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Aerospace Medicine and Human Performance

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Aerospace Medicine and Human Performance

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This journal, representing the members of the Aerospace Medical Association, is published for those interested in aerospace medicine and human performance. It is devoted to serving and supporting all who explore, travel, work, or live in hazardous environments ranging from beneath the sea to the outermost reaches of space.

AEROSPACE MEDICAL ASSOCIATION is an organization devoted to charitable, educational, and scientific purposes. The Association was founded when the rapid expansion of aviation made evident the need for physicians with specialized knowledge of the flight environment. Since then, physicians have been joined in this Association by professionals from many fields and from many countries, all linked by a common interest in the health and safety of those who venture into challenging environments.

AEROSPACE MEDICINE AND HUMAN PERFORMANCE, formerly *Aviation, Space, and Environmental Medicine*, is published monthly by the Aerospace Medical Association, a non-profit charitable, educational, and scientific organization of physicians, physiologists, psychologists, nurses, human factors and human performance specialists, engineers, and others working to solve the problems of human existence in threatening environments on or beneath the Earth or the sea, in the air, or in outer space. The original scientific articles in this journal provide the latest available information on investigations into such areas as changes in ambient pressure, motion sickness, increased or decreased gravitational forces, thermal stresses, vision, fatigue, circadian rhythms, psychological stress, artificial environments, predictors of success, health maintenance, human factors engineering, clinical care, and others. This journal also publishes notes on scientific news and technical items of interest to the general reader, and provides teaching material and reviews for health care professionals.

MEMBERSHIP—The Aerospace Medical Association welcomes members interested in aerospace medicine and human performance. Membership applications may be obtained online at www.asma.org or from the Aerospace Medical Association's headquarters at 631 US Highway 1, Suite 307, North Palm Beach, FL 33408, or phone the Membership Department at (703) 739-2240 x 107; skildall@asma.org.

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Aerospace Medicine and Human Performance

OCTOBER 2025 VOLUME 96 NUMBER 10

Boundless Frontiers Relentless Progress

ANNUAL SCIENTIFIC MEETING

DATES ARE CHANGING!

Our next AsMA-UHMS Annual Scientific Meeting will be in Denver, CO, **May 17-21, 2026**. Important dates include:

- **Oct. 1, 2025:** On or around this date, the abstract submission site will open.
- **Jan. 4, 2026:** The abstract submission site will close at 11:59 p.m. EST. NO exceptions...submit early!
- **Jan. 31, 2026:** Submitters will be notified of accepted or declined abstracts by 5:00 p.m. EST.
- **Feb. 28, 2026:** No more updates to accepted abstracts will be permitted after 11:59 p.m. EST.

The Need For SPEED

Farther, faster, together.

The Aerospace Medical Foundation is working to accelerate its efforts by empowering the next generation of Aerospace Medicine scientists who will take humans to deep space. In order to achieve these objectives, they are setting a goal in the "Need for Speed" campaign of $5 million by AsMA's 100th Anniversary! Donations can be in cash or in stock and can be made by credit card or PayPal through the AsMAFoundation.org website. AsMA Members: consider joining the Heritage Society and include the Foundation in your estate planning.

Support the Foundation!

With your help we can accelerate to Mach 10 by 2029!

SUBSONIC MACH < 1.0

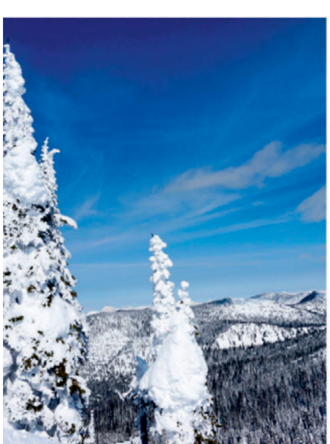
$680,000

Undersea and Hyperbaric Medical Society

2026 WINTER SYMPOSIUM

Converging Frontiers: Advancing Human Optimization and Risk Reduction in Sea, Land and Sky

January 26-28

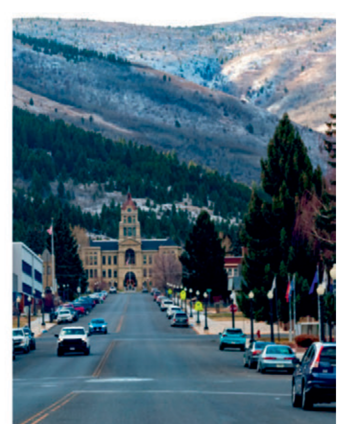


The Lodge at Whitefish Lake

Join us - Save the Date!

The Lodge at Whitefish Lake is situated between Whitefish Lake and the Viking Creek Wetland Preserve, just minutes from the heart of downtown Whitefish.

Inspired by the grand lodges of the past, with all the conveniences of the present, The Lodge brings a sense of leisure and grace to the Montana travel experience. Surrounded by mountains with the pristine waters of Whitefish Lake at our back door, and all the amenities of a full-service resort hotel,



2026 AsMA & UHMS Annual Scientific Meeting
"Boundless Frontiers—Relentless Progress"
Sheraton Denver Downtown Hotel
Denver, CO, United States; May 17–21, 2026

Call for Abstracts Deadline: Jan. 4, 2026; *NO Exceptions!*

The 2026 AsMA-UHMS Annual Scientific Meeting will be held in Denver, CO, United States. The theme for the 2026 Annual Scientific Meeting is **"Boundless Frontiers—Relentless Progress."** With emerging technology and new entrants into the aviation and space environment, it is now more important than ever to encourage the next generation of young people to consider entering career fields like aerospace medicine, engineering, aviation, maintenance, air traffic control, and remotely piloted vehicle operations, to name a few. To quote a staff member, "if a young person can't see it, they can't be it." Many of our youth have no awareness of the career opportunities in aerospace medicine. We need to be out in our schools and youth organizations telling our story. In addition, AsMA members will need to maintain a full awareness, and in many cases, a working knowledge of the innovations so we can better respond to needs of the aviation and space communities. The future will require us to think differently as the airspace system changes.

The Annual Scientific Meeting is the premier international forum to learn and discuss evolving trends and multidisciplinary best practices in research, clinical applications, human performance, and flight safety. The 2026 AsMA-UHMS Annual Scientific Meeting welcomes abstracts in the many areas related to Aerospace Medicine. For a complete list, see the box on p. 2 of this form.

AsMA ABSTRACT SUBMISSION PROCESS

LIMIT: 350 words/2500 characters including spaces; NO Tables or Figures or References should be included in the abstract. All abstracts must be submitted via the electronic submission system link on the meeting website: *https://asma-uhms-asm.org/abstracts/asma-call-for-abstracts.html*.

ATTENTION: You MUST use personal email addresses when entering your abstracts and those of your co-authors.

ABSTRACT PRESENTATION TYPES

The Annual Scientific Meeting highlights four types of presentation formats.

1. Interactive Presentations (Posters): Individual interactive (poster) presentations are integrated into a session, grouped by topic. The presentation must be submitted as a PowerPoint with up to a maximum of 10 slides. Video and audio clips can be embedded. They will be displayed digitally. Posters are on display for two full days, each in an assigned space. Authors will be asked to present their poster for a single designated 90-min period on one of these days.

2. Slide: Standalone 15-minute slide presentation with questions/discussion that will be integrated into an oral slide session, grouped by topic. PowerPoint presentations will be organized by topic area and presented during 90-minute blocks of time, 6 periods of 15 minutes each. Individual PowerPoint Oral presentations are limited to 15 minutes, including 3–5 minutes for questions and discussion.

3. Panel: Invited Presentation that will link to support a Panel Overview containing five (non-case study) or six (case study) abstracts presented as a cohesive whole. Panels also have 90 minutes, ideally 5 presentations of 15 minutes each followed by a 15-minute discussion period.

4. Workshop: Invited Presentation that will link to and support a Workshop Overview. Overview abstracts should reflect the material to be presented in this long format for up to 8 hours of CME credit.

PRESENTATION CATEGORIES

There are two presentation categories based on the topic. (Templates and examples are provided for each type and will be available on the abstract submission website). Authors will be required to enter abstract text under the headings as described below.

1. Original Research: Material that is original in nature and has not been previously presented. Original analysis of a hypothesis involving data collection and analysis. Headings include Introduction, Methods, Results, and Discussion.

2. Education: Typically, a discussion of information that is already available.

a. Program/Process Review: Description of a program or process that is used to solve a problem or accomplish a task. Headings include Background, Description, and Discussion.

b. Tutorial/Review: An educational session intended as a review of established material. Headings include Introduction, Topic, and Application.

c. Case Study: A single clinical or human performance event. Headings include Introduction, Case Description, and Discussion.

PANEL GUIDANCE

Panels must be composed of a coordinated sequence of 5 abstracts that flow logically from one to another supporting the central theme. Panels must contain abstracts that allow 15 minutes of structured discussion at the end of the session.

Case Study Panels: Case Study Panels can have 6 abstracts and are intended to highlight a particular institution, community, or aeromedical issue, usually presented from the same institution or aeromedical community.

It is the responsibility of the Panel Chairperson to enter all supporting abstracts and to ensure that all supporting abstracts clearly describe how each supports the Panel theme. If the Panel theme is not clearly identified and/or the abstracts do not support a central theme, the Scientific Program Committee may decline the proposed Panel in total. Unrelated abstracts from a laboratory or organization do not constitute a Panel (unless they are Case Studies).

Panel Chairs are also responsible for preparing questions and discussion points to facilitate a moderated discussion with the audience during the sixth period. Each Panel speaker should cite or link directly to the Panel theme, and at the end of their talk should provide a logical segue to the next abstract.

WORKSHOP GUIDANCE

Rules for workshops and the review process are similar to those for Panels (above). Individual abstracts must be entered for each invited presenter and all necessary information must be entered in the same manner as all other abstracts, including financial disclosure statements. Course materials should be made available for registrants.

A separate registration fee is charged for Workshops registration. For additional information contact Gisselle Vargas, Deputy Executive Director, at gvargas@asma.org.

AsMA ABSTRACT SUBMISSION PROCESS

All abstracts must be submitted via the electronic submission system linked to on the association's website: *https://asma-uhms-asm.org/abstracts/asma-call-for-abstracts.html*. Click on the link to the abstract submission site--available on the AsMA home page and

Meetings page on or about September 1, 2025. Authors with questions regarding the abstract submission process should contact AsMA directly at (703) 739-2240, x101 (Mrs. Rachel Trigg), email rtrigg@asma.org or x102 (Mrs. Stella Sanchez), email ssanchez@asma.org.

The following information is required during the submission process: Abstract title, presenting author information (including complete mailing and email addresses and telephone numbers), topic area (from list provided on back of form), contributing authors names, emails and institutions, abstract content **(LIMIT: 350 words/2500 characters including spaces), at least 2 Learning Objectives** (the Accreditation Council for Continuing Medical Education requires this for all presentations). In addition, three (3) multiple choice or True/False questions and answers are required for each Interactive Presentation, Slide, and Panel presentation for enduring materials for CME credit. Read instructions online for additional details. ***Interactive presentations must be uploaded as a PowerPoint in advance of the meeting no later than February 23, 2026, 11:59 PM ET.***

PLEASE NOTE: All Presenters (including panelists) are required to register for the meeting. *There is a discounted fee for non-member presenters. Registration limited to the day of presentation will be available on site.*

Financial Disclosure/Conflict of Interest/Ethics

Abstracts will not be accepted without a financial disclosure form. The form is included as part of the website abstract submission process. The presenting author must agree to comply. Scientific presentations at AsMA-sponsored events will adhere to the highest standards of scientific ethics, including appropriate acknowledgment or reference to scientific and/or financial sources. Presenters must avoid the endorsement of commercial products in their abstracts and during their presentations. There must be no advertisements on Posters, slides, or handout materials.

Presentation Retention Policy

AsMA will use live capture technology to record all oral presentations during the meeting. Recorded presentations will be made available to registrants after the meeting. Authors are required to provide permission for live capture and a nonexclusive license to repurpose the content. PDF copies of Poster presentations must be uploaded to the designated submission site.

Permissions and Clearances

It is the author's responsibility to obtain all necessary permissions and clearances prior to submission of the abstract. AsMA assumes no liability or responsibility for the publication of any submitted material.

Acceptance Process

Abstracts will be reviewed by a minimum of three members of the AsMA Scientific Program Committee. Acceptance will be based on the abstract's originality, relevance, scientific quality, and adherence to the guidelines provided. Criteria for non-acceptance include, but are not limited to: insufficient, inconsistent, or ambiguous data; commercialism; or reviews of previously published literature. Abstracts must be 100% complete upon submission, including all final data and results. How well authors abide by submission and format guidelines will also be one of the criteria used to determine acceptance of abstracts.

Presenters are limited to one Slide OR Interactive Presentation AND one Panel presentation unless given specific prior permission by the Scientific Program Committee Chair, Amanda Lippert, at sciprog@asma.org. Following review by the Scientific Program Committee in January, all contributors will receive a notification of acceptance or non-acceptance by email. Accepted abstracts will be published in *Aerospace Medicine and Human Performance*.

While the Scientific Program Committee strives to honor the presenter's desired presentation format, for reasons such as space limitations or dissimilar content, an abstract may be changed to an alternative presentation format. Assignment of an abstract to either a poster or a slide presentation will be recommended by the Scientific Program Committee, but the final decision will be made by the Program Committee Chair.

Abstract Withdrawal

Withdrawing abstracts is strongly discouraged. However, if necessary, a request to withdraw an abstract should be sent to Amanda Lippert, the Scientific Program Chair, at sciprog@asma.org and Rachel Trigg at rtrigg@asma.org. The request for withdrawal must include the abstract title, authors, ID number, and reason for withdrawal. Abstract withdrawal decisions must be sent to the Scientific Program Chair as soon as possible.

Mentorship

Optional review / feedback for all presenters at AsMA 2026

AsMA is continuing its mentorship initiative for all authors for the 2026 Scientific Meeting. You have the option to submit a draft of your abstract to a group of senior AsMA members for review and feedback. If you have questions about this opportunity, please e-mail sciprog@asma.org. E-mail your abstract to sciprog@asma.org no later than December 15, 2025. The Program Mentor Group will review provide feedback via e-mail by December 22, 2025. The abstract will still need to be finalized in the submission system.

TOPIC AREAS: (These will be listed on a drop-down menu on the submission site. They are used to organize the abstracts into sessions.)

1: Human Performance
- 1.1 Personnel Selection
- 1.2 Training
- 1.3 Hypobaric & Hyperbaric Physiology
- 1.4 Thermal Physiology
- 1.5 Acceleration / Vibration/ Impact
- 1.6 Fatigue
- 1.7 Neurophysiology & Sensory (inc. Vision, Auditory, Vestibular, Spatial Disorientation)
- 1.8 Aerospace Human Factors & Psychology
- 1.9 Aerospace Human Systems Integration

2: Clinical Medicine
- 2.1 Aviation Medicine
- 2.2 Health Promotion and Wellness Programs
- 2.3 Medical Standards / Aircrew Health
- 2.4 Occupational / Environmental Medicine
- 2.5 Operational Medicine
- 2.6 Hyperbaric Medicine

3: Travel and Transport Medicine
- 3.1 Travel Medicine
- 3.2 Aeromedical Transport / Air Evacuation
- 3.3 Air Transport Medicine
- 3.4 Commercial
- 3.5 Pandemic Preparedness

4: Space Medicine
- 4.1 Space Medicine
- 4.2 Space Operations

5: Safety and Survivability
- 5.1 Escape / Survival
- 5.2 Flight Safety / Accident Investigation

6: Other
- 6.1 History of Aerospace Medicine
- 6.2 Ethics

Follow the link on our website: *https://asma-uhms-asm.org/abstracts/asma-call-for-abstracts.html*

- **Submission hard deadline: Sunday, January 4, 2026, 11:59 PM ET (there will be no extensions)**
- Notice of acceptance by Saturday, January 31, 5 pm ET.
- **No updates to abstracts will be accepted after Saturday, February 28, 2026, 11:59 PM ET**
- **Interactive presentations (posters): PDF/PPT must be submitted to the UHMS by Monday, February 23, 11:59 PM ET - NO updates will be accepted after this date, not even on site.**

Aerospace Medical Association

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(703) 739-2240, Ext. 107 | (703) 739-9652 FAX
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OUR MEMBERSHIP APPLICATION IS AVAILABLE ONLINE. GO TO ***www.asma.org*** *AND CLICK ON "MEMBERSHIP"*

Please Send CV or Bio to the Journal Department: rtrigg@asma.org

You will automatically receive access to the online journal with your membership.

PLEASE PRINT – (Last Name, First Name, Middle Initial) ______ (Military Rank, Service, Corps) ______ (Degrees) ______

(Mailing Address) ______

(City, State, Zip, Country) ______

(Email address) ______ (Work Phone / Mobile Phone) ______

(Date of Birth) ______ (Gender) ______ (Area of Specialty) ______

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MEMBERSHIP RATES: (check one)

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- ☐ Student[2] $50
- ☐ Resident[3] $175
- ☐ Allied Membership[4] $50
- ☐ Technician $130
- ☐ 3-Year Membership $820

[1]**Must be 65 yrs old + 25 yrs of AsMA membership**
[2]**Requires proof of full-time student status**
[3]**Requires proof of Medical Residency**
[4]**Requires residence in Low or Low-Middle Income country**
(see list online: https://www.asma.org/membership/individual**)**

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☐ Pay by Check Check Number: ______

Signature: ______
(Required for credit card transactions)

☐ *Life Membership $5,500*

NOTE: Payment **MUST** be made by check.

Please contact AsMA Membership Department at skildall@asma.org for details.

☐ Bank Transfer

NOTE: all Bank Transfers must include a $35.00 US processing fee.

Please contact AsMA Membership Department at skildall@asma.org for bank details.

For United States Federal Income Tax purposes, you can deduct as a charitable contribution the price of the membership renewal less the estimated cost of your ***Aerospace Medicine and Human Performance*** journal subscription. We estimate the cost to produce the journal to be $100 per year. Any membership contribution in excess of $100 per year is tax deductible.

For Non-U.S. members, the entire membership fee is related to the activities of the Aerospace Medical Association to improve the professional knowledge and practice of its members. This includes subscription to the Association's professional journal, itself part of the education effort of the Association.

Specialties: Please select from the following list of specialties all that apply to you.

- ☐ Administrative Medicine – physicians
- ☐ Aerospace and Aviation Medicine
- ☐ Aerospace Flight Nursing
- ☐ Aerospace Human Factors & Human Engineering
- ☐ Aerospace Physiology
- ☐ Airline Medical Director
- ☐ Allergy
- ☐ Anesthesiology
- ☐ Aviation Medical Examiner
- ☐ Biochemistry
- ☐ Bioengineering
- ☐ Biomedical Engineering
- ☐ Biophysics
- ☐ Cardiology or cardiovascular disease
- ☐ Certified in Aerospace Physiology
- ☐ Dermatology
- ☐ Development & Manufacturing Industry
- ☐ Diplomate, ABPM, Cert in Aero Med
- ☐ Emergency Medicine
- ☐ ENT
- ☐ Environmental Sciences
- ☐ Epidemiology
- ☐ Family Practice
- ☐ Forensic Medicine
- ☐ Gastroenterology
- ☐ General Practice
- ☐ General Surgery
- ☐ Geriatrics
- ☐ Hand Surgery
- ☐ Human Performance
- ☐ Human Systems Integration
- ☐ Hyperbaric Medicine
- ☐ Industrial or Occupational Medicine
- ☐ Industrial or Traumatic Surgery
- ☐ Internal Medicine
- ☐ Legal Medicine
- ☐ Life Insurance Medicine
- ☐ Life Science
- ☐ Maxillofacial Surgery
- ☐ Medical Anthropology
- ☐ Military Command
- ☐ Neurological Surgery
- ☐ Neurology
- ☐ Nuclear Medicine
- ☐ Nursing/Patient Transport
- ☐ Obstetrics and Gynecology
- ☐ Occupational Diseases
- ☐ Ophthalmology
- ☐ Optometry
- ☐ Orthopedic Surgery
- ☐ Otolaryngology and Otology
- ☐ Pathology
- ☐ Pediatrics
- ☐ Pharmacology
- ☐ Physical Medicine & Rehabilitation
- ☐ Physiology
- ☐ Plastic Surgery
- ☐ Preventive Medicine – General
- ☐ Proctology
- ☐ Psychiatry
- ☐ Psychology
- ☐ Public Health
- ☐ Pulmonary Disease
- ☐ Radiology & Roentgenology
- ☐ Research and Research Scientist
- ☐ Rheumatology
- ☐ Space Medicine
- ☐ Sports Medicine
- ☐ Surgery
- ☐ Thoracic Surgery
- ☐ Toxicology
- ☐ Tropical Medicine
- ☐ Urology

Please consider joining one or more of the following Constituent Organizations:

- Aerospace Human Factors Association
- Aerospace Medicine Student and Resident Organization
- Aerospace Nursing and Allied Health Professionals Society
- Aerospace Physiology Society
- American Society of Aerospace Medicine Specialists
- International Airline Medical Association
- International Association of Military Flight Surgeon Pilots
- Life Sciences & Biomedical Engineering Branch
- Society of NASA Flight Surgeons
- Society of U.S. Air Force Flight Surgeons
- Society of U.S. Army Flight Surgeons
- Society of U.S. Naval Flight Surgeons
- Space Medicine Association
- Space Surgery Association

August Executive Committee Meeting

Warren Silberman, D.O.

As this was John Peters' and my first Executive Committee meeting following our annual meeting, given the many accomplishments, I decided to dedicate my newsletter to this event.

This particular meeting always occurred the day after the annual site visit for our next annual meeting. In this case, it was held at the Sheraton Downtown Denver. Our members should recall that this was the site of our 2017 Scientific Meeting and again in 2021 after we missed the meeting in 2020 due to the pandemic. In prior years, the meetings lasted one and a half days; however, due to changes in the meeting structure, we finished at 12:45 on the first day! This was secondary to the proposal of our new Executive Director, with my complete agreement, to simplify the meeting process. From this meeting onward, we will conduct meetings to discuss items presented by our four Vice Presidents, provided by their respective committees, and then incorporate them into the meeting agenda. The responsibilities of each committee chair will be to elevate issues based on an "SBAR". This acronym stands for "Situation, Background, Assessment, and Recommendation." So, should a committee come up with an issue, they will have to answer each one of those items before they forward it to their responsible Vice President.

I am not going into real depth on the notable items, so should you want some more details, feel free to ask one of us.

Prior to our Annual Meeting in Atlanta, the Church across the street from our Alexandria headquarters (HQ) asked our Executive Director if AsMA was interested in selling the building. As you may have heard, with the requirement for all government employees to return to their places of business, there is an excess of empty properties in Virginia. That, along with the aging of the actual building and the fact that the monthly upkeep was costing AsMA more money than the organization was putting into the property, your Governance team voted to explore the possibility of the Church purchasing the property. Well, after a lengthy but standard process, the Church accepted our offer of $1.5 million. The AsMA staff will visit HQ in late September to clean out and mail essential documents to be archived. The rest will be sent to our new HQ in North Palm Beach, FL. Our new mailing address will be 631 N. US Highway 1, Suite 307, North Palm Beach, FL, and we will be co-located with the Undersea and Hyperbaric Medical Society (UHMS).

Since AsMA will no longer have a presence in Virginia, the Governance team also voted to incorporate in Florida.

A longstanding issue with choosing meeting sites for our annual meetings has been providing a per diem rate to all scientific meeting attendees. As our members should know, there is a significant number of members who are military and government. This became a substantial issue from 2029 and beyond, where AsMA's requirement for per diem was being challenged. Jeff Sventek, AsMA's outgoing Executive Director, incoming Executive Director John Peters, and the team from AIM pushed forward with an idea to negotiate a 5-year agreement with a single brand versus focusing on individual markets. The result was Marriott and Hyatt bidding for 5 years of our scientific meeting. Well, they were successful and, after reviewing the offers, your Governance team decided on the Marriott Corporation. Our three annual meetings are already planned. They will be in 2026, Denver, CO; 2027, Dallas, TX; and 2028, New Orleans, LA. So, beginning in 2029, which is AsMA's 100th Anniversary, we will be having meetings at hotels exclusively belonging to the Marriott corporation. The 2029 meeting is to be held at the San Francisco Marriott Marquis Hotel from June 12 to 24.

It was discussed and agreed at the meeting that our committee chairs be vetted much more carefully by their respective Vice Presidents. The committee chairs need to provide much more timely responses to issues that arise during their tenure and agree in writing to accept their responsibilities. The Vice Presidents were tasked with developing a process to assess the performance of their committee chairs. The committee chairs should respond to issues within approximately 20 days of their initiation. This is where the creation of an "SBAR" will occur. The SBARs will then be collected by the respective Vice President and become the issues discussed at each meeting. We still want the committees to provide us with meeting reports that will continue to be part of the "supplement" to our meeting minutes.

Your AsMA management team has been diligently working on evaluating the organization's outsourced information systems and platforms. The team intends to create our next generation of systems in-house rather than purchasing outsourced systems that are inflexible and expensive.

As you are aware, we have discontinued printing our monthly journal, limiting ourselves to printing copies at the expense of AsMA and the requester. This had become an added expense with minimal return, prompting the management team to seek a group willing to print our Journal and handle the requester directly, rather than through AsMA. The AsMA team has partnered with Sheridan Connect to provide an on-demand print system for individuals who prefer print journals. To remind our members, you can now print specific articles or the entire journal on your own! A remarkable milestone was acknowledged at the meeting by our Treasurer. This was the first time in the history of the AsMA Journal that the expenses of the journal were less than the cost to the Association!

DOI: https://doi.org/10.3357/AMHP.PP9610.2025

CONTACT DETAILS:
Email: President@asma.org • **Website:** www.asma.org • **Facebook:** Aerospace Medical Association • **X:** @Aero_Med • **YouTube:** @Aero_Med

Exercise Heat Stress Responses in Unacclimatized Endurance- and Resistance-Trained Women

Barbara N. Sanchez; Sam Soufi; Catherine Saenz; William J. Kraemer; Elaine C. Lee; Jeff S. Volek; Carl M. Maresh

INTRODUCTION: Sex-specific responses to heat stress are not well characterized in women with different training backgrounds. This study examined physiological and perceptual responses to moderate-intensity exercise in the heat among endurance-trained (ET) and resistance-trained (RT) women.

METHODS: In a counterbalanced crossover design, 17 (8 ET, 9 RT) healthy, well-trained, heat-unacclimatized women performed a 75-min walking exercise session at 60% $\dot{V}O_{2peak}$ (maximum volume of oxygen consumption) in both Hot (33°C, 50% relative humidity) and Neutral (21°C, 50% relative humidity) conditions. Rectal temperature (T_{rec}), heart rate (HR), minute ventilation ($\dot{V}_e$), blood lactate, urine specific gravity, and body mass loss were assessed. Perceptual measures included overall, central, and local ratings of perceived exertion (RPE), thermal sensation, thermal comfort, thirst, and the Environmental Symptoms Questionnaire.

RESULTS: Across both groups, T_{rec}, HR, $\dot{V}_e$, and perceptual responses were significantly elevated in Hot vs. Neutral. No group differences were observed in T_{rec}, HR, $\dot{V}_e$, or perceptual ratings. RT women exhibited significantly higher post-exercise lactate levels in Hot, but this did not correspond to higher RPE or Environmental Symptoms Questionnaire scores. $\dot{V}O_{2peak}$ was a significant predictor of RPE responses in Neutral but not Hot. No moderation effect of training group was observed.

DISCUSSION: ET and RT women experienced comparable physiological and perceptual strain during prolonged exercise in the heat. Despite metabolic differences, perceptual responses were consistent across training backgrounds. These findings highlight the role of training stimulus over $\dot{V}O_{2peak}$ in thermoregulatory outcomes and support inclusive heat tolerance recommendations for active women across training disciplines.

KEYWORDS: thermoregulation, perceived exertion in heat, environmental stress, exercise training adaptation.

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Climate change has led to more frequent hot weather conditions, increasing the risk of heat-related illness across occupational and recreational settings. As a result, populations will be increasingly challenged to maintain labor and exercise activities in hot environments. By 2020, the global average temperature had risen by 1.2°C compared to preindustrial levels, with record breaking temperatures continuing in the years following the Paris Agreement of 2015.[1] This trend underscores the need to better understand exercise-heat stress responses across diverse populations to protect and optimize human performance. Given the rising participation of women in endurance sports, resistance training, and labor-intensive occupations,[2,3] this study contributes to closing the gender gap in exercise-heat stress research.[2,4] Women may differ in thermoregulatory responses due to sex-specific physiological characteristics, including lower sweat gland density, higher body fat percentage, and generally lower absolute maximum volume of oxygen consumption ($\dot{V}O_{2max}$) values—all of which

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can impair heat dissipation.[4] Despite these known differences, most prior research has focused on men, creating a critical knowledge gap regarding how training background influences thermoregulation in women.[4]

In addition, limited research has addressed how differences in training modality—specifically endurance vs. resistance training—impact responses to exercise in the heat.[5] While endurance training has been extensively studied in this context,[6,7] resistance training remains underexplored. Although $\dot{V}O_{2max}$ is often cited as a key predictor of thermoregulatory capacity, Ravanelli et al.[5] argue that it is the endurance training stimulus itself, not $\dot{V}O_{2max}$ per se, that drives these adaptations. Intense resistance training may induce partial heat-acclimation-like adaptations, such as changes in sweating efficiency or core temperature regulation. Given the prevalence of physically demanding tasks that involve lifting, carrying, and pushing and pulling against an external load, resistance training represents an understudied area in environmental physiology research, especially for women.

Although not yet well understood, resistance training may influence mechanisms such as orthostatic tolerance,[8] heat shock protein expression,[9] and Akt signaling,[10] which may contribute to improved heat tolerance. These physiological pathways may support thermoregulatory adaptations in resistance-trained individuals. Yet resistance training may not confer the same benefits as endurance training, such as increased sweat rate or more efficient heat dissipation,[6,11] potentially resulting in reduced heat loss. Little is known about how resistance training affects thermoregulation, making this study particularly novel in examining unacclimatized resistance-trained women. This also allows us to explore whether resistance training elicits comparable heat-adaptive benefits despite typically lower $\dot{V}O_{2max}$ values.[5] Together, these contrasting possibilities underscore the importance of directly comparing endurance- and resistance-trained women to determine whether different training modalities produce distinct or overlapping thermoregulatory advantages.

The exacerbated physiological and psychological strain that accompanies increased thermal stress impairs exercise performance. Alongside physiological metrics, perceptual responses reflect the complex integration of internal and external cues that shape an individual's sense of effort, discomfort, and strain.[12] The rating of perceived exertion (RPE) scale is a widely used tool for quantifying perceptual load, often correlating with physiological measures such as heart rate (HR), workload, ventilation rate, and oxygen consumption ($\dot{V}O_2$).[13,14] Additional measures such as thermal sensation and thirst provide further insight into tolerance and self-regulated behavior during exercise in the heat, informing safer and more effective performance strategies.

The scarcity of data on women in this area underscores the importance and novelty of the present study. We examined physiological and perceptual responses during prolonged moderate-intensity exercise in both hot and thermoneutral conditions among unacclimatized endurance- or resistance-trained women. Based on prior literature indicating that endurance training mimics heat acclimation-related adaptations,[6,15] we hypothesized that endurance-trained women would exhibit more favorable—or less impaired—responses to exercise heat stress compared to resistance-trained women. This study contributes to a more complete understanding of how training backgrounds affect thermoregulatory performance in women and offers practical implications for female exercisers, athletes, servicewomen, and occupational workers in hot environments. Understanding how women with different training backgrounds respond to exercise in the heat, particularly without prior acclimatization, is a novel and important question that this study directly addresses.

METHODS

Subjects

The study protocol was approved in advance by The Ohio State University Institutional Review Board (#2022H0312) and each subject provided written informed consent before participating. Two groups of healthy, trained women ages 18–35 yr participated in this study. Subjects were recruited through online advertisement, printed flyers, and word-of-mouth referrals, drawing both from the university campus and the surrounding local community. Subjects were screened for eligibility using a structured questionnaire assessing health history, heat exposure, menstrual cycle characteristics, and physical fitness history. Inclusion criteria required subjects to be healthy, physically active women (engaging in structured exercise at least 2–3 times per week for the past 3 mo) without a history of cardiovascular, metabolic, or respiratory disease. Exclusion criteria included musculoskeletal injuries that could limit movement, prior heat-related illness, or frequent exposure to extreme heat (≥90°F/32.2°C) in the past 3 mo. None of the subjects reported a history of heat-related illness, cardiovascular, metabolic, or respiratory disorders, nor occasional environmental (i.e., >90°F/32.2°C) or habitual (sauna/hot tub use) heat exposure during the previous 3 mo.

A total of 20 subjects were initially recruited for the study. Of these, two did not meet the performance benchmarks required for classification as endurance or resistance trained and were excluded. One additional subject withdrew after completing one exercise visit, citing personal reasons unrelated to the study. Thus, 17 subjects completed all study procedures and were included in the final analysis.

Training classification was determined through self-reported exercise history and validated by performance benchmarks. Nine women were classified as resistance-trained (RT). These subjects self-identified as resistance exercisers and demonstrated an advanced resistance training status, as described by Santos Junior et al.[16] Specifically, they were able to bench press ≥60% and back squat ≥120% of their bodyweight. These performance criteria reflect advanced neuromuscular adaptations, and the skill required for the proper execution of these lifts.[16]

The other eight women were classified as endurance-trained (ET). These subjects self-identified as endurance exercisers and demonstrated a $\dot{V}O_{2peak}$ of ≥46.5 mL · kg^{-1} · min^{-1} for ages 20–29 and ≥37.5 mL · kg^{-1} · min^{-1} for ages 30–35. These values fall within the 80th percentile of endurance fitness as defined by the American College of Sports Medicine.[17]

Procedure

Study data collection occurred during the winter months in the U.S. Midwest, where outdoor temperatures rarely exceeded 50°F (10°C). All trials were scheduled when subjects were free of premenstrual symptoms. Subjects completed three laboratory visits, including one for performance testing and two for experimental exercise in an environmental chamber (Tescor, Inc., Warminster, PA, United States). Each laboratory visit was separated by a minimum of 72 h to allow for adequate recovery between sessions and minimize residual fatigue effects.

To minimize potential confounding factors, subjects followed standardized pre-experimental instructions before all study visits. These included maintaining proper hydration by consuming 500 mL of water before bed and another 500 mL upon waking, refraining from strenuous physical activity and prolonged heat exposure for 48 h, obtaining sufficient sleep (7–9 h recommended), and consuming an adequate meal at least 2 h before testing. Additionally, subjects were instructed to consume similar menus 24 h prior to each exercise visit to promote dietary consistency. Although these standardized pre-experimental instructions were followed, individual differences in fluid intake, retention, or previous hydration behaviors may have contributed to the baseline thirst differences between groups. No formal 24-h hydration recall questionnaire was administered, but subjects verbally confirmed adherence to the pre-experimental instructions upon arrival.

During the performance testing visit, subjects underwent body composition analysis, aerobic fitness assessment, and maximal strength testing. Body composition was assessed via dual-energy x-ray absorptiometry (Lunar iDXA™, GE HealthCare, Chicago, IL, United States) to determine total body fat percentage, lean mass, and bone mineral density. Subjects were positioned according to manufacturer guidelines and the scanner was calibrated before each session. Aerobic fitness was evaluated using an individualized graded exercise test on a treadmill using a metabolic cart (ParvoMedics, Salt Lake City, UT, United States). Specifically, the protocol consisted of an initial speed of 3.0 mph, 0% incline, for 2 min. This was followed by 2 min at 4.0 mph and 5.0 mph, respectively, at 0% incline. After which, increases in speed and/or incline were made each minute as previously determined, in collaboration with the subject, until they reached volitional exhaustion. $\dot{V}O_{2peak}$ was determined when at least two of the following criteria was met: a plateau in oxygen consumption despite increasing workload, a respiratory exchange ratio ≥1.10, or attainment of age-predicted maximal HR.[17] Maximal strength was assessed using 1-repetition maximum assessments for the bench press and back squat exercises following the National Strength and Conditioning Association Guidelines.[18] Subjects performed a standardized warm-up consisting of submaximal sets, followed by successive maximal attempts with 2–3 min of rest between attempts. The heaviest successfully lifted weight with proper form was recorded as the 1-repetition maximum. All lifts were performed using free weights with trained personnel supervising for safety and proper technique in accordance with the described guidelines and included proper depth, controlled movement, and maintenance of neutral spine alignment.[18]

This study followed a counterbalanced crossover design, where each subject completed two experimental exercise sessions: one in a hot environment [Hot: 33°C, 50% relative humidity (RH)] and one in a neutral environment (Neutral: 21°C, 50% RH). The order of conditions was randomized to minimize order effects. Experimental sessions were scheduled in one of two available time slots (07:00–09:30 or 10:00–12:30), with each subject maintaining the same time slot across both visits for consistency. The specific number of subjects assigned to each time slot for Hot and Neutral conditions was not recorded. The time elapsed since waking was not controlled but was assumed consistent within individuals across sessions. During exercise sessions, subjects wore lightweight, moisture-wicking athletic clothing (shorts and a short-sleeved shirt) and athletic shoes to maintain consistency across trials while minimizing external thermal influences.

Upon arrival at the laboratory, subjects provided a urine sample for hydration status and pregnancy testing. Euhydration was confirmed with a urine specific gravity (USG) (TS400, Reichert Technologies®, Depew, NY, United States) value of ≤1.025. None of the subjects tested positive for pregnancy.

Once hydration was confirmed, subjects had their body mass recorded. Subjects were asked to wear the same exercise attire for both Hot and Neutral exercise sessions. An HR monitor (Polar H10, Kempele, Finland) was secured and a rectal thermistor (DataTherm®II, GeraTherm Medical AG, Geratal, Germany) was self-inserted 10 cm beyond the external anal sphincter to measure core temperature (T_{rec}). Subjects then entered the environmental chamber and rested for 15 min before completing a modified Environmental Symptom Questionnaire (ESQ).[19]

The exercise protocol consisted of a continuous 75-min treadmill walk at 60% $\dot{V}O_{2peak}$. Treadmill speed and grade were initially set using standard metabolic equations to approximate the workload corresponding to 60% $\dot{V}O_{2peak}$. During the first 15 min of exercise, oxygen consumption was continuously monitored using a metabolic cart to verify that subjects were exercising at the target intensity. If $\dot{V}O_2$ measurements deviated from the desired 60% $\dot{V}O_{2peak}$, slight adjustments to speed or grade were made to maintain the prescribed intensity. Subsequently, $\dot{V}O_2$ was reassessed for 3-min intervals at the 30-, 45-, 60-, and 75-min marks, with further adjustments as necessary to ensure consistent exercise intensity throughout the session.

The selection of a 75-min exercise duration at 60% $\dot{V}O_{2peak}$ was based on its relevance to inducing significant thermoregulatory responses, which are critical for understanding physiological adaptations in various populations. This combination of duration and intensity has been widely used in research to study heat acclimation and thermoregulation. For instance, protocols involving 60–90 min of exercise at moderate intensities have been shown to effectively promote heat acclimation and elicit substantial thermoregulatory adaptations.[20] Additionally, exercising at 60% $\dot{V}O_{2peak}$ represents a moderate intensity that is sustainable for most individuals, ensuring subject safety while still providing meaningful data on physiological and perceptual responses to prolonged exercise in different environmental conditions.

Physiological measures, including HR, minute ventilation ($\dot{V}_e$), and T_{rec}, were recorded at 15-min intervals throughout the exercise session. HR and T_{rec} data were collected from a single time point, specifically during the last 10 s of each 15-min interval. $\dot{V}_e$ was averaged over the final minute of each 15-min interval to account for fluctuations in ventilation rate and provide a stable representation of respiratory effort. Subjects wore a metabolic mask only during the designated measurement periods to collect ventilation and oxygen consumption data. The mask was worn continuously for the first 15 min of exercise and then for 3-min sampling periods at the 30-, 45-, 60-, and 75-min marks. At all other times, the mask was removed to minimize discomfort and avoid influencing perceptual responses such as thermal sensation and breathing effort.

To ensure subject safety, T_{rec} was continuously monitored throughout the exercise session. If a subject's T_{rec} reached 39.7°C (103.5°F), the session would be immediately stopped, and the subject would be removed from the environmental chamber to undergo active cooling procedures, including cold water ingestion and resting in a cool environment. In addition to physiological monitoring, perceptual measures were assessed every 15 min, allowing subjects to report any discomfort or early signs of heat strain. The metabolic mask was removed outside of designated measurement periods, reducing potential respiratory discomfort. No adverse events occurred during the study.

Perceptual ratings were collected in a predetermined order at the end of each 15-min interval: overall RPE (O-RPE), central RPE (C-RPE), local RPE (L-RPE), thermal sensation (TS),[21] thermal comfort (TC),[22] and Thirst.[23] Subjects verbally stated their ratings while referencing a printed scale that displayed both numerical values and descriptive terms to ensure consistent interpretation. Subjects were given 30 mL of water every 15 min after data collection was complete.

For differentiated RPEs, the Borg 6-20 scale[24] was used to assess O-RPE, C-RPE, and L-RPE. These ratings were collected immediately after the metabolic mask was removed, with subjects first rating overall exertion, followed by breathing exertion (C-RPE), and finally local exertion (L-RPE).

For TS, subjects used the 9-point Zhang scale,[21] an expansion of the original American Society of Heating, Refrigerating and Air-Conditioning Engineers 7-point scale. The modification improved sensitivity in heat conditions by extending the scale range from −4 ("very cold") to +4 ("very hot"), with 0 representing thermal neutrality. Subjects were instructed to rate their overall perception of temperature, rather than specific body parts, and verbally report their response while referencing the printed scale.

For TC, subjects rated their level of comfort using a 4-point scale, ranging from 4 ("very uncomfortable") to 1 ("comfortable").[22] They were advised to consider both physiological and psychological perceptions of heat when making their ratings.

For Thirst perception, a 9-point thirst scale was used, where 1 represented "not thirsty at all" and 9 indicated "very, very thirsty".[23] Subjects were instructed to assess their subjective sensation of thirst rather than their desire for fluid intake.

These instructions were verbally explained to subjects before data collection, allowing them to ask questions to ensure comprehension. This approach ensured that perceptual measures were consistently applied across all trials.

Although multiple perceptual scales were collected during exercise, subjects were given clear and concise instructions on how to rate their perceptions, and each scale served as a quick perceptual check. To minimize cognitive load, subjects were instructed to provide their immediate, instinctive (or "gut") response without overanalyzing. The sequence of ratings remained consistent across all trials (O-RPE, C-RPE, L-RPE, TS, TC, and Thirst), allowing subjects to become familiar with the process. Given that each rating required only a brief response and based on extensive prior researcher experience in this regard, the perceptual assessments were determined not to impose significant cognitive demand.

Prior research has indicated that exercise may influence thermal perception, potentially reducing thermal sensation compared to passive heat exposure due to mechanisms such as exercise-induced analgesia.[25] To mitigate this potential bias, subjects were specifically instructed to focus on their immediate thermal perception at the moment of assessment rather than retrospective comparisons to prior sensations. Additionally, maintaining a standardized sequence of perceptual ratings at each time point helped reinforce familiarity with the process, potentially reducing variability in responses over time. While this methodological approach aimed to enhance the reliability of TS and TC ratings, we acknowledge that some degree of perceptual alteration due to exercise remains a potential limitation.

After completing the exercise, subjects underwent a 2-min walking cooldown, followed by post-exercise lactate measurements and a final ESQ. Upon exiting the environmental chamber, subjects had their post-exercise body mass and USG measured, which concluded the visit.

Statistical Analysis

All data were expressed as mean ± SD unless otherwise specified. A two-way mixed analysis of variance with the repeated factor of time (six levels: 0, 15, 30, 45, 60, and 75 min) and the nonrepeated factor of exercise type (ET, RT) was used to analyze HR, T_{rec}, $\dot{V}_e$, TS, TC, and Thirst between Hot and Neutral conditions. Similarly, a two-way mixed analysis of variance with the repeated factor of time (five levels: 15, 30, 45, 60, and 75 min) was used to analyze RPE for overall, local, and central exertion. Differences in ESQ scores between pre- and post-exercise were assessed using independent and paired-sample *t*-tests. Cohen's *d* was used to determine the effect size of differences in variable means.

Where significant results were found, post hoc analyses were conducted with a Bonferroni correction for multiple comparisons. To evaluate the role of aerobic fitness on perception, multiple linear regression was used to assess whether $\dot{V}O_{2peak}$ predicted O-RPE, C-RPE, and L-RPE at 75 min in each environment. Moderation analyses were conducted using the Process macro (Model 1) to assess whether the training group moderated the relationship between $\dot{V}O_{2peak}$ and RPE. The level of statistical significance was set at $P < 0.05$ for all analyses. Statistical analyses were performed using SPSS 28.0 for Windows (SPSS, Chicago, IL, United States).

RESULTS

Subjects were classified into endurance-trained (ET, $N = 8$) and resistance-trained (RT, $N = 9$) groups based on self-reported exercise history and performance testing results (**Table I**). As expected, ET women reported significantly more weekly endurance training, while the RT group performed significantly more weekly resistance training (both $P < 0.001$, $d > 2.5$; see Table I for descriptive data and 95% CIs). Significant group differences were observed for $\dot{V}O_{2peak}$ and both strength ratios (all $P \leq 0.002$, $d > 1.8$). Full values and confidence intervals are shown in Table I.

Relative exercise intensity during the 75-min walking protocol was consistent and did not significantly differ between ET and RT groups or between Hot and Neutral conditions at any time point (all $P > 0.05$), confirming that all subjects exercised at comparable intensities (~60% $\dot{V}O_{2peak}$). Average physiological responses across all exercise time points (15–75 min) for Hot and Neutral conditions are presented in **Table II**. These include HR, T_{rec}, $\dot{V}_e$, postexercise lactate, percent body mass loss, and USG. All values are reported as mean ± SD, with statistical comparisons reflecting condition effects.

HR progressively increased over time in both conditions and was significantly higher in Hot (**Fig. 1**) (165.2 ± 10.3 bpm) than Neutral (154.7 ± 9.1 bpm, $P < 0.05$). A significant main effect of time was observed [Hot: $F(4,60) = 65.47$, $P < 0.001$, $\eta^2 = 0.81$; Neutral: $F(4,60) = 57.38$, $P < 0.001$, $\eta^2 = 0.79$], with HR significantly elevated from baseline at 15 min and continuing to rise throughout exercise in both conditions. In Neutral, the increase was less pronounced and plateaued after 45 min. Although HR was higher in Hot, no significant interaction between time and condition was found [$F(4,60) = 2.315$, $P = 0.098$]. A three-way interaction among time, condition, and training group was also not significant [$F(4,60) = 1.827$, $P = 0.145$], indicating similar HR patterns between ET and RT groups across conditions.

T_{rec} increased over time in both conditions, with a more pronounced rise in Hot (**Fig. 2**). Average T_{rec} in Hot was 38.4 ± 0.3°C, significantly higher than Neutral (37.9 ± 0.2°C, $P < 0.05$). A significant main effect of time was observed in Hot [$F(4,60) = 32.26$, $P < 0.001$, $\eta^2 = 0.68$], with increases from baseline beginning at 15 min and continuing through the end of exercise (all $P < 0.05$). Neutral T_{rec} also showed a significant time effect [$F(4,60) = 25.41$, $P < 0.001$, $\eta^2 = 0.63$], though the increase was more gradual and plateaued after 45 min. A significant time × condition interaction was observed [$F(4,60) = 3.912$, $P = 0.027$, $\eta^2 = 0.30$], indicating greater heat retention in Hot. No significant three-way interaction was found [$F(4,60) = 2.089$, $P = 0.115$], suggesting similar T_{rec} responses between ET and RT groups.

$\dot{V}_e$ increased over time in both conditions, with significantly higher values in Hot (53.2 ± 8.7 L · min^{-1}) than Neutral (47.6 ± 7.9 L · min^{-1}, $P < 0.05$). In Hot, a significant main effect of time was observed [$F(4,60) = 21.57$, $P < 0.001$, $\eta^2 = 0.59$], with $\dot{V}_e$ increasing from baseline at 30 min and remaining elevated thereafter (all $P < 0.05$). Neutral also showed a significant but less pronounced time effect [$F(4,60) = 18.94$, $P < 0.001$, $\eta^2=0.56$]. A significant time × condition interaction [$F(4,60) = 4.301$, $P = 0.045$, $\eta^2 = 0.26$] indicated greater ventilatory strain in Hot. No significant three-way interaction was observed [$F(4,60) = 1.665$, $P = 0.184$], suggesting similar $\dot{V}_e$ responses between ET and RT groups.

Lactate levels increased significantly from pre- to postexercise in both conditions, with a greater rise in Hot (**Fig. 3**). In Hot, post-exercise lactate was significantly higher than pre-exercise for both ET [$t(7) = 3.62$, $P = 0.008$, $d = 1.28$] and

Table I. Subject Demographic and Performance Characteristics.

VARIABLE	ET	RT	*d*	95% CI FOR MEAN DIFFERENCE (ET–RT)
Age	23.88 ± 3.31	25.00 ± 4.90	−0.27	−6.06, 5.26
Weight (kg)	60.49 ± 4.68	65.03 ± 8.52	−0.65	−8.15, 2.75
Height (cm)	170.65 ± 5.78	166.67 ± 4.46	0.78	−4.23, 5.63
Body fat %	23.11 ± 5.15	22.18 ± 4.38	0.20	−7.55, −4.35
Lean Mass (kg)	44.63 ± 2.91	48.32 ± 7.25	−0.65	−5.39, 2.59
Weekly Endurance Training (h/wk)	6.94 ± 3.23†	0.33 ± 1.00	2.69	4.04, 9.15
Weekly Resistance Training (h/wk)	1.38 ± 1.92†	7.00 ± 1.75	−3.07	−7.53, −3.71
$\dot{V}O_{2peak}$	55.57 ± 5.39*	46.20 ± 4.66	1.87	4.13, 14.61
Squat to Body Mass Ratio	1.01 ± 0.24†	1.50 ± 0.18	−2.36	−0.71, −0.27
Bench to Body Mass Ratio	0.62 ± 0.10†	0.91 ± 0.18	−2.04	−0.44, −0.14

Data presented as mean ± SD. Statistical comparisons reflect group differences. 95% confidence intervals are reported for between-group differences.
ET: endurance trained; RT: resistance trained; CI: confidence interval.
*Significantly different than RT ($P = 0.002$).
†Significantly different than RT ($P < 0.001$).

Table II. Average Physiological Responses during Exercise by Condition and Group.

VARIABLE	HOT ET	HOT RT	*P* (HOT)	*d* (HOT)	NEUTRAL ET	NEUTRAL RT	*P* (NEUTRAL)	*d* (NEUTRAL)
Heart rate (bpm)	163.8 ± 9.7	166.5 ± 10.9	0.496	0.35	153.5 ± 8.7	155.9 ± 9.6	0.571	0.29
Rectal temperature (°C)	38.3 ± 0.3	38.5 ± 0.3	0.246	0.62	37.8 ± 0.2	38.0 ± 0.2	0.583	0.28
Minute ventilation ($L \cdot min^{-1}$)	52.4 ± 8.1	54.1 ± 9.2	0.652	0.23	46.9 ± 7.3	48.3 ± 8.4	0.710	0.20
Body Mass Loss (%)	0.92 ± 0.35	1.33 ± 0.44	0.260	0.58	0.51 ± 0.28	0.65 ± 0.34	0.409	0.42
Post-Exercise USG	1.021 ± 0.006	1.020 ± 0.007	0.674	0.21	1.014 ± 0.005	1.015 ± 0.005	0.718	0.19

Values are presented as mean ± SD. Statistical comparisons reflect condition effects.
ET: endurance trained; RT: resistance trained; USG: urine specific gravity.

RT groups [$t(8) = 4.89$, $P = 0.001$, $d = 1.63$]. In Neutral, pre-to-post increases were smaller; the change was not statistically significant for ET [$t(7) = 2.05$, $P = 0.078$, $d = 0.72$], but was significant for RT [$t(8) = 2.41$, $P = 0.041$, $d = 0.84$]. Postexercise lactate was significantly higher in Hot than Neutral for both groups ($P < 0.05$), indicating greater anaerobic demand in the heat. Additionally, RT women had significantly higher postexercise lactate than ET women in Hot [RT: 3.21 ± 1.13 $mmol \cdot L^{-1}$; ET: 1.44 ± 0.22 $mmol \cdot L^{-1}$; $t(15) = 4.20$, $P < 0.001$, $d = 2.04$, 95% CI (0.90, 2.70)], suggesting a greater anaerobic contribution in resistance-trained individuals.

Both body mass and USG changed significantly following exercise, reflecting fluid loss. Body mass decreased in both conditions, with a significantly greater loss in Hot (1.13 ± 0.42%)

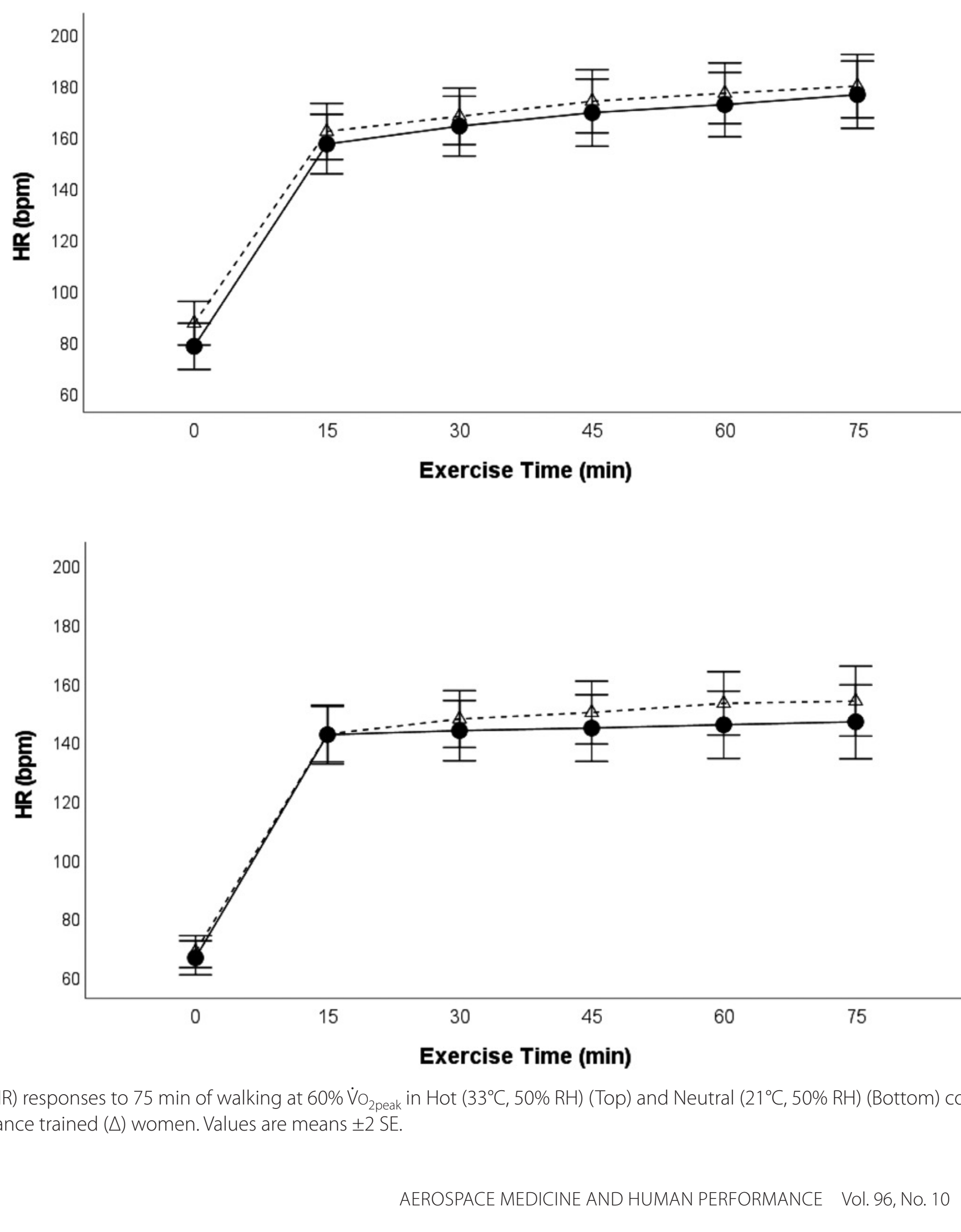

Fig. 1. Heart rate (HR) responses to 75 min of walking at 60% $\dot{V}O_{2peak}$ in Hot (33°C, 50% RH) (Top) and Neutral (21°C, 50% RH) (Bottom) conditions in endurance trained (•) and resistance trained (Δ) women. Values are means ±2 SE.

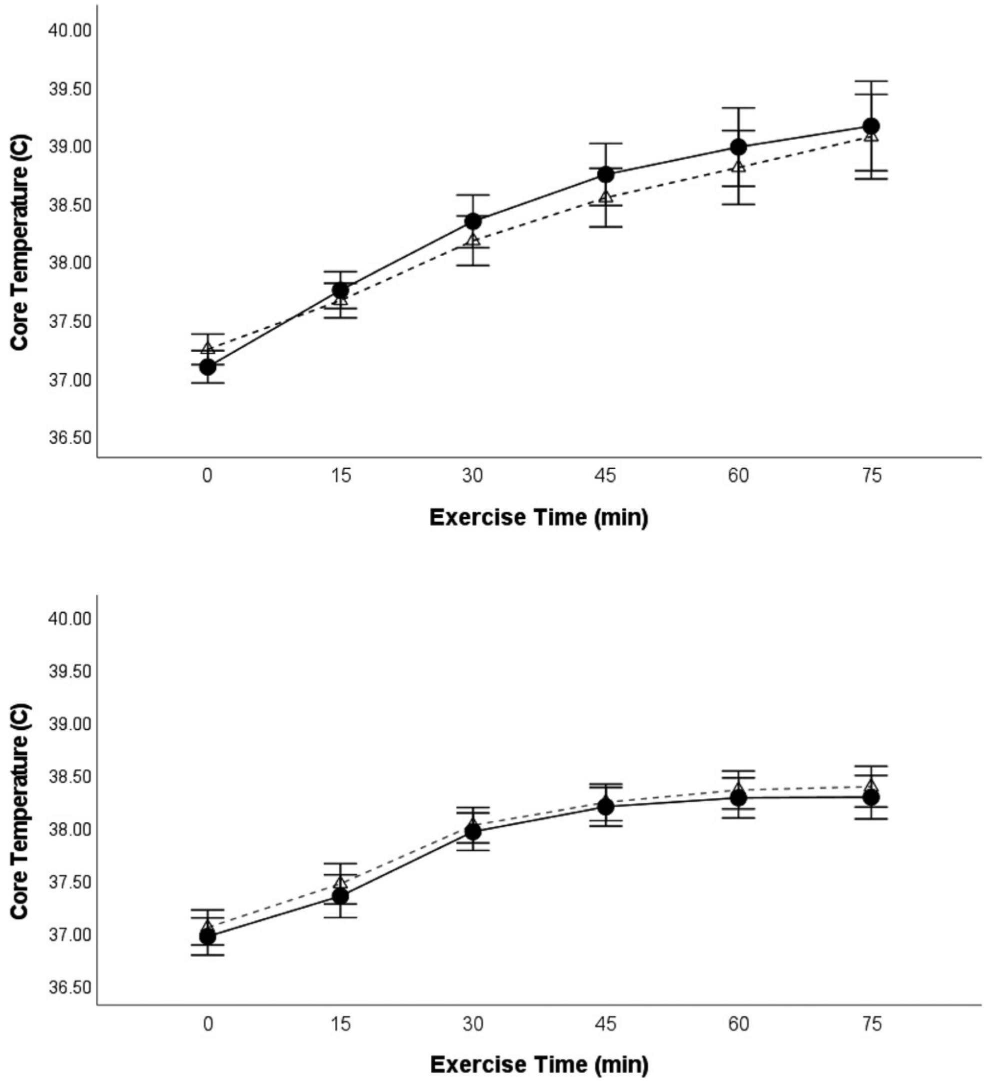

Fig. 2. Core temperature (°C) responses to 75 min of walking at 60% $\dot{V}O_{2peak}$ in Hot (33°C, 50% RH) (Top) and Neutral (21°C, 50% RH) (Bottom) conditions in endurance trained (•) and resistance trained (Δ) women. Values are means ±2 SE.

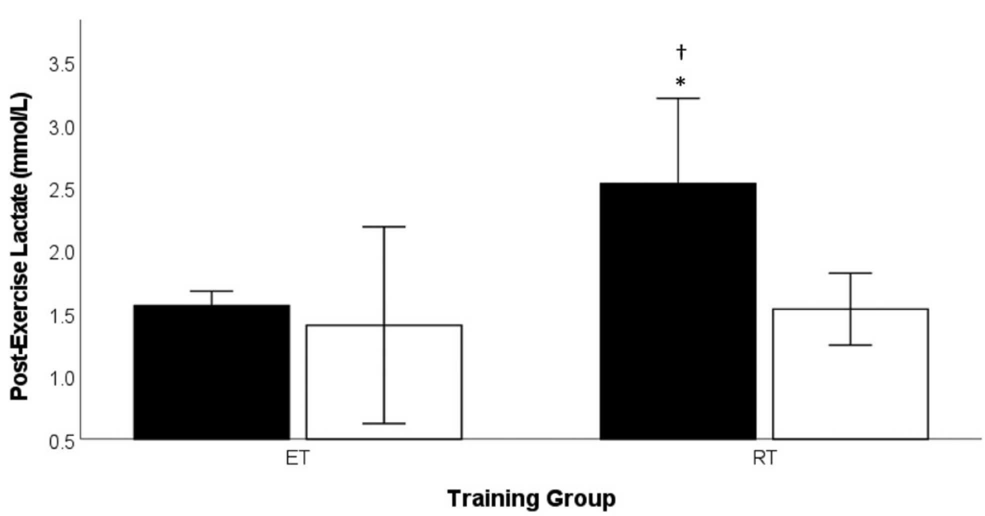

Fig. 3. Post-exercise lactate values after 75 min of walking at 60% $\dot{V}O_{2peak}$ in Hot (33°C, 50% RH; black bars) and Neutral (21°C, 50% RH; white bars) conditions in endurance trained (ET) and resistance trained (RT) women. Values are means ±2 SE. *Significantly higher than ET Hot ($P < 0.001$). †Significantly higher than RT Neutral ($P = 0.015$).

compared to Neutral [0.58 ± 00.31%; $t(16) = 5.12$, $P < 0.001$, $d = 1.36$, 95% CI (0.33, 0.76)]. Pre-exercise USG values confirmed euhydration at the start of each session, with no significant difference between Hot (1.012 ± 0.005) and Neutral [1.011 ± 0.004; $t(16) = 0.63$, $P = 0.537$, $d = 0.15$, 95% CI (−0.003, 0.005)]. Post-exercise USG was significantly higher in Hot (1.020 ± 0.006) than Neutral [1.015 ± 0.005; $t(16) = 3.42$, $P = 0.003$, $d = 0.83$, 95% CI (0.002, 0.008)], indicating greater dehydration in the heat. No significant group differences were observed for percent body mass loss [ET:0.92 ± 0.35%, RT: 0.89 ± 0.40%; $t(15) = 0.17$, $P = 0.867$, $d = 0.08$, 95% CI (−0.36, 0.43)] or USG change [Hot: ET Δ = 0.008 ± 0.004, RT Δ = 0.009 ± 0.005; $t(15) = 0.43$, $P = 0.674$, $d = 0.21$, 95% CI (−0.004, 0.006)], indicating similar hydration responses across groups.

Perceptual responses are summarized in **Table III**. O-RPE increased over time in both conditions, with significantly higher ratings in Hot during the later stages. A significant main effect of time was found in Hot [$F(4,60) = 27.44$, $P < 0.001$, $\eta^2 = 0.65$], with values rising from baseline at 30 min and peaking at 75 min (all $P < 0.05$). Neutral also showed a significant time effect [$F(4,60) = 24.91$, $P < 0.001$, $\eta^2 = 0.62$], though values remained lower throughout. A significant time × condition interaction [$F(4,60) = 4.95$, $P = 0.042$, $\eta^2 = 0.25$] indicated greater perceived effort in Hot, particularly after 45 min. No significant three-way interaction was observed [$F(4,60) = 0.645$, $P = 0.435$], suggesting similar O-RPE trends between groups. At 60 min in Neutral, RT women reported significantly higher O-RPE than ET women ($P = 0.028$, $d = 0.97$); however, this isolated difference does not appear to carry practical significance given the overall pattern of responses.

C-RPE increased over time in both conditions, with greater elevations in Hot. A significant main effect of time was observed in Hot [$F(4,60) = 23.19$, $P < 0.001$, $\eta^2 = 0.61$], with increases from baseline beginning at 30 min (all $P < 0.05$). Neutral also showed a significant time effect [$F(4,60) = 19.84$, $P < 0.001$, $\eta^2 = 0.57$], though values were consistently lower. A significant time × condition interaction [$F(4,60) = 4.55$, $P = 0.050$, $\eta^2 = 0.22$] indicated a more rapid rise in C-RPE in Hot. No significant three-way interaction was found [$F(4,60) = 0.477$, $P = 0.500$], suggesting similar responses between ET and RT groups.

L-RPE gradually increased over time in both conditions and was higher in Hot during the later stages. A significant main effect of time was found in Hot [$F(4,60) = 19.05$, $P < 0.001$, $\eta^2 = 0.56$], with increases beginning at 30 min (all $P < 0.05$). Neutral showed a similar but less pronounced trend [$F(4,60) = 17.77$, $P < 0.001$, $\eta^2 = 0.54$]. A near-significant time × condition interaction [$F(4,60) = 3.963$, $P = 0.065$, η2 = 0.21] suggested greater local fatigue in Hot. No significant three-way interaction was observed [$F(4,60) = 0.064$, $P = 0.804$], indicating consistent L-RPE responses across training groups.

TS increased over time in both conditions, with greater discomfort reported in Hot. A significant main effect of time was found in Hot [$F(5,75) = 41.29$, $P < 0.001$, $\eta^2 = 0.73$], with TS rising from baseline at 15 min and remaining elevated throughout ($P < 0.05$). Neutral also showed a significant but smaller increase [$F(5,75) = 19.31$, $P < 0.001$, $\eta^2 = 0.56$]. A significant

Table III. Perceptual Responses in ET and RT Women Across Hot and Neutral Exercise Conditions.

	THERMAL SENSATION		THERMAL COMFORT		THIRST		O-RPE		C-RPE		L-RPE	
TIME	ET	RT	ET	RT	ET	RT	ET	RT	ET	RT	ET	RT
Hot												
0	1.38 ± 0.52	0.89 ± 0.60	2.25 ± 0.71	1.56 ± 0.73	3.38 ± 0.74	2.78 ± 1.09	—	—	—	—	—	—
15	2.50 ± 0.54	2.11 ± 0.78	2.75 ± 0.89	2.67 ± 0.50	5.00 ± 0.93	4.00 ± 1.50	12.50 ± 1.31	13.22 ± 1.86	10.50 ± 2.07	11.56 ± 1.88	12.50 ± 3.02	14.00 ± 1.80
30	2.75 ± 1.04	2.44 ± 0.88	2.88 ± 0.99	2.78 ± 0.44	5.50 ± 1.41	4.44 ± 1.51	13.88 ± 1.96	124.22 ± 1.64	12.13 ± 2.36	12.44 ± 2.65	13.63 ± 3.34	15.11 ± 1.83
45	3.13 ± 1.13	2.56 ± 1.01	3.13 ± 1.13	3.00 ± 0.71	5.50 ± 1.77	5.33 ± 1.87	14.88 ± 2.95	15.33 ± 1.80	13.50 ± 3.46	12.89 ± 2.76	13.88 ± 3.52	15.89 ± 2.32
60	3.25 ± 0.89	3.11 ± 1.05	3.13 ± 1.13	3.00 ± 0.71	6.00 ± 2.00	5.89 ± 1.90	15.25 ± 2.96*	16.22 ± 2.77*	13.25 ± 3.24	13.89 ± 3.55	14.13 ± 3.31	16.11 ± 2.98
75	3.13 ± 0.84	3.00 ± 1.00	3.00 ± 1.07	3.22 ± 0.67	6.63 ± 2.07	6.44 ± 1.81	15.25 ± 3.54*	16.78 ± 3.42*	13.63 ± 3.54*	15.11 ± 4.01*	14.63 ± 3.50	16.67 ± 3.54
Neutral												
0	−1.75 ± 0.71	−2.22 ± 0.83	1.63 ± 0.52	2.11 ± 0.93	3.25 ± 1.28*	1.44 ± 1.59	—	—	—	—	—	—
15	0.13 ± 0.64	0.56 ± 0.73	1.75 ± 0.71	1.89 ± 0.78	4.13 ± 1.55*	2.67 ± 1.00	10.75 ± 1.58	11.44 ± 2.13	9.63 ± 1.60	9.89 ± 2.37	11.25 ± 2.44	12.89 ± 1.36
30	0.88 ± 0.64	1.00 ± 0.71	2.00 ± 0.76	1.78 ± 0.67	4.38 ± 1.85	3.33 ± 1.41	11.50 ± 1.77	12.67 ± 1.80	10.50 ± 0.93	10.67 ± 2.55	12.13 ± 1.64	13.56 ± 1.42
45	1.13 ± 0.84	1.22 ± 0.83	2.00 ± 0.76	2.00 ± 0.87	4.13 ± 1.89	3.89 ± 1.76	11.75 ± 2.05	13.56 ± 2.40	11.00 ± 1.85	10.89 ± 2.62	11.50 ± 2.07	13.44 ± 1.81
60	1.13 ± 0.84	1.22 ± 0.97	1.88 ± 0.84	1.89 ± 0.78	4.13 ± 1.89	4.00 ± 1.94	11.38 ± 1.85†	13.44 ± 1.67	10.75 ± 1.91	11.56 ± 3.05	11.38 ± 2.50	13.56 ± 2.19
75	1.25 ± 0.89	1.11 ± 0.93	1.75 ± 0.71	2.00 ± 0.87	4.38 ± 1.77	4.33 ± 2.00	11.50 ± 2.00	13.11 ± 1.54	10.50 ± 1.77	11.44 ± 3.13	11.63 ± 2.62	13.33 ± 1.87

Values are presented as mean ± SD.
ET: endurance trained; RT: resistance trained; O-RPE: overall rating of perceived exertion; C-RPE: central rating of perceived exertion; L-RPE: local rating of perceived exertion.
*Significant difference between Hot and Neutral at corresponding time point ($P < 0.05$).
†RT significantly higher than ET at that time point ($P < 0.05$).

time × condition interaction [$F(5,75) = 8.549$, $P = 0.010$, $\eta^2 = 0.32$] indicated higher thermal discomfort in Hot, particularly in later stages. No significant three-way interaction was observed [$F(5,75) = 0.85$, $P = 0.372$], suggesting similar TS patterns across groups.

TC decreased over time in both conditions, with greater discomfort reported in Hot. A significant main effect of time was found in Hot [$F(5,75) = 35.85$, $P < 0.001$, $\eta^2 = 0.70$], with TC decreasing from baseline at 15 min and continuing to decline ($P < 0.05$). Neutral also showed a significant but smaller decrease [$F(5,75) = 18.22$, $P < 0.001$, $\eta^2 = 0.55$]. A significant time × condition interaction [$F(5,75) = 6.734$, $P = 0.014$, $\eta^2 = 0.30$] indicated greater thermal discomfort in Hot, especially after 45 min. No significant three-way interaction was observed [$F(5,75) = 2.519$, $P = 0.133$], indicating similar TC responses across groups.

Thirst increased over time in both conditions, with higher ratings in Hot (**Fig. 4**). A significant main effect of time was observed [$F(5,75) = 15.94$, $P < 0.001$, $\eta^2 = 0.52$], with increases from baseline beginning at 30 min ($P < 0.05$). Neutral also showed a significant time effect [$F(5,75) = 12.88$, $P < 0.001$, $\eta^2 = 0.46$], though values remained lower. A significant time × condition interaction [$F(5,75) = 5.600$, $P = 0.032$, $\eta^2 = 0.28$] indicated greater thirst in Hot, particularly later in the trial. No significant three-way interaction was found [$F(5,75) = 1.218$, $P = 0.287$], suggesting similar responses between groups. ET women reported higher thirst at baseline [ET: 3.25 ± 1.28; RT: 1.44 ± 1.59, $t(15) = 2.71$, $P = 0.015$, $d = 1.26$, 95% CI (0.41,3.21)] and at 15 min [ET: 4.13 ± 1.55, RT: 2.67 ± 1.00, $P = 0.034$, $d = 0.88$, 95% CI (0.12,2.81)] in Neutral. While all subjects followed standardized hydration protocols, individual variability in pre-session fluid behavior may have contributed to these differences.

Table IV presents ESQ responses before and after the 75-min walk at 60% $\dot{V}O_{2peak}$ in Hot and Neutral conditions. ESQ scores increased significantly from pre- to post-exercise in both conditions, with a greater increase in Hot. In Hot, postexercise scores rose significantly for both ET [$t(7) = 3.56$, $P = 0.009$, $d = 1.26$, 95% CI (4.64, 21.60)] and RT groups [$t(8) = 4.81$, $P = 0.001$, $d = 1.60$, 95% CI (6.22, 17.00)], reflecting heightened

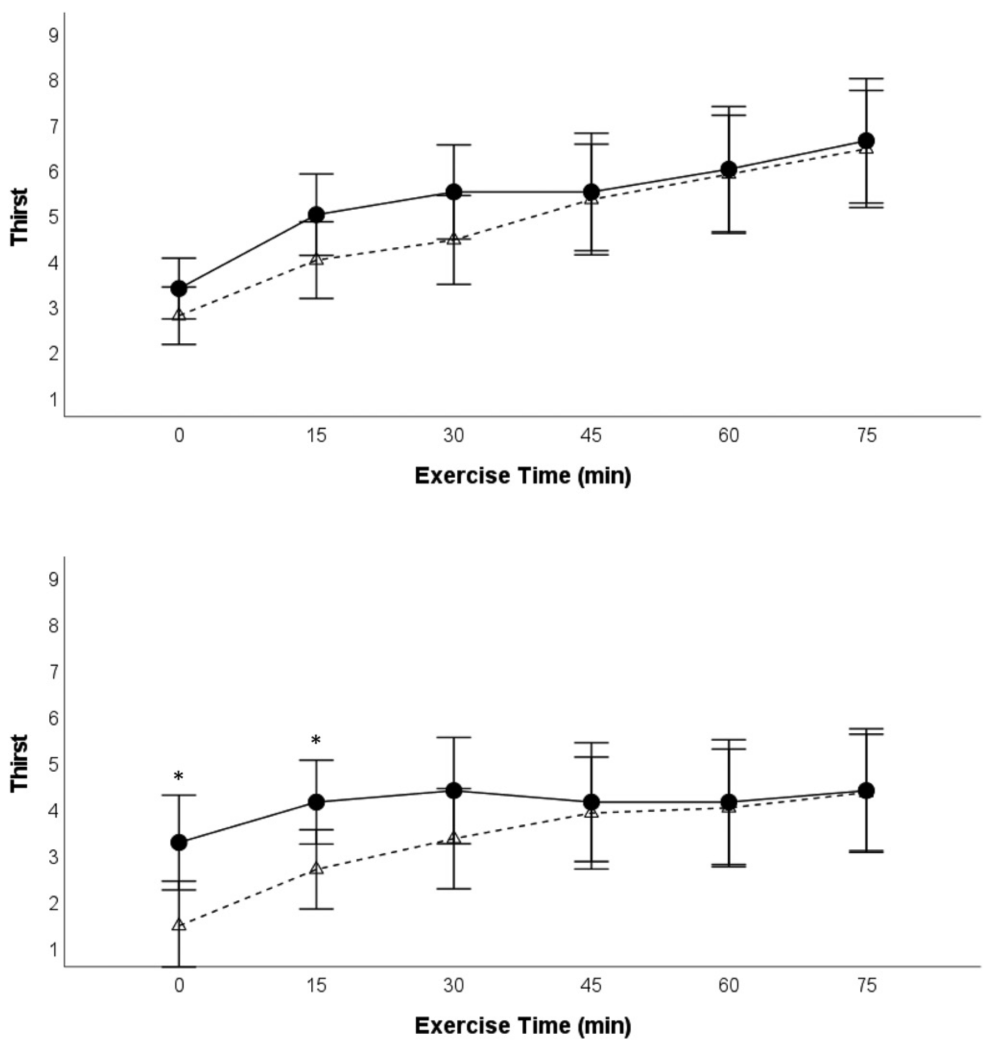

Fig. 4. Thirst responses to 75 min of walking at 60% $\dot{V}O_{2peak}$ in Hot (33°C, 50% RH) (Top) and Neutral (21°C, 50% RH) (Bottom) conditions in endurance trained (•) and resistance trained (Δ) women. Values are means ±2 SE. *Significantly different between groups ($P < 0.05$).

Table IV. Environmental Symptoms Questionnaire (ESQ) Responses Pre- and Post-Exercise in Hot and Neutral Conditions.

	ET HOT		RT HOT		ET NEUTRAL		RT NEUTRAL	
MEASURE	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**
Pre-exercise ESQ total score	6.63	2.07	5.67	3.64	4.25	2.19	6.78	5.04
Post-exercise ESQ total score	19.75*	11.77	17.78‡	8.21	5.88*	1.25	8.89	6.75
ΔESQ total score	13.13†	10.43	12.11†	7.56	1.63	2.00	2.11	6.31

Values are presented as mean ± SD.
ET: endurance trained; RT: resistance trained.
*Significantly higher than pre-exercise value ($P < 0.05$).
†Significantly higher than ΔESQ Neutral value ($P < 0.01$).
‡Significantly higher than pre-exercise value ($P < 0.001$).

physiological and psychological strain. In Neutral, post-exercise increases were observed but smaller, reaching significance for RT [$t(8) = 2.19$, $P = 0.059$, $d = 0.77$] but not for ET [$t(7) = 1.65$, $P = 0.138$, $d = 0.58$]. Post-exercise ESQ scores were significantly higher in Hot than Neutral for both groups ($P < 0.05$), indicating greater overall stress in the heat. No significant group differences were observed post-exercise within either condition ($P > 0.05$), suggesting training background did not strongly influence symptom reporting.

Regression analyses revealed that $\dot{V}O_{2peak}$ significantly predicted lower overall RPE (B = −2.07, $P = 0.017$, $R^2 = 0.469$) and local RPE (B = −0.232, $P = 0.040$, $R^2 = 0.370$) at minute 75 in the Neutral condition, indicating that aerobic fitness is associated with reduced perceived exertion in a thermoneutral environment. However, $\dot{V}O_{2peak}$ was not a significant predictor of perceptual or physiological responses in the Hot condition, suggesting that the benefit of aerobic fitness may be diminished under heat stress. Moderation analysis showed no significant $\dot{V}O_{2peak}$ × training group interaction effects, and separate correlation analyses within each group (ET and RT) also revealed no associations. These findings indicate that the observed relationships between fitness and RPE were not dependent on training background.

DISCUSSION

This study examined physiological and perceptual responses to a continuous 75-min bout of walking at 60% $\dot{V}O_{2peak}$ in both Hot (33°C, 50% RH) and Neutral (21°C, 50% RH) conditions in ET and RT women. The findings revealed that ET and RT women demonstrated comparable physiological and perceptual responses to prolonged moderate intensity walking under both hot and thermoneutral conditions. These results contrast with our initial hypothesis that endurance training would yield superior thermoregulatory outcomes. Rather, the data suggest that distinct physiological adaptations from both training modalities may converge to support similar tolerance of exercise heat stress.

Endurance training is classically associated with increased plasma volume, cardiac output, and sweating efficiency, whereas resistance training may enhance tolerance to high-intensity effort via greater buffering capacity, muscle mass, and repeated exposure to metabolically stressful bouts that could mimic some aspects of heat adapatation.[6,11] As Ravanelli et al. noted,[5] it may be the training stimulus—rather than $\dot{V}O_{2peak}$ alone—that drives improvements in thermoregulation. The lack of group differences in key physiological and perceptual markers, despite higher post-exercise lactate in RT women during Hot, underscores the potential for training type diversity in developing heat resilience.

Several contextual factors may explain the similarity in perceptual and physiological responses between ET and RT women. Women tend to exhibit different thermoregulatory responses than men, such as lower sweat rates and great reliance on dry heat loss, which may result in more uniform perceptions of exertion and thermal strain across training types.[26] Additionally, both ET and RT women in this study reported similar environmental exposures, with most training indoors or in climate-controlled settings, which may have induced overlapping thermoregulatory adaptations regardless of exercise modality.[5] Shared environmental conditions during habitual training may partially explain the convergence in heat tolerance, particularly in the absence of recent extreme heat exposure. Furthermore, the exercise intensity (60% $\dot{V}O_{2peak}$), while sufficient to induce thermoregulatory strain, may not have been high enough to fully differentiate between the physiological limits of endurance vs. resistance-trained individuals. Prior work has shown that differences in perceptual responses across training backgrounds may only emerge at higher intensities or during maximal efforts.[27,28] Thus, it is possible that the moderate intensity, shared training environments, and female-specific traits collectively contributed to the comparable results observed.

The physiological responses observed in this study further support the conclusion that both ET and RT women experienced similar thermal and cardiovascular strain across environmental conditions. HR, T_{rec}, and $\dot{V}_e$ were all significantly elevated in the Hot condition compared to Neutral, consistent with prior studies examining exercise heat stress.[14,22] Importantly, no significant group differences merged in these variables, indicating that RT women tolerated and responded to heat exposure in a manner similar to their ET counterparts, despite differences in training mode and $\dot{V}O_{2peak}$. While post-exercise lactate was significantly higher in RT women in Hot, this did not correspond to higher differentiated RPE, suggesting a potential dissociation between metabolic strain and perceived effort among RT subjects. Similar findings have been observed in resistance-trained individuals who demonstrate greater buffering capacity and tolerance for lactate accumulation.[26] Additionally, percent body mass loss and post-exercise USG were comparable between groups, confirming that hydration status was well-controlled and unlikely to account for perceptual or physiological variation. Taken together, these physiological findings reinforce the conclusion that training background did not meaningfully influence thermoregulatory or cardiovascular strain during moderate-intensity exercise in the heat.

Perceptual responses, including O-RPE, C-RPE, L-RPE, TS, TC, Thirst, and the ESQ, closely mirrored the physiological data, increasing with exercise duration and environmental stress, but without significant differences between training groups. This alignment between perceptual and physiological measures reinforces the validity of perceptual scales as tools for monitoring strain in exercise-heat contexts, particularly in applied settings such as athletic performance, occupational tasks, and military service.[29] The inclusion of the ESQ provided additional insight into subtle symptoms of heat strain that may not be captured by traditional RPE or thermal comfort scales, supporting its use as a complementary tool for assessing multisystem responses to environmental stress. The differentiated RPE approach further allowed for nuanced analysis of central and peripheral strain, aligning with previous literature emphasizing the role of region-specific perception in heat stress assessment. [24,25]

The current study addresses a substantial gap in the literature. Namely, the lack of research on resistance-trained women in an exercise-heat setting.[4,28] With women comprising a growing proportion of athletes, servicewomen, and labor-intensive occupations, it is essential to understand how varied training backgrounds influence heat stress tolerance. By demonstrating that resistance training may support similar thermoregulatory and perceptual outcomes to endurance training, this study advocates for broader inclusion of training modalities in exercise-heat research, particularly in underrepresented women.

There were some limitations to the study design that may have impacted the implications of the presented findings. Participant menstrual cycle phase was not controlled during scheduling, which may have influenced physiological and perceptual response. However, this decision was made to enhance the practical relevance of the findings, as women frequently exercise in varying environmental conditions without regard to menstrual phase. To reduce confounding effects, subjects were advised not to attend study visits if they were experiencing premenstrual distress or feeling unwell.

Contraceptive use and type were documented, though not used as grouping variables. Three ET and seven RT women reported using non-hormonal contraception, two ET and two RT used oral contraceptives, and three ET women used hormonal intrauterine devices. While the study was designed to compare training background rather than reproductive status, per se, it is possible that hormonal variations influenced perceptual responses. Prior work by Minahan et al.[30] found that women using oral contraceptives reported higher RPE during cycling in the heat compared to naturally menstruating women.

The potential influence of exercise itself on thermal perception should also be considered. Prior research[11] suggests that exercise may dampen thermal perception compared to passive heat exposure, potentially due to exercise-induced analgesia or altered sensory processing during physical exertion. Although subjects were instructed to rate their sensations instinctively and assessments were collected in a consistent manner, it remains possible that exercise modulated their thermal perception.

Future studies should incorporate objective markers of thermal strain, such as skin temperature or sudomotor activity, alongside perceptual scales. A within-subject comparison of active vs. passive heat exposure could further clarify how exercise alters thermal perception and symptom awareness.

In conclusion, both endurance-trained and resistance-trained women experienced comparable physiological and perceptual strain during prolonged moderate-intensity exercise in both hot and thermoneutral conditions. These findings suggest that distinct training modalities can produce functionally similar responses to heat stress, offering practical implications for training design, readiness assessment, and health protection across a variety of active women.

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Abnormal Pattern of Spondylosis and Postflight Neck Flexibility in Fifth-Generation Fighter Pilots

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INTRODUCTION: Cervical spine degeneration occurs naturally, often has biomechanical effects on spinal function, and can be accelerated by daily loading environments such as whole-body vibration. Military fighter pilots routinely experience high-magnitude G_z loading with added helmet mass and head-neck in nonneutral orientations. This study characterized spinal degeneration in fighter pilots and identified functional consequences.

METHODS: A total of 18 fifth-generation fighter pilots received cervical spine MRI scans with secondary clinical reviews. Type and location of degenerative changes were noted. Cervical spine range of motion (CROM) was measured before flight and as soon as possible postflight. Cervical spine degenerative changes were correlated to preflight CROM and changes in postflight CROM.

RESULTS: All enrolled pilots had 2 or more cervical spine disc bulges (average 3.5 per pilot), foraminal stenosis occurred in 17/18 pilots (average 2.8 cervical spine levels), and uncovertebral hypertrophy was evident in 17/18 pilots (average 2.4 cervical spine levels). Spinal degenerative findings were not correlated to preflight CROM. Total incidence of degenerative findings was strongly negatively correlated to postflight reductions in extension, lateral bending, and axial rotation CROM.

DISCUSSION: The pattern of degenerative changes in fighter pilots was remarkably different from that of civilians and was characterized by much higher incidence of degenerative changes and degenerative changes biased toward the upper cervical spine, despite the severity of individual degenerative findings being relatively modest. Correlation to postflight CROM changes, but not preflight CROM, implies a pain-mediated mechanism as opposed to altered biomechanics associated with degeneration of spinal tissues.

KEYWORDS: biomechanics, cervical spine, intervertebral disc, stenosis, $+G_z$.

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Cervical spine degeneration begins around the time of skeletal maturity and progresses with age. Degenerative changes include desiccation of the nucleus pulposus, fissure of the annulus fibrosus, bony osteophyte formation, and inflammatory changes of the uncinate processes and zygapophyseal joints. Intervertebral foraminal stenosis is an important consequence of these structural changes due to its role in nerve root impingement and radiculopathy, and can result from multiple independent mechanisms, including reduced intervertebral disc height, posterolateral disc bulge, and uncovertebral or zygapophyseal joint arthropathy. Posterior disc bulge and retrolisthesis can also contribute to central canal stenosis, which can lead to symptoms of myelopathy. Cervical spine degeneration can be associated with a number of pain mechanisms, including mechanical, radiculopathic, and myelopathic

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symptoms, although the degenerative cascade often occurs without significant symptoms.[1] However, due to the structural nature of these changes, cervical spine biomechanical dysfunction is often a primary outcome.

Studies have highlighted age- and degeneration-associated biomechanical dysfunction in terms of reductions in cervical spine range of motion (CROM).[2,3] For example, reduced CROM occurred early in asymptomatic males, with large reductions across the three primary planes of motion between the third and fifth decades.[2] Miyazaki reported a more complex relationship by correlating degeneration grade with segmental motion,[3] demonstrating increased motion associated with early degenerative changes followed by reduced motion for more severe degeneration. That description was in line with the accepted pattern of dysfunction, instability, and stabilization often used to characterize the course of spinal degeneration. However, the pattern of altered segmental biomechanics can vary between spinal levels within an individual, will be dependent on the specific characteristics of degenerative changes at that level (i.e., annular laxity associated with disc height loss vs. bridging osteophytes), and changes in total CROM will be the cumulative effect of biomechanical changes across all levels of the cervical spine.

The daily biomechanical environment may accelerate degenerative spinal changes for some individuals. Although evidence of an association between occupational environment and accelerated spinal degeneration is mixed, some studies reported an effect of whole-body vibration. For example, incidence of severe lumbar spine degeneration was higher in train engineers who experience whole body vibration as part of their occupation compared to sedentary factory workers.[4] Similarly, occupational loading in heavy machine drivers was related to the presence of lumbar spine disc degeneration.[5] The types of loading experienced in these occupations subject the spinal soft tissues to repeated biomechanical loads at a frequency that may exceed the ability of the tissues to recover and lead to accumulating fatigue-related damage in the chronic phase.

Military fighter pilots experience repeated nonphysiological loads as a part of flight training activities. High G_z accelerations, coupled with head-supported mass and nonneutral head-neck orientations, produce nonphysiological loads borne by the cervical spine[6] that can contribute to development and acceleration of degenerative changes. However, while some studies reported premature and more frequent cervical spine degenerative changes in fighter pilots compared to controls,[7,8] other studies found no differences in cervical spine degeneration.[9] The presence of premature cervical spine degenerative changes in fighter pilots could affect their functional capacity given the associated reduction in spinal biomechanics.[10] Therefore, the objective of this study was to describe degenerative changes in fighter pilot cervical spines and characterize the possible association with altered postflight CROM.

METHODS

Subjects

Fighter pilots of fifth-generation aircraft from the 115[th] Fighter Wing of the Wisconsin Air National Guard were recruited to voluntarily participate in this longitudinal study. All pilots within the fighter wing were invited to participate. Fifth-generation fighters represent the newest military fighter aircraft platform with advanced technological developments, first introduced into the fleet in the early part of the 21[st] century. It has advances in stealth technology, avionics, network-centric capabilities, agility, and maneuverability as some examples. These features enable enhanced survivability, situational awareness, and operational effectiveness in contested environments. The study protocol was approved by the Institutional Review Boards at the Medical College of Wisconsin (protocol number PRO00043926) and Air Force Research Laboratory (Air Force protocol number FWR20230061X). A total of 20 pilots provided written informed consent and enrolled in the study. Two pilots were not able to participate in the MRI protocol.

The remaining 18 pilots participated in baseline and flight training assessments between October 2023 and January 2024. Baseline assessments were conducted at the time of enrollment and flight training assessments were conducted an average of 41 ± 18 d later. Baseline assessments consisted of demographic and flight history questionnaires, neck pain questionnaires, anthropometry measurements, and Upright MRI. Flight training assessments consisted of a questionnaire on recent flight experience and dynamics, pre- and postflight functional assessments, and pre- and postflight pain assessments. All 18 pilots completed preflight functional assessments within 48 h of the targeted flight training exercise (16/18 on the evening before) and 16/18 pilots completed postflight functional assessments on the date of flight training; 2 pilots completed postflight functional assessments the morning after flight training.

Equipment and/or Materials

Upright MRI scans were performed using a 0.6 T Upright MRI scanner (Fonar Corporation, Melville, NY, United States) at Upright MRI of Deerfield (Deerfield, IL, United States). The Upright MRI scanning technique was chosen because the upright seated posture produces a preload on the cervical spine associated with weight-bearing of the head.[11] That preload can change the orientation of the cervical spine and reproduce clinical symptoms in patients with neck pain. Subjects were instructed to remain seated in an upright posture inside the scanner, with their head maintained level and facing forward. The scanning protocol included standard clinical T1 and T2 weighted scans.

Procedure

Deidentified scans were automatically provided to a Board-Certified Diagnostic Radiologist who performed secondary clinical reviews and provided standardized cervical spine MR imaging reports for each subject. Secondary reviews were provided on a fee-for-service basis and the Radiologist was not affiliated with the study and had no knowledge of the study protocol or objectives, or any individual pilot's medical and flight histories. Imaging reports documented degenerative changes, including intervertebral disc bulge, foraminal stenosis, central canal stenosis, uncovertebral joint arthropathy, and facet joint arthropathy. The presence of these degenerative changes was documented at each spinal level (C2/3 through C7/T1). Studies reported high intra- and interobserver agreement in the identification and grading of intervertebral disc bulge/herniation[12] and stenosis.[13] Cumulative incidence of MRI findings was calculated as the total number of degenerative findings for disc bulge, foraminal stenosis (unilateral or bilateral), osteophyte, and uncovertebral joint arthropathy across all cervical spine levels (C2/3 through C7/T1) for each enrolled pilot. Cumulative incidence of MRI findings was a value between 0 (no degenerative findings) and 24 (max of 4 at each of 6 spinal levels).

T2 weighted MRI scans were used to grade each intervertebral disc according to the Pfirrmann scale with a value between 1 (normal) and 5 (severely degenerated).[14] Two individuals from the Principal Investigator's laboratory independently graded degeneration of all cervical spine intervertebral discs. One of the technicians repeated Pfirrmann grading for all discs at least 1 d following the initial assessment. Intra- and interobserver reliability was assessed using the intraclass correlation coefficient (ICC). Total Pfirrmann score was the sum of the individual scores for each cervical spine disc between C2/3 and C7/T1. Total Pfirrmann score was a value between 6 (all normal discs) to 30 (Grade 5 at each of 6 cervical spine intervertebral discs).

Enrolled pilots participate in approximately 100 flight training exercises per year focused on a variety of training scenarios. Our protocol included assessment of flight-related changes in CROM. For this analysis, we chose a single flight-training exercise to measure CROM on the day prior to flight training and as close as possible to the conclusion of flight training. The protocol specifically targeted basic fighter maneuver (BFM) training (i.e., dogfighting), during which the pilots experience repeated high-magnitude accelerations.

Active CROM was measured prior to and immediately after flight training using a CROM device (Performance Attainment Associates, Lindstrom, MN, United States). The examiner for CROM was a certified athletic trainer who has a clinical background in testing neck and back ROM. Pilots were positioned seated on a bench with arms at their sides. CROM was quantified for three trials of flexion, extension, right and left lateral bending, and right and left axial rotation (total $N = 18$ trials) in randomized order. The pilots were instructed on how to move their head for each movement (flexion: "chin to chest", extension: "look up", lateral bending: "ear to shoulder", and rotation: "turn to the right/left") and CROM was measured by the same study team member for all pilots. No instruction was given with reference to pain level the pilot may/may not have experienced during movement. Average CROM was calculated across the three trials in each direction for each subject. Lateral bending and axial rotation CROM were the sum of right and left directions. Postflight change in CROM was assessed as the difference between pre- and postflight CROM, divided by the preflight CROM. A negative value indicated reduced postflight compared to preflight CROM.

Statistical Analysis

Cervical spine degeneration scores were correlated to the magnitude of postflight changes in CROM using Pearson's correlation analysis (RStudio 2023.03.0, Posit Software, Boston, MA, United States). Cumulative incidence of MRI findings and total Pfirrmann scores were the primary correlations. However, cumulative and level-by-level findings of specific degeneration types (e.g., intervertebral foraminal stenosis, disc bulge, etc.) were also correlated to postflight changes in CROM.

Groupwise comparisons were also performed. Paired *t*-tests were used to compare postflight CROM to preflight CROM. Analysis of Variance (ANOVA) was used to compare spinal degeneration scores, demographics/anthropometry, pain scores, and preflight CROM between groups of enrolled fighter pilots. Specific *P*-values and correlation coefficients are reported individually to assess the strength of each correlation or groupwise comparison.

RESULTS

Enrolled pilots (mean age: 38.4 ± 5.7 yr; mean ± SD) had an average of 14.1 ± 5.9 yr military flight history and a total of 2181 ± 924 military flight hours. Across the entire population, 88% of all military flight hours were logged in the F-35, F-16, or F-18. Total military flight hours were positively correlated with pilot age [$r(\text{df}) = 0.910(16)$; $P < 0.0001$] and years of military flight experience [$r(\text{df}) = 0.947(16)$; $P < 0.0001$].

Cervical spine MRI scans revealed no acute traumatic injuries for any enrolled pilot. However, imaging reports described a variety of cervical spine degenerative changes. Disc bulge was the most common (**Table I**). Of the 18 pilots, 16 had between

Table I. Incidence of Cervical Spine Degenerative Findings Across the 18 Enrolled Fighter Pilots.

DEGENERATIVE FINDING	NUMBER (%) OF LEVELS	AVERAGE NUMBER PER PILOT	MINIMUM NUMBER	MAXIMUM NUMBER
Intervertebral Disc Bulge	63 (58)	3.5	2	6
Intervertebral Foraminal Stenosis	54 (50)	2.4	1	6
Uncovertebral Joint Arthropathy	44 (41)	2.4	0	4
Osteophytes	28 (26)	1.6	0	4
Central Canal Stenosis	24 (22)	1.3	0	4
Zygapophyseal Joint Arthropathy	5 (5)	0.3	0	3
Retrolisthesis	4 (4)	0.2	0	1

Total: 108 cervical spinal levels.

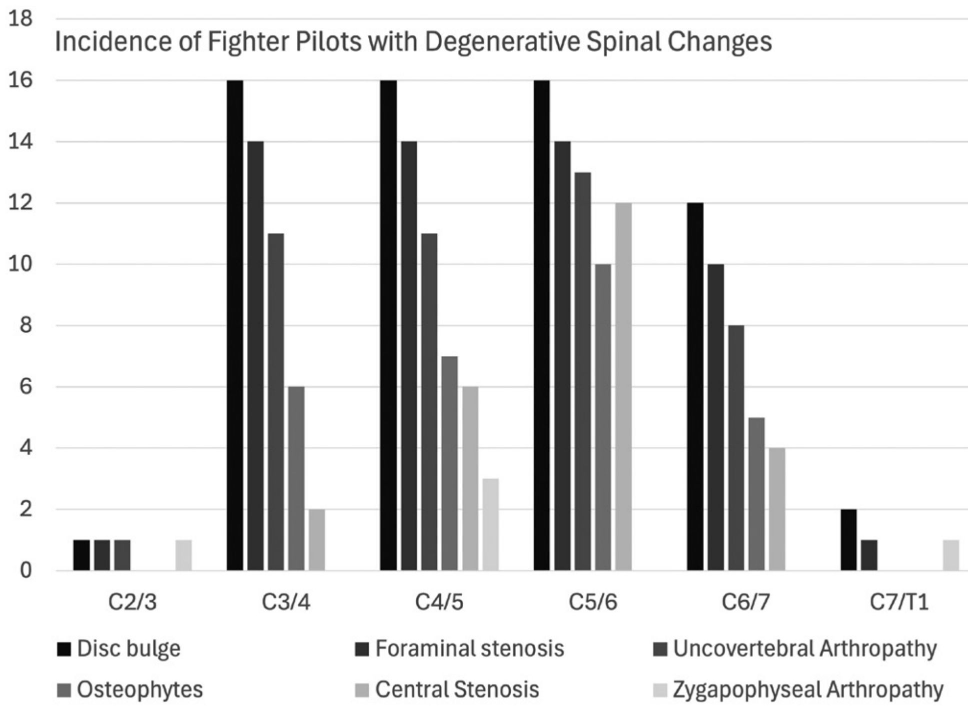

Fig. 1. Incidence and spinal levels for cervical spine degenerative changes identified during secondary clinical reviews of MRI scans across the 18 fifth-generation fighter pilots enrolled in this study.

2 and 4 cervical spine levels with disc bulge; 2 pilots had disc bulge at 5 or 6 spinal levels (C2/3 through C7/T1). The incidence of cervical spine disc bulges per pilot was not dependent on age ($P = 0.829$; df = 16) or total military flight hours ($P = 0.702$; df = 16). Disc bulges were most frequently identified at the C3/4 through C6/7 spinal levels (**Fig. 1**).

Intervertebral foraminal stenosis was the next most common degenerative finding and was closely associated with intervertebral disc bulge. In fact, all but two spinal levels with foraminal stenosis (96%) also had disc bulge. Of 54 spinal levels with foraminal stenosis, 49 demonstrated bilateral occurrence (5 had unilateral stenosis), and 48 of 54 spinal levels with foraminal stenosis were graded as mild. Intervertebral foraminal stenosis was identified primarily at C3/4 through C6/7 spinal levels. The number of cervical spine levels with foraminal stenosis per pilot increased with pilot age [r(df) = 0.440(16); $P = 0.068$] and total military flight hours [r(df) = 0.462(16); $P = 0.054$]. Older and more experienced pilots had higher incidence of foraminal stenosis.

Uncovertebral joint arthropathy was most common in the middle cervical spine (C3/4 to C5/6). Older [r(df) = 0.613(16); $P = 0.007$] and more experienced [r(df) = 0.652(16); $P = 0.003$] pilots had higher incidence of uncovertebral arthropathy. Osteophytes and central canal stenosis were less common, occurring primarily at the C5/6 spinal level with reduced incidence cranially and caudally. Zygapophyseal arthropathy was the least common degenerative finding. Of the five levels with zygapophyseal arthropathy, three occurred in one pilot (C2/3, C4/5, and C7/T1).

Summing the incidence scores for the four most common findings (disc bulge, foraminal stenosis, uncovertebral arthropathy, and osteophytes) across the six cervical spinal levels (i.e., cumulative incidence), pilots had an average incidence of 10.3 ± 3.6 (mean ± SD) cervical spine degenerative findings (range: 5–18). Cumulative incidence of MRI findings had positive correlations with both pilot age [r(df) = 0.558(16); $P = 0.016$] and total military flight hours [r(df) = 0.506(16); $P = 0.032$], wherein older and more experienced pilots had higher incidence of MRI findings.

Focusing on a level-by-level basis, pilots had very few degenerative findings identified on MRI reports at C2/3 and C7/T1 (average: 0.17). A majority of findings were present at C3/4 (2.5 ± 1.4 findings), C4/5 (2.6 ± 1.3 findings), C5/6 (2.9 ± 1.4 findings), and C6/7 (1.9 ± 1.5 findings). These findings indicate that pilots had an average of between 2.5–2.9 of the four most common MRI findings at each spinal level from C3/4 through C5/6. The most frequent combination included disc bulge with foraminal stenosis and uncovertebral joint arthropathy.

All 108 intervertebral discs across the 18 enrolled pilots were graded using the Pfirrmann scale to quantify severity of disc degeneration. Our assessments achieved moderate interobserver reliability (0.594) and moderate intraobserver reliability (0.707). A majority of discs (60.2%) were scored as Pfirrmann Grade 1, 34.3% were scored as Grade 2, 4.6% were Grade 3, and 0.9% were Grade 4. Disc degenerative changes were most frequent in the upper cervical spine and became less frequent caudally (**Fig. 2**). For example, 72.2% and 66.7% of C2/3 and C3/4 discs were Grade 2 or higher compared to only 11.1% and 0% of C6/7 and C7/T1 discs. Total Pfirrmann score was dependent on spinal level ($P < 0.0001$) and was positively correlated with pilot age [r = 0.381(16); $P = 0.119$]. Total Pfirrmann score did not have a strong correlation to cumulative incidence of MRI findings ($P = 0.539$; df = 16).

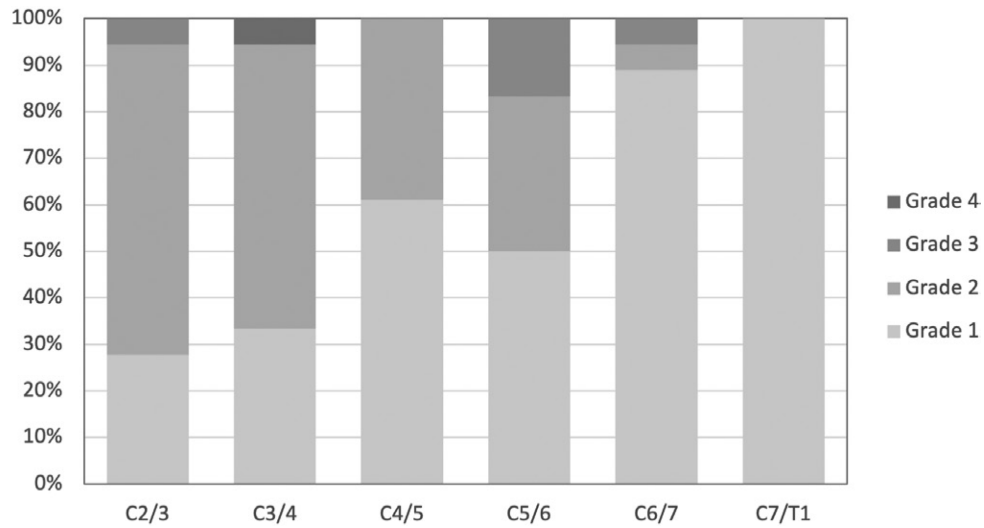

Fig. 2. Pfirrmann grade distribution for cervical spine intervertebral discs for the 18 enrolled fighter pilots in this study.

Flight training assessments were targeted toward more aggressive activities. To that end, assessments for 15 of 18 pilots were performed at the time of BFM training. The other three pilots performed Defensive Counter Air (DCA)-type training. Flight training lasted an average of 1.5 ± 0.4 h, with DCA training being longer (2.3 ± 0.3 h) than BFM training (1.3 ± 0.2 h). Of 18 pilots, 9 reported acceleration characteristics from their flight training. All nine pilots performed BFM training, had a mean peak acceleration of 7.8 ± 1.2 g's, and exceeded 5 g's an average of 4.0 ± 1.5 times.

None of the pilots had flight training on the day of their preflight assessment. In the 7 d prior to the targeted flight training exercise, pilots participated in flight training an average of 1.7 ± 0.8 times for an average of 2.5 ± 1.2 h. Preflight CROM for flexion, extension, lateral bending, and axial rotation are presented in **Table II**. None of the preflight CROM metrics had strong correlations with the number of flights or the total duration of flight training in the previous 7 d. There were 16 pilots who completed their postflight CROM assessment on the day of flight training, an average of 69 min (range: 22–167 min) following completion of flight training. The remaining two pilots completed their CROM assessments the morning following their flight training.

A total of 11 pilots demonstrated increased and 7 pilots demonstrated decreased postflight flexion CROM. Change in postflight flexion CROM was not dependent on age ($P = 0.870$; df = 16) or flight hours ($P = 0.990$; df = 16). Paired t-test revealed that postflight flexion CROM was not different from preflight ($P = 0.469$)

Postflight CROM for the remaining three planes were all reduced compared to preflight. Extension, lateral bending, and axial rotation demonstrated large reductions in postflight CROM compared to preflight. There were 14 pilots who demonstrated reduced postflight extension and lateral bending CROM, and 13 pilots who demonstrated reduced axial rotation CROM. Postflight CROM reductions for each of the three directions were positively correlated to CROM reductions for each of the other two directions [Rs >0.70 (df = 16); $P < 0.005$]. Postflight reductions in CROM for all three directions were not strongly correlated to age, duration, or type (i.e., BFM vs. DCA) of flight training for that assessment.

The magnitude of change in postflight flexion CROM was not strongly correlated with any MRI findings. Pilots with higher incidence of cervical spine degeneration had greater postflight reductions in extension, lateral bending, and axial rotation (**Fig. 3**). Correlations for postflight CROM changes in extension, lateral bending, and axial rotation were most consistent for cumulative incidence of MRI findings. Cumulative incidence of MRI findings (i.e., the total number of disc bulges, foraminal stenosis, osteophytes, and uncovertebral arthropathy identified in each pilot's cervical spine) was negatively correlated to postflight change in extension CROM [r(df) = −0.499(16); $P = 0.035$], lateral bending CROM [r(df) = −0.470(16); $P = 0.049$], and axial rotation CROM [r(df) = −0.493(16); $P = 0.038$].

Pilots with higher incidence of cervical spine foraminal stenosis had greater postflight reductions in CROM. Total foraminal stenosis score was negatively correlated to postflight change

Table II. Preflight And Postflight Cervical Spine Range of Motion (CROM), Along with Percent Change in Postflight CROM.

CROM DIRECTION	PREFLIGHT (°)	POSTFLIGHT (°)	PERCENT CHANGE	*P*-VALUE
Flexion	50.8 ± 11.0	52.1 ± 13.1	+2.6	0.469
Extension	57.8 ± 16.7	53.3 ± 18.2	−7.8	0.009
Lateral Bending	82.3 ± 18.6	76.1 ± 24.2	−7.5	0.018
Axial Rotation	131.9 ± 27.0	124.4 ± 33.1	−5.7	0.021

Lateral bending and axial rotation CROM were a total of right plus left CROM.

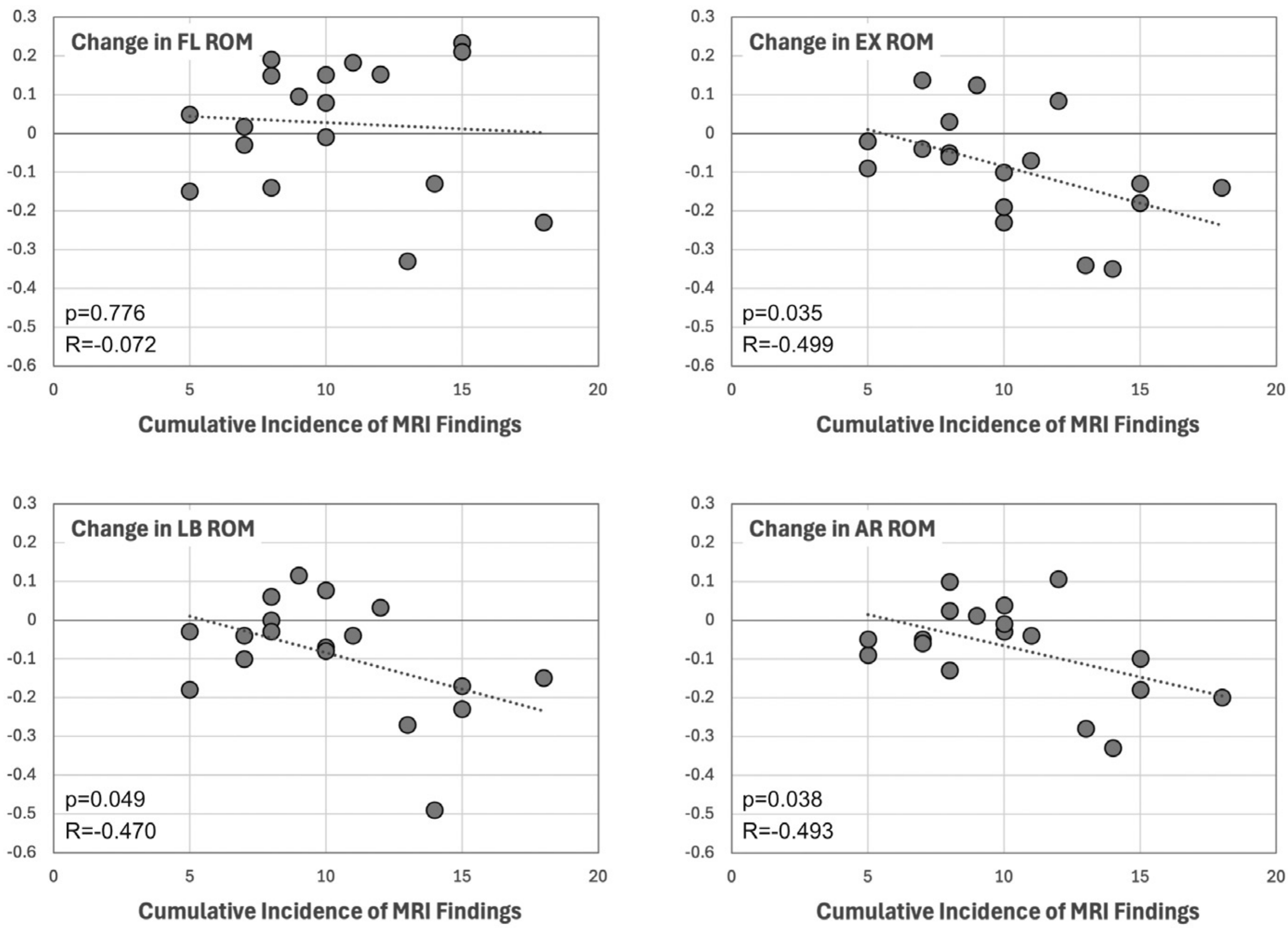

Fig. 3. Cumulative incidence of MRI findings was correlated ($P < 0.05$) to postflight changes in extension (EX), lateral bending (LB), and axial rotation (AR) CROM, but not flexion (FL) CROM.

in extension CROM [r(df) = −0.534(16); P = 0.0224], lateral bending CROM [r(df) = −0.601(16); P = 0.0083], and axial rotation CROM [r(df) = −0.475(16); P = 0.0462]. Correlations for postflight changes in extension CROM and lateral bending CROM were stronger for total foraminal stenosis score than for cumulative incidence of MRI findings. This may indicate a fundamental role of foraminal stenosis in limiting postflight CROM for fighter pilots.

The cumulative incidence of cervical spine disc bulge did not have strong correlation with postflight changes in any of the cervical spine ranges of motion. This finding was somewhat surprising given the strong association between cervical spine disc bulge and intervertebral foraminal stenosis, mentioned earlier, and the finding of a strong negative correlation between total foraminal stenosis score and postflight reductions in CROM. However, cumulative uncovertebral arthropathy had a negative correlation with postflight change in axial rotation CROM [r(df) = −0.516(16); P = 0.029], and negative correlations with postflight change in extension CROM [r(df) = −0.419(16); P = 0.084] and postflight change in lateral bending CROM [r(df) = −0.466(16); P = 0.051]. Pilots with higher incidence of cervical spine uncovertebral arthropathy had greater postflight reductions in CROM. Total Pfirrmann score was not correlated to postflight changes in CROM.

DISCUSSION

The major findings from this study were: 1) our group of fifth-generation fighter pilots displayed a unique pattern of cervical spine degenerative changes relative to civilian populations; and 2) the incidence of cervical spine degenerative changes per pilot was strongly correlated with postflight changes in CROM. The unique pattern of cervical spine degenerative changes was characterized by an unusually high incidence of degenerative changes across the cervical spine as well as a preponderance of degenerative changes in the upper cervical spine in comparison to civilian populations. These findings were consistent across the enrolled fighter pilot population, were generally correlated with pilot age and experience, and were remarkably different from the civilian population as described below.

One of the more striking aspects of the cervical spine degeneration profile in these pilots was the high incidence of degenerative findings. Every enrolled pilot had a minimum of two

Table III. Cervical Spine Location of Intervertebral Disc Protrusion in Asymptomatic Subjects Compared to the Current Fighter Pilot Population.

STUDY	NO. OF SUBJECTS (AGE, yr)	INCIDENCE OF INTERVERTEBRAL DISC PROTRUSION (%)				
		C2/3	C3/4	C4/5	C5/6	C6/7
Ernst et al[16]	30 (19–69)	--	--	21	33	26
Lehto[18]	89 (28–63)	0	2	13	17	4
Matsumoto[17]	497 (10–60+)	2	8	14	27	20
Current Study	18 (28–49)	6	89	89	89	67

cervical spine intervertebral disc bulges, with an average of 3.5 across the subject population. This incidence was much higher than the reported incidence of bulging discs in civilians, where only 80% of 104 civilian males ages 30–39 yr had one or more cervical spine disc bulge,[15] with an average of two per subject. The location of disc bulges was also unique relative to the civilian population (**Table III**), where disc bulges were most common in the middle and lower cervical spine. However, 89% of fighter pilots in this study had disc bulge at each level from C3/4 through C5/6, and 61% had disc bulge at C6/7. Therefore, this population demonstrated intervertebral disc bulges that occurred much more commonly at upper/middle cervical spine levels (C3/4 and C4/5) than the civilian population.[16–18]

Present findings of intervertebral disc degenerative changes were also different from the civilian population. Disc degenerative changes were not overly severe, with an average score of 1.48 across the entire population, but were remarkably different in the pattern compared to civilians, wherein fighter pilots had the highest Pfirrmann scores in the upper cervical spine (C2/3 and C3/4). Disc degeneration in the general population was cited to have the highest Pfirrmann scores at the C5/6 spinal level, with lower scores cranially and caudally.[19] Therefore, the pattern of intervertebral disc degenerative changes in these fighter pilots, characterized by highest Pfirrmann scores in the upper cervical spine, represents a unique profile compared to the normal age-related degeneration pattern. Given the similarity in age between these fighter pilots and civilian volunteers in literature, the differing spinal degeneration profiles are most likely attributable to the flight environment to which the fighter pilots are regularly exposed.

Findings of accelerated degenerative changes in the cervical spine for this group of fighter pilots were consistent with other studies.[7,8] For example, Petren-Mallmin and Linder reported significantly increased cumulative cervical spine disc protrusion scores in their population of experienced fighter pilots (ages 28–49 yr) compared to age-matched controls.[7] Hämäläinen and colleagues supported the current level-based findings by demonstrating significantly increased occurrence of posterior nuclear extension at the C3/4 spinal level in experienced fighter pilots compared to ground crew controls.[8] This finding is particularly relevant given that present findings of high incidence of disc bulge at C3/4 was one of the strongest differences from age-matched asymptomatic civilians. Hamalainen also reported very high incidence of nuclear extension in their fighter pilots at the C3/4 to C6/7 spinal levels, mirroring the findings from this study. Other studies attributed cervical spine degenerative changes in fighter pilots to a natural aging process that was not dependent on high-G exposures.[9,20] However, despite reporting that cervical spine degenerative changes seemed to be more associated with older age, Landau and colleagues identified that fighter pilots had 65% greater average highest severity cervical spine degeneration grades and a higher average number of affected discs than transport pilots, despite the fighter pilot population being an average of 12 yr younger than the transport pilots in that study.[20] Regardless, this study identified a unique pattern of cervical spine degeneration in fighter pilots that was characterized by a high incidence of degenerative changes both across the population and within individual pilots when compared to data from large samples of age-matched civilians published in literature. Importantly, another major outcome from this analysis was that the total incidence of degenerative changes per pilot was associated with reduced postflight CROM, which implied a reduced in-flight functional deterioration for pilots with increased degenerative changes.

The findings of accelerated upper cervical spine degenerative changes are both striking and can be explained by the biomechanical environment experienced by fighter pilots during flight training. Enrolled pilots participate in approximately 100 flight training exercises per year and BFM training often exposes pilots to peak accelerations exceeding 8 g's while wearing combat helmets that exceed 4.5 lb. BFM training also requires pilots to position themselves in non-neutral head-neck orientations[21] to maintain airspace awareness. The check-six position, in particular, involves axially rotating the head, which causes pre-stress to the spinal soft tissues in the upper cervical spine prior to the application of g-induced loads. The check-six position has commonly been associated with neck pain in fighter pilots.[22] Repeated exposures to this type of environment can lead to mechanical fatigue and damage preferentially affecting soft tissues of the upper cervical spine that eventually contribute to accelerated degenerative changes.

This study identified strong correlations between cumulative incidence of cervical spine degenerative changes and immediate postflight changes in CROM. Interestingly, degenerative cervical spine changes were not correlated to preflight CROM. This likely implicates flight-related pain flare-ups as the primary mechanism for postflight reductions in CROM, as opposed to altered segmental flexibility associated with disc degeneration and joint arthropathy. Support for this hypothesis is that total Pfirrmann scores were not strongly correlated to postflight changes in CROM, whereas total incidence of foraminal stenosis had some of the strongest correlations identified in this study. Prior biomechanical research demonstrated that lumbar spine foraminal dimensions, including cross-sectional area, demonstrated the greatest reductions during ipsilateral lateral bending and axial rotation, whereas extension had only modest reductions and flexion actually increased foraminal dimensions.[23] Disc bulge also increased during extension, lateral bending, and axial rotation. These biomechanical findings track closely with present results, indicating strongest correlations of cumulative foraminal stenosis and total MRI findings with axial rotation and lateral bending. Importantly, axial rotation and lateral bending are also the spinal motions that pilots engage in during "check-six" maneuvers. We anticipate these flight-related reductions in CROM to be transient, which is consistent with prior reports of flight-related pain flare-ups,[24,25] and for CROM to eventually return to baseline levels.

Correlations between postflight changes in CROM and cervical spinal degenerative changes were largely driven by five pilots (28% of the subject population) with the highest total incidence of MRI findings (Fig. 3). Removal of those pilots from the analysis resulted in essentially no meaningful correlation between postflight changes in CROM and cervical degeneration. Interestingly, those five pilots had the highest scores for total foraminal stenosis, total uncovertebral arthropathy, and total disc bulge. In fact, three of these pilots demonstrated at least one cervical spinal level with moderate foraminal stenosis and no other pilot across the entire population demonstrated more than mild stenosis. Total Pfirrmann scores for these five pilots were in the top half of all enrolled pilots, but were otherwise not remarkable. Accordingly, this finding clearly demonstrates a role for the incidence and severity of spinal degenerative findings, particularly related to foraminal stenosis, in postflight reductions in CROM and, presumably, flight-related neck pain.

The 5 pilots demonstrating remarkable postflight reductions in CROM were also different from the other 13 pilots according to a number of demographic, anthropometric, neck pain, and flight-related characteristics (**Table IV**). Groupwise analysis revealed that the five pilots had significantly higher cumulative incidence of MRI findings and greater incidence of specific degenerative findings as outlined above. They were also older and taller, had 36% more total military flight hours, and had larger neck circumference with longer neck lengths. The five pilots had higher baseline NDI scores, although reported postflight pain scores were not different. However, a possible explanation for the lack of differences in postflight pain scores might lie in the format of the Brief Pain Inventory questionnaire. All 5 pilots with strong postflight CROM changes reported experiencing more than usual or typical pain in the past week (self-report occurred at the time of the flight assessment), whereas only 6 of the remaining 13 pilots reported the same. Based on the structure of the Brief Pain Inventory questionnaire, pilots were not asked about current pain levels if they did not report more than usual pain in the past week. Therefore, under reporting of current pain in the 13 pilots without postflight CROM changes may have artificially increased the group pain scores since the 7 pilots without unusual pain were not included in the group average. This may partially explain similar current pain scores between the two groups. Finally, the five pilots with postflight changes in CROM tended to have reduced preflight CROM, particularly in flexion. Based on this groupwise analysis, these five pilots form a separate phenotype with a consistent profile that contributes to reduced postflight neck function through biomechanical, anthropometrical, and pain-related characteristics. Further analyses aimed at the identification of other plausible phenotypes within the larger sample are currently being conducted.

Table IV. Descriptive Measures Showing a Unique Phenotype of Pilots That Demonstrate Remarkable Postflight Reductions in Cervical Spine Range of Motion (CROM).

METRIC	GROUP 1 (*N* = 5)	GROUP 2 (*N* = 13)	*P*-VALUE
Spinal Degeneration			
Total Incidence of MRI Findings	15.4 ± 2.3	8.6 ± 2.0	0.001
Foraminal Stenosis Incidence	4.4 ± 0.9	2.5 ± 1.0	0.004
Disc Bulge Incidence	4.4 ± 0.9	3.2 ± 0.9	0.032
Uncovertebral Arthropathy Incidence	3.8 ± 0.4	1.9 ± 1.0	<0.001
Demographics/Anthropometry			
Age (years)	41.2 ± 3.7	37.3 ± 6.0	0.124
Career Flight Hours	2700 ± 543	1982 ± 978	0.070
Height (cm)	183.9 ± 6.6	175.8 ± 7.7	0.057
Neck circumference (base, cm)	42.7 ± 1.6	39.5 ± 2.9	0.011
Neck length (cm)	13.0 ± 1.6	11.8 ± 1.6	0.180
Pain Scores			
Baseline NDI	9.2 ± 5.1	4.5 ± 3.3	0.109
Pain at Assessment	4.0 ± 2.4	4.3 ± 1.6	0.796
Max Pain 24 h prior to Assessment	4.2 ± 2.3	5.5 ± 1.6	0.322
Avg Pain 24 h prior to Assessment	3.4 ± 2.1	3.5 ± 1.1	0.925
Pre-flight Range of Motion			
Flexion CROM	42.5 ± 6.7	53.9 ± 10.8	0.019
Extension CROM	47.0 ± 17.3	61.9 ± 15.1	0.137
Lateral Bending CROM	73.6 ± 13.6	85.7 ± 19.6	0.167
Axial Rotation CROM	114.8 ± 36.8	138.5 ± 20.3	0.232

Group 1: five pilots who had postflight CROM reductions; Group 2: =the remaining 13 pilots who did not have remarkable postflight changes.

In addition to identifying specific findings of cervical spine degeneration (e.g., disc bulge and foraminal stenosis), this study incorporated a novel grading system to quantify cumulative incidence of cervical spine degenerative changes for each pilot. This grading system was based on the idea that clinical reports of neck pain are often not attributable to a single degenerative finding, but a combination of several defects that contribute to the total degeneration state. Therefore, counting the number of degenerative findings and scoring the cumulative level of degenerative changes at both the segmental and cervical spine levels allowed us to quantify the complete degeneration state across the pilot population. Clinical studies support this assertation. In a study of over 3000 participants, Kasch and colleagues identified that patients with 5 or more MRI findings had greater pain severity at baseline and over 6 yr compared to subjects who had no MRI findings.[26] A similar study reported that MRI imaging evidence of multiple degenerative findings, including disc bulge and spondylosis, was more common in adults 50 yr of age or younger with back pain compared to asymptomatic individuals.[27] In the present study, this unique analysis demonstrated strong correlations for postflight changes in extension, lateral bending, and axial rotation CROM with cumulative cervical spine degeneration state. In fact, of all the individual degeneration type scores, only total foraminal stenosis had stronger correlations with postflight changes in CROM. This clearly demonstrates the utility of using an assessment of the cumulative degeneration state across the entire cervical spine compared to focusing on a single spinal level or type of degeneration.

A limitation is that MRI clinical secondary reviews were performed by a single Diagnostic Radiologist. We felt this was acceptable for multiple reasons. Firstly, the Radiologist was not associated with this study and had no knowledge of the study objectives or subject medical history. Secondly, the types of degenerative changes that were a focus of this analysis were previously shown to have high interrater repeatability. For example, identification of disc bulge using the North American Spine Society, American Society of Neuroradiology, and American Society of Spine Radiology Combined Task Force classification system for lumbar discs[28] resulted in excellent intra- and interobserver agreement for raters, including musculoskeletal radiologists and orthopedic surgeons.[29] Another study reported that disagreement between raters in the diagnosis of intervertebral disc bulge and foraminal stenosis was generally not related to the presence or absence of these findings, but the precise scoring (i.e., mild, moderate, severe).[30] Similarly, Pfirrmann and colleagues[31] demonstrated moderate to substantial inter- and intraobserver agreement for radiologists and orthopedic surgeons in the identification and grading of foraminal stenosis and nerve root compression. Given the excellent agreement between radiologists and surgeons in the identification and grading of spinal degenerative changes, and the fact that MR images from our subjects were all graded by the same unaffiliated individual, we felt justified in using only one radiologist for our MRI secondary reviews.

Despite the novel and important data presented in this manuscript, this analysis does have limitations that can serve as useful guidance to researchers contemplating similar studies. Firstly, secondary clinical reviews were performed by a single radiologist. As discussed above, we feel justified in the decision to use a single radiologist due to the high level of repeatability of the reported MRI metrics. However, comparison of MRI findings between multiple radiologists could have reduced the risk of possible Type I and Type II errors, providing a higher level of confidence in these results. Similarly, these conclusions were based on the cumulative incidence of MRI findings without accounting for the severity of these spinal degenerative changes. Grading the clinical severity (i.e., mild/moderate/severe) or measuring the size/dimensions of disc bulges and stenosis may add a higher level of sensitivity in these results and remains a focus of our ongoing longitudinal analyses. Another limitation is the lack of a control population in this analysis. A cohort of age- and sex-matched civilians would provide a more direct comparison for degeneration and CROM findings in our enrolled fighter pilots. However, a benefit of the current method of comparing our findings to large populations of civilians is that the data in literature and across studies are likely to be more representative of the population in general given the large sample size, which would be difficult to replicate in a study such as this. Finally, one of the major findings from this study, the correlation of spinal degeneration incidence to postflight CROM changes, was derived primarily from a subsample of five pilots. While the number of pilots is somewhat limited, as discussed above, it represents a sizable percentage of the entire enrolled population. Small sample sizes are not uncommon in this type of study[20,24,32] and, given the statistical strength of these findings and the significant differences between this cohort and the other pilots, we have confidence in these results and feel justified in our conclusions.

This study identified a unique pattern of cervical spine degenerative changes in this group of fifth-generation fighter pilots characterized by high incidence and unique location compared to civilians. All pilots demonstrated a high number of cervical spine degenerative changes, including an average of 3.5 spinal levels with intervertebral disc bulge and 2.4 spinal levels with foraminal stenosis. Severity of these changes was not remarkable, although location of degenerative changes was biased toward the upper cervical spine. This unique degeneration profile likely results from high G-loads to which fighter pilots are routinely exposed with head-neck in non-neutral orientation during flight training. These non-neutral orientations involve axial rotation, which is facilitated by motion of the upper cervical segments and causes pre-stress on the soft tissues of the upper cervical spine. Repeated exposure to these loads can result in accumulating damage to the upper cervical spine tissues that manifests as degenerative changes, including disc bulge and inflammation of the uncovertebral and facet joints. These changes contribute to intervertebral foraminal stenosis, which was a major finding in this study.

Interestingly, our analysis demonstrated that the incidence and severity of degenerative changes were not correlated to baseline CROM, but were strongly correlated to postflight CROM changes. These correlations were strongest for axial rotation and lateral bending, motions that incorporate segmental rotation through either primary or coupled relationships and reduce foraminal dimensions on the ipsilateral side. Therefore, postflight reductions in CROM were not likely a biomechanical phenomenon, since baseline CROM was not correlated to spinal degeneration, but associated with acute flight-related pain symptoms that limit CROM mainly in bending modes that involve the upper cervical spine, where degenerative changes were most evident. It should be noted that correlations between spinal degeneration and postflight changes in CROM were driven by a subgroup of five pilots, as discussed in detail above. Therefore, these findings would be strengthened by continued analysis and replication in other studies. Ongoing analyses of baseline and flight-related pain symptoms, as well as comprehensive phenotypes in this fighter pilot population may add clarity to this scenario.

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Prevalence and Risk Factors of Metabolic-Associated Fatty Liver Disease in the Korean Air Force

Du Hyun Song; Boncho Ku

INTRODUCTION: This study investigated the prevalence and risk factors of metabolic-associated fatty liver disease (MAFLD) in the Korean Air Force population (2020–2022), comparing nonpilot and pilot groups.

METHODS: Participants over 40 yr were classified into MAFLD or non-MAFLD groups. MAFLD was defined as hepatic steatosis on ultrasonography plus one of the following: overweight/obesity, type II diabetes, or metabolic deregulations. Variables analyzed included body mass index (BMI), alanine aminotransferase (ALT), uric acid, fasting plasma glucose, lipid profile, triglycerides, albumin, and exercise habits.

RESULTS: Among 1044 participants (667 pilots, 377 nonpilots), MAFLD prevalence was 30.3%, significantly lower in pilots (27.7%) than in nonpilots (34.7%). For nonpilots, BMI [odds ratio (OR) = 3.41], diabetes (OR = 8.32), and ALT (OR = 1.91) were significant factors, although the small sample size limited broader conclusions. Among pilots, BMI (OR = 3.77), uric acid (OR = 1.83), ALT (OR = 1.98), triglycerides (OR = 1.50), and dyslipidemia (OR = 7.97) were strongly associated with MAFLD. Uric acid levels had a greater association with MAFLD in pilots compared to nonpilots.

DISCUSSION: This study highlights the distinct prevalence and risk factors of MAFLD in pilots vs. nonpilots. Uric acid, in particular, emerged as a significant risk factor for pilots, suggesting its potential use for targeted risk assessment in this group. The findings underscore the importance of tailored preventive strategies for MAFLD in occupational groups.

KEYWORDS: pilots, fatty liver, metabolic syndrome, aviation medicine, military personnel.

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Obesity, recognized by the World Health Organization (WHO) as a chronic disease requiring long-term treatment, has become an increasing concern in modern society. In South Korea, the prevalence of obesity has consistently increased over the past decade, now affecting 36.6% of the total population, with rates of 46.2% in men and 27.3% in women.[1] This rising prevalence of the disease is closely linked to the development of various comorbid conditions, including diabetes and metabolic syndrome.[2,3] Furthermore, obesity is a significant risk factor for the development of fatty liver diseases, particularly nonalcoholic fatty liver disease (NAFLD), which is a leading cause of chronic liver disease. Previous studies have reported the prevalence of NAFLD in Korea to range from 15–50%.[4,5]

Recently, there has been a paradigm shift toward recognizing metabolic-associated fatty liver disease (MAFLD) as a more accurate representation of fatty liver conditions linked to metabolic disorders such as obesity, type II diabetes, and dyslipidemia. In 2020, the Asia-Pacific Association for the Study of the Liver (APASL) introduced the term MAFLD to refine and update the NAFLD concept, emphasizing the critical role of metabolic health in the disease's pathogenesis and progression. This transition underscores the necessity for more comprehensive and precise diagnostic criteria.[6,7]

Despite the growing recognition of MAFLD, there is a lack of research in Korea, particularly concerning its prevalence and characteristics within specific populations, such as the military.

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Pilots, for example, face unique challenges due to their profession, including long-distance flights, irregular meal patterns, and circadian rhythm disruptions, which may predispose them to metabolic disorders, including MAFLD.[8] The presence of MAFLD in pilots not only threatens individual health but also raises significant aviation safety concerns, as the disease could progress to more severe liver conditions or exacerbate other metabolic syndromes.

Given the critical nature of this issue, there is a pressing need for targeted studies on the prevalence, risk factors, and management of MAFLD within the military population. Thus, this study investigated the prevalence and associated risk factors of MAFLD in the Republic of Korea Air Force, comparing pilots to nonpilots ages 40 yr or older.

METHODS

Subjects

This study was conducted at the Korean Air Force Aerospace Medical Center, which routinely performs health checkups for both pilots and nonpilots. The standard screening process for individuals ages 40 and older included an abdominal ultrasound. We collected data from 1044 individuals who underwent health checkups at the center between January 2020 and December 2022 by reviewing electronic medical records (EMRs).

This study was reviewed and approved by the Institutional Review Board (IRB) of the Korean Air Force Aerospace Medical Center (IRB number: 136367-202403-HR-01-00). All procedures were conducted in accordance with the protocol approved by the ethics committee, ensuring adherence to ethical standards throughout the study.

Procedure

The following variables were extracted from the EMRs: age, gender, height, weight, body mass index (BMI), waist circumference, smoking status, alcohol consumption, blood pressure, exercise level, blood test results, hepatitis B and C status, abdominal ultrasound findings, presence of fatty liver, and degree of fatty liver. We categorized the study population into two occupational groups: pilots and nonpilots. The nonpilot group consisted of military personnel engaged in nonflying roles, such as administrative or technical support duties, and did not belong to any aircrew category. We further subdivided the pilot group into low-acceleration and high-acceleration pilots based on their exposure to different levels of acceleration forces. We assessed additional demographic and health-related information, including age, gender, alcohol consumption, smoking status, exercise level, presence of diabetes, hypertension, and hyperlipidemia, using a structured questionnaire. Experienced personnel at the center performed measurements of height, weight, waist circumference, and blood pressure. An experienced radiologist performed abdominal ultrasonography to determine the presence and extent of fatty liver disease based on the Hamaguchi criteria ultrasonographic grading system. Blood samples were collected on the same day as the abdominal ultrasound and analyzed in the laboratory.

MAFLD was diagnosed using the following criteria: fatty liver confirmed by abdominal ultrasound plus overweight/obesity, diabetes, or other metabolic abnormalities. Metabolic abnormalities were defined by the presence of two or more of the following criteria: 1) waist circumference ≥90 cm for men or ≥80 cm for women; 2) systolic blood pressure (SBP) ≥130 mmHg, diastolic blood pressure (DBP) ≥85 mmHg, or the use of antihypertensive medication; 3) triglyceride (TG) levels ≥150 mg · dL^{-1} or the use of antihyperlipidemic medication; 4) high-density lipoprotein cholesterol (HDL) levels <40 mg · dL^{-1} for men or <50 mg · dL^{-1} for women; and 5) presence of prediabetes, defined as a fasting blood glucose level ≥100 mg · dL^{-1}, HbA1c level ≥5.7%, or current treatment of diabetes.

Statistical Analysis

All statistical analyses were conducted using R statistical software (version 4.4.0, released on April 14, 2024) (R Core Team 2024). Statistical significance was defined as *P*-value less than 0.05 ($\alpha = 0.05$) for all tests. Continuous variables were summarized as means with SDs, and categorical variables were presented as frequencies and percentages. Demographic characteristics, anthropometric measurements, clinical information, and biochemical and hematological results were compared with Welch's independent two-sample *t*-test for continuous variables or the Chi-squared test for categorical variables. Multiple logistic regression analyses were conducted for the total population and subgroups stratified by occupational specialty, adjusting for age, smoking status, alcohol consumption, exercise level, hypertension, dyslipidemia, diabetes, and hepatitis status to investigate the association between MAFLD and each risk factor considered in this study.

To further investigate the independent associations between risk factors, additional multiple logistic regressions corresponding to the total population and subgroups stratified by occupational specialty were conducted, using all risk factors and the same confounders as in the previous analyses. For two multiple logistic regression models derived from the occupational-stratified subgroups, the differences in the association magnitudes of estimated logistic regression coefficients corresponding to risk factors were identified using the simple Z test.[9] For all logistic regression analyses, all variables, including risk factors and confounders, were standardized with means of 0 and SDs of 1.

RESULTS

Table I summarizes the subjects' demographics, anthropometric measurements, clinical information (vital signs, substance use, and metabolic- and liver-related diseases), and laboratory test results. In this study, the prevalence of MAFLD among the 1044 subjects was 316 (30.3%). The prevalence of MAFLD in the pilot group was 27.7% (185 out of 667), which was statistically significantly lower ($P = 0.018$) than that in the nonpilot

Table I. Demographic Characteristics of the Study Population by MAFLD Status.

CHARACTERISTIC	OVERALL N = 1,044*	NON-MAFLD N = 728*	MAFLD N = 316*	WELCH'S $t/\chi^{2\dagger}$	df†	P-VALUE†
Age	49.14 (4.87)	49.13 (4.91)	49.17 (4.77)	−0.13	615	0.899
Occupational Specialty: Pilot	667 (64%)	482 (66%)	185 (59%)	5.6	1	0.018
Aircraft speed				8.6	2	0.013
Non-Pilot	377 (36%)	246 (34%)	131 (41%)			
Low acceleration	190 (18%)	128 (18%)	62 (20%)			
High acceleration	477 (46%)	354 (49%)	123 (39%)			
Height (cm)	173.52 (5.02)	173.45 (5.11)	173.68 (4.81)	−0.70	632	0.484
Weight (kg)	75.86 (9.04)	72.98 (7.61)	82.48 (8.61)	−17	538	<0.001
BMI ($kg \cdot m^{-2}$)	25.12 (2.55)	24.18 (1.99)	27.27 (2.39)	−20	512	<0.001
Waist Circumference (cm)	84.30 (6.64)	82.03 (5.48)	89.54 (6.10)	−19	545	<0.001
Systolic BP (mmHg)	125.73 (10.89)	124.31 (10.72)	129.01 (10.60)	−6.6	605	<0.001
Diastolic BP (mmHg)	81.44 (7.62)	80.70 (7.56)	83.16 (7.49)	−4.9	604	<0.001
Smoking	674 (65%)	454 (62%)	220 (70%)	5.1	1	0.024
Alcohol	880 (84%)	624 (86%)	256 (81%)	3.7	1	0.055
Regular exercise	997 (95%)	693 (95%)	304 (96%)	0.52	1	0.470
Hypertension	136 (13%)	68 (9.3%)	68 (22%)	29	`	<0.001
Dyslipidemia	61 (5.8%)	30 (4.1%)	31 (9.8%)	13	1	<0.001
Diabetes	43 (4.1%)	13 (1.8%)	30 (9.5%)	33	1	<0.001
Hepatitis	31 (3.0%)	19 (2.6%)	12 (3.8%)	1.1	1	0.299
White blood cells ($10^3/\mu L$)	5.66 (1.37)	5.46 (1.27)	6.12 (1.48)	−6.8	523	<0.001
Red blood cells ($10^6/\mu L$)	4.92 (0.34)	4.88 (0.32)	5.01 (0.36)	−5.6	548	<0.001
Hemoglobin ($g \cdot dL^{-1}$)	15.24 (0.97)	15.13 (0.94)	15.49 (0.99)	−5.4	573	<0.001
Hematocrit (%)	44.92 (2.74)	44.67 (2.67)	45.51 (2.80)	−4.5	574	<0.001
Platelets ($10^3/\mu L$)	237.53 (48.50)	234.60 (48.36)	244.27 (48.21)	−3.0	601	0.003
BUN ($mg \cdot dL^{-1}$)	14.50 (3.34)	14.62 (3.36)	14.24 (3.28)	1.7	612	0.092
Creatinine ($mg \cdot dL^{-1}$)	0.96 (0.13)	0.96 (0.12)	0.97 (0.13)	−1.5	552	0.123
Uric acid ($mg \cdot dL^{-1}$)	6.24 (1.27)	6.07 (1.16)	6.65 (1.43)	−6.4	504	<0.001
Total protein ($g \cdot dL^{-1}$)	7.30 (0.36)	7.27 (0.35)	7.37 (0.38)	−3.8	556	<0.001
Albumin ($g \cdot dL^{-1}$)	4.61 (0.24)	4.59 (0.23)	4.66 (0.24)	−4.0	577	<0.001
Total bilirubin ($mg \cdot dL^{-1}$)	0.99 (0.39)	1.01 (0.39)	0.96 (0.38)	1.9	615	0.057
SGOT (AST) ($IU \cdot L^{-1}$)	27.83 (11.53)	26.34 (8.17)	31.28 (16.40)	−5.1	385	<0.001
SGPT (ALT) ($IU \cdot L^{-1}$)	29.37 (16.82)	24.84 (11.59)	39.82 (21.67)	−12	396	<0.001
Alkaline phosphatase ($IU \cdot L^{-1}$)	207.61 (50.07)	204.21 (49.86)	215.46 (49.75)	−3.4	600	<0.001
Gamma-GT (GGT) ($IU \cdot L^{-1}$)	40.66 (32.70)	36.16 (27.95)	51.01 (39.78)	−6.0	455	<0.001
Glucose ($mg \cdot dL^{-1}$)	100.84 (13.47)	98.73 (11.47)	105.72 (16.19)	−7.0	458	<0.001
Total cholesterol ($mg \cdot dL^{-1}$)	201.17 (35.39)	201.00 (32.88)	201.55 (40.65)	−0.21	502	0.830
Triglyceride ($mg \cdot dL^{-1}$)	133.09 (84.91)	115.35 (68.92)	173.94 (102.50)	−9.3	443	<0.001
HDL-cholesterol ($mg \cdot dL^{-1}$)	54.58 (11.77)	57.02 (11.74)	48.96 (9.75)	12	713	<0.001
LDL-cholesterol ($mg \cdot dL^{-1}$)	130.88 (33.87)	129.82 (31.86)	133.32 (38.03)	−1.4	516	0.153

*Mean (SD); *N* (%).

†Welch's two-sample *t*-test; Pearson's Chi-squared test.

BUN: blood urea nitrogen; SGOT (AST): glutamic-oxaloacetic transaminase (or aspartate aminotransferase) test; SGPT (ALT): serum glutamic pyruvic transaminase (or alanine aminotransferase) test; Gamma GT (GGT): gamma-glutamyl transferase; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

group (34.7%, 131 out of 337). The mean age of the total population was 49.14 ± 4.87 yr and no statistical difference in mean age was observed between the non-MAFLD (49.13 ± 4.91) and MAFLD groups (49.17 ± 4.77). Similar to previous findings,[10–12] bodyweight, BMI, and waist circumference were significantly higher in the MAFLD group compared to the non-MAFLD group. Among the biochemical and hematological results analyzed in this study, except for blood urea nitrogen (BUN), total bilirubin, and HDL, the MAFLD group showed higher values than the non-MAFLD group. Furthermore, with the exception of platelets, BUN, Creatinine (Cr), total bilirubin, total cholesterol (CHOL), and low-density lipoprotein cholesterol (LDL), there were significant differences (P < 0.001) between the MAFLD and non-MAFLD groups.

Table II presents the unadjusted and adjusted odds ratios (ORs) estimated for each risk factor, obtained from univariate and logistic regression analyses, respectively, for the total population and subgroups stratified by occupational specialty. The risk factor most strongly associated with MAFLD across all analysis groups and models was BMI, with the following ORs: total population, unadjusted = 5.35 [95% confidence interval (CI): 4.31–6.73], adjusted = 5.29 (95% CI: 4.24–6.71); nonpilot group, unadjusted = 6.05 (95% CI: 4.24–9.05), adjusted = 6.18 (95% CI: 4.25–9.43); pilot group, unadjusted = 4.92 (95% CI: 3.77–6.57), adjusted = 5.03 (95% CI: 3.80–6.81). Similar to BMI, waist circumference also exhibited a strong positive association with MAFLD across all analysis groups and models, with ORs ranging from 4.32–5.84, 95% CI lower bounds ranging from 3.28–4.01, and 95% CI upper bounds ranging from 5.62–8.93 for both unadjusted and adjusted models. In the total population, BUN [unadjusted OR = 0.89 (95% CI: 0.78–1.02), adjusted OR = 0.89 (95% CI: 0.77–1.03)]

Table II. Unadjusted and Adjusted Association of Risk Factors with MAFLD According to Occupational Specialty.

	TOTAL (*N* = 1044)				NON-PILOT (*N* = 377)				PILOT (*N* = 667)			
	UNADJUSTED (df = 1042)		ADJUSTED (df = 1034)		UNADJUSTED (df = 375)		ADJUSTED (df = 367)		UNADJUSTED (df = 665)		ADJUSTED (df = 657)	
RISK FACTOR	**OR (95% CI)***	**Wald Z; *P***	**OR (95% CI)***	**Wald Z; *P***	**OR (95% CI)***	**Wald Z; *P***	**OR (95% CI)***	**Wald Z; *P***	**OR (95% CI)***	**Wald Z; *P***	**OR (95% CI)***	**Wald Z; *P***
BMI	5.35 (4.31, 6.73)	14.76; <0.001	5.29 (4.24, 6.71)	14.22; <0.001	6.05 (4.24, 9.05)	9.34; <0.001	6.18 (4.25, 9.43)	8.99; <0.001	4.92 (3.77, 6.57)	11.26; <0.001	5.03 (3.80, 6.81)	10.89; <0.001
Waist circumference	4.69 (3.81, 5.86)	14.09; <0.001	4.68 (3.76, 5.91)	13.35; <0.001	5.62 (3.96, 8.32)	9.14; <0.001	5.84 (4.01, 8.93)	8.67; <0.001	4.25 (3.28, 5.62)	10.56; <0.001	4.32 (3.28, 5.81)	10.07; <0.001
Systolic BP	1.57 (1.37, 1.82)	6.22; <0.001	1.51 (1.30, 1.75)	5.43; <0.001	1.37 (1.11, 1.70)	2.91; 0.0036	1.40 (1.12, 1.77)	2.91; 0.0036	1.71 (1.41, 2.10)	5.38; <0.001	1.62 (1.33, 1.99)	4.72; <0.001
Diastolic BP	1.40 (1.22, 1.61)	4.72; <0.001	1.36 (1.18, 1.57)	4.17; <0.001	1.30 (1.07, 1.59)	2.57; 0.0103	1.29 (1.05, 1.60)	2.42; 0.0155	1.46 (1.21, 1.79)	3.80; <0.001	1.44 (1.18, 1.77)	3.53; <0.001
WBC	1.62 (1.41, 1.86)	6.81; <0.001	1.51 (1.30, 1.75)	5.51; <0.001	1.53 (1.23, 1.90)	3.85; <0.001	1.36 (1.08, 1.72)	2.56; 0.0105	1.66 (1.39, 2.00)	5.48; <0.001	1.60 (1.33, 1.94)	4.88; <0.001
Hgb	1.50 (1.30, 1.74)	5.41; <0.001	1.55 (1.33, 1.81)	5.60; <0.001	1.39 (1.12, 1.75)	2.87; 0.0041	1.46 (1.15, 1.87)	3.06; 0.0022	1.62 (1.34, 1.97)	4.84; <0.001	1.63 (1.34, 2.01)	4.76; <0.001
PLT	1.22 (1.07, 1.39)	2.94; 0.0033	1.18 (1.02, 1.35)	2.28; 0.0224	1.07 (0.88, 1.30)	0.67; 0.5024	0.98 (0.79, 1.21)	−0.17; 0.8644	1.33 (1.11, 1.60)	3.10; 0.0019	1.33 (1.10, 1.61)	3.00; 0.0027
BUN	0.89 (0.78, 1.02)	−1.67; 0.0950	0.89 (0.77, 1.03)	−1.59; 0.1108	0.84 (0.67, 1.03)	−1.64; 0.1007	0.81 (0.64, 1.02)	−1.78; 0.0751	0.95 (0.80, 1.13)	−0.60; 0.5481	0.97 (0.81, 1.16)	−0.32; 0.7468
Creatinine	1.11 (0.98, 1.27)	1.60; 0.1100	1.15 (1.00, 1.32)	1.97; 0.0491	1.08 (0.87, 1.35)	0.73; 0.4657	1.10 (0.88, 1.39)	0.83; 0.4049	1.18 (1.00, 1.40)	1.91; 0.0558	1.20 (1.01, 1.43)	2.02; 0.0431
Uric acid	1.60 (1.39, 1.84)	6.60; <0.001	1.69 (1.46, 1.96)	6.90; <0.001	1.34 (1.08, 1.67)	2.67; 0.0075	1.37 (1.09, 1.73)	2.65; 0.0079	1.83 (1.52, 2.21)	6.35; <0.001	1.95 (1.60, 2.38)	6.59; <0.001
Protein	1.30 (1.14, 1.49)	3.82; <0.001	1.30 (1.13, 1.50)	3.62; <0.001	1.25 (1.02, 1.55)	2.14; 0.0323	1.28 (1.03, 1.61)	2.16; 0.0305	1.33 (1.12, 1.60)	3.21; 0.0013	1.31 (1.09, 1.58)	2.87; 0.0042
Albumin	1.31 (1.15, 1.50)	3.99; <0.001	1.32 (1.14, 1.52)	3.83; <0.001	1.20 (0.98, 1.47)	1.77; 0.0776	1.24 (0.99, 1.54)	1.88; 0.0605	1.42 (1.19, 1.71)	3.88; <0.001	1.37 (1.14, 1.66)	3.33; <0.001
T. Bilirubin	0.87 (0.76, 1.00)	−1.88; 0.0604	0.90 (0.78, 1.04)	−1.44; 0.1496	1.00 (0.80, 1.24)	−0.02; 0.9852	1.09 (0.86, 1.37)	0.69; 0.4918	0.83 (0.68, 0.99)	−2.03; 0.0421	0.81 (0.67, 0.98)	−2.17; 0.0302
AST	1.74 (1.46, 2.10)	6.02; <0.001	1.69 (1.40, 2.04)	5.48; <0.001	2.06 (1.52, 2.87)	4.43; <0.001	2.23 (1.59, 3.20)	4.51; <0.001	1.58 (1.28, 1.97)	4.09; <0.001	1.49 (1.20, 1.87)	3.52; <0.001
ALT	3.02 (2.50, 3.69)	11.13; <0.001	2.83 (2.34, 3.46)	10.35; <0.001	3.56 (2.60, 5.02)	7.56; <0.001	3.36 (2.45, 4.77)	7.12; <0.001	2.68 (2.13, 3.45)	8.00; <0.001	2.55 (2.01, 3.29)	7.47; <0.001
ALP	1.25 (1.09, 1.42)	3.31; <0.001	1.24 (1.08, 1.42)	3.05; 0.0023	1.37 (1.10, 1.70)	2.82; 0.0048	1.34 (1.06, 1.71)	2.44; 0.0147	1.17 (0.99, 1.38)	1.85; 0.0641	1.17 (0.98, 1.39)	1.77; 0.0774
GGT	1.59 (1.38, 1.86)	6.09; <0.001	1.56 (1.34, 1.84)	5.57; <0.001	1.31 (1.08, 1.61)	2.61; 0.0089	1.31 (1.07, 1.64)	2.45; 0.0142	1.88 (1.52, 2.38)	5.56; <0.001	1.88 (1.50, 2.40)	5.32; <0.001
Fasting glucose	1.75 (1.50, 2.06)	6.96; <0.001	1.65 (1.39, 1.98)	5.62; <0.001	1.58 (1.29, 1.98)	4.19; <0.001	1.53 (1.20, 1.99)	3.30; 0.0010	1.90 (1.52, 2.40)	5.50; <0.001	1.81 (1.43, 2.33)	4.74; <0.001
TG	2.17 (1.84, 2.57)	9.14; <0.001	2.19 (1.85, 2.62)	8.82; <0.001	1.68 (1.36, 2.10)	4.65; <0.001	1.74 (1.40, 2.23)	4.70; <0.001	2.76 (2.18, 3.54)	8.18; <0.001	2.83 (2.21, 3.67)	8.01; <0.001
HDL	0.42 (0.35, 0.50)	−9.69; <0.001	0.43 (0.36, 0.52)	−9.01; <0.001	0.44 (0.33, 0.58)	−5.73; <0.001	0.47 (0.34, 0.62)	−5.08; <0.001	0.41 (0.32, 0.51)	−7.65; <0.001	0.42 (0.33, 0.52)	−7.30; <0.001
LDL	1.11 (0.97, 1.27)	1.53; 0.1254	1.27 (1.10, 1.46)	3.29; 0.0010	1.00 (0.81, 1.23)	−0.02; 0.9815	1.12 (0.89, 1.41)	0.97; 0.3335	1.24 (1.05, 1.48)	2.45; 0.0143	1.38 (1.15, 1.66)	3.40; <0.001

*OR: odds ratio; CI: 95% confidence interval; df: degree of freedom. Unadjusted and adjusted ORs and Wald 95% CIs were obtained from univariate and multiple logistic regression models, respectively. Multiple logistic regressions include age, smoking, alcohol, regular exercise, and metabolic and related diseases (hypertension, dyslipidemia, diabetes, and hepatitis) as covariates. All continuous risk factors are standardized with mean of 0 and SD of 1.

BMI: body mass index; BP: blood pressure; WBC: white blood cells; Hgb: hemoglobin; PLT: platelet count; BUN: blood urea nitrogen; T bilirubin: total bilirubin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: Alkaline phosphatase; GGT: gamma-glutamyl transferase; TG: triglycerides; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

and total bilirubin [unadjusted OR = 0.87 (95% CI: 0.76–1.00), adjusted OR = 0.90 (95% CI: 0.78–1.04)] showed negative associations with MAFLD, but the results were not statistically significant. All other hematological and biochemical indicators, except these two, showed statistically significant associations with MAFLD. CHOL [unadjusted OR = 1.02 (95% CI: 0.89–1.16), adjusted OR = 1.15 (95% CI: 1.00–1.33)], Cr [unadjusted OR = 1.11 (95% CI: 0.98–1.27), adjusted OR = 1.15 (95% CI: 1.00–1.32)], and LDL [unadjusted OR = 1.11 (95% CI: 0.97–1.27), adjusted OR = 1.27 (95% CI: 1.10–1.46)] exhibited statistically significant associations after the adjustment for confounders. HDL [unadjusted OR = 0.42 (95% CI: 0.35–0.50), adjusted OR = 0.43 (95% CI: 0.36–0.52)] showed a negative association with MAFLD, while multiple hematological and biochemical indicators considered in this study displayed positive associations with MAFLD. Both the nonpilot and pilot groups showed this tendency. However, the association magnitudes of MAFLD with all hematological and biochemical markers, excluding aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP), were estimated to be stronger in the pilot group compared to the nonpilot group.

Table III displays the results of the multiple logistic regression analysis using all risk factors as explanatory variables for the total population, nonpilot, and pilot groups. BMI (OR = 3.23, 95% CI: 2.24–4.70), ALT (OR = 1.81, 95% CI: 1.35–2.47), uric acid (UA, OR = 1.48, 95% CI: 1.21–1.82), fasting glucose (FG, OR = 1.35, 95% CI: 1.09–1.69), HDL (OR = 0.73, 95% CI: 0.57–0.93), LDL (OR = 1.27, 95% CI: 1.04–1.56), albumin (ALB, OR = 1.36, 95% CI: 1.06–1.75), TG (OR = 1.30, 95% CI: 1.07–1.61), and regular exercise (OR = 2.75, 95% CI: 1.10–7.31) were independently associated with MAFLD in the total population.

In the nonpilot group, only BMI (OR = 3.41, 95% CI: 1.76–6.96), diabetes (OR = 8.32, 95% CI: 1.79–41.25), and ALT (OR = 1.91, 95% CI: 1.03–3.59) were identified as independent factors associated with MAFLD. In the pilot group, BMI (OR = 3.77, 95% CI: 2.35–6.19), UA (OR = 1.83, 95% CI: 1.40–2.42), ALT (OR = 1.98, 95% CI: 1.18–2.20), TG (OR = 1.50, 95% CI: 1.09–2.10), and dyslipidemia (OR = 7.97, 95% CI: 1.32–57.35) were factors independently associated with MAFLD. A comparison of risk factors for MAFLD between nonpilots and pilots revealed that the association magnitude of UA in pilots (OR = 1.84, 95% CI: 1.41–2.42) was statistically significantly higher than that in nonpilots (OR = 1.13, 95% CI: 0.79–1.60), as indicated by the Z-test for the difference between regression coefficients from the independent models ($P = 0.0294$). However, when pilots were stratified by acceleration exposure, the association remained significant in both high-acceleration (adjusted OR = 3.02, 95% CI: 1.54–6.61) and low-acceleration groups (adjusted OR = 1.77, 95% CI: 1.28–2.48), as shown in **Table IV**. Although the odds ratio was numerically higher in the high-acceleration group, the difference between the two groups was not statistically significant ($P = 0.1836$).

DISCUSSION

The diagnostic criteria for MAFLD are more comprehensive than those for NAFLD and MAFLD is closely associated with metabolic diseases such as obesity, diabetes, and hyperlipidemia. This comprehensive approach facilitates the evaluation and management of the patient's overall health status. Additionally, the strong correlation with metabolic disorders facilitates the prediction of future complications, making focusing on MAFLD advantageous for establishing effective treatment strategies. In particular, the health of pilots is a critical factor in the safe operation of an aircraft. During a flight, various situations may arise that require quick and accurate judgment, as well as a healthy physical condition, to prevent potential accidents. Consequently, the effective health management of pilots is of paramount importance to ensure flight safety.

Previous studies have reported that the prevalence of MAFLD ranges from approximately 30–40%.[10–12] This study found that the prevalence was approximately 30% among the entire study population. However, prevalence estimates from previous studies typically include both sexes and a wide range of ages. Previous studies have shown that MAFLD prevalence peaks in individuals in their 40s and is generally higher in men compared to women.[13,14] Given that the participants in our study were predominantly men in their 40s and 50s, the observed prevalence may be considered low compared to other studies.

Moreover, the occupational group analysis revealed a lower prevalence of MAFLD among pilots, approximately 28%, compared to other studies. This lower prevalence may be attributed to the active health management practices implemented for pilots. The Republic of Korea Air Force conducts annual physical examinations and biennial comprehensive health assessments for pilots to identify potential risk factors for flight safety. Flight surgeons actively manage the health of pilots when they identify health issues, potentially contributing to the lower prevalence of MAFLD in this occupational group.

The relationship between socioeconomic status and the risk of fatty liver disease has been well documented in several studies.[15,16] Individuals with low socioeconomic status are at higher risk for fatty liver disease and MAFLD, largely due to factors such as low physical activity and unhealthy eating habits.[17] In contrast, pilots are required to engage in continuous learning and maintain a high level of education to ensure safe flights. Their income is generally higher than that of other military personnel due to additional allowances, and they belong to a higher-income group compared to those in other occupational sectors. These factors likely contribute to the lower prevalence of MAFLD observed among pilots.

In the total population, risk factors for MAFLD were identified as BMI, ALT, LDL, TG, and FG, similar to previous studies and, in the pilot group, the analysis identified several significant risk factors for MAFLD, including BMI, dyslipidemia, ALT, UA, FG, and TG.[10,12,18] Of particular note is the finding regarding UA levels, which exhibited a significantly

Table III. Multivariable Logistic Regression Analysis for MAFLD According to Occupational Specialty.

RISK FACTOR	TOTAL (df = 1014) OR (95% CI) exp (β_T)	TOTAL Wald Z; *P*	NON-PILOT (df = 347) OR (95% CI) exp (β_{NP})	NON-PILOT Wald Z; *P*	PILOT (df = 637) OR (95% CI) exp (β_P)	PILOT Wald Z; *P*	$\beta_{NP} - \beta_P$; *P**
Age	1.11 (0.91, 1.36)	1.05; 0.2951	0.83 (0.56, 1.24)	−0.91; 0.3610	1.22 (0.94, 1.58)	1.52; 0.1276	0.385; 0.1114
BMI	3.23 (2.25, 4.70)	6.24; <0.001	3.41 (1.76, 6.96)	3.51; 0.0005	3.77 (2.35, 6.19)	5.39; <0.001	0.101; 0.8137
Waist circumference	1.34 (0.93, 1.94)	1.58; 0.1152	1.82 (0.93, 3.60)	1.75; 0.0801	1.05 (0.66, 1.68)	0.20; 0.8383	−0.551; 0.1867
Sys BP	1.27 (0.97, 1.67)	1.74; 0.0821	1.29 (0.83, 2.04)	1.12; 0.2626	1.38 (0.95, 2.02)	1.67; 0.0957	0.066; 0.8254
Dia BP	0.97 (0.74, 1.27)	−0.25; 0.8037	0.94 (0.61, 1.47)	−0.26; 0.7961	0.97 (0.66, 1.41)	−0.17; 0.8620	0.024; 0.9359
Smoking	0.86 (0.57, 1.31)	−0.70; 0.4856	1.19 (0.54, 2.70)	0.43; 0.6646	0.74 (0.43, 1.27)	−1.07; 0.2825	−0.473; 0.3370
Alcohol	0.55 (0.33, 0.94)	−2.20; 0.0275	0.33 (0.13, 0.85)	−2.30; 0.0213	0.74 (0.37, 1.49)	−0.84; 0.3991	0.805; 0.1770
Regular exercise	2.75 (1.10, 7.31)	2.11; 0.0348	2.80 (0.67, 13.86)	1.35; 0.1770	2.32 (0.60, 9.92)	1.19; 0.2336	−0.188; 0.8567
Hypertension	1.16 (0.65, 2.05)	0.50; 0.6197	1.76 (0.71, 4.34)	1.23; 0.2196	0.77 (0.33, 1.80)	−0.59; 0.5532	−0.821; 0.1937
Dyslipidemia	1.89 (0.87, 4.08)	1.62; 0.1043	1.27 (0.47, 3.31)	0.48; 0.6299	7.97 (1.32, 57.35)	2.18; 0.0289	1.838; 0.0863
Diabetes	2.87 (0.96, 8.96)	1.85; 0.0642	8.32 (1.79, 41.25)	2.66; 0.0079	1.50 (0.25, 11.27)	0.42; 0.6733	−1.712; 0.1711
Hepatitis	1.52 (0.55, 4.05)	0.82; 0.4101	1.23 (0.18, 6.93)	0.23; 0.8214	2.78 (0.78, 9.65)	1.60; 0.1090	0.815; 0.4664
WBC	1.04 (0.85, 1.28)	0.42; 0.6750	1.02 (0.69, 1.49)	0.10; 0.9170	1.09 (0.84, 1.43)	0.65; 0.5184	0.068; 0.7754
RBC	0.94 (0.66, 1.33)	−0.33; 0.7421	0.84 (0.44, 1.57)	−0.55; 0.5843	1.04 (0.66, 1.63)	0.18; 0.8533	0.220; 0.5800
HGB	1.34 (0.84, 2.15)	1.24; 0.2138	0.90 (0.36, 2.32)	−0.21; 0.8304	1.48 (0.83, 2.68)	1.31; 0.1908	0.494; 0.3788
HCT	0.86 (0.53, 1.39)	−0.62; 0.5374	1.15 (0.45, 2.82)	0.30; 0.7620	0.75 (0.40, 1.41)	−0.88; 0.3775	−0.424; 0.4530
PLT	1.13 (0.93, 1.38)	1.24; 0.2133	0.93 (0.66, 1.29)	−0.44; 0.6614	1.29 (0.98, 1.70)	1.83; 0.0669	0.330; 0.1346
BUN	0.88 (0.72, 1.08)	−1.23; 0.2203	0.76 (0.53, 1.08)	−1.53; 0.1260	0.95 (0.73, 1.23)	−0.37; 0.7102	0.224; 0.3150
Creatinine	0.96 (0.79, 1.18)	−0.38; 0.7003	1.08 (0.74, 1.58)	0.39; 0.6942	0.89 (0.69, 1.15)	−0.88; 0.3769	−0.192; 0.4093
Uric acid	1.48 (1.21, 1.81)	3.79; <0.001	1.13 (0.79, 1.60)	0.66; 0.5089	1.84 (1.41, 2.42)	4.43; <0.001	0.490; 0.0294
Protein	0.83 (0.65, 1.07)	−1.43; 0.1530	0.78 (0.48, 1.25)	−1.03; 0.3020	0.83 (0.59, 1.17)	−1.07; 0.2829	0.065; 0.8296
Albumin	1.36 (1.06, 1.74)	2.41; 0.0162	1.45 (0.92, 2.29)	1.60; 0.1097	1.34 (0.96, 1.87)	1.70; 0.0891	−0.081; 0.7769
T. Biliruin	1.01 (0.83, 1.23)	0.13; 0.8933	1.29 (0.88, 1.91)	1.29; 0.1954	0.89 (0.69, 1.13)	−0.97; 0.3331	−0.378; 0.1070
AST	1.01 (0.82, 1.28)	0.09; 0.9244	1.35 (0.84, 2.77)	0.87; 0.3827	0.64 (0.36, 1.01)	−1.68; 0.0938	−0.751; 0.0851
ALT	1.81 (1.35, 2.46)	3.86; <0.001	1.91 (1.03, 3.59)	2.01; 0.0444	1.99 (1.31, 3.14)	3.06; 0.0022	0.042; 0.9141
ALP	1.10 (0.91, 1.34)	0.98; 0.3269	1.22 (0.85, 1.76)	1.08; 0.2791	1.09 (0.84, 1.40)	0.65; 0.5145	−0.116; 0.6080
GGT	0.93 (0.75, 1.14)	−0.67; 0.5008	0.95 (0.70, 1.27)	−0.37; 0.7145	0.97 (0.69, 1.33)	−0.20; 0.8450	0.020; 0.9273
Fasting glucose	1.35 (1.09, 1.69)	2.75; 0.0059	1.08 (0.77, 1.55)	0.42; 0.6778	1.61 (1.18, 2.20)	3.05; 0.0023	0.406; 0.0844
TG	1.30 (1.07, 1.61)	2.51; 0.0120	1.28 (0.95, 1.78)	1.58; 0.1138	1.49 (1.09, 2.10)	2.41; 0.0159	0.153; 0.5027
HDL	0.73 (0.57, 0.93)	−2.53; 0.0113	0.86 (0.56, 1.31)	−0.69; 0.4911	0.74 (0.53, 1.03)	−1.76; 0.0781	−0.150; 0.5862
LDL	1.26 (1.03, 1.55)	2.27; 0.0231	1.29 (0.90, 1.86)	1.39; 0.1642	1.29 (0.99, 1.70)	1.86; 0.0630	0.001; 0.9956

All continuous covariates are standardized with mean of 0 and SD of 1.

*Difference between two beta coefficients from independent logistic regression models. The significant difference was evaluated using Z test as follows: Z = (β ̂_NP-β ̂_P)/√(σ ̂_(β_NP)^2 + σ ̂_(β_P)^2).

OR: odds ratio; CI: 95% confidence interval; df: degree of freedom; BMI: body mass index; BP: blood pressure; WBC: white blood cells; Hgb: hemoglobin; PLT: platelet count; BUN: blood urea nitrogen; T bilirubin: total bilirubin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: Alkaline phosphatase; GGT: gamma-glutamyl transferase; TG: triglycerides; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

Table IV. Unadjusted Estimated Means of Blood Test Measures According to Occupational Specialty Within the MAFLD Group.

BLOOD TEST MEASURE	MAFLD: NO				MAFLD: YES			
	NON-PILOT*	PILOT*	MD (95% CI) †	t; P-VALUE†	NON-PILOT*	PILOT*	MD (95% CI) †	t; P-VALUE†
WBC	5.57 (5.41, 5.74)	5.41 (5.29, 5.53)	0.17 (-0.04, 0.37)	1.58; 0.114	6.17 (5.94, 6.40)	6.08 (5.89, 6.27)	0.08 (-0.21, 0.38)	0.56; 0.578
RBC	4.87 (4.82, 4.91)	4.89 (4.86, 4.92)	−0.02 (-0.07, 0.03)	−0.92; 0.357	4.97 (4.91, 5.03)	5.04 (5.00, 5.09)	−0.07 (-0.15, 0.00)	−1.90; 0.058
Hgb	15.1 (14.9, 15.2)	15.2 (15.1, 15.3)	−0.10 (-0.25, 0.05)	−1.35; 0.178	15.4 (15.2, 15.5)	15.6 (15.4, 15.7)	−0.20 (-0.41, 0.01)	−1.83; 0.067
HCT	44.6 (44.3, 45.0)	44.7 (44.4, 44.9)	−0.06 (-0.48, 0.36)	−0.29; 0.772	45.3 (44.8, 45.7)	45.7 (45.3, 46.1)	−0.40 (-1.01, 0.21)	−1.29; 0.198
PLT	241.8 (235.7, 247.8)	230.9 (226.6, 235.3)	10.8 (3.4, 18.2)	2.87; 0.004	245.6 (237.3, 253.9)	243.3 (236.4, 250.3)	2.28 (-8.51, 13.07)	0.41; 0.679
BUN	14.4 (14.0, 14.8)	14.7 (14.4, 15.0)	−0.33 (-0.84, 0.18)	−1.26; 0.207	13.8 (13.2, 14.4)	14.6 (14.1, 15.0)	−0.76 (-1.51, -0.02)	−2.00; 0.045
Creatinine	0.93 (0.92, 0.95)	0.97 (0.96, 0.98)	−0.03 (-0.05, -0.02)	−3.59; 0.000	0.94 (0.92, 0.96)	0.99 (0.97, 1.01)	−0.05 (-0.07, -0.02)	−3.25; 0.001
Uric acid	6.08 (5.92, 6.23)	6.06 (5.95, 6.17)	0.02 (-0.18, 0.21)	0.16; 0.876	6.45 (6.24, 6.67)	6.79 (6.61, 6.96)	−0.33 (-0.61, -0.05)	−2.35; 0.019
Protein	7.27 (7.22, 7.31)	7.27 (7.24, 7.31)	−0.01 (-0.06, 0.05)	−0.24; 0.810	7.36 (7.29, 7.42)	7.37 (7.32, 7.43)	−0.02 (-0.10, 0.06)	−0.45; 0.656
Albumin	4.58 (4.55, 4.61)	4.60 (4.58, 4.62)	−0.02 (-0.05, 0.02)	−0.90; 0.368	4.63 (4.59, 4.67)	4.68 (4.64, 4.71)	−0.05 (-0.10, 0.01)	−1.73; 0.084
T. Biliruin	0.94 (0.89, 0.98)	1.04 (1.01, 1.08)	−0.11 (-0.16, -0.05)	−3.53; 0.000	0.94 (0.87, 1.00)	0.97 (0.92, 1.03)	−0.04 (-0.12, 0.05)	−0.86; 0.393
AST	26.6 (25.2, 28.0)	26.2 (25.2, 27.2)	0.37 (-1.37, 2.10)	0.42; 0.676	33.2 (31.2, 35.1)	29.9 (28.3, 31.6)	3.22 (0.69, 5.75)	2.50; 0.013
ALT	25.6 (23.6, 27.5)	24.5 (23.1, 25.8)	1.10 (-1.26, 3.45)	0.91; 0.362	42.0 (39.3, 44.6)	38.3 (36.1, 40.5)	3.65 (0.21, 7.08)	2.08; 0.038
ALP	205.3 (199.1, 211.6)	203.6 (199.2, 208.1)	1.68 (-5.97, 9.34)	0.43; 0.666	220.8 (212.2, 229.3)	211.7 (204.5, 218.9)	9.10 (-2.06, 20.26)	1.60; 0.110
GGT	42.2 (38.2, 46.1)	33.1 (30.3, 35.9)	9.06 (4.17, 13.95)	3.64; 0.000	53.5 (48.0, 58.9)	49.3 (44.7, 53.9)	4.22 (-2.91, 11.34)	1.16; 0.246
Fasting glucose	99.9 (98.3, 101.5)	98.1 (97.0, 99.3)	1.79 (-0.21, 3.80)	1.76; 0.079	107.8 (105.5, 110.0)	104.3 (102.4, 106.2)	3.51 (0.59, 6.43)	2.36; 0.019
T. Cholesterol	197.6 (193.2, 202.0)	202.7 (199.6, 205.9)	−5.09 (-10.50, 0.32)	−1.85; 0.065	193.5 (187.5, 199.6)	207.2 (202.2, 212.3)	−13.7 (-21.6, -5.8)	−3.41; 0.001
TG	130.4 (120.4, 140.4)	107.7 (100.5, 114.8)	22.7 (10.4, 35.0)	3.62; 0.000	182.7 (168.9, 196.4)	167.8 (156.2, 179.3)	14.9 (-3.0, 32.8)	1.63; 0.103
HDL	55.5 (54.1, 56.9)	57.8 (56.8, 58.8)	−2.35 (-4.06, -0.64)	−2.69; 0.007	48.3 (46.3, 50.2)	49.5 (47.8, 51.1)	−1.19 (-3.69, 1.30)	−0.94; 0.348
LDL	124.6 (120.4, 128.8)	132.5 (129.5, 135.5)	−7.90 (-13.04, -2.75)	−3.01; 0.003	124.5 (118.8, 130.2)	139.6 (134.7, 144.4)	−15.1 (-22.6, -7.6)	−3.94; 0.000

MD: mean difference; CI: 95% confidence interval; WBC: white blood cells; RBC: red blood cells; Hgb: hemoglobin; HCT: hematocrit; PLT: platelet count; BUN: blood urea nitrogen; T bilirubin: total bilirubin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: Alkaline phosphatase; GGT: gamma-glutamyl transferase; T. cholesterol: total cholesterol; TG: triglycerides; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

*Estimated means and 95% CIs based on linear models with interaction term between occupational specialty and MAFLD.

†Estimated mean difference between nonpilot and pilot groups within MAFLD group and its 95% CI.

stronger association with MAFLD in pilots compared to nonpilots. This suggests that the unique occupational stress experienced by pilots may contribute to an elevated risk of developing MAFLD. Previous studies have established a link between elevated UA levels and occupational stress, particularly in jobs characterized by irregular work hours.[19] The high-stress environment of aviation, where pilots must maintain flight stability, manage irregular schedules, and adhere to strict dietary regimens, may exacerbate this risk.[20] Moreover, when the pilot group was classified by high-acceleration and low-acceleration pilot subgroups, this association remained significant in both pilot subgroups. Although the adjusted odds ratio was numerically higher in the high-acceleration group, the difference between the two groups was not statistically significant. These findings suggest that elevated UA is a consistent and independent risk factor for MAFLD across different operational roles among pilots. Consequently, our study suggests that interventions aimed at modulating UA levels—whether through dietary modifications or pharmacological treatments—could be an effective strategy for reducing the risk of MAFLD in this population.

The results of this study highlight the importance of comprehensive health management in reducing the prevalence of MAFLD among pilots. The findings regarding UA levels, in particular, warrant further investigation to elucidate the mechanisms at play and to develop targeted interventions that could further mitigate the risk of MAFLD in this high-stress occupational group.

Previous studies have reported that exercise level, alcohol consumption, smoking status, and waist circumference are independently associated with the incidence of MAFLD.[17] However, our study found no association between these factors and MAFLD among pilots. This may be attributed to the effective health management system in place for Korean Air Force pilots, where strict health regulations are enforced. Pilots who are obese or have metabolic syndrome face potential penalties, such as being restricted from flight duties, if their condition is not adequately managed.

This study has several limitations. First, we were unable to evaluate all age groups due to the constraints imposed by age-specific screening items, which may have limited the generalizability of our findings across different age demographics. Second, the study lacked comprehensive data on the participants' lifestyle and nutritional habits, which could have influenced the observed associations. Most critically, the study's restriction to men precluded any analysis of sex-based differences. This limitation is primarily due to the nature of the military setting, where men significantly outnumber women. Additionally, the number of female pilots—a specialized occupation—was insufficient to allow meaningful statistical analysis.

Despite these limitations, the study possesses a notable strength: it is the first of its kind in Korea to include active pilots as participants. Pilots represent a unique population that receives extensive health monitoring due to the physical demands of the profession. This study's findings can serve as a valuable reference for managing the health of pilots and may inform future research in this area. Further studies are warranted to explore the health outcomes of pilots in more diverse and inclusive populations, particularly to address the gaps identified in this research.

In conclusion, a notable difference in the prevalence of MAFLD was observed between the pilot and nonpilot groups. Specifically, UA emerged as a distinctive risk factor in pilots compared to nonpilots. This finding suggests that UA could be used as a specific marker for assessing MAFLD risk in the pilot population, highlighting the need for targeted health monitoring and intervention strategies within this group.

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Medical Reporting Behavior of Military, Commercial, and General Aviation Pilots

Panagiotis Kioulepoglou; Ilias Makris

INTRODUCTION: Pilots are undoubtedly among employees who undergo rigorous medical evaluations to ensure they are fit to fly. However, accidents like the Germanwings Flight 9525 highlight that medically unfit individuals can still end up in the cockpit.

METHODS: This study sought to investigate Greek pilots' attitudes toward medical reporting, given that the available national research is very limited. Semistructured interviews were conducted and analyzed through Thematic Analysis with subjects (*N* = 18) from general, military, and commercial aviation in Greece during the first quarter of 2024. Cross-sectoral differences were identified through Content Analysis.

RESULTS: The primary barrier to medical reporting, identified by 16 out of 18 subjects (88% of the sample), was the fear of losing their pilot license, which would have major consequences for their income and way of life. Additionally, concerns about the perceived damage to professional identity and a deep passion for flying contributed to their reluctance to disclose medical issues. A general tendency to conceal medical problems from the Aeromedical Examiner during the annual medical certificate renewal was identified, particularly when such issues were considered of minor importance (61% of the sample).

DISCUSSION: Although the findings align with international research, this study identified a more pronounced tendency among subjects to conceal medical issues they perceived as unimportant. The establishment of compulsory loss-of-pilot-license insurance was the major mitigation measure proposed by the interviewees. Nonetheless, its effectiveness remains questionable according to the literature, and further research is recommended in this area.

KEYWORDS: medical reporting, Greek pilots, reporting barriers, under-reporting.

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Without a doubt, aviation stands as one of the industries worldwide with the highest emphasis on safety. According to the National Transportation Safety Board, accident rates are dropping significantly year by year and are by no means comparable to those of the previous century.[1] In this regard, aviation authorities have placed significant emphasis on ensuring pilots are physically and mentally prepared to meet all necessary standards, thereby enhancing safety performance. Consequently, all eligible pilots undergo annual medical evaluations to assess and renew their medical certification upon meeting the required standards.[2]

However, a percentage of reported accidents worldwide have been attributed to health issues of pilots who reported for duty despite being unfit.[3] Furthermore, research indicates that 0.33–2.4% of all general aviation accidents in the United States are attributed to pilot suicide, underlining the possibility of an unfit individual entering the cockpit.[4] In most cases, the pilots withhold information about their medical condition from their Aeromedical Examiner (AME) during their annual medical check and falsely declare themselves as fit to fly. Thus, the failure of pilots to disclose medical issues raises concerns regarding

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their reporting culture with direct consequences to aviation safety. Recognizing the limited scope of relevant research in Greece, the reporting culture of Greek pilots regarding their medical conditions is identified as a research gap that requires attention.

Although a precise definition of reporting culture remains challenging to pinpoint, researchers have described it as an organizational climate where employees feel comfortable to report adverse events openly and honestly.[5] The concept of reporting culture gained attention in the late 20th century when figures like James Reason, Sheryl Chappell, et al. emphasized its significance in safety. In essence, establishing an effective safety culture requires that critical issues be communicated freely and without hesitation.[6] To that end, the main focus of safety departments was on the reporting behavior of pilots, particularly with regard to incident reporting, given that it is absolutely necessary to report an incident in order to develop safety measures against its reoccurrence.[6]

Nevertheless, another important aspect of reporting behavior, i.e., the reporting intention of pilots regarding their medical issues, has caused concerns over the years. Evidently, many pilots concealed issues regarding their health, for various reasons, and reported as fit to fly, with direct implications to the safety of the flight.[7]

Unfortunately, this tendency led to one of the most shocking moments in aviation history, the Germanwings Flight 9525 in 2015 where 150 lives were lost when the aircraft crashed into the French Alps without obvious cause. It was later discovered that the first officer intentionally maneuvered the aircraft to the ground, as he was experiencing severe psychotic episodes of depression that went unnoticed by both the AMEs and the airline company.[8] Apart from the Germanwings case, EgyptAir Flight 990 in 1999 (217 fatalities) and SilkAir Flight 185 in 1997 (104 fatalities) remind us of the reoccurring nature of this issue.[3] It is also emphasized that many anecdotal theories suspect the disappearance of Malaysian flight MH370 in 2014 to be the result of pilot suicide.[9]

Fortunately, accidents resulting from pilot suicide or incapacitation are rare. Between 1974–2007, there were only 9 reported cases of suicide (suspected and confirmed) by aircraft in Germany (18 fatalities), which is approximately 6 suicide flights per 1000 aviation accidents. This ratio aligns with relevant literature, which estimates it to be between 0.33–2.4%, which is still considered low. However, it is highlighted that these figures might be significantly underestimated, as it is often very challenging for accident investigators to distinguish a pilot suicide from an ordinary accident, especially when no messages are left by the deceased.[10] In addition, the recorded suicide accidents are just the tip of the iceberg, as it is reasonable to assume that many flights may have been accomplished uneventfully by pilots with unreported medical issues. While the existence of the problem is apparent, the array of studies regarding the medical reporting intention of pilots is considered limited on a worldwide scale and almost absent in many countries.

In 2019 Hoffman et al. surveyed 613 male and female pilots in the United States, revealing that 38.8% had withheld information from a physician, and 60.2% had delayed or avoided seeking medical care due to concerns about their flying status.[11] Interestingly, replicating results were obtained by Hoffman et al. in 2022, where it was found that more than 1 in 2 pilots ($N = 3765$) avoided healthcare due to fears of losing their medical certificate.[7] Similarly, a survey by Strand et al. found that 12% of 1616 Norwegian aviation employees (including pilots and air traffic controllers) had under-reported or concealed a medical condition[12]. Additionally, over half of the subjects in this study were aware of colleagues who had under-reported medical issues. Remarkably, the most profound excuse for not reporting a medical issue in that study was the belief that their condition was not affecting flight safety. Also, 69% of them attributed their under-reporting to fears of negative career impact.

Furthermore, Canfield et al. supported in 2016 that only 6–8% of pilots who committed suicide by aircraft had previously disclosed their medical condition to a medical expert.[13] Arguably, the reasons behind the concealment could be diverse, albeit the most dominant cause was the fear of negative career impact. Moreover, Pinsky et al. named several other possible factors of medical under-reporting such as lack of perceived confidentiality, embarrassment, shame, fear of losing the aviator's identity, a feeling that nothing would change, or fear that they would be viewed as unreliable by colleagues.[14] Finally, another reason for under-reporting medical issues could be the macho attitude, that is, the belief that seeking help for a medical issue is a sign of weakness.[15] This attitude has been observed among veterans of the U.S. military in the past[16] and it can be assumed that military pilots might have similar thoughts.

This study sought to investigate Greek pilots' attitudes toward medical reporting, given that the available national research is very limited. As a result, a qualitative approach was preferred to facilitate exploration of specific traits, attributes, and views of subjects in depth. Additionally, including military, commercial, and general aviation pilots as subjects was seen as a way to facilitate comparisons between these groups and prevent bias arising from differences among these sectors. Consequently, the main research questions of the study are: "What is the attitude of Greek pilots toward medical reporting? What are the main barriers? What, if anything, can be done to facilitate medical reporting according to them?"

METHODS

Subjects

Initially, the study protocol was reviewed by the University of Peloponnese Research Ethics and Deontology Committee and was granted an exemption. All procedures involved were anonymous and voluntary, and each subject provided written informed consent before participating. Furthermore, all gathered data were anonymized after the interview sessions took place. The official recruiting of subjects occurred during the first quarter of 2024, using a combination of convenience and purposive sampling strategies. Eligible subjects were required to be currently used as certified pilots within a Greek aviation organization, with a minimum of 3 yr of professional experience. Pilots engaged in general aviation on a nonpermanent basis—such as for recreational or part-time purposes—were excluded, as their perspectives on medical reporting were expected to differ, especially in relation to career progression and financial stability. To ensure the authenticity of subjects' professional roles, all invitations were distributed through the researchers' professional networks.

Additionally, efforts were made to enhance the sample's representativeness by maximizing diversity in background and demographic characteristics, including gender, age, marital status, education, and more. Having said that, equal numbers of pilots, i.e., six, from general, military, and commercial aviation, were purposefully recruited with ages spanning from 27–54 yr. As expected, the participation of only two female subjects in the study reflected the minority status of women in the pilot population, comprising approximately 5%.[17] Furthermore, 15 out of 18 subjects were married, and 10 of them were parents at the time of the study. Lastly, their tenure (years in their organization) ranged from 3–22 yr.

Equipment and Materials

All interviews were conducted in viva voce using a basic recording device that lacked file transfer capability, ensuring adherence to data protection measures. Subsequently, all data were permanently deleted upon completion of the transcribing procedure. Moreover, the interview schedule was designed by drawing on previous research about pilots' attitudes toward medical reporting.[7,12] Lastly, all developed transcripts were analyzed through use of ATLAS.ti qualitative analysis software (version 8.4.24.0, Lumivero/ATLAS.ti Scientific Software Development GmbH, Berlin, Germany).

Procedure

A qualitative approach using semistructured interviews was chosen as the most suitable method for this study, with the primary focus being on the perspectives of Greek pilots regarding medical reporting according to the research questions. The analysis integrated core principles of Thematic Analysis[18] with elements of Content Analysis, such as the quantification of recurring codes. The coding techniques were data-driven, as there was no prior national-level knowledge on the topic. Through an iterative three-cycle analysis, the generated codes and themes highlighted subjects' perceptions toward their intention to disclose medical issues at their organization/authority.

The interview sessions were conducted to explore subjects' perspectives without a predetermined number at the beginning of the study. Instead, additional sessions continued until no new insights emerged from the subjects, achieving the point known as data saturation.[19] Based on prior research employing similar methodologies,[20] a minimum of 10 interviews was estimated as appropriate for this type of analysis. Eventually, the final number was shaped to include 18 interviews—1 per subject, as data saturation signs were apparent from the 10th session onward.

To that end, each session commenced with a brief collection of demographic details of the subject and personal questions regarding their career path in aviation. Then the discussion narrowed down to medical reporting strategies of their organization and individual perspectives about it, such as facilitators and barriers when it comes to disclosing a medical condition, etc. During this process, each subject received a tailored set of probes and prompts to uncover any additional underlying factors affecting their views on voluntary medical reporting. Finally, closing questions were used to identify any perspectives that subjects might not have previously shared.

It is worth emphasizing that all interviews were conducted in Greek to ensure subjects' comprehension. The duration of sessions varied from 15–45 min. Following data collection, all recordings were transcribed verbatim manually, with an initial reading aimed at capturing the main ideas and identifying inconsistencies (data cleansing). Throughout this process, all transcripts underwent complete anonymization.

Statistical Analysis

A three-cycle combination of Thematic and Content Analysis was used to enable the meaningful interpretation of subjects' perspectives and quantify repetitive code patterns across the transcripts. This process entailed a repetitive series of reading, reflecting, editing, and evaluating codes, aimed at eliciting meaningful themes. The coding techniques followed Saldaña's guidelines, prioritizing the retention of essential findings pertinent to the project's context and ensuring conciseness in the final findings.[21] To ensure discernability among general, military, and commercial aviation pilots, a unique identifier—[G], [M], or [C]—was appended to the end of each generated code to indicate the pilot's sector. After the analysis, codes that appeared in all three sectors were merged into one code without any identifiers, demonstrating that the corresponding code originated from all three groups. Furthermore, to bolster the accuracy of the findings, triangulation was used via cross-coding procedures among the researchers.[22] Finally, all analysis outputs were translated into English for publication purposes. A research flow diagram is provided in **Fig. 1**.

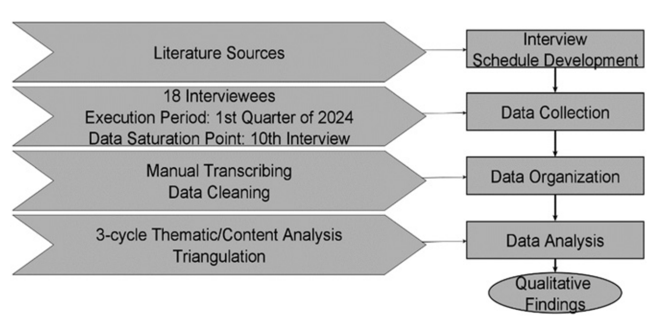

Fig. 1. Research flow summary.

RESULTS

Thematic analysis of 18 transcripts resulted in the creation of 80 codes and 3 emerging themes. Nevertheless, after the merging of reoccurring codes across the three groups of subjects, the number of extracted codes was reduced to 35. The first theme, "Medical Reporting Attitudes", encompasses the subjects' perspectives on medical reporting and outlines the primary barriers that prevent them from seamlessly reporting health issues to their organization or medical examiner. The second theme, "Special Attributes", emerged from observed differences among general, military, and commercial aviation subjects. The final theme, "Mitigation Measures", entailed all the possible solutions that could facilitate reporting of medical issues, as those were described by the subjects. A thematic map summarizes the product of this analysis in **Fig. 2**.

The first theme, Medical Reporting Attitudes, highlighted subjects' general beliefs and attitudes toward reporting a medical condition to their organization or to AMEs during their annual medical check. Surprisingly, all subjects expressed some level of anxiety about formally disclosing a medical issue. However, their fear was more pronounced when it came to reporting an issue to the AME during their medical certificate renewal. This tendency was described by subject five (P05), a 42-yr-old general aviation pilot, who said that "No, I don't believe that anyone would conceal a medical issue to the company", whereas when he was asked regarding the annual medical check, he responded differently: "That's a different story. I think that most of them [his colleagues] would avoid mentioning anything to their AME…"

According to the subjects, the primary reason for this reluctance was the threat of losing their medical certificate, i.e., disqualification as a pilot and, possibly, a transition to a nonflying duty with usually degraded salary and growth opportunities. That said, all of them supported the belief that every extra piece of information being revealed to the AME is one step closer to the loss of their pilot license. P13, a female general aviation pilot, encompassed the whole perspective in her phrase "Concealing what is concealable":

> "Now I see [understand the point of the question]. The general rule is… concealing what is concealable from the AME… That's the whole thing in a few words. Inside the company, there is always a higher degree of understanding, and usually a reasonable solution can be found. Without having the AME involved…"

The majority of subjects expressed concerns regarding their future, particularly with regard to their financial survivability. They admitted that getting "grounded" could mean a considerable, or total loss of income, with direct consequences to their family lifestyle, livelihood issues, etc. To that end, 11 out of 18 subjects admitted that they seek medical treatment privately and secretly when they can. They also pointed out that the process of revealing medical issues to the AME was stressful on its own. P18, a 33-yr-old commercial pilot, underscored this:

> "The most important aspect of the problem is that your whole career is at risk. The more problems you disclose to the AME, the closer you are to your loss of license. Even if what you are revealing is not significant, it may become in the future. And if nothing

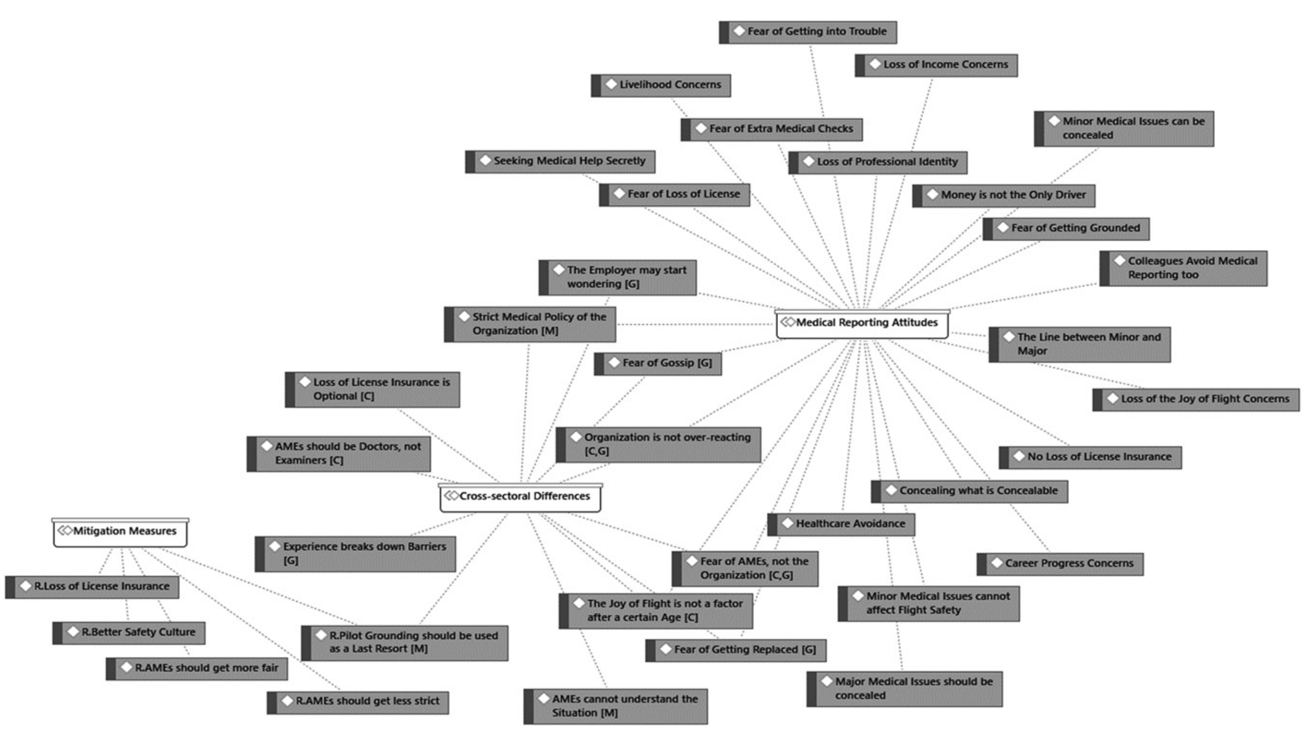

Fig. 2. Visual illustration of thematic analysis findings.

happens in the end, the whole process of getting extra medical checks is wearing you down psychologically. So, you find a doctor privately, and this is it…"

Additionally, more than half of the subjects supported that, in the spirit of flight safety, minor medical issues that have no impact to flying performance may be concealed, whereas major ones should be reported no matter the consequences. P06, a 40-yr-old military pilot, insisted that "It's up to the nature of the [medical] problem. I would initially try to estimate its importance. In case it was that important… to cost my life or lead to an accident, I would report it… even to the medical examiner". Then, specific probes were asked by the interviewer to outline the extent of what was considered minor/major medical issue on behalf of the pilots. P15, a 47-yr-old pilot, said: "For example, I would not disclose a dermatological issue. I think it's of no significance, but I would surely reveal symptoms of dizziness, let's say". On the same wavelength, P18 maintained that: "Problems with my vision, hearing, or perception of events are critical. In contrast, issues like skin conditions, allergies, or sexually transmitted diseases are less important to be reported". Additional conditions that certain participating pilots deemed as minor included certain blood test indices. For example, P16 would not disclose elevated cholesterol, triglycerides and blood sugar levels. Likewise, P12 would not report hemorrhoids to their AME, considering it a minor condition.

Conversely, three subjects contended that major medical problems should be concealed from the AME and be addressed privately with a personal doctor, as revealing such issues is more likely to harm their careers. P04, a 40-yr-old general aviation pilot, stated the following:

> "It depends… If it was a minor issue I would report it. If it was something more severe, influencing my ability to work… I would try to elicit as much information as possible regarding it… and try to deal with it privately… before I tell it to the examiner."

Lastly, a small portion of the interviewees expressed a secondary concern regarding medical reporting, apart from the impact on their career. Thus, 11 out of 18 pilots insisted that they were afraid to report medical issues due to concern over losing their ability to enjoy the beauty of flight per se. They also mentioned that losing their pilot license is considered an act of "being degraded" as they lose their professional identity. P03, a 30-yr-old military pilot, summed the interviewees' perspectives in the following lines:

> "To me, flying plays a vital role in my life… it is one of the most important ones. It is something that helps me psychologically. For the time I spend on the aircraft, my mind gets empty from ordinary concerns, my focus is on the flight itself, I am detached from daily habits like the cellphone… It is something that elevates my whole ego. That's why, because I really love it, I cannot imagine myself without the joy of the flight in my life. It means so much to me beyond its significance as an employment."

The second theme, Cross-Sectoral Differences, focused on codes that were not appearing in every group of pilots, highlighting differences across the three aviation sectors, i.e., general, military, and commercial, with regard to medical reporting. Generally, code recurrence on this theme was low (usually two or three subjects), underlining that pilots' perspectives were generally aligned across the interviews. Nevertheless, in terms of reporting barriers, P04, a 40-yr-old general aviation pilot, mentioned gossip and fear of replacement as barriers when it comes to medical reporting, whereas military and commercial pilots did not make any similar statements:

> "By the moment I report a medical issue, the employer may start wondering about my potential as a pilot and possibly start looking for another pilot to hire… and the colleagues, once they are aware of my situation, they will start talking too… you know."

Another interesting difference was the willingness of general and commercial aviation pilots to report medical issues to their organization but not to the AMEs. P07, a 54-yr-old commercial pilot, said: "I would report it to the company. Not to the examiner. I would reveal to the examiner the least possible. It's a matter of livelihood, you have to protect your income, lifestyle, family, etc." On the other hand, there were no such mentions from the military subjects as they implied that reporting to the organization or the AME is essentially the same thing.

Finally, two commercial pilots insisted that the beauty of flight after a certain age is not a factor and salary is the sole reason behind medical under-reporting. P12, a 29-yr-old commercial pilot, maintained: "Generally, after a certain age, and especially after you have a family… you care only about your income. Romance is good, but it won't put food on the table…", implying that the beauty of flight alone is not a game-changer.

The third and final theme, Mitigation Measures, is a summary of what the interviewees suggested for more effective and easy medical reporting. Subjects' proposals were found to be scattered except one, i.e., the introduction of an obligatory loss-of-pilot-license insurance. P08, a 42-yr-old commercial pilot, shed light on the current situation through his words: "There are 3rd party agreements in which every pilot can participate voluntarily. If you wish, they deduct an amount from your salary so as to provide a compensation in case you lose your pilot license". Having said that, 13 out of 18 subjects admitted that securing their income would definitely lead to more substantial medical reporting. P10, a 37-yr-old general aviation pilot, underscored this: "Of course it will. This goes without saying. Obviously, it's all about our income, and for this reason nobody will hesitate to report anything to the examiner should his/her income is secured. I believe that loss of license insurance should be regulated rather than being optional". Nonetheless, certain dissenting voices from 11 interviewees insisted that money is not the only driver and even with insurance coverage, reporting medical issues to the examiner would be challenging, as they do not want to risk their professional identity or lose the joy of flying, as described in Theme 1.

Apart from the insurance solution, other recommendations focused on the safety culture of pilots as a remedy. P06, a military pilot, answered regarding his suggestions on the matter: "I think that a better safety culture along with more focused training would be the solution to this problem. Development of a better culture aiming at aviation safety… which I believe is getting better as the years go by…". Finally, three subjects claimed that doctors and examiners should be less strict and make use of the pilot disqualification option as a last resort.

The emergence of Theme 2 necessitated a deeper exploration of the differences between general, military, and commercial aviation subjects. To achieve this, basic principles of Content Analysis were applied to provide a comprehensive view of the sample's homogeneity by illustrating the recurrence of codes across the three pilot groups. Apparently, major differences between the groups were not identified, as the codes with the most repetitions were found in all three groups of pilots. Nonetheless, specific codes that received more repetitions in certain groups are discernible in **Fig. 3** and provide a supplementary picture of pilots' perspectives along with the presented themes. Indicatively, military pilots seem to have less concerns regarding their income when it comes to medical reporting, as they have two less repetitions in the "Loss of Income Concerns" code than the other two groups.

Another example is the tendency of commercial pilots to be more reluctant to report minor medical issues compared to the other two groups as they get higher recurrence scores in the relative codes, e.g., "Minor medical issues should be concealed."

DISCUSSION

The findings of this study provided a snapshot of Greek pilots' attitudes toward reporting of medical issues. Overall, the narratives of the interviewees are consistent with similar international research which acknowledges that the main barrier for a pilot to report a health condition to their AME or organization is the fear of damaging their career and the subsequent financial consequences to their families and lifestyle.[7,12] The prevalence of this fear is considered substantial as every single subject of the study demonstrated a degree of reluctance to disclose medical issues for this reason.

Moreover, 11 subjects insisted that the fear of losing their professional identity acts as a barrier on its own due to their passion for flying. This fear was also referenced in Pinsky et al.'s study, along with several other barriers such as lack of perceived confidentiality, embarrassment, shame, learned helplessness effect, macho attitude, and fear of being viewed as unreliable by colleagues.[14] Of those, some were identified in this study also, namely the fear of embarrassment and shame as a result of gossip between colleagues. P10, a general aviation pilot, said: "If it was a medical issue that wouldn't affect flight safety, I would normally conceal it just to avoid the whispers…" Finally, this study reported two instances where subjects feared being labeled as unreliable, specifically in relation to their employer rather than their colleagues.

From the examiner's perspective, it was observed that a considerable portion of subjects frequently withheld information about medical conditions they perceived as minor or irrelevant—such as dermatological issues or sexually transmitted

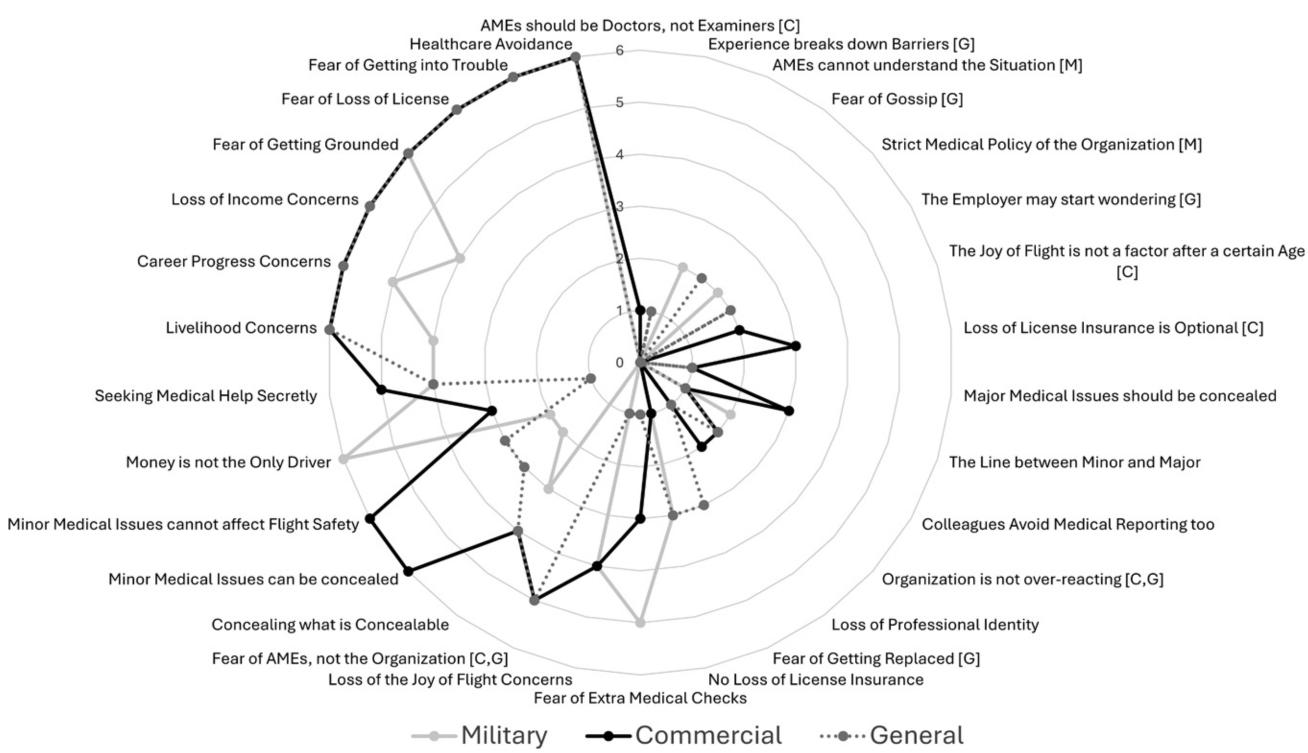

Fig. 3. Spider graph of recurring codes between groups.

infections—believing these had no impact on flight safety. Therefore, it is recommended that examiners probe further into conditions pilots may consider insignificant during medical examinations.

According to the interviewees, there is a tendency among pilots to conceal medical events of minor severity as these could not affect flying performance or the safety of the flight. It would be reasonable to assume that such practices may not entail any risks to flight safety, as minor health events, like the common flu or temporary back pain, are typically manageable.

However, the real problem occurs when the line between major and minor medical conditions becomes blurred. P15 and P18 underlined that "minor" medical problems such as "dermatological issues, allergies, and sexually transmitted diseases" may not be reported, which at first glance seems a logical thought. Nevertheless, it is underlined that even a minor medical condition such as an allergy could prove to be critical under certain circumstances.

To that end, medical literature is straightforward that every medical symptom should be fully investigated by an expert before it is treated as "minor".[23] Furthermore, many scientific papers have underlined the increased likelihood of poor self-diagnosis, especially in recent years where the availability of online medical-related stuff is immense.[24] It is also emphasized that self-diagnosis involves a high degree of subjectivity, which can result in incorrect conclusions, even by highly skilled individuals such as pilots.[25]

Given that the primary barrier to medical reporting has its roots in the financial concerns of pilots, the establishment of a "Loss of License Insurance" as a mitigation measure was reasonably proposed. According to the interviewees, this insurance should be regulated and implemented in every aviation organization to achieve the expected benefits. However, in Strand et al.'s study, it was identified that pilots with loss of license insurance concealed their medical conditions even more than those without insurance.[12] Considering the current study's subjects who claimed that "Money is not the only driver" on their decision to conceal or disclose a medical issue, it becomes unclear whether such mitigation measures would ultimately resolve the problem.

Concerning limitations, the potential for generalizing this study's findings is limited by typical inhibitors of qualitative research, such as the use of nonprobability sampling and the small number of subjects. Additionally, caution must be exercised when quantifying certain qualitative indicators, such as code recurrence, to avoid potentially misleading interpretations. Nevertheless, as Greek aviation organizations adhere to the same regulatory authorities (such as ICAO and EASA) as with the rest of Europe, it could be speculated that parallels might be drawn between Greek and European pilots. This speculation is also strengthened by the fact that the findings of this study are generally in line with other similar European studies. Consequently, despite the limited generalizability prospects, this research may act as a basis for future studies to be built upon. Thus, it is envisaged that future studies with bigger sample sizes may complement present results and hopefully lead to holistic solutions. Furthermore, future research may additionally focus on under-reporting from a medical perspective so as to identify specific symptoms/diseases that are usually not reported during the typical aeromedical examinations.

In conclusion, the subjects of this study were found to be skeptical toward medical reporting as all of them admitted having under-reported or having the tendency to under-report medical issues formally. The most substantial barriers were leaning toward the fear of losing the pilot's license due to a reported health problem. This fear was linked with possible consequences such as reduced income, alteration of lifestyle, and degradation of their professional identity. Encouragingly, the majority of subjects underlined that major medical issues should be reported no matter the consequences. That said, approximately half of them admitted that minor medical issues might be concealed as they cannot jeopardize the safety of the flight.

Despite the differences between general, commercial, and military aviation sectors, variations in the findings were minimal, indicating an increased homogeneity within the sample. Furthermore, the subjects' reflections and perspectives aligned with those from previous international studies in the field. They suggested mandating a regulated and compulsory loss of license insurance for all employed pilots to ensure medical reporting can occur without fear of financial repercussions in the event of pilot disqualification. This mitigation measure, combined with the development of a strong safety culture, was considered the ideal approach for ensuring smooth medical reporting in the aviation industry.

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Pilot Preconditions and Errors Identified in Indonesian Aviation Accident Investigation Reports

Inne Yuliawati; Budi Sampurna; Tjhin Wiguna; Imam Subekti; Aria Kekalih; Widura Imam Mustopo; Hervita Diatri; Wawan Mulyawan

INTRODUCTION: Human factors are responsible for 80% of accidents and 50% of serious incidents. The Human Factor Analysis and Classification System allows the identification of contributing factors, including pilot preconditions, as the imminent layer prior to errors. This study aimed to investigate the association of pilot preconditions and errors to accidents and serious incidents from 2007–2024 in Indonesia.

METHODS: This was a cross-sectional study design with secondary data from the investigation reports published by the National Transport Safety Committee (NTSC) from 2007–2024 in Indonesia, downloaded from the NTSC website, August 12–31, 2024. The study focused on pilot-error-related investigation reports, analyzing preconditions and errors. Internal validation was conducted with the NTSC investigators. Statistical analysis using nonparametric tests was carried out to assess the association between preconditions, errors, and incident severity (Accidents and Serious Incidents).

RESULTS: A total of 245 investigation reports were downloaded, amounting to 253 aircraft, with 8 aircraft involved in near collisions, and 186 pilot-error-related investigations selected as subject analysis. The study found that pilots with Adverse Mental States had a 3.87 times higher risk [95% confidence interval (CI) = 1.77–8.47] for accidents, while pilots with Physical Mental Limitation had a 3.35 times higher risk (95% CI = 1.50–7.45). In addition, pilots with Skill-Based Errors had a 3.07 times higher risk (95% CI = 1.38–6.83) for accidents.

DISCUSSION: Aviation accidents and serious incidents are caused by multiple contributing factors, and the complexity of human factors emphasizes the need for a multifaceted approach to mitigating pilot error.

KEYWORDS: human factor, pilot error, preconditions, accidents, serious incidents.

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Human factors have been known to be responsible for 70–80% of aviation accidents and serious incidents.[1–3] In regard to human errors, researchers have stated that the contribution of human errors to accidents in aviation was mostly derived from pilot error, which accounts for 80% of accidents and 50% of serious incidents in the United States.[4–5] Pilots hold considerable value in aviation safety as they contribute notably in managing flight operational tasks. Thus, it is pivotal to identify the human factors contributing to errors, especially the risk factor of pilots.

In order to prevent human errors, investigation and research were conducted to identify the contributing human factors, and ultimately the risk factors, of pilots.[6,7] Identifying a pilot's risk factors for errors should begin from the preconditions that represent the cognitive process, which is a cumulative interaction of psychological, physiological, and psychosocial factors of human capabilities and limitations. There are several models that have been developed to understand human factors.[8–10]

Wiegmann and Shapell developed The Human Factor Analysis and Classification System (HFACS) to identify the human factors that contribute to human error. The HFACS has been applied to understand the human factor elements associated with aircraft accidents and serious incidents. In detail, the

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HFACS structure consists of four layers that are interlinked, working in concert with each other to not only enumerate unsafe acts or errors but also highlight faults within higher cognitive processes. The HFACS begins at the fourth or highest level, the Organizational Influences, then progressively moves to the third level or the Unsafe Supervision, then to the second level or the Precondition of Unsafe Acts, then lastly to the first level or Unsafe Acts.

The framework of the HFACS begins from the fourth layer, which is the Organizational Influences layer and consists of Resource Management, Organizational Climate, and Organizational Process. The third layer, Unsafe Supervision, comprises Inadequate Supervision, Planned Inappropriate Operation, Failed to Correct Problem, and Supervisory Violation. The second layer is the Precondition of Unsafe Acts, which encompasses the Physical Environment, Technological Environment, Adverse Mental State, Adverse Physiological State, Physical Mental Limitation, Crew Resource Management, and Personal Readiness. The first layer is the Unsafe Acts, involving Errors and Violation. The Errors comprise Decision Error, Skill-Based Errors, and Perceptual Errors. Violation comprises Routine and Exceptional Violation.[11,12]

In regards to preconditions of unsafe acts, the classification of pilot preconditions that HFACS recognizes are Adverse Mental State, Adverse Physiological State, Physical/Mental Limitation, Crew Resource Management and Personal Readiness. While for classification of errors, pilots could experience Decision Errors, Skill-Based Errors, and/or Perceptual Errors, unless accurate mitigation is executed accordingly in a timely manner. Precondition is the imminent layer of cognitive process that regulates the preventive measures prior to errors.[10–12] Thus, precondition for pilots is the key factor that catalyzes the cognitive process in delivering the measures to prevent errors.

Because Indonesia is an archipelago country consisting of 17,380 islands with mountainous terrain and 38 provinces with more than 300 ethnicities, air transport is supported by 201 airports (33 of which are international), 61 commercial airlines, and 30 charter/commuter and general aviation aircraft. For example, at Soekarno-Hatta International airport, the busiest airport connecting domestic and international flights in Indonesia, the average aircraft movement in April 2024 was 80 aircraft movements per hour. The busy activities of air transport and the geographical location of Indonesia are crucial for our economic growth, but at the same time, create a challenge for aviation safety. Pilots, as notable contributors in managing flight operational tasks, pose a high risk in aviation safety that derives from intense workload (such as extended flight times and flying multiple sectors), stress, teamwork, flying across mountainous terrain, and landing on slope runways. Thus, pilots' risk factors for errors consist of physiological, psychological, and psychosocial aspects.

In terms of implementing aviation safety, Indonesia as a contracting state of the International Civil Aviation Organization (ICAO) has to implement a Safety Management System (SMS) which includes human factors as recommended practices. The implementation of human factors into SMS regulation in Indonesia was not optimal due to lack of evidence-based data. In addition, based on the aircraft investigation reports from 2014–2023, the National Transport Safety Committee (NTSC)[13,14] as the independent committee whose duty is to investigate transportation accidents and serious incidents in Indonesia, recorded that human factors accounted for 66 out of 69 such events. However, the data from these investigation reports were not evaluated optimally through the application of the HFACS model. Therefore, aviation safety with pilots as the key factors requires a proactive approach in identifying the preconditions of pilots and mitigating errors. This makes our paper a pilot study, analyzing the human factors associated with the errors and preconditions which lead to numerous accidents and serious incidents in Indonesia. Thus, the data from this research will serve as a substantial recommendation in the human factor aspect of SMS implementation in Indonesia. The study aimed to analyze the association between preconditions and errors in accidents and serious incidents that were related to pilot errors in Indonesia from 2007–2024.

METHODS

Procedure

The study obtained ethics approval from the Medical Research Ethics Committee, Faculty of Medicine, the University of Indonesia with certificate number KET1139/UN2.F1/ETIK/PPM.00.02/2024, dated August 5, 2024.

This is a retrospective cross-sectional study of secondary data from the investigation reports that have been published by the NTSC from 2007–2024. The data was downloaded from the Investigation Reports database of the NTSC, collected from August 12–31, 2024, along with an internal validation process to identify the independent and dependent variables based on HFACS classification. There were 245 investigation reports downloaded, implicating 253 aircraft, with 8 experiencing near misses or collisions between 2 aircraft.

The analysis of independent and dependent variables was done by identifying key information, specifically located in the sections of Findings and Contributing Factors, within each report's narrative. Then, the classification of the variables was evaluated based on HFACS. The flowchart of data analysis is described in **Fig. 1**. In order to ensure a detailed and accurate understanding of the HFACS model, a process of internal validation was performed in order to correctly identify the independent variables from the narratives. As a consequence, the analysis was conducted together with the help of five experts in human factors working as investigators from the NTSC, who were either directly involved as the investigator(s) in charge or at least assisted in reporting the narrative(s). One of the experts has a degree in aviation medicine as a specialist doctor, as well as five years of experience as an investigator for the NTSC. Two of the experts are psychologists specialized in aviation human factors and two other experts are pilots, possessing more than 10 yr of experience as investigators for the NTSC and completion of HFACS training.

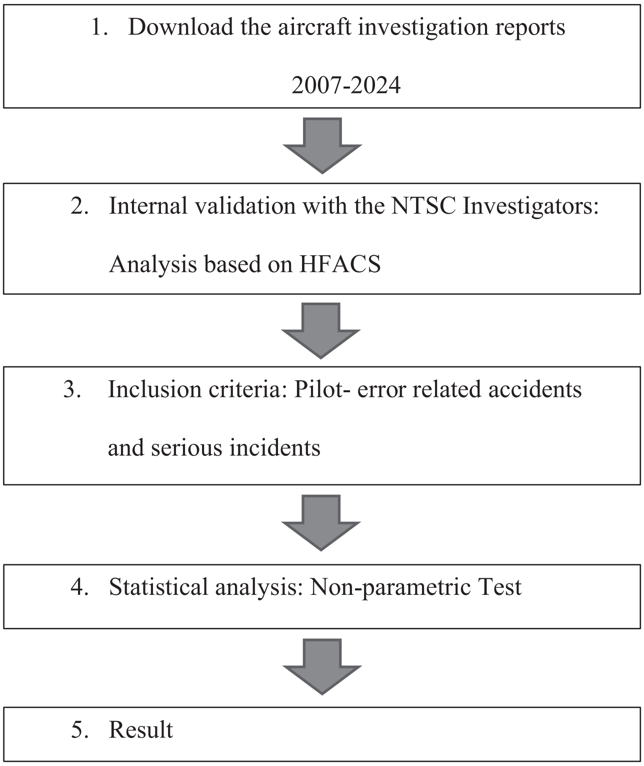

Fig. 1. Flowchart of data analysis.

The internal validation was conducted online by having discussions with experts in a meeting platform from August 12–31, 2024. The discussions started from the latest to the oldest investigation report on the NTSC website, and the analysis with internal validation came after each report was downloaded. Since the experts were directly involved in the investigation or at least participated as assistants in writing the reports, and the NTSC regularly has monthly meetings to discuss the reports, the discussion came to a collaborative conclusion effectively. The interrater reliability was not calculated because there were minimal discrepancies between experts, and when there was a discrepancy, the analysis led to a united conclusion.

For the coding of descriptive and analytical data, the independent and dependent variables were coded and categorized accordingly. The inclusion criteria for this study were aircraft accidents and serious incidents that were related to pilot errors. Pilot error was defined as an error performed solely by a pilot, or a co-occurrence between pilots or between pilots and other aviation personnel [such as Air Traffic Controllers (ATC), cabin crew, technicians, or ground crew].

The dependent variable was the Severity of Incident, categorized into Serious Incident (coded as 0) and Accident (coded as 1). The independent variables, based on HFACS, were preconditions of pilots, which consisted of five classifications of preconditions and three classifications of errors. If a precondition or error was present, it was coded as 1, while an absence of either the preconditions or errors was coded as 0.

In terms of preconditions, the first was Adverse Mental State, coded as present when one of the following conditions was reported in the Findings or Contributing Factors section of the narrative: stress, loss of situational awareness, mental fatigue/burnout, distraction, or channelized attention. Secondly, Adverse Physiological State was coded as present when one or more of the following conditions was reported: fatigue, hypoxia, spatial disorientation, or any medical condition. Thirdly, Crew Resource Management was coded as present when one of the following conditions appeared: lack of communication, steep authority, lack of teamwork, failure to conduct preflight briefing, or failure of leadership. Fourthly, Physical Mental Limitation was coded as present when one of the following conditions appeared: limitations in motoric movement or sensory input; or insufficient reaction. Lastly, Personal Readiness was coded as present when one of the following conditions was stated: lack of experience/competency, unscheduled flight, drinking alcohol or sedative medication, lack of information, or decrease of medical fitness.[9–11]

Regarding errors, the first is the Perceptual Error, categorized as present when one of the following was apparent: errors due to visual illusion or spatial disorientation; or errors due to misjudged distance/altitude measurement or ATC clearance. Secondly, Skill-Based Error was categorized as present when one of the following was exhibited: breaking in visual scanning, inadvertent use of flight controls, poor technique/airmanship, failure to comply with manuals/procedures, failure to prioritize attention, or over-reliance on automation. Lastly, Decision Error was categorized as present when one or more of the following conditions were reported: inappropriate maneuver, inadequate knowledge/skill, exceeded ability, or wrong response to emergency. [9–11] The dependent variable or outcome was then categorized into either Accidents or Serious Incidents.

Statistical Analysis

The accuracy, completeness, and consistency were analyzed to avoid missing data prior to statistical analysis. The statistical analysis was performed using the 22nd version of the IBM (Armonk, NY, United States) Statistical Package for the Social Sciences (SPSS) software. Descriptive statistics of variables were performed to assess their prevalence. Since all the variables were categorical, proportional analysis with a Chi-squared test or Fisher's exact test was done to assess the association between the dependent and independent variables. Subsequently, multivariate analysis with logistic regression was then carried out to analyze the candidate variables with a P-value of <0.2, indicating that the variables have a significant relationship for further analysis, which allows more comprehensive interactions and improves prediction accuracy. From these tests, the P-value of <0.05 was determined to be statistically significant.

Model diagnostic and validation were assessed with a Hosmer-Lemeshow test to measure the goodness of fit or its limitations within the context of the study. Additionally, the multicollinearity test was used to detect the presence of a strong correlation between independent variables in a regression model by looking at the Variance Inflation Factor (VIF) value. Correction for multiple testing was assessed with the False

Discovery Rate (FDR) to control the Type I error rate, or false positive errors, in statistical testing.

RESULTS

The total investigation report downloaded included 245 reports, amounting to 253 aircraft, 8 of which were involved in near misses or near collisions. The number of aircraft that experienced accidents was 148 (58.5%) and serious incidents was 105 (41.5%). In terms of the format of investigation reports, there were: 166 (67.8%) final reports, which were completed to reach a conclusion; 71 (28.9%) preliminary reports, which have the factual information but have not been concluded; 5 (2.1%) short summaries, which are short, complete reports; 2 (0.8%) first interim statements, which are preliminary reports that have not been completed within 1 yr; and 1 (0.4%) safety recommendation, which is a recommendation to establish urgent corrective actions. Human errors appeared in 195 (77.1%) aircraft accidents and serious incidents. Among the human-errors-related accidents and serious incidents, 186 related to pilot errors (73.5%), 5 (2%) related to technician errors, 2 (0.8%) related to air traffic controller (ATC) errors, 1 related to cabin crew errors, and 1 related to tractor driver errors appeared in 1 (0.4%) accidents and serious incidents, consecutively. Thus, 67 aircraft accidents and serious incidents were dropped, and 186 pilot-error-related accidents and serious incidents were selected to be analyzed. In terms of the pilot error co-occurrence, 158 (84.9%) related to errors caused by pilot and pilot errors, with 101 (63.9%) involved in accidents and 57 (36.1%) involved in serious incidents; 16 errors were related to pilot and ATC errors; 6 (3.8%) related to pilot and technician errors; 3 (1.9%) related to pilot and flight operation officers; and 3 (1.9%) related to pilot and cabin crew errors.

The characteristics of aircraft showed that from 186 aircraft, 88 had Commercial Airworthiness Operation Certificates (AOC), of which 33.6% experienced accidents and 67.1% experienced serious incidents. In terms of type of aircraft, 101 turboprop or single-engine (Beechcraft, Embraer, Fokker, MA 60, and Cessna) experienced accidents and serious incidents in Indonesia from 2007–2024. In addition, among 177 aircraft, 128 were multi-crew operations, with 67.3% having experienced accidents and 79.5% having experienced serious incidents.

In terms of the characteristics of pilots, some data were missing in the reports, thus the data proportions were based on availability. The characteristics of pilots showed that 112 out of 125 (89.6%) were Indonesian, 129 out of 131 (98.5%) were male, and 2 out of 131 (1.5%) were female, with 1 female pilot experiencing an accident and 1 female pilot experiencing a serious incident. As for the type of license, 20 out of 128 (15.6%) had an Airline Transport Pilot License (ATPL), 94 (73.4%) had a Commercial Pilot License (CPL), 9 (7.0%) had a Student Pilot License (SPL), and 4 (3.1%) had a Private Pilot License (PPL). As for the class of medical certificate, 114 out of 128 (89.1%) had a Class 1 Medical certificate and 14 (10.1%) had a Class 2 Medical Certificate.

Based on the analysis of the report narrative, the data indicates that a pilot could experience one precondition or more, along with one error or more, at the same time. Hence, the proportions of precondition and error categories did not accumulate to 100%. In 186 cases of pilot-related errors, 91 (48.9%) experienced Adverse Mental State, 82 (32.7%) experienced Adverse Physiological State, 43 (23.1%) experienced Physical Mental Limitation, 105 (56.6%) experienced problems in Crew Resource Management, and 80 (43%) experienced problems in Personal Readiness. In terms of Unsafe Acts or Errors, 123 (66.1%) experienced Perceptual Errors, 63 (33.9%) experienced Skill-Based Errors, and 86 (46.2%) experienced Decision Errors. The preconditions of pilots that caused errors are described in **Table I**, and the errors that the pilots experienced are described in **Table II**.

Bivariate analysis using a Chi-squared statistical test showed a significant association ($P < 0.05$) between Adverse Mental State [$P = 0.032$; odds ratio (OR) = 1.91; 95% confidence interval (CI) = 1.05–3.46], Physical Mental Limitation ($P = 0.038$; OR = 1.88; 95% CI = 1.03–3.40), Skill-Based Errors ($P = 0.015$;

Table I. Analysis of Pilot Preconditions, *N* = 186.

	SEVERITY OF INCIDENTS	
PRECONDITIONS	**ACCIDENTS**	**SERIOUS INCIDENTS**
Adverse Mental State		
Stress	18 (16.4)	8 (10.5)
Loss of situational awareness	26 (23.6)	12 (15.8)
Mental fatigue	3 (2.7)	4 (5.3)
Distraction	8 (7.3)	4 (5.3)
Channelized attention	6 (5.5)	3 (3.9)
No	49 (44.5)	45 (59.2)
Adverse Physiological State		
Fatigue	10 (9.1)	15 (19.7)
Spatial disorientation	8 (7.3)	3 (3.9)
Hypoxia	2 (1.8)	1 (1.3)
Obstructive Sleep Apnoea	1 (0.9)	0
Enteritis	0	1 (1.3)
Heart Failure	0	1 (1.3)
Musculoskeletal injury	1 (0.9)	0
Paresis of cochlea	1 (0.9)	0
No	87 (79.1)	55 (72.4)
Physical mental Limitation		
Limitation in motoric	1 (0.9)	0
Limitation in sensory input	32 (29.1)	16 (21.1)
Insufficient reaction	26 (23.6)	14 (18.4)
No	51 (46.4)	46 (60.5)
Crew Resource Management		
Lack of communication	18 (16.4)	22 (28.9)
Steep authority	2 (1.8)	0
Lack of teamwork	22 (20.0)	11 (14.5)
Failure to conduct briefing	5 (4.5)	9 (11.8)
Failure of leadership	11 (10.0)	5 (6.6)
No	52 (47.3)	29 (38.2)
Personal Readiness		
Sleep restriction	1 (0.9)	5 (6.6)
Lack of experience/ competency	29 (26.4)	17 (22.4)
Unscheduled flight	1 (0.9)	0
Alcohol/ sedatives	1 (0.9)	0
Lack of information	14 (12.7)	12 (15.8)
Decrease of medical fitness	1 (0.9)	2 (2.6)
No	63 (57.3)	40 (52.6)

Table II. Characteristic of Errors, $N = 186$.

ERRORS	SEVERITY OF INCIDENTS ACCIDENTS	SERIOUS INCIDENTS
Perceptual Error		
Error due to visual illusion	20 (18.2)	10 (13.2)
Error due to spatial disorientation	14 (12.7)	5 (6.6)
Error due to misjudge distance/ altitude/speed	40 (36.4)	28 (36.8)
Error due to misjudge ATC clearance	4 (3.6)	3 (3.9)
No	32 (29.1)	30 (39.5)
Skill-Based Error		
Breaking in visual scanning	6 (5.5)	4 (5.3)
Inadvertent use of flight controls	4 (3.6)	0
Poor technique/ airmanship	19 (17.3)	8 (10.5)
Failed to comply with manuals/ procedures	9 (8.2)	5 (6.6)
Failed to prioritize attention	7 (6.4)	0
Over-reliance in automation	1 (0.9)	2 (2.6)
No	64 (58.2)	57 (75.0)
Decision Error		
Inappropriate maneuvers	11 (10.0)	4 (5.3)
Inadequate knowledge/ skill	4 (3.6)	6 (7.9)
Exceeded ability	3 (2.7)	11 (14.5)
Wrong response to emergency	24 (21.8)	23 (30.3)
No	68 (61.8)	32 (42.1)

OR = 2.23; 95% CI = 1.16–4.28), Decision Errors ($P = 0.008$; OR = 0.45; 95% CI = 0.25–0.82), and the Severity of Incidents. However, Perceptual Error ($P = 0.180$; OR = 1.52; 95% CI = 0.82–2.81) with a P-value of <0.2 and having a theoretical justification for the association with the dependent variable were taken into account for multivariate analysis. This consideration allows more comprehensive interactions among variables and improves prediction accuracy.

Model diagnostics and validation were assessed using a Hosmer-Lemeshow goodness of fit, the result of which showed a P-value of 0.753 (more than 0.05), indicating that there was no significant difference between the observed and expected proportions. Thus, the model has an adequate fit to the data and can be considered appropriate for predicting the data.

Table III. Multivariate Analysis.

VARIABLE	SEVERITY OF INCIDENTS ACCIDENTS N (%)	INCIDENTS N (%)	P-VALUE	ADJUSTED ODDS RATIO (95% CI)
Adverse Mental State				
Yes	61 (67.0)	30 (33.0)	<0.001	3.87 (1.77–8.47)
No	49 (51.6)	46 (48.4)		1.00 (reference)
Physical Mental Limitation				
Yes	59 (67.0)	29 (33.0)	0.003	3.35 (1.50–7.45)
No	51 (52.0)	47 (48.0)		1.00 (reference)
Perceptual Error				
Yes	77 (62.6)	46 (37.4)	0.130	1.76 (0.85–3.66)
No	33 (52.4)	30 (47.6)		1.00 (reference)
Skill-Based Error				
Yes	45 (71.4)	18 (28.6)	0.006	3.07 (1.38–6.83)
No	65 (52.8)	58 (47.2)		1.00 (reference)
Decision Error				
Yes	42 (48.8)	44 (51.2)	0.143	0.60 (0.30–1.19)
No	68 (68.0)	32 (32.0)		1.00 (reference)

Additionally, the multicollinearity among independent variables was assessed to ensure that the regression results were not influenced by interdependent predictors. The result showed that the VIF for all independent variables was <10 and collinearity tolerance was >0.1, which indicated no significant multicollinearity between independent variables.

Table III showed a multivariate analysis using a logistic regression statistical test that presented a significant association ($P < 0.05$) between Adverse Mental State ($P < 001$; adjusted OR = 3.87; 95% CI = 1.77–8.47), Physical Mental Limitation ($P = 0.003$; adjusted OR = 3.35; 95% CI = 1.50–7.45), and Skill-Based Error ($P = 0.006$; adjusted OR = 3.07; 95% CI = 1.38–6.83) as the factors and the Severity of Incidents. A correction for multiple testing was assessed with the FDR to control the Type I error rate, or false positive errors, in statistical testing. The result showed that the corrected P-values of the significant variables were less than the threshold (FDR threshold = 0.05). The result indicated that corrected P-values were significant for Adverse Mental State, Physical Mental Limitation, and Skill-Based Error.

DISCUSSION

The analysis of the investigation reports showed that the preconditions and errors that contributed to accidents or serious incidents were multifactorial. A pilot could experience multiple preconditions that could lead to not only one error, but multiple errors at the same time if not mitigated efficiently. Thus, it is beneficial to learn from the investigation report to elaborate on the recommended practices in enhancing aviation safety. For example, the investigation report of the Merpati Airline flight on May 17, 2011, near Utarom Airport, Kaimana Papua with MA60 type of aircraft: the data from the accident report indicated five preconditions and two errors. The first precondition was Adverse Mental State, which was categorized from loss of situational awareness that was caused by a regression in competency. The second precondition was Adverse Physiological State, which was categorized from fatigue because the accident occurred during the fourth sector of the day. The third precondition was Physical Mental Limitation, which was categorized from a lack of sensory input given that the flight was executed under Visual Flight Rule during final approach with visibility of 2 km. The fourth precondition of Crew Resource Management was due to steep authority, lack of communication, lack of teamwork, and absence of crew briefing. The last precondition was Personal Readiness, which was categorized due to both pilots having insufficient experience and inadequate training on the type of aircraft.[15]

The number of sectors is one of the risk factors for fatigue, because take-off and landing are the most crucial phases of flight that increase workload for pilots. The accident was during the fourth sector, which cumulatively could cause fatigue, and the workload of flight operational tasks became more prominent because low visibility during approach caused the crew to experience lack of sensory input. The workload increased even more due to the absence of briefing during approach and lack of communication and teamwork in the cockpit, thus the crew could not synchronize the plan to conduct the approach. The pilot in command (PIC) tried to mitigate the preconditions, but the action was inappropriate since the PIC showed regression in competency, asking for flaps that were not available for the type of aircraft he was flying—instead, the PIC asked for flaps that were available for the type of aircraft he had mastered previously. Regrettably, the second-in-command (SIC) did not recommend any correction. The lapse of professional judgement between the PIC and SIC showed ineffective Crew Resource Management.[15] Crew Resource Management is essential for effective teamwork and communication in the cockpit. It includes skills such as leadership, communication, decision-making, and conflict resolution among the flight crew.[15,16] Thus, none of these preconditions could be mitigated effectively due to lack of teamwork and the fact that both pilots had insufficient experience and inadequate training. The preconditions occurring in sync created the loss of situational awareness that progressively deviated into Perceptual Errors due to misjudgment of distance/altitude and airspeed, as well as Skill-Based Errors due to a failure to comply with manual/procedures.

Regarding Crew Resource Management, the SIC was a newly recruited pilot who was acting as the monitoring pilot and had a total flight time of only 234 h on the MA60. Meanwhile, the PIC had the experience of 34 yr in the company, was acting as the flying pilot, and had a total flight time of 190 and 6982 h on the MA60 and the Fokker types of aircraft, respectively. The background of the pilots and the lack of communication and teamwork suggested that there was a steep authority in the cockpit. In this research, lack of communication had the highest proportion in Crew Resource Management, which was experienced by 40 (21.5%) pilots, while lack of teamwork caused 33 (17.7%) pilots to experience accidents and serious incidents. However, the analysis showed that the precondition of Crew Resource Management was not significantly associated with the severity of incidents. The rationale for this result from the analysis was that other preconditions contributed prior to the precondition of Crew Resource Management and in sync/interrelated with other preconditions, which progressively contributed to Perceptual Error and Decision Error. Communication and teamwork are very important in aviation because every movement of the aircraft at airports and along the flight path is guided by ATCs. In addition, communication between pilots requires effective cooperation either as the flying pilot (the pilot who controls the aircraft) or the monitoring pilot (the pilot who monitors and reads the checklist). Communication and cooperation in Crew Resource Management involve a complex psychosocial interaction, requiring role comprehension, cockpit task management, and personal culture to complement each other.

Analyzing further to the higher level of the HFACS, it was revealed that the Supervisory level also contributed to errors. This was supported by the fact that the management of the airline did not perform any oversight concerning the pilot's performance and readiness in exercising flight operation. The airline manual of operations stated that pilots were allowed to operate an MA60 only if they had achieved the required minimum of 250 flight hours in training. Regrettably, the airline management failed in adhering to the aircraft's manual and thus did not identify the fact that neither pilot had sufficient competency for operating the aircraft. In the concept of HFACS, safety commitment starts from the highest level, which was in this case the inadequate supervision from the organization to manage its resources and assets, including human, facility, and training budget. It is crucial for the management of airlines to organize and supervise every aspect of human factors for an effective mitigation program in aviation safety.

In terms of mitigation, the precondition of Personal Readiness has a great impact in aviation safety because adequate training that benefits competency and skill. Personal Readiness for pilots determines both availability and capability for flight duty. Availability is the readiness for flight duty in terms of being fit, and capability is the readiness for flight duty in terms of being competent. Lack of competency could cause poor technique or airmanship and compromises aviation safety, leading to accidents. Competency is essential for pilots to have the required capability for operating aircraft. Capability focuses more on pilots' cognitive thinking, which consists of memory, perception, attention, and the competency and skill that the pilot achieves through learning. In the concept of HFACS, failure in cognitive thinking can be categorized as the precondition of Adverse Mental State or Physical Mental Limitation.

The availability aspect of Personal Readiness includes contributing risk factors such as sleep restriction, unscheduled flights, drinking alcohol, lack of information, and injury or decrease of medical condition. Availability is not only focused on cognitive thinking but also the supporting resources, including physiological and physical condition. Sleep restriction could derive from workload that forces pilots to have unscheduled flights, exceed flight and duty time limitations, and have shorter sleep periods. Sleep restriction may cause fatigue that may impair pilots' performance; in the concept of HFACS, fatigue is categorized as the precondition of Adverse Physiological State. Other factors that may impair pilots' performance, especially in cognitive thinking, include: drinking alcohol immediately before flight duty; limited access to information about unfamiliar terrain or weather that has never been experienced before; injuries that could limit musculoskeletal range of movement; and medical conditions that could cause incapacitation. The availability of pilots' Personal Readiness is influenced by other factors that require attentive measures.

This accident was one of the examples in which all five preconditions were related in sync, creating errors that were ineffectively mitigated and described the result of this study. Another accident that had complex contributing factors was Investigation Report KNKT.15.12.28.04, concerning the Kalstar Aviation aircraft on December 21, 2015. The contributing factors were Crew Resource Management (due to steep authority and lack of teamwork), Personal Readiness (caused by lack of competency), and Decision Error (due to exceeded capabilities and inappropriate maneuvers). In terms of Crew Resource Management, the steep authority was caused by a significant power difference between the PIC and the SIC. Both pilots flew an Embraer-type aircraft which had only been operated for a short while by Kalstar. The SIC, who acted as the flying pilot, was a 26-yr-old pilot with a total flight time of 557 h and 25 min on the Embraer-type aircraft. Meanwhile, the PIC, who acted as the monitoring pilot, was a 46-yr-old pilot with a total flight time of 598 h on the Embraer-type aircraft. Data from the Voice Cockpit Recorder (VCR) showed that the PIC dominated the conversation, evidenced by the PIC giving multiple instructions which were immediately followed by the SIC. Additionally, the NTSC stated that another contributing factor at the supervisory level of HFACS was a lack of oversight by the airline management. The internal supervision on pilots' performance was not conducted by the airline management.[16] The lack of competency and poor Crew Resource Management caused Skill-Based Errors and Decision Errors. The errors caused an overshot, high-speed landing right on the middle of the landing strip, ultimately resulting in heavy damages to the aircraft.[16]

Another example was the accident involving an aircraft from Perseroan Terbatas: Spirit Avia Sentosa (FlyingSAS) at the mountains of Anem, Oksibil, on April 12, 2017, at 03:40 UTC (12:40 Eastern Indonesia Time). The preconditions that contributed to the accident were Adverse Physiological State (fatigue and daytime sleepiness) and Personal Readiness (due to decrease of medical fitness). In terms of error, Decision Error was present progressively with the state of exceeded capability. The airline management also contributed through lack of supervision, which caused a noncompliance with the standard flight operation procedure.[17]

One accident in Indonesia that had a major impact and garnered significant attention worldwide was when Lion Air Flight JT 160 crashed into the Java Sea after taking off on September 20, 2018. The preconditions involved were as follows: Technological Environment (because the Maneuvering Characteristic Augmentation System design of Boeing 737-8 MAX aircraft did not meet the standard of airworthiness), Adverse Mental State (because of stress and channelized attention), and Personal Readiness (due to lack of competency). Regarding errors, Skill-Based Error (caused by inadequate training) and Decision Error (caused by exceeded capabilities) were present. Although the biggest contributing factor of the accident was unstandardized technology, it must be noted that human error also impacted the outcome of this accident, mainly due to the lack of knowledge in operating the related technology as well as subpar training.[18]

In terms of a serious incident, the NTSC reported on the Batik Air flight from Kendari to Cengkareng on January 25, 2024, during which both the PIC and SIC were asleep in the cockpit for 28 min. The preconditions were Adverse Mental State from burnout, Adverse Physiological State from fatigue, and Personal Readiness from sleep restriction. The errors that derived from these preconditions were Decision Errors from exceeded capabilities. The preconditions of pilots that happened in such serious incidents bring attention to the importance of fatigue management and safety reports. It is not only in pilots' best interest to report conditions that might compromise their flight performance, but it is also in the essence of aviation safety.[19,20] The safety report should include fatigue or stress, and it is the airline management's responsibility to support the safety report as the highlight of aviation safety. IMSAFE, which is an acronym for Illness, Medication, Stress, Alcohol, Fatigue, and Emotion, is often valued as the self-checklist before conducting flight duty, and pilots should report accordingly when a concern arises. Fatigue management requires collaboration and coordination between pilots and the airline management, mainly to share responsibilities in encouraging safety reports and mitigating the preconditions of pilots.[21,22]

Referring to the investigation reports above, the contributing factors to accidents or serious incidents were multifactorial, all the way from the highest level, which is the organizational, and descending to the supervision level and the precondition level. The factors from each level consisted of a plethora of variables, all of which cumulatively compromise the cognitive function of the pilots and eventually play considerable roles in causing multiple errors. The mitigation of these detrimental variables should be established efficiently as soon as possible to further decrease unnecessary risk in aviation.[23,24]

Although the result of this study did not show a significant association between Adverse Physiological State, Crew Resource Management, Personal Readiness, Perceptual Error, and Decision Error, it is apparent that aviation accidents and serious incidents are caused by multiple factors at play. The rationale for the absence of association was that each precondition or error contributed in sync with other preconditions and errors that could cause accidents or serious incidents if not optimally mitigated.

The study recognized that the preconditions of technology and environment were potential confounding factors; these were overcome by focusing the analysis on accidents and serious incidents that were related to pilot error. Nevertheless, the contribution of technology and environment depends on the humans who operate the technology and adapt to the environment.

This study recommends further research to investigate the correlation of each precondition to each error and, subsequently, to aviation accidents and serious incidents, for all aviation personnel. More importantly, the result emphasized the need to address the implementation of mitigation programs as part of the Safety Management System (SMS) and the Fatigue Risk Management System (FRMS) in Indonesia, which requires a strong safety commitment starting from the management of organizations, not only within the operators but in conjunction with the regulator bodies. A commitment for aviation safety can start from a simple task prior to flight duty. For example, this could be declaring the IMSAFE checklist and safety report for any of the IMSAFE items marked as "yes." Compliance with the safety report should begin from the airline management by giving an example, supporting the safety report as shared responsibility, and supervising the safety report in accordance to the SMS or FRMS program.

In a nutshell, the cognitive function of the pilots in each of the reports discussed in this study failed to respond accordingly to the multiple preconditions and errors in a timely manner, and thus resulted in disaster. As human factors are complex, there cannot truly be a sole factor that causes errors. Instead, the aviation industry needs to focus on the possible mitigations that could be performed and could yield effective results by understanding the underlying causes of such errors.

In conclusion, the preconditions of pilots in Indonesia that were associated with accidents and serious incidents from 2004–2024 are Adverse Mental State and Physical Mental Limitation. In terms of errors, Skill-Based Error was associated significantly with accidents and serious incidents. Aviation accidents and serious incidents are caused by multiple contributing factors, and there cannot truly be a sole factor that causes errors. The complexity of humans emphasizes the need for a multifaceted approach to mitigating error.

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Magnesium Alterations in Human Spaceflight

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INTRODUCTION: Magnesium is essential for numerous physiological processes. Changes in magnesium homeostasis during spaceflight could impact astronaut health, particularly as mission durations increase. This review examines trends in serum, urine, and intake-based magnesium data from published human spaceflight studies.

METHODS: A systematic search was conducted using scientific and government agency databases. Inclusion criteria were English studies of adult astronauts in spaceflight reporting magnesium measurements (serum, urine, or intake). Magnesium data were extracted across in-flight, landing day, and postflight time points. Percent change from baseline was calculated and regression analyses evaluated trends over time.

RESULTS: A total of 20 studies were included. In-flight data showed an early increase in urine magnesium (+19.3% ± 3.6%) without significant trends over time, while serum magnesium remained stable initially but increased with longer flight duration ($\beta = 0.03$). On landing day, serum magnesium was similar (−3.92% ± 0.94%) with a nonsignificant trend toward baseline thereafter ($\beta = 0.15$), whereas urine magnesium decreased significantly (−30.01 ± 6.74%), followed by a significant trend toward baseline over time ($\beta = 1.16$).

DISCUSSION: Microgravity may be associated with early renal magnesium losses and a progressive increase in serum magnesium. This could be a result of initial fluid shifts and neurohormonal changes, followed by progressive loss from bone and muscle, potentially exacerbated by insufficient dietary intake. Data are limited to missions less than 6 mo, leaving long duration consequences unknown. Further research is needed to confirm trends and explore underlying mechanisms.

KEYWORDS: magnesium, electrolytes, spaceflight physiology, microgravity, nutrition, astronaut health.

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Space exploration is characterized by exposure to extreme conditions that disrupt normal physiological processes and pose a risk to human health. NASA and its international partners have planned future missions to soon establish the Lunar Gateway and Artemis Base Camp on the Moon, with Mars as a longer-term objective. There is a critical need for meticulous research to ensure optimal human health in space, especially as mission durations and distances increase.[1,2] Mitochondrial dysfunction has emerged as a key biological phenomenon in astronauts during spaceflight. Impairment of mitochondrial adenosine triphosphate (ATP) synthesis may lead to accumulation of toxic metabolites, reactive oxygen species, and apoptosis.[3–5]

Magnesium ions (Mg^{2+}), the second most abundant intracellular cations, serve as essential cofactors in hundreds of enzymatic reactions, many involving ATP production.[6] Mg^{2+} is primarily absorbed in the small intestines via passive and active transport mechanisms, with residual Mg^{2+} excreted in the feces.[6,7] After absorption, Mg^{2+} distributes across intracellular compartments, primarily bone (50–60%), muscle (25–30%), and other soft tissue (20–25%), with less than 1% present in serum.[7,8] Magnesium homeostasis is maintained through gastrointestinal absorption, renal filtration and reabsorption (primarily in the loop of Henle), and exchange with intracellular stores.[6,8,9] Magnesium status and the extent of magnesium filtration are influenced by diet, renal function, inflammation,

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bone and muscle mobilization, hormones, medications, and sex, among other factors.[6,7] Hypomagnesemia is typically induced by intestinal or renal losses, with re-equilibration from intracellular compartments occurring over days to weeks.[9] The currently accepted reference range for serum magnesium is 0.75–0.95 mmol · L^{-1},[10,11] although recent literature suggests a more stringent range of 0.85–0.95 mmol · L^{-1} to correct for chronic latent deficiencies.[8,12,13]

Epidemiological studies have found that magnesium insufficiency may be associated with inflammation, cardiovascular diseases, metabolic syndrome, bone metabolism, stress, and other disorders.[6] Clinical manifestations of hypomagnesemia include neuromuscular, cardiovascular, and electrolyte abnormalities.[7] In the context of spaceflight, magnesium loss has been hypothesized to contribute to peripheral vascular and renal dysfunction,[14,15] cardiac conditions such as "Apollo 15 syndrome,"[16] "Neil Armstrong syndrome,"[17,18] and myocardial injury,[19] as well as renal stone formation.[20]

The broad range of intracellular functions of Mg^{2+} underscores its importance in supporting mitochondrial function, regulating physiological systems, and preventing both acute and chronic conditions on Earth and in space. To better understand Mg^{2+} dynamics in microgravity, a systematic review was conducted of studies evaluating serum and urine magnesium levels and magnesium intake in astronauts, and the data was synthesized to identify trends across spaceflight missions.

METHODS

This systematic review was registered under Prospero (#CRD42024501014), deemed exempt from human subjects research under Scripps Institutional Review Board (#IRB-25-8535), and conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis. A comprehensive search was initially conducted in Medline (OVID), Scopus (Elsevier), the Cochrane Library Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials, and was augmented with keyword searching in the NASA Task Book and NASA Life Sciences data archive in January 2024. An updated search with expanded search strings was performed in May 2024. An additional search was performed in July 2024 using the Defense Technical Information Center collection via the Dimensions platform to capture declassified U.S. government research.

The specific PICO research question asked was: do astronauts (population) experience changes in serum or urinary magnesium levels (outcome) during spaceflight (intervention) compared to Earth-based conditions (comparison)? Eligibility criteria were predefined before the literature search. Inclusion criteria were: 1) full-text articles in English; 2) studies of adult astronauts in spaceflight of any duration; and 3) original studies reporting at least one measurement of serum or urine magnesium or magnesium intake before, during, or after flight. Studies were excluded if they were: 1) non-English, 2) animal studies, or 3) studies conducted in non-microgravity environments (i.e., bedrest or centrifuge studies).

Titles, abstracts, and the full-text articles were screened in Covidence by two authors, with conflicts resolved by a third. Studies were extracted from Covidence to a spreadsheet to categorize studies based on sample size, flight duration, flight name, type of magnesium collected, collection interval surrounding flight, flight day, and return day. To ensure methodological rigor and transparency, a Cochrane Risk of Bias In Nonrandomized Studies of Interventions (ROBINS-I) assessment was conducted and cross-checked by two authors. Due to inherent limitations in spaceflight research, select domains were excluded from final bias assessment.

Study characteristics and individual magnesium values were synthesized into a customized Microsoft Excel (Microsoft Corporation. Redmond, WA, United States; version 2504) sheet. When raw data values were not explicitly reported, values were extracted from figures using WebPlotDigitizer (Ankit Rohatgi. Version 5.2). Serum magnesium concentrations were converted to mmol · L^{-1} using appropriate conversion factors.[13] All magnesium values were normalized to percent change from baseline. Weighted averages were calculated for each flight interval and source, and trends were analyzed via linear regression using R statistical language (R Foundation for Statistical Computing, Vienna, Austria; version 4.4.1) and the ggplot2 package (Hadley Wickham; version 3.5.2). All data for single time-points are reported as means with SD, while model estimates are reported as the regression coefficient and standard error. A *P*-value less than 0.05 was considered statistically significant and is reported alongside the test statistic returned with the relevant degrees of freedom. Short duration flight is defined as flight duration of 30 d or less, whereas long duration is greater than 30 d.

RESULTS

Literature Search

Fig. 1 displays a flowchart of the screening and study selection process. The database search yielded 6296 articles and 18 articles were obtained from other sources, of which 978 duplicates were removed. Of the 5336 remaining studies, 96 were eligible for full-text review and 20 studies met inclusion criteria.

Extracted studies included missions ranging from Gemini VII to International Space Station (ISS) expeditions. The longest duration of in-flight magnesium collection was recorded on flight day 180. Among studies describing analytical methods, atomic absorption spectrophotometry was most commonly used. Two studies were excluded due to duplicate results already reported in another publication.[21,22] Two studies reported magnesium values in graphical form without numerical data.[23,24] The WebPlotDigitizer was unsuccessful in transcribing these figures, but these studies were included for qualitative analysis. Data on urine magnesium excretion and maximum diuresis following a postflight water load test on return day 2 after short duration flight were omitted from

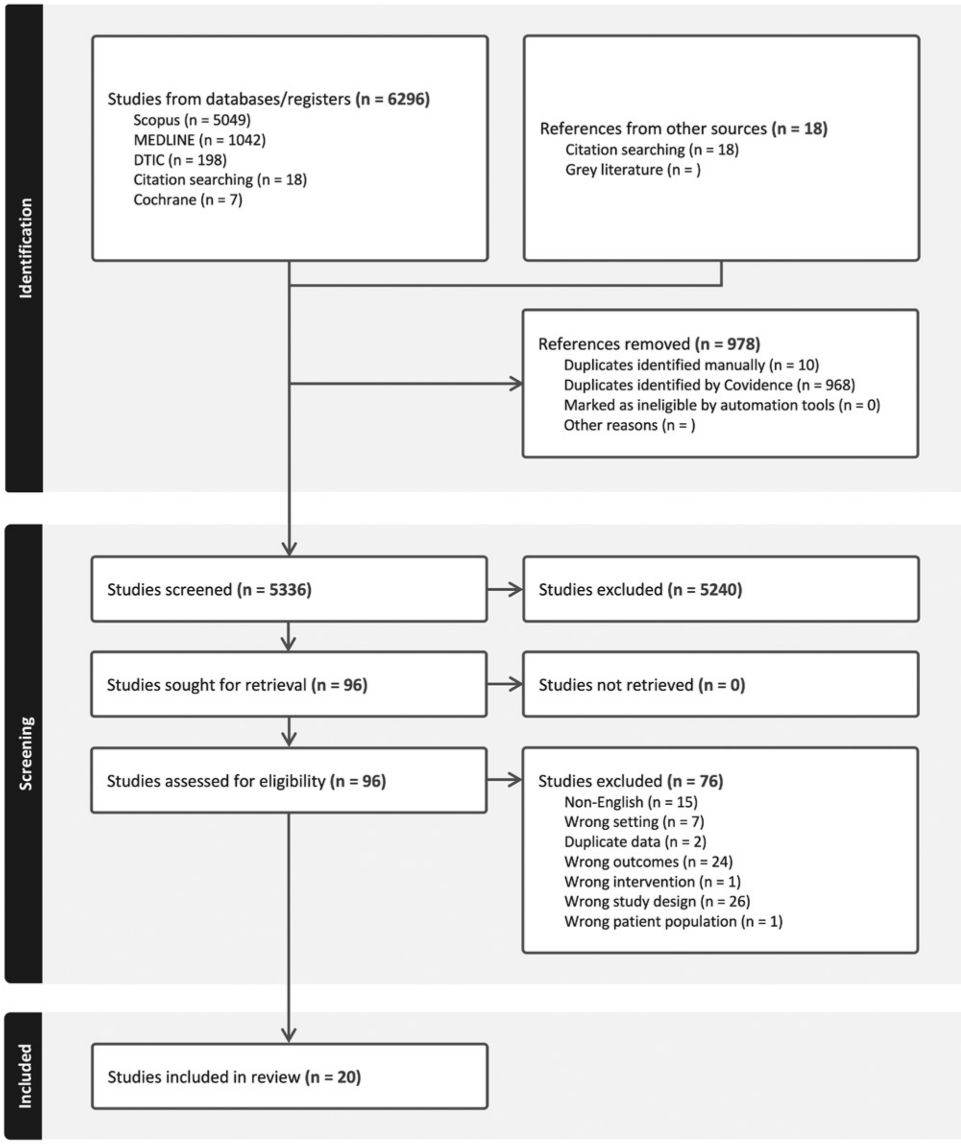

Fig. 1. Flowchart of the study selection process.

the regression model,[25] but are described qualitatively for completeness.

Description of Studies

The 20 studies varied in magnesium sources (serum, urine, or intake), units reported, flight duration, timing of sample collections, astronaut demographics (often not reported), and sample sizes. Several studies reported missing data, resulting in variable sample sizes across collection days.

Overall, the combined sample size across all studies was 1130 astronauts, though overlap among studies and cohorts is likely. When broken down by flight interval, in-flight magnesium values were collected from 148 astronauts in 16 cohorts across 11 studies, landing day magnesium values were collected from 905 astronauts in 18 cohorts across 11 studies, and postflight magnesium values were collected from 382 astronauts in 26 cohorts across 15 studies. Many cohorts assessed two different magnesium sources in the same astronauts. The largest single-cohort sample size was 504, and measured serum magnesium on landing day after short duration flight. Four studies had sample sizes of two, with individual astronauts' data reported. One study included only a single participant. A summary of the studies is presented in **Table I**.

In Flight

Leach-Huntoon et al. report that electrolyte serum concentrations generally decrease early in flight due to fluid loss, along with a suppression of aldosterone and an increase in antidiuretic hormone (ADH) and angiotensin I.[32] Smith et al. reports a statistically significant increase in serum magnesium by flight day 120 ($N = 39$) and a statistically significant increase in urine magnesium by flight day 15 ($N = 43$). Both serum and urine remained elevated through the end of their 180-d mission. In these cohorts, serum and urine magnesium were also separated

Table I. Summary of Studies Reporting Magnesium Measurements.

STUDY	N	FLIGHT DURATION	PREFLIGHT	IN FLIGHT	LANDING DAY	POSTFLIGHT
Lutwak et al.[26]	1	Short	U, I	U, I		U, I
	1	Short	U, I	U, I		U, I
Leach & Rambaut[27]	9	Long	S, U	U	S	S, U
Leach et al.[28]	32	Short	S		S	
	23	Short	U		U	
Whedon et al.[23]	1	Short	U	U		U
	1	Short	U	U		U
	1	Short	U	U		U
Grigor'ev et al.[25]	1	Short	S, U	U	U	S, U
	1	Short	S, U		U	S, U
Smith et al.[29]	9	Long	I	I		I
Leach[30]	8	Short	S, U		S, U	S, U
Grigor'ev et al.[31]	1	Long	U, I			U, I
	1	Long	U, I			U, I
Leach-Huntoon et al.[32]	6	Short	S	S	S	S
Cintron[33]	1	Short	U	U		
Leach[34]	9	Short	S		S	
	133	Short	S		S	
Grigoriev et al.[35]	8	Short	U			U
	4	Long	U			U
	18	Long	U			U
	6	Long	U			U
Grigoriev et al.[36]	143	Short	S			S
Vorobiev et al.[37]	1	Short	U	U		U
	1	Long	U	U		U
Whitson et al.[38]	6	Short	U, I	U, I	U, I	U, I
D'Aunno et al.[39]	5	Short	S		S	S
	7	Long	S		S	S
Smith et al.[40]	11	Long	U		U	
Grigoriev et al.[41]	60	Long	S, U		U	S, U
Smith & Zwart[42]*	39	Long	S	S	S	S
	504	Short	S		S	
	43	Long	U	U	U	U
	8	Short	U		U	
Smith et al.[24]	27	Unknown		I		

*Studies that analyzed the relationship of magnesium with the interim resistive exercise device, the advanced resistive exercise device, and bisphosphonates; U = urine magnesium collected; I = magnesium intake collected; S = serum magnesium collected.

into groups based on differing bone density-related countermeasures: interim resistive exercise device, advanced resistive exercise device (ARED), and those who took bisphosphonates along with ARED access. Serum magnesium was significantly higher on flight day 15 in the bisphosphonates group and on flight day 180 for the ARED group. As for urine magnesium, all groups were higher on flight day 15 compared to baseline. Lastly, in a subset of 33 crewmembers with sublingual tissue magnesium determinations, a similar trend of higher serum (significance on flight day 180) and urine magnesium in flight was observed. Although there were statistically significant differences, all values remained within normal ranges.[42]

In a study of two Gemini VII astronauts, Lutwak et al. reported urinary excretion did not change during the first week of flight. Significantly increased amounts of magnesium in one astronaut were excreted the second week of flight and excretion fell dramatically toward the end of flight. Magnesium intake in both astronauts was markedly decreased in flight. This study also reported decreases in fecal magnesium. Overall, a net negative magnesium balance was reported,[26] the only study to report this. Leach and Rambaut reported an increase in urine magnesium on flight day 1 through 28 average and flight day 29 through 59 average, but a slight decrease thereafter compared to preflight in 9 astronauts. They also noted an increased ADH in the early in-flight period.[27] Whedon et al. reports that magnesium, potassium, and sodium were lost in modest but substantial amounts during the in-flight phase of Skylab II in a sample size of three, and the increased excretion was almost exclusively by urine as opposed to feces.[23] While Grigor'yev et al. does not directly address in-flight urine magnesium, the data demonstrates a decreased urine magnesium by day 4 of flight, but an increased urine magnesium at day 27 in flight in one astronaut compared to baseline.[25] In a sample size of one, Cintron reports a trend to an increased excretion of magnesium early in flight, alongside calcium, phosphate, and uric acid.[33] Vorobiev et al. does not directly address in-flight urine magnesium, but data reveals differing trends in both astronauts studied. One astronaut had decreased urine magnesium on flight days 6 and 12 with no change on flight day 18. The other astronaut had a markedly lower preflight urine magnesium value and demonstrated increases in urine magnesium on flight days 7, 12, and 17.[37] Whitson et al. reports urine magnesium was unchanged during short duration flight in a sample size of six, though there was a trend to a decrease early in flight and increase late in flight. Phosphate, oxalate, and sulfate were also unchanged. Magnesium intake was significantly decreased at all intervals in flight.[38] A figure in Smith et al. visualizes daily magnesium intake in 27 ISS astronauts (20 male, 7 female). While not directly addressed, it appears that half of the male astronauts on average did not meet their recommended dietary allowance (RDA) of 420 mg $\cdot$ d^{-1} while the majority of female astronauts did for their RDA of 320 mg $\cdot$ d^{-1}. This study also reports a positive relationship between energy intake and magnesium intake during spaceflight, similar to on Earth.[24]

Postflight

Leach assessed serum magnesium in 2 different cohorts, one consisting of 9 astronauts from Skylab flights in durations ranging from 28–84 d and the other of 133 astronauts from 28 different Space Shuttle flights in durations ranging from 2–11 d. This study reported significant decreases upon landing in both flight programs alongside uric acid.[34] Leach et al. reported a decrease from baseline in serum magnesium in 32 astronauts immediately postflight following short duration Apollo missions, accompanied by decreases in potassium but not sodium or chloride. Significant decreases in urine magnesium, sodium, potassium, and chloride in the first 24 h postflight in 23 astronauts was also reported. Furthermore, food consumption was variable and generally below basal requirements.[28] Smith et al. reported a significant decrease in urine magnesium and phosphorus in 11 astronauts on landing day after long duration flight, possibly due to decreased dietary intake. Over half of crewmembers were reported to have urinary magnesium concentrations below a clinical threshold of 3.0 mmol $\cdot$ d^{-1} and the presence of select oxidative stress markers in urine postflight was noted.[40]

While landing day is not directly addressed, Leach and Rambaut reported a statistically significant decrease in serum magnesium in nine astronauts after flights ranging from 28–84 d. In addition, they reported decreases in postflight total daily output of magnesium.[27] Grigor'yev et al. also does not directly address landing day changes but reports a decrease in urine magnesium in two astronauts upon return from a short duration Salyut-4 flight. Postflight serum magnesium and calcium were increased, whereas sodium and potassium were decreased. Notably, a water load test was performed on return day 2 which demonstrated increased renal excretion of magnesium and calcium.[25] Leach reports that serum magnesium, sodium, and uric acid decreased on landing day in eight astronauts after a short duration flight, and reversed toward baseline within 3–5 d. In terms of urine magnesium, the most consistent changes in six astronauts after short duration flight were decreases within 24 h of landing, alongside sodium, potassium, chloride, uric acid. Of note, it specified that several cohorts of astronauts in this study consumed electrolyte beverages and/or eight salt tablets and 1 L of water in the hours before landing.[30] While not directly addressed, Leach-Huntoon reported a decreased serum magnesium on landing day in six astronauts after short duration flight, with near baseline values thereafter on return days 3 and 10.[32] Although Whitson et al. reported urine magnesium did not change throughout their study in six astronauts after short duration flight, a decrease was observed on landing day with a near baseline value 7–10 d postflight. In addition, dietary magnesium and potassium were significantly less immediately after flight.[38] D'Aunno et al. reported no changes in serum magnesium or other electrolytes on landing day and postflight in a cohort of five astronauts after short duration flight and seven astronauts after long duration flight. Pertaining to cardiac function, they reported that there were no electrolyte changes sufficient to impact cardiac conduction or repolarization but found that long duration flight was associated with QTc interval prolongation. This trend is visualized on landing day and 3 d postflight.[39] Grigoriev et al. reported that there were no statistical variations in blood magnesium, total calcium, sodium, chlorine, or osmotically active substances on the first day after long duration flight in 60 astronauts comprising 28 different flights. However, a significant decrease in urine magnesium and calcium on landing day was reported, with a decrease in diuresis as well. Urine magnesium and calcium excretion remained low through postflight day 3, whereas sodium and potassium were similar to preflight.[41] Smith et al. reports that urine magnesium was no different from preflight in two different cohorts on landing day after short duration flight, one with 8 astronauts and the other with 504 astronauts.[42] In the same cohort of astronauts described previously with in-flight serum and urine values from Smith et al. with sample sizes of 39 and 43, both serum and urine magnesium were significantly lower than preflight on landing day, and urine magnesium remained low for 48 h. Serum and urine magnesium returned to baseline values on postflight day 30.[42]

Grigoriev et al. reports a significant reduction of serum magnesium, potassium, and phosphates on the first day after short duration flight in 143 astronauts, with an increase in chloride, aldosterone, and angiotensin I. They hypothesize these changes suggest shifts in water-salt homeostasis during spaceflight and recommend further analysis regarding whether these are a compensatory effect or an onset of pathology.[36] Grigor'yev et al. reports an increased excretion of bivalent ions after long duration flight in two Salyut-6 astronauts, with no change in diuresis likely due to intake of fluid and salt supplements late in flight. A load test with potassium chloride was conducted preflight and on return day 2, and both astronauts had faster excretion of magnesium, calcium, and potassium during the test compared to preflight.[31] Whedon et al. did not directly address postflight magnesium, but as previously described for in-flight data, they reported significant losses of body magnesium in three astronauts who underwent short duration flight.[23] Grigoriev et al. reports an increased urine magnesium and calcium excretion 1 d after varying flight durations, that being 8 astronauts after short duration flight and 3 different cohorts of 4, 6, and 18 astronauts after long duration flight. They also cite their previous study (published in Russian) which demonstrated increased urine magnesium excretion after long duration flight despite decreased diuresis, and during a water load test postflight.[35] Lutwak et al., as previously described for in-flight data, reported a net positive postflight magnesium balance through return day 4, likely owing to increased dietary intake and decreased loss from urine and feces.[26] Vorobiev et al., as previously described for in-flight data, reported decreases in urine fluid, sodium, potassium, and osmotically active compounds, but increases in magnesium and calcium. Of note, one astronaut underwent short duration flight and the other long duration flight; the increase in urine magnesium and calcium postflight was more pronounced in the astronaut who underwent long duration flight.[37]

Analysis Across Studies

Based on a more stringent serum magnesium reference interval (0.85–0.95 mmol · L^{-1}), as suggested by recent literature,[8,12,13] one in-flight value (flight day 15; total N = 39), six landing day values (total N = 702), and six postflight values (return days 1, 2, 3, and 30; total N = 192) were below the lower limit. In contrast, using the conventional range (0.75–0.95 mmol · L^{-1}),[10] no values fell below threshold. No values exceeded the upper limit in either range.

For urine magnesium, using a deficiency threshold of 80 mg · d^{-1} (3.29 mmol · d^{-1}),[7,8] 2 in-flight values (flight days 12 and 17; total N = 1), 4 landing day values (total N = 19), and 7 postflight values (return days 1, 3, 6, and 12; total N = 63) fell below the threshold. Two astronauts from different studies also had low preflight urine magnesium values.

For magnesium intake, values from 4 short duration flights (total N = 13) and 1 landing day value (total N = 6) fell below both a 250 mg · d^{-1} deficiency threshold and the 350 mg · d^{-1} RDA for ISS crewmembers. Notably, in one cohort of six astronauts, both urine magnesium and intake were below their respective thresholds on landing day.[38]

Serum magnesium showed no significant initial change from baseline with flight [−0.01 ± 0.83%, $t(7) = -0.011$, $P = 0.991$], but a significant upward trend was observed over time [β = 0.03, $t(7) = 3.455$, $P = 0.011$; **Fig. 2**]. On landing day, serum magnesium was no different from baseline [−3.92 ± 0.94%, $t(1.06) = -5.969$, $P = 0.096$], followed by a similarly nonsignificant trend toward baseline in the postflight period [β = 0.15, $t(23) = 1.857$, $P = 0.076$; Fig. 2].

In contrast, urine magnesium showed an initial significant increase from baseline [+19.31 ± 3.58%, $t(12) = 5.395$, $P <$ 0.001], with no significant in-flight trend over time [β = 0.03, $t(12) = 0.689$, $P = 0.504$; **Fig. 3**]. On landing day, urine magnesium was significantly decreased from baseline [−30.01 ± 6.74%, $t(3.05) = -8.960$, $P = 0.002$], followed by a significant upward trend back toward baseline [β = 1.16, $t(40) = 4.238$, $P <$ 0.001] over time (Fig. 3).

Risk of Bias

Using the Cochrane ROBINS-I, most studies were determined to have a low overall risk of bias, supporting the reliability of the data synthesized in this review (**Fig. 4**). One exception was Smith et al., which presented magnesium intake data for 27 astronauts solely through a figure.[24] This study lacked essential methodological details such as astronaut recruitment, baseline characteristics, data collection methods, and analysis details. The absence of these details contributed to a classification of a severe risk of bias.

DISCUSSION

To our knowledge, this is the first review to synthesize serum, urine, and intake data to evaluate magnesium changes during and after spaceflight. Recent literature suggests magnesium deficiency should be considered if subjects exhibit serum concentrations less than 0.85 mmol · L^{-1}, urine excretion less than 80 mg · d^{-1} (3.29 mmol · d^{-1}), and intake less than 250 mg · d^{-1}.[8] However, none of the 20 studies included in this review assessed all 3 of the aforementioned magnesium sources concurrently,

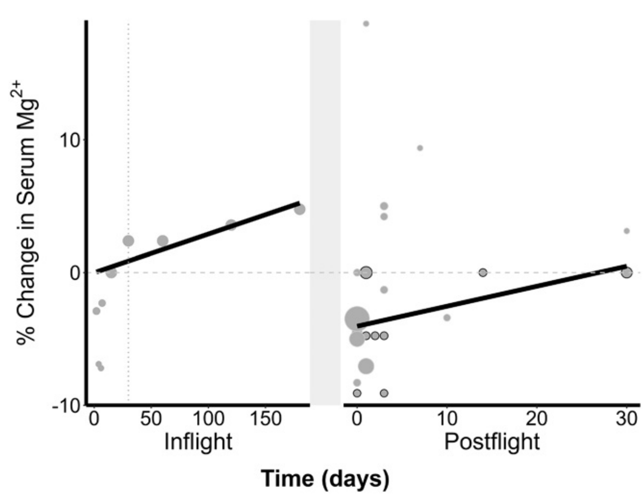

Fig. 2. Changes in serum Mg^{2+} from baseline to both in flight and upon return to Earth. All circular data points represent a single study, with its size reflecting the number of participants (range 2–504) and presence of a black outline representing long duration flight. The linear trendline is weighted according to the sample size in each individual study.

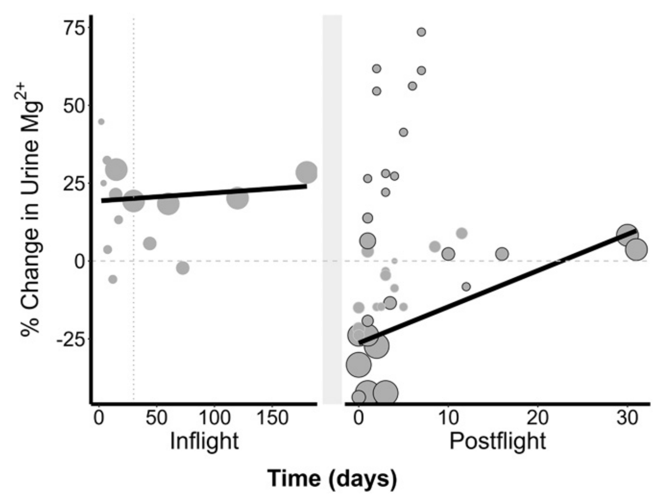

Fig. 3. Changes in urine Mg^{2+} from baseline to both in flight and upon return to Earth. All circular data points represent a single study, with its size reflecting the number of participants (range 1–60) and presence of a black outline representing long duration flight. The linear trendline is weighted according to the sample size in each individual study.

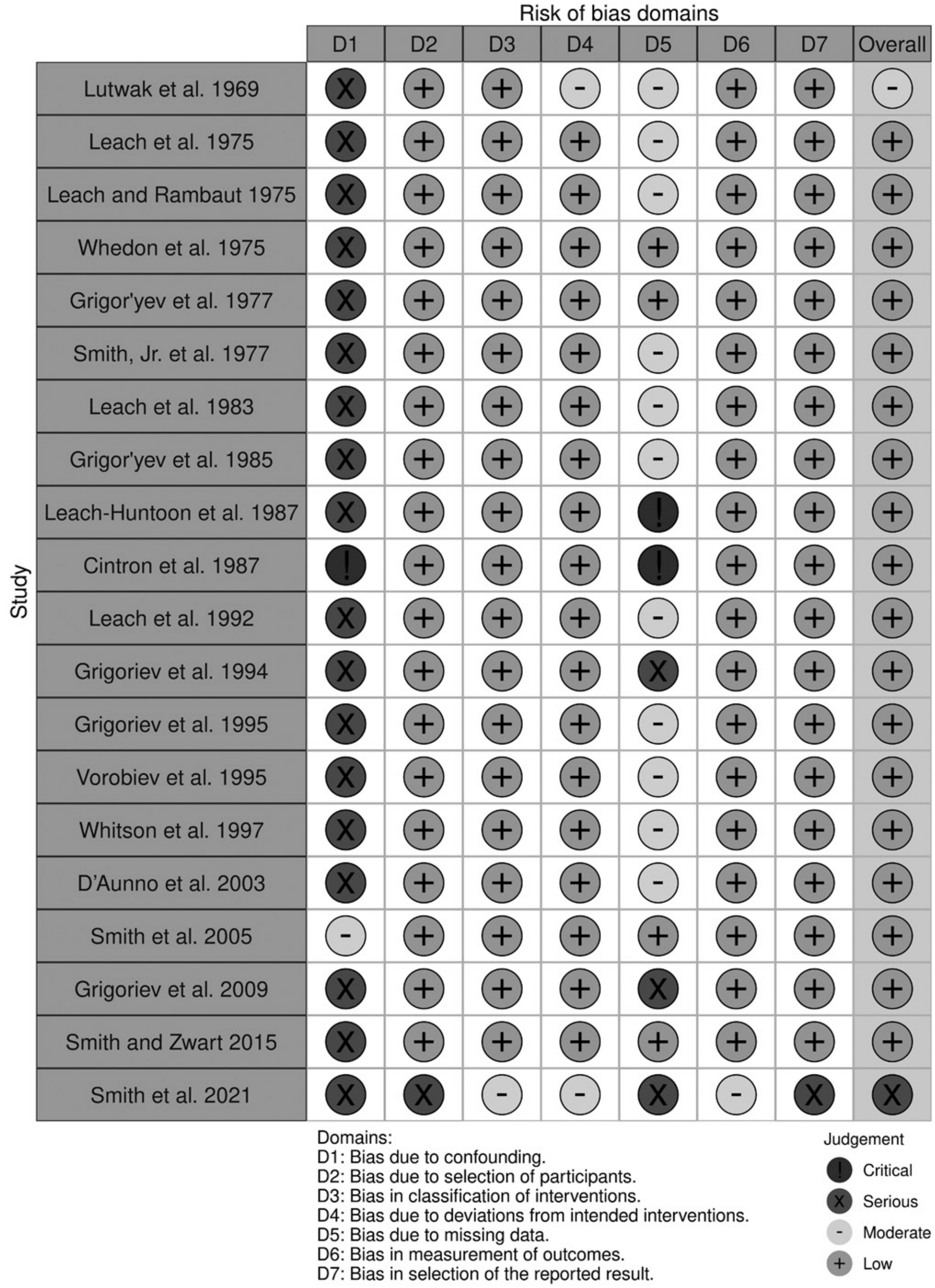

Fig. 4. Cochrane ROBINS-I assessment.

and few collected more than one metric on the same day. Of these, only one study demonstrated a trend toward deficiency, showing both decreased magnesium intake and urine excretion on landing day.[38]

A trend of increasing serum magnesium with longer flight duration and elevated urine magnesium throughout flight was identified, predominantly driven by a single study with relatively large sample sizes.[42] The longest time point with in-flight magnesium data was 180 d, but the trends from this review suggest that serum magnesium may continue to increase and urine magnesium may remain elevated on longer flights. On landing day, multiple studies reported a sharp decline in both serum and urine magnesium compared to baseline. Postflight, these values gradually returned to baseline. Interestingly, in healthy individuals on Earth, the serum magnesium levels exhibit minimal daily variation, with one study finding typical within-subject biological variation of 3.2% within a 24-h period. This same study showed that 24-h urinary magnesium had a within-subject biological variation of 36%.[43] Therefore, while statistical significance was only observed for urine magnesium, which may somewhat be related to physiological variation, the variability in postflight values may also reflect rapid volume repletion, nutritional changes, renal adaptation to Earth's gravity, and other confounding factors.

Despite normal or elevated concentrations in flight, serum or urine magnesium alone does not represent total magnesium status or whether the body is in equilibrium with its intracellular compartments. Magnesium is an intracellular electrolyte and serum levels can be regulated by hormones and renal mechanisms.[44] As a result, serum magnesium can remain within clinical reference ranges in the presence of total body depletion because intracellular sources serve as a reservoir.[8] Some investigators have explored alternative methods for evaluating magnesium status in spaceflight, such as saliva, sublingual epithelial, or fractional excretion of magnesium (FEMg), though these methods remain contentious.[7] One study found an increase of salivary magnesium concentrations in astronauts despite increased fecal and urinary magnesium, but did not correlate this with serum levels.[45] Smith et al. found no significant change in sublingual tissue magnesium concentrations before and after flight, and no association with in-flight exercise type or bisphosphonate use.[42] While some terrestrial studies report a correlation between epithelial magnesium and intracellular status, one involving cardiac biopsies in a small cohort of cardiac surgery patients and the other linking to dysrhythmia risk,[46,47] this method has not been validated and is not likely to be generalizable to healthy astronauts.[7]

Magnesium intake during spaceflight is also concerning. Despite NASA's RDA of 420 $mg \cdot d^{-1}$ for men and 320 $mg \cdot d^{-1}$ for women in exploration missions lasting up to 365 d,[48] in-flight intake often fell below these thresholds across multiple studies. This dietary insufficiency, coupled with potential changes in gastrointestinal absorption, could compromise astronaut health, especially on longer missions.

A potential relationship between magnesium status and bone mineral content (BMC) is supported by postflight and postmortem findings. In an autopsy result from cosmonauts who died after a 24-d Salyut-1 mission, some magnesium bone concentrations were 12–32% lower than terrestrial control subjects.[49] Similarly, Smith et al. reported that as postflight BMC declined, serum and urine magnesium area under the curve increased, specifically in astronauts with ARED access.[42] This finding is consistent with the high concentration of magnesium in bone tissue. While the ARED is intended to preserve BMC, it requires extensive energy expenditure and may necessitate an even higher magnesium intake.[24]

Interestingly, FEMg remained unchanged and consistently greater than 2% in Smith et al.[42] Assuming the FEMg equation can be extrapolated to spaceflight, this would suggest that any observed magnesium loss may not be solely due to reduced dietary intake but rather altered renal reabsorption or redistribution from intracellular stores. Further complicating the interpretation of renal function, some studies reported differences in urine concentrations of bivalent ions vs. univalent ions in postflight periods, including after a water load test.[25,37,41] This suggests potential ion-specific reabsorption variations either due to microgravity or upon return to gravity.

Although this review identifies measurable changes in magnesium homeostasis during spaceflight, numerous confounding factors in space make it challenging to determine the exact mechanisms driving these trends. Given these complexities, the following hypotheses provide potential explanations for the observed magnesium alterations.

Impaired magnesium reabsorption. Upon entering microgravity, fluid shifts lead to central blood volume expansion and altered renal hemodynamics.[50] In response, the kidneys undergo functional adaptations, including increased glomerular filtration rate and changes in tubular reabsorption,[51] which may result in increased urinary excretion and impaired reabsorption due to altered fluid balance and neurohormonal response.[52] Studies have also reported changes in ADH, aldosterone, and angiotensin, which may support this mechanism.[27,28,32] Further, the results of a postflight water load test suggest persistent alterations in magnesium reabsorption,[25] either due to lingering effects of spaceflight or as a new adaptation upon return to Earth.

Reduced bone mineral content. Microgravity causes reductions in bone mineral density due to decreased mechanical loading.[53] Magnesium plays a key role in the structural integrity of bone, with approximately 50–60% of total body Mg^{2+} stored in the bone matrix.[54] A decline in bone mineral density during spaceflight may reduce magnesium incorporation into bone tissue, resulting in a shift of magnesium into circulation. This is supported by the observed relationship between magnesium area under the curve and BMC in flight, as well as magnesium levels found in postflight bone autopsy samples.[42,49] This redistribution may also serve as a compensatory mechanism to maintain homeostasis in response to early magnesium losses from urine and intake.

Tissue loss and muscular atrophy. Approximately 25–30% of intracellular magnesium is stored in muscle tissue, where it supports protein synthesis, energy production, and muscle contraction.[55] Reduced mechanical loading in microgravity may promote catabolism of muscle and soft tissue, leading to a shift of intracellular magnesium into circulation.[56] This hypothesis is supported by studies reporting astronaut weight loss,[28,35,40] many of which attribute these reductions to lean body mass or direct muscle loss.[23,30] Results from a postflight potassium chloride load test suggested impaired tissue potassium retention in the setting of urinary potassium loss,[35] which alludes to persistent muscular atrophy upon return to Earth. This potassium wasting may also be a direct result of hypomagnesemia due to magnesium's effect on renal outer medullary potassium channels.[57] Additional evidence includes findings of net negative nitrogen and phosphorus balances along with increases in blood urea nitrogen and serum creatinine in astronauts, all of which are biomarkers consistent with muscle breakdown.[23,26,30] These changes may reflect another compensatory mechanism to maintain magnesium homeostasis in response to losses from urine and diet.

Poor magnesium intake. Limited in-flight dietary data suggest that astronauts frequently do not meet the magnesium RDA. In addition to inadequate intake, absorption of magnesium is easily impaired due to changes in gastrointestinal pH and transit time.[7] These factors can reduce the bioavailability of magnesium even if intake is sufficient. While urine magnesium responds relatively quickly to changes in dietary intake, serum magnesium is more buffered and may remain stable initially.[12] This delay in serum response may partially explain why serum magnesium was unchanged during early phases of spaceflight, even if total body stores are declining.

Physiological Implications of In-Flight Magnesium Variations

Persistent magnesium losses during spaceflight may trigger mobilization from intracellular stores, which in turn could impair several physiological processes. At a cellular level, magnesium supports mitochondrial structure and function by maintaining membrane potentials and enhancing ATP synthesis.[58,59] Deficiencies in Mg^{2+} may lead to mitochondrial dysfunction, reduced ATP production, and increased reactive oxygen species, which contributes to oxidative damage.[60] Magnesium is also essential for DNA and RNA stability, and facilitates protein synthesis through ribosomal integrity.[61,62]

Intracellular magnesium disturbances may also have systemic consequences. Magnesium plays a key role in regulating calcium and potassium channels, maintaining electrochemical gradients necessary for intracellular signaling, neuromuscular function, and electrolyte secretion.[55,63,64] As a natural calcium antagonist, Mg^{2+} modulates calcium influx into cells,[63] initiating the interaction between actin and myosin filaments for muscle contraction while also facilitating muscle relaxation.[62] When magnesium homeostasis is altered, this magnesium-calcium balance is disrupted, leading to sustained calcium influx, hyperexcitability, and potential clinical symptoms such as muscle cramps or spasms.[65]

Through its regulation of voltage-gated ion channels, magnesium influences neurotransmitter release, resting membrane potential, and generation of action potentials–all which are critical to cardiovascular performance.[63,66] Cardiovascular complications have been observed during spaceflight[16,17,19] owing to magnesium deficits as a potential contributing factor. However, while arrhythmias have been reported during and after spaceflight, they have not been linked to electrolyte abnormalities.[39,67] Nonetheless, magnesium alterations may exacerbate inflammation and endothelial dysfunction, potentially increasing the risk of other cardiovascular perturbations.[68]

As an inhibitor of oxalate crystallization, magnesium alterations could increase the risk of nephrolithiasis.[69] The risk of renal stone formation has been well-documented in astronauts and remains a recognized hazard during long duration space missions.[20,40]

Limitations

Interpreting these data in aggregate is challenging due to the substantial heterogeneity among the included studies. For instance, landing day and postflight results should be interpreted cautiously, as electrolyte and volume repletion commonly occur prior to and after landing. Additionally, spaceflight protocols and countermeasures have evolved over time, meaning older studies in this review may not reflect current standards.

Pharmaceutical use, such as diuretics, was not reported in a majority of the studies and may have influenced electrolyte status. Astronaut demographics were rarely described, though based on historical trends,[70] most astronauts were likely male, limiting the generalizability to current or future astronaut cohorts. Several studies reported issues with sample collection, often resulting in mismatched sample sizes or flight days. Poorly described methodology and data sources may also have led to unintentional duplication of results. While analog studies (i.e., bedrest) were excluded, this may have omitted important implications on intracellular magnesium loss. Furthermore, several non-English publications were excluded which may have contained relevant data. Lastly, this study did not examine potential confounders such as calcium, potassium, vitamin D, vitamin B12, cortisol, or other biological or hormonal components which may also impact magnesium values.

Pertaining to risk of bias assessment, domain 1 (confounding) was excluded from the final evaluation, as all studies uniformly suffered from confounding due to uncontrolled baseline characteristics of astronauts, an inherent limitation of spaceflight research. Domain 5 (missing data) was also excluded from the final evaluation, as none of the studies addressed data completeness. However, given the stringent reporting requirements of government-sponsored spaceflights, it was presumed the available data were comprehensive.

Future Spaceflight Considerations

Maintaining magnesium homeostasis is important to ensure optimal human health and performance during long duration spaceflight. While existing studies suggest there is no concern for magnesium deficiency in missions lasting 4–6 mo,[24,42] this review highlights concerns for longer missions based on both the paucity of available data and observed trends indicating possible alterations over time. Additionally, the rapid magnesium changes on landing day warrants further investigation, especially as this physiological adaptation may differ from that of extraterrestrial environments such as the Moon or Mars.

In order to address renal magnesium loss in flight, a more complete understanding of urine magnesium excretion and renal reabsorption will be crucial to clarify the underlying mechanism of magnesium regulation. Musculoskeletal countermeasures offer one of the most promising strategies to preserve intracellular magnesium by mitigating BMC loss and muscle atrophy. Optimizing dietary magnesium intake may require an understanding of in-flight gastrointestinal absorption as well as continued efforts to develop and standardize meal plans. Furthermore, long-term food stability, particularly under extreme conditions like ionizing radiation exposure, should be considered.[71] More creative, sustainable strategies may be required for long duration missions, such as the growth and cultivation of extraterrestrial agriculture with magnesium-rich dietary sources.[72,73]

While magnesium supplementation may prevent dietary deficiencies, excess magnesium may be excreted in urine if tissue losses reduce the body's ability to store magnesium. However, since urinary excretion alone does not indicate total body magnesium status, a magnesium load test in flight and upon return to Earth may provide a more accurate assessment. Some studies have proposed additional strategies to address potential magnesium deficiency during long duration space missions, including subcutaneous products for magnesium delivery,[74] gene therapy approaches,[75] and careful selection of astronaut candidates.[76] While oral magnesium supplementation may suffice, pharmaceutical stability and storage constraints should be considered for exploration missions.

Serum and urine magnesium measurements, when combined with dietary intake tracking, is one of the most practical, noninvasive methods to assess overall magnesium status.[7] Future studies should attempt to collect magnesium using these three modalities concurrently, ideally alongside BMC, lean body mass, components of protein catabolism, exercise, medications, hormones, other electrolytes, and diuresis in order to better understand overall magnesium status during and after spaceflight. Finally, data collection will be needed from missions longer than 6 mo in duration, and during exercise and extravehicular activity.

The increased urine Mg^{2+} excretion observed immediately in microgravity, coupled with the incremental increase in serum magnesium over flight duration, suggests significant implications for cellular and physiological function. This pattern may reflect initial renal loss due to fluid shifts and neurohormonal changes, followed by progressive loss from bone and muscle, potentially exacerbated by insufficient dietary intake. Serum magnesium levels mostly remained within clinical reference ranges, though this could mask underlying deficiencies. Current data are limited to missions up to 180 d, which raises questions about how these trends change in long duration exploration missions. Further research is needed to confirm the trends identified in this study and identify possible countermeasures as humanity prepares for prolonged space missions.

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Post-COVID-19 Neurocognitive Screening in Routine Pilot Aeromedical Evaluations

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INTRODUCTION: One crucial aspect of flight safety is being able to detect medical or neuropsychological conditions during aeromedical examinations. However, subtle but safety-significant post-COVID-19 neurocognitive impairments may go unreported or undetected. The Trail Making Test (TMT) and Symbol Digit Modalities Test (SDMT) can detect these impairments in domains essential to pilot performance, though further investigation is needed to assess their effectiveness and clinical utility in routine pilot aeromedical examinations. This short communication presents preliminary findings for using these tests.

METHODS: A study identified the TMT and SDMT as appropriate screening tools for evaluating pilot neurocognitive performance after COVID-19. Mixed methods were then used to compare the screening tools' performance between post-COVID-19 cases and healthy controls, while also assessing their acceptability and feasibility in routine aeromedical examinations for pilots.

RESULTS: Post-COVID-19 neurocognitive disorders affect skills that are essential for pilot performance. Receiver operating characteristic curve analyses showed the diagnostic accuracy of the screening tests, with area under the curve values of 0.853 for TMT Part B, 0.817 for the SDC version of SDMT, and 0.769 for TMT Part A, indicating their effectiveness in identifying cognitive impairments. Airline pilots considered screening an important flight safety intervention.

DISCUSSION: Airline pilots, together with international aviation psychologists and aviation medicine experts, endorsed the safety-critical importance and value of screening pilots for post-COVID-19 impairments. Given the numerous practical implications of implementing such a strategy, we recommend that pilots be screened for potential post-COVID-19 neurocognitive impairments. A larger study is necessary to validate these preliminary findings and recommendations.

KEYWORDS: screening implications, pilots, post-COVID-19, aeromedical examinations.

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Acute COVID-19 survivors deal with post-COVID-19 conditions that affect their neurocognitive functioning, leading to impairments such as reduced working memory, poor concentration, and impaired situational awareness.[1] These cognitive deficits can impact pilots' performance, raising flight safety concerns. Civil aviation safety authorities acknowledge these long-term effects but have varying policies for detecting post-COVID-19 impairments and implementing risk mitigation strategies. Policies that rely on visible impairments during medical exams, or on proxies such as hospitalization for the acute phase of COVID-19 infection potentially miss pilots who had mild acute COVID-19 infections and self-managed or were treated in the community, who nonetheless have developed post-COVID-19 impairments. As the development of post-COVID-19 conditions, also known as Long COVID, is possible after each acute COVID-19 infection or reinfection, the number of likely impaired pilots will continue to rise.

A concern is that pilots may downplay or conceal mild neurocognitive deficits that nonetheless pose risks to flight safety. Studies have shown that pilots underreport medical conditions

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during aeromedical evaluations due to certification concerns.[2,3] Pilots may also experience cognitive dysfunction of which they are unaware following COVID-19 infection.[4] Situations where pilots are hesitant to disclose symptoms or are unaware of their impairments could have consequences for aviation safety, as standard medical examinations may not detect these impairments. Furthermore, while individual performance assessments may be sensitive to detect more severe impairments, emerging evidence indicates that there are likely persistent neurocognitive changes below the threshold for detection in acute COVID-19 survivors without subjective symptoms.[5] Thus, integrating quick and effective clinical neurocognitive screening tests into routine pilot aeromedical evaluations is crucial to mitigate potential flight safety risks secondary to post-COVID-19 neurocognitive impairments.

While we have previously identified the Trail Making Test (TMT) and Symbol Digit Modalities Test (SDMT) as potentially appropriate tests for identifying post-COVID-19 cognitive dysfunction,[6] confirmation and validation of our findings from larger pieces of research are still required. The main objective of this short communication is, therefore, to discuss the potential implications for routine aeromedical evaluations of pilots with post-COVID-19 conditions based on our preliminary findings.

METHODS

Initially, literature syntheses on pilot performance, post-COVID-19 conditions, and their long-term impacts, including screening tests relevant to assessing pilot cognitive performance post-COVID-19, were undertaken. A total of 13 neurocognitive screening tools were evaluated, with the TMT and SDMT identified as the most reliable for assessing deficits crucial to pilot cognitive performance and aviation safety.

Subjects

Following ethics approval from the University of Otago Human Ethics Committee (Reference Numbers H23/126/127), using mixed-methods, TMT parts A and B and the Symbol Digit Coding (SDC) version of the SDMT were compared between post-COVID-19 cases and healthy controls. Subjects in the age range of 18–65 yr old, with a history of acute COVID-19 infection, who had post-COVID-19 conditions signs and symptoms were included in the study. There were 48 participants who consented to participate. However, some informed the researchers that they could not undergo formal screening tests due to illness or symptom intensification during the rehearsal trial, resulting in 32 Long COVID participants completing the full screening test. Subjects who were seriously ill (unable to provide the required information) or had severe Post-Exertional Malaise Syndrome, which would make it unsafe to undergo the test during data collection, or who were unable to write and read were excluded from the study.

For the control group, anyone between 18–65 yr of age and who did not currently have any COVID-19 or post-COVID-19 related signs and symptoms was eligible to participate. A total of 23 healthy controls participated in the study. Six airline pilots between 21–65 yr of age who actively worked in airline flying operations and had no reported post-COVID-19 conditions were also included. All procedures complied with the ethical requirements of the Institutional Human Ethics Committee and the 1964 Declaration of Helsinki and its subsequent revisions or equivalent ethical standards. All participants who volunteered for the study signed an informed consent form before participation. Participants were self-selected based on their interests and availability.

Procedure

Participants first confirmed their eligibility and provided sociodemographic data, then completed an online supervised 5-min screening using the TMT and SDMT. The TMT consists of two parts: in Part A, participants are required to connect a series of encircled numbers from 1–25 in ascending order as quickly as possible. Part B of the TMT is similar, but involves connecting alternating encircled numbers (1–13) and letters (A–L) in both numerical and alphabetical order. In the SDC version of the SDMT, participants must match numbers to the corresponding symbols as quickly and accurately as possible using a symbol-number key displayed on a computer screen. Airline pilots were invited to complete an online survey and asked to provide feedback through a semistructured, brief, and anonymous questionnaire containing six questions specifically designed for this study. The questionnaire mainly assessed the acceptability and feasibility of the screening tests in routine aeromedical examinations. They also had the opportunity to share their experiences of participating in the screening test and their overall satisfaction with the screening session.

Statistical Analysis

The Mann-Whitney *U*-test was used to identify differences between the groups (cases and controls) in the distributions of screening test scores. Receiver operating characteristic curve analyses were performed to compare and evaluate the diagnostic accuracy of the screening tests using the area under the curve. The significance level for all analyses was set at 5%.

RESULTS

The initial literature synthesis identified a range of neuropsychological and neuropsychiatric effects of COVID-19, including both physical and mental fatigue, which can affect an individual's performance. Essential cognitive skills, attention, and executive functions, were found to be vital for pilot safe flying, indicating they should be part of routine aeromedical examinations due to their vulnerability to COVID-19's long-term impacts. Two screening tests, TMT

Table I. Area Under the Curve for TMT Parts A and B and the SDC Version of the SDMT.

				95% CONFIDENCE INTERVAL	
TEST RESULT VARIABLE(S)	AREA UNDER THE ROC CURVE	STANDARD ERROR	SIG.*	LOWER BOUND	UPPER BOUND
TMT-A total (ms)	0.769	0.067	0.001	0.638	0.900
TMT-B total (ms)	0.853	0.050	0.000	0.755	0.952
SDC-SDMT in 90 s	0.817	0.056	0.000	0.708	0.927

TMT: Trail Making Test; SDC: Symbol Digit Coding; SDMT: Symbol Digit Modalities Test; ROC: receiver operating characteristic.
*The significance (Sig.) level was 0.05.

and SDMT, were selected as being effective in assessing these critical cognitive skills for pilots, being quick, cost-effective, and easy for Aviation Medical Examiners (AMEs) to administer in different formats to prevent practice effects. Their objective nature can also help an AME identify subtle impairments and recommend possible further comprehensive neuropsychological evaluations in conjunction with flight simulators and real-world operations.

Preliminary evaluations showed that individuals with post-COVID-19 conditions performed significantly worse on the administered screening tests compared to healthy controls. The Mann-Whitney *U*-test confirming persistent cognitive impairments across administered screening tests, with a large effect size for TMT Part B [r = −0.59; Z = −4.43; $P < 0.001$] and the SDC version of the SDMT [r = 0.53; Z = 3.98; $P < 0.001$], and a medium effect size for TMT Part A [r = −0.45; Z = −3.37; $P < 0.001$]. The area under the receiver operating characteristic curve analysis yielded values of 0.853 for TMT Part B, 0.817 for the SDC version of the SDMT, and 0.769 for TMT Part A (all $P < 0.001$) (**Table I**). Feedback from pilots indicated strong support for these screening tests. They found the tests easy to understand and execute, encountering no challenges or technical difficulties while performing the tests, as the screening tests were neither burdensome nor time-consuming (**Fig. 1** and **Fig. 2**). They recognized the potential effectiveness of screening tests in identifying cognitive impairments and endorsed their

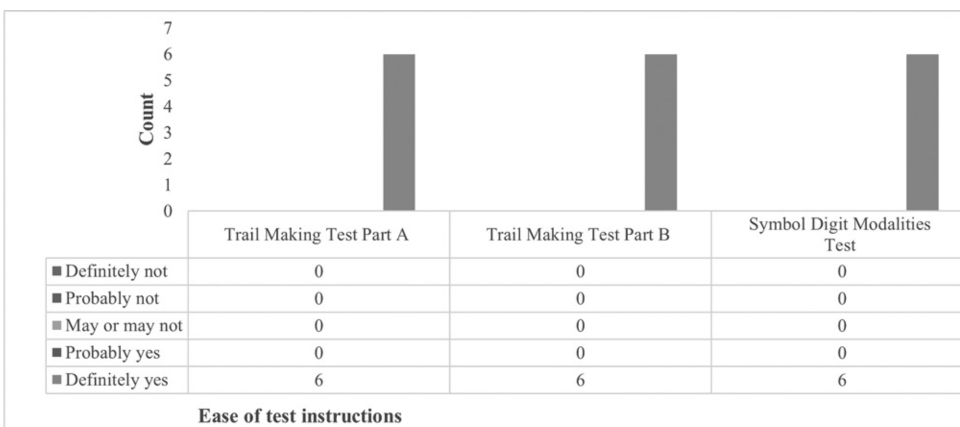

Fig. 1. Responses of participant airline pilots on whether the test instructions are easy to understand and follow.

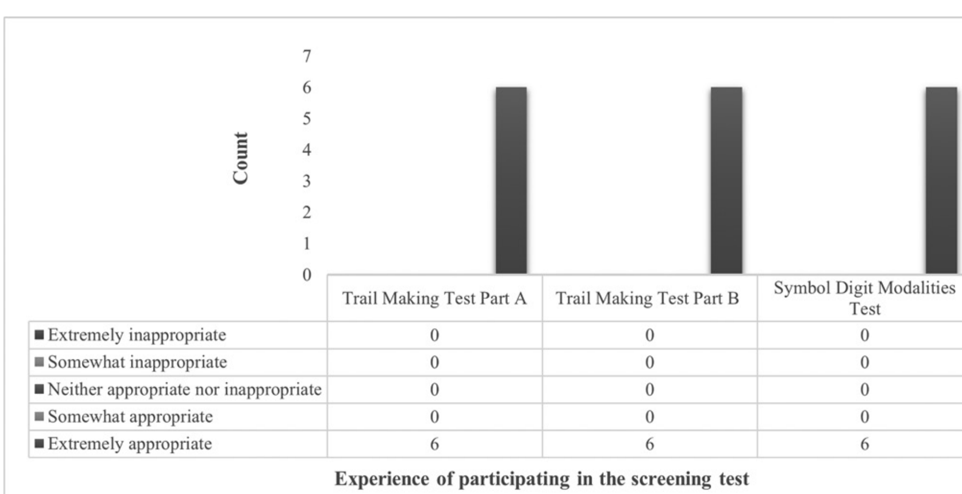

Fig. 2. Responses of participant airline pilots on their overall experience of taking part in the screening test session.

integration into routine evaluations as advantageous for pilots and the aviation sector.

DISCUSSION

This short communication highlights the need for routine universal screening for possible neurocognitive deficits in pilots infected with COVID-19. The main implications are that pilots could and should be screened. The aerospace scientific community should consider potential opportunities for more substantial research to validate the findings of our demonstration project. For instance, by establishing aircrew-specific norms, regulatory agencies could consider validating these tests for standard routine pilot aeromedical assessments, enhancing aviation safety and pilot health.

Post-COVID-19 neurocognitive impairments, including executive dysfunction and attention deficits, have been widely reported in both hospitalized COVID-19 survivors and those managed in the community.[7,8] These impairments can negatively affect pilot performance, underscoring the necessity for screening long-term neurocognitive effects resulting from COVID-19 with valid and reliable screening tools that are efficient and easy to apply. Routine medical certification examinations could be enhanced by testing to identify those pilots for whom additional performance information is required by triangulating with information available to the airline, such as simulator checks or in-flight operational performance evaluations. If the screening test indicates possible neurocognitive impairment that is inconsistent with normal performance on other parameters, further assessment would likely be unnecessary. This would reduce the need for referrals for costly and time-intensive neuropsychological assessments.

Our previous findings, based on existing literature and consultation with an international panel of experts in aviation medicine and aviation psychology, led to the selection of the TMT and SDMT as suitable screening tools for use in routine aeromedical evaluations.[6] They assess the cognitive skills crucial for pilot flight performance, focusing on attention and executive function domains. Evaluating and maintaining these cognitive functions in pilots is also a pivotal element of flight safety. These findings illustrate the applicability of incorporating the TMT and SDMT into regular aeromedical examinations to offer potential benefits with respect to enhancing flight safety and promoting pilots' well-being.

The preliminary findings of TMT and SDMT assessments concerning their discriminative accuracy among individuals with post-COVID-19 conditions compared to healthy controls demonstrate a performance difference in test scores, with the Mann-Whitney *U*-test revealing a statistically significant difference between the two groups. The nonnormal distribution of test scores and statistically significant differences suggest that some individuals who have experienced post-COVID-19 conditions face ongoing neurocognitive challenges. These findings indicate that TMT and SDMT are ideal tools for assessing COVID-19-associated neurocognitive impairment, aligning with recent research that reports these tools can detect cognitive impairments in post-COVID-19 conditions.[9,10]

Regulatory agencies and other stakeholders tend to take the view that simulator checks can detect cognitive impairment; however, it is not likely to be the most reliable method for detecting cognitive deficits. One reason for this is that simulator checks follow an established format and pilots can forecast the tasks they will perform or are asked to perform during simulator checks.[11] The second reason is that pilots are already skilled and practice the tasks that are going to be checked during simulator assessment; this allows them to maintain those skills and repeatedly perform tasks when they become stressed during testing. Moreover, overlearned skills may be retained during the early stages of cognitive impairment. There is also a risk that pilots with subtle but significant neurocognitive impairments who meet acceptable standards might pass simulator checks.

It is also important to recognize that screening may reveal impairments not solely related to post-COVID-19 neurocognitive issues. Factors such as alcohol use, medical conditions such as poorly controlled hypertension or early dementia, and temporary conditions such as fatigue or stress can also contribute to impairment. Aeromedical experts should consider these confounding factors when interpreting results and be cognizant of the need for comprehensive evaluations to accurately diagnose the cause of impairments.

During the assessment of the clinical utility of screening tests, evaluating their feasibility and acceptability in terms of time, practicability, technical resources, etc., is crucial.[12] Our preliminary evaluation of the clinical utility of the screening test indicates that the TMT and SDMT are practical to administer and have good usability in aeromedical screening examinations. Participating pilots found the test interface user-friendly and reported that the steps for test administration were easy to understand, remember, and follow. This positive reception suggests that implementing these screening tests as part of routine aeromedical evaluations for pilots could be an effective strategy to enhance flight safety, especially concerning post-COVID-19 neurocognitive impairments.

There are detailed neuropsychological batteries currently used in aviation settings, such as the CogScreen-Aeromedical Edition. However, in a routine aeromedical evaluation setting, such tests are likely to be overly demanding in terms of time and resources and unlikely to be cost-effective. They require administration by neuropsychologists, who are a scarce resource and would cause considerable waiting times for testing. In contrast, TMT and SDMT are simple, straightforward, and cost-free to use, and AMEs or Flight Surgeons can administer and interpret these tests in aeromedical settings, making them convenient, practical, and economical options.

Effective screening tests aim to minimize both false positives and false negatives by considering the tradeoffs between the accuracy of the tests and the potential impacts of errors on safety, operations, and pilot well-being. False positives (when a screening test incorrectly identifies a healthy pilot as having a condition) have consequences, such as stress, delays, and costs associated with unnecessary further evaluations and follow-up tests, including unnecessary treatments. False negatives (when a screening test fails to identify a condition in a pilot who actually has it) have their own impacts, including undiagnosed conditions that can lead to flight safety risks, compromising passengers, crew, and resources.

Further studies with large sample sizes are needed to validate these screening tests within a pilot population and to establish a normative dataset specific to aircrew. In addition, investigation of additional psychometric properties of these screening tests, such as their content and face validity, criterion validity, inter- and intrarater reliability and test-retest reliability in the pilot population, is warranted. Evaluating the risk-benefit ratio of screening thousands of healthy pilots with cognitive assessment tools is also crucial in moving forward, compared to the number of cognitive deficits identified.

In conclusion, the initial findings of our assessment have provided preliminary data suggesting that pilots could and should be screened for post-COVID-19 neurocognitive impairments, given the practical implications of implementing screening in routine aeromedical evaluations. To conduct further studies, funding and research support will now be sought from the aerospace medicine community, as our initial evaluations justified the need for a more comprehensive research study.

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Headache and Neurological Deficits with Cerebrospinal Fluid Lymphocytosis in a Helicopter Pilot

Emma L. Wetmore; Robert Haddon; Carrie E. Robertson; Clayton T. Cowl; Wiaam Y. Elkhatib; Ivan Garza

BACKGROUND: The syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis (HaNDL syndrome) consists of migraine-like headache episodes with >4 h of hemiparesthesia, dysphasia, and/or hemiparesis plus cerebrospinal fluid lymphocytic pleocytosis. While the rarity of HaNDL syndrome often precludes reassurance of the nature of this syndrome, it has consistently been identified as a benign condition that lasts no longer than 3 mo.

CASE REPORT: In the first week of a viral illness, a 29-yr-old male helicopter pilot experienced acute-onset "stumbling" when walking, "nonsensical speech," migraine-like headache, scintillating scotomata, and paresthesias of the tongue and bilateral extremities that lasted for 4–6 h. Work-up included lumbar puncture, revealing lymphocytic pleocytosis. A week later, he experienced word-finding difficulty, right-sided numbness/paresthesia, and severe occipital headache lasting 3 h. A third episode with sensory symptoms involving the tongue and right arm and leg occurred for a few hours 25 d after the onset of the first episode. Symptoms resolved spontaneously. A month following initial discharge, he denied symptom recurrence. Repeat lumbar puncture 4 mo later showed resolution of his pleocytosis. He was considered neurologically recovered 3 mo after symptom onset.

DISCUSSION: This patient's transient episodes were consistent with HaNDL syndrome. His symptom resolution involving three episodes within 25 d reflects the transient nature of this condition. It is critical to recognize HaNDL syndrome as a benign, monophasic disorder that resolves within a maximum of 3 mo so that future pilots with a recent history of HaNDL syndrome may safely and expeditiously return to work.

KEYWORDS: HaNDL, headache, transient, pilot.

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Pilots are required to maintain an acceptable level of health to ensure optimal performance during their occupational duties. Neurological conditions especially can significantly impact a pilot's ability to make quick decisions, react to shifting situations while flying, ensure proper coordination with flight controls, and maintain spatial awareness. Without these components, safe flight operation cannot be done and both personal and public safety risk increases. FAA regulations therefore mandate stringent neurological assessments for pilots, including medical history, neurological examinations, and neuropsychological testing, if necessary. Conditions of high concern include cerebrovascular disease, seizure disorders, traumatic brain injuries, and degenerative nerve disease.

The syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis (HaNDL syndrome) consists of migraine-like headache episodes with >4 h of hemiparesthesia, dysphasia, and/or hemiparesis plus cerebrospinal fluid lymphocytic pleocytosis. While the rarity of HaNDL syndrome often precludes reassurance of the nature of this syndrome, it has consistently been identified as a benign condition that lasts no longer than 3 mo.

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CASE REPORT

A 29-yr-old male helicopter pilot presented to an Aviation Medical Examiner (AME) due to concern for multiple episodes of transient neurological symptoms complicating his ability to return to work. He sought renewal of an FAA Class II Medical Certificate. This patient experienced three distinct neurological episodes confined within a 25-d time period 3 mo before presenting to our service and, thereafter, remained completely asymptomatic. This started with a viral illness involving fatigue and a bilateral occipital headache that followed familial viral exposure. He experienced an acute onset of “stumbling” when walking, “nonsensical speech,” a severe headache, and paresthesias of his whole tongue and bilateral upper and lower extremities 2 d later that lasted for 4–6 h. The headache was associated with scintillating scotomata in his visual fields, photophobia, phonophobia, nausea, and vomiting. He was fully aware and oriented during this episode. He presented to the emergency department where he was afebrile and his vitals were stable. He was admitted to a neuro-ICU for 1 night for further workup and monitoring. He had a head CT without contrast, head and neck CT angiogram with contrast, and brain MRI without contrast that were unremarkable. A routine EEG was notable for mild diffuse slowing with focal slowing in the left frontotemporal and central head region. He had a lumbar puncture notable for 171 nucleated cells/mcL (normal 0–5 cells/mcL) with predominant (93%) lymphocytes (normal 40–80%), 3 red blood cells (normal 0 red blood cells), 88 mg · dL^{-1} protein (normal 0–35 mg · dL^{-1}), and 65 mg · dL^{-1} glucose (normal approximately 67.2 mg · dL^{-1} based on a serum glucose of 112 mg · dL^{-1}) with a negative gram stain and no growth on bacterial or viral cultures. He did have extensive laboratory work-up notable for a negative toxicology screen, a negative respiratory viral panel, a pan-negative bacterial and viral cerebrospinal fluid (CSF) polymerase chain reaction (PCR) panel [including CSF cytomegalovirus (CMV), herpes simplex virus 1 and 2 (HSV1, HSV2), human herpes virus 6, and varicella zoster virus], and a serum CMV IgG >8.0 AI (normal <0.9 AI) and IgM 3.6 AI (normal <0.9 AI). He was loaded with levetiracetam and started on acyclovir and antibiotics for central nervous system coverage for presumed meningitis/encephalitis due to his lymphocytic pleocytosis. He was discharged the following day on levetiracetam 750 mg BID out of an abundance of caution due to not all testing being returned. Due to this hospitalization, he was placed on short-term disability from his job as a pilot pending future evaluation of his ability to fly.

A week after discharge, he experienced a similar episode with word finding difficulty, numbness/paresthesias on his right side, and a severe occipital headache lasting 3 h. This headache was associated with photophobia, phonophobia, and nausea. He again presented to the emergency department and was admitted to the hospital for 2 d. He had a repeat head CT and brain MRI without contrast which were unremarkable. However, a head and neck CT angiogram (CTA) with contrast did show mild asymmetric decrease in caliber and opacification of the M2 and M3 branches of the anterior temporal segment of the left middle cerebral artery, suggestive of possible anatomic variation vs. vasculitis. A 24-h video EEG was unremarkable. He was tapered off levetiracetam and started on topiramate for presumed “complicated migraines.”

About a week later, during a period of stress and physical exertion, he experienced a third episode involving only numbness/paresthesias of the tongue, right arm, and right leg. His symptoms resolved within hours with no medical intervention. His topiramate was briefly increased to 75 mg daily, although due to side effects, including restlessness, this medication was ultimately discontinued.

A few days later, he saw the aforementioned AME regarding his return to work as a pilot. At the time, he denied recurrences of his episodes. An epileptologist was then electronically consulted for his opinion on the case. He expressed skepticism that the cause of his symptoms was exclusively migraine, seizure, or viral encephalitis due to the quick resolution of symptoms without significant intervention. This provider postulated that his symptoms could be secondary to the Headache and Neurological Deficits with cerebrospinal fluid Lymphocytosis (HaNDL) syndrome. He was then referred to an American Board of Psychiatry and Neurology-certified neurologist and United Council for Neurologic Subspecialties-certified headache specialist to weigh in on the possible contribution of migraine headaches to his symptoms. He was seen by this headache specialist 1 mo later. The patient reported that at baseline, he experienced occasional mild, dull, holocephalic headaches that were triggered by stress or lack of sleep. He stated that he did not need medication for these headaches as they were not bothersome. This headache specialist suspected his symptoms would likely prove to be secondary to HaNDL syndrome. He recommended follow-up with a cerebrovascular neurologist for his prior CTA findings of mild left middle cerebral artery (MCA) attenuation, consultation from an infectious disease specialist for his positive CMV serology, and obtaining a paraneoplastic panel for possible autoimmune causes of his symptoms. This panel was remarkable for a mildly elevated GAD65 antibody at 0.05 nmol · L^{-1} (normal <0.02 nmol · L^{-1}).

The patient saw a cerebrovascular neurologist 3 mo after his first episode for his CTA findings of mild left MCA attenuation possibly suggestive of vasculitis. A repeat MRI of the brain was performed which showed normal MCA caliber without vessel enhancement. Due to his lack of symptoms for 3 mo, it was believed that vasculitis was not a likely cause of his symptoms. Additionally, an infectious diseases specialist was consulted for his positive CMV serology, who concluded that his initial viral symptoms a month prior to his hospitalization could have represented an acute CMV infection, but was not a clear cause of his presenting complaints, especially due to his negative CSF CMV PCR. Further, around this time, the patient also saw an autoimmune neurologist for his GAD65 antibody positivity. Due to his low GAD65 antibody titer, it was believed that this was an unlikely cause of his neurological symptoms.

Repeat lumbar puncture 4 mo after his initial symptom onset showed resolution of his pleocytosis, with 2 total nucleated cells/mcL (normal 0–5 cells/mcL), 41 mg · dL^{-1} protein (normal 0–35 mg · dL^{-1}), and 52 mg · dL^{-1} glucose, with unremarkable CSF autoimmune encephalitis panel, Ma2 antibody, myelin oligodendrocyte glycoprotein antibody, oligoclonal bands, CMV PCR, flow cytometry, and bacterial culture. His AME considered him fit to return to his job as a pilot at this time, and the AME applied for reinstatement of his aeromedical certification under Special Issuance. This was granted 4 mo later on Special Issuance with required follow-up visits with his neurologist every 6 mo. At two consecutive follow-up visits with the headache specialist that occurred 6 mo and 13 mo after his initial onset of symptoms, the patient had a normal neurological exam and denied any additional headaches or transient episodes with neurological symptoms. A few months after his second uneventful neurology follow-up and 16 mo after his initial neurological clearance, his full unrestricted Class II FAA medical certificate was granted. He continues flying helicopters without issue.

DISCUSSION

The above description of the patient's transient episodes of headache and neurological deficits with subsequent extensive and unremarkable laboratory and imaging workup is consistent with HaNDL syndrome. According to the current International Classification of Headache Disorders (ICHD-3), HaNDL consists of migraine-like headache episodes that are associated with >4 h of hemiparesthesia, dysphasia, and/or hemiparesis, as well as cerebrospinal fluid lymphocytic pleocytosis (>15 white blood cells per microliter) not better accounted for by another ICHD-3 diagnosis.[1] The differential diagnosis for HaNDL syndrome is broad and warrants a thorough neurological evaluation to rule out such serious conditions as stroke, seizure, meningoencephalitis, and/or paraneoplastic disease. Common tests for the evaluation of patients presenting with possible HaNDL syndrome include neurovascular brain imaging, EEG, and CSF analysis.[2]

Interestingly, our patient reported symptoms of a viral illness in the days immediately before his presentation and shortly after his children in daycare had been ill. Further, he had a positive CMV serology (both IgG and IgM) at his initial presentation; however, he notably had a negative CMV PCR in his CSF. Multiple prior case reports have indicated that there is a possible link between HaNDL syndrome and viral illnesses. This was first postulated in 1983[3] and has since expanded to include possible links between HaNDL and CMV,[3,4] human herpes virus 6,[5] and Epstein-Barr virus.[6] Notably, it does not seem that cases are clustered in particular times of the year when certain viral illnesses may be more common.[7,8] It has been postulated that viral illnesses may lead to symptoms associated with HaNDL syndrome due to viral-induced immune system dysfunction, causing an aseptic inflammation that irritates the cerebral vasculature.[4,6] It should also be noted that there have been three reported cases of an association of HaNDL syndrome with channelopathies, including CACNA1H.[9,10] The patient described in this report did not have testing for such a condition and clinically is not currently part of the criteria for diagnosis of HaNDL syndrome. Upon literature review, it does appear that cases of HaNDL syndrome associated with the CACNA1H channelopathy, to the best of our knowledge, resolve in less than 3 mo, which is consistent with other known cases of the condition.

While chronic conditions could result in denial of a pilot's ability to safely operate an aircraft and receive medical certification, the pilot described above underwent extensive neurological evaluation for his symptoms and was determined to have HaNDL syndrome. HaNDL syndrome is a benign, monophasic disorder that does not recur after 3 mo.[11] Literature has consistently documented the brevity of this syndrome, which includes case series from Berg et al. and Gómez-Aranda et al., which cumulatively reported 90 patients who stopped having episodes within 90 d of initial symptom onset.[7,8] Unfortunately, the rarity of this condition often precludes recognition of the brevity of the syndrome. Accordingly, we recommend a stand-down time of 3 mo given the safety-sensitive nature of aviation-related operations. We hope that this case report outlines the importance of recognizing HaNDL syndrome as a benign, monophasic disorder that lasts for a maximum of 3 mo, so that future pilots with a recent history of HaNDL syndrome may safely and expeditiously return to work.

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Pachychoroid Neovasculopathy, Intravitreal Injection, and Implications for Aeromedical Decision Making

Wei Yun Lily Yang; Isaac Wei Jie Chay; Hou Boon Lim; Marcus Chiang Lee Tan; Brian See; Jason Weizheng Low

BACKGROUND: Optimal visual function is essential in aviation to ensure flight safety and mission effectiveness. Pachychoroid neovasculopathy is a relatively recently recognized clinical entity of choroidal neovascularization, belonging to the pachychoroid spectrum, for which intravitreal therapy (IVT) is the standard of care. The main aeromedical considerations are degradation of visual function from disease progression, which could preclude aircrew from flying duties, and the compatibility of IVT with flying.

CASE REPORT: A trained Republic of Singapore Air Force aircrew operator on board the Fokker-50 first presented with a reduction in visual acuity at his annual aircrew medical examination, for which he was restricted from flying duties for further evaluation. He was diagnosed with central serous chorioretinopathy and treated conservatively, but subsequently developed pachychoroid neovasculopathy. He was started on monthly IVT for 3 mo before being placed on a treat-and-extend regimen. After 10 mo of treatment totalling five doses of aflibercept IVT, he achieved resolution of subretinal fluid and recovery of visual acuity, stereopsis, and color vision. He was returned to flying duties upon full recovery, with a close follow-up regimen with his attending ophthalmologist and flight surgeon.

DISCUSSION: Pachychoroid neovasculopathy can cause degradation of visual function and visual incapacitation, posing differential threats to flight safety and mission success based on an aircrew's vocational roles. The aviation environment could also influence disease progression. Furthermore, aeromedical considerations for IVT are increasingly relevant as IVT becomes the standard of care for prevalent conditions, including neovascular age-related macular degeneration and diabetic macular edema.

KEYWORDS: central serous chorioretinopathy, intravitreal therapy, anti-vascular endothelial growth factor, flight safety, fitness for flying, aviation medical standards.

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Pachychoroid disease is a relatively recent term describing an increase in the choroidal thickness due to dilatation of the large outer oval choroidal vessels (Haller's layer) and compression of the smaller inner choroid vessels in the choriocapillaris and Staller's layer.[1] Disease entities within the pachychoroid spectrum include pachychoroid pigment epitheliopathy, central serous chorioretinopathy (CSCR), pachychoroid neovasculopathy (PNV), and polypoidal choroidal vasculopathy (PCV). CSCR typically affects middle-age men with a type A personality who work in high stress environments; moreover, with an annual incidence of 9.9–27 per 100,000 men,[2] it is therefore expected to be relatively common among military aircrew. PNV itself is postulated to be a late complication in patients with chronic CSCR, who subsequently develop type 1 choroidal neovascularization (CNV) due to longstanding retinal pigment epithelium (RPE) dysfunction and serous pigment epithelial detachment (PED)[3].

The primary aeromedical concerns of PNV relate to visual incapacitation from poor quality of vision, as well as treatment considerations with intravitreal therapy (IVT). Aeromedical

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considerations for IVT are increasingly relevant as IVT becomes the standard of care for prevalent eye conditions, including neovascular age-related macular degeneration (AMD), diabetic macular edema, and central retinal vein occlusion. Moreover, there exist factors in the aviation environment, such as gas expansion with hypobaria that could interact with air bubbles or subretinal fluid (SRF). Although these physiological extremes are typically inevitable in flying operations, the effects of IVT on aeromedical risk should be deliberated vis-à-vis operational requirements.

CASE REPORT

The aviator was a 44-yr-old man, a trained Republic of Singapore Air Force (RSAF) nonpilot operator on the Fokker-50 platform. He had a history of right eye stable and left eye progressive keratoconus, for which he underwent a single session of left eye corneal cross-linking in January 2015. He was returned to flying duties after demonstrating good and stable vision with the aid of spectacles. He was a nonsmoker and did not report the use of regular medications, including exogenous steroids, phosphodiesterase inhibitors, or antiarrhythmics.

The aviator was first diagnosed with left eye acute CSCR by his attending retina specialist in August 2022. Spectral domain optical coherence tomography (SD-OCT) of the macula revealed neurosensory detachment at the fovea with SRF and a small serous PED **(Fig. 1)**. His best corrected visual acuity (BCVA) was otherwise normal and met prescribed visual standards then, and he was visually asymptomatic. As this was his first episode of CSCR, his retina specialist opted to manage him conservatively with observation. He was also on follow-up with a corneal specialist for bilateral keratoconus. Corneal topography and refractive error were stable after cross-linking and he was planned for fitting of new rigid gas permeable contact lenses.

He was subsequently noted at his annual aircrew medical examination in November 2022 to have a reduction in his BCVA of 0.30 LogMAR (20/40 Snellen) in the left eye. The right eye BCVA with contact lenses was 0.00 LogMAR (20/20 Snellen). Ishihara, Titmus, and Amsler grid testing were unremarkable. Rabin cone contrast test scores were 95 (protan), 100 (deutan), and 100 (tritan) in the left eye, and 100 for all three cones in the right eye. A dilated fundus examination revealed presence of mottling at the macula with no macular hemorrhage. The right eye was normal on clinical examination. On review with a flight surgeon, he reported no visual complaints in the preceding months, with no central scotoma, micropsia, reduced contrast sensitivity, or metamorphopsia on Amsler grid testing. He reported no difficulties with ground duties, driving, and activities of daily living. He was restricted from flying duties for further evaluation and treatment.

At the follow-up review with his retina specialist in February 2023, dilated retina examination revealed a focal PED at the macula with no macula hemorrhage or drusen **(Fig. 2A)**. SD-OCT revealed almost full resolution of the SRF, but persistence of the subfoveal PED. Notably, interval development of intraretinal fluid was seen, suggestive of choroidal neovascularization **(Fig. 2B).** Fluorescein angiography did not demonstrate much hyperpermeability, but indocyanine green angiography (IGCA) showed late staining network plaque, indicating a

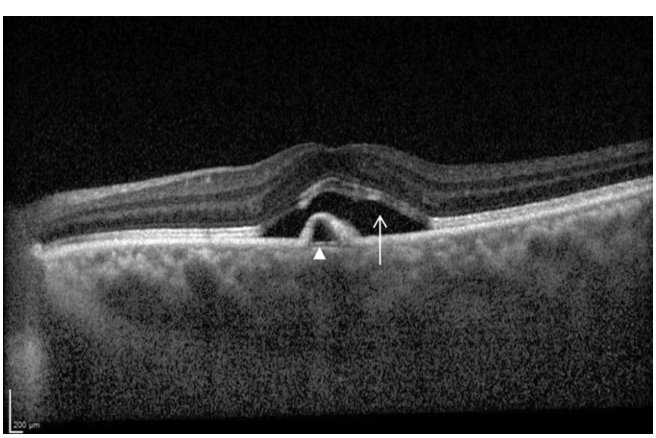

Fig. 1. Spectral domain optical coherence tomography of the left eye at first presentation in August 2022 showing neurosensory detachment with subretinal fluid (arrow). There is a small serous pigment epithelial detachment (arrowhead).

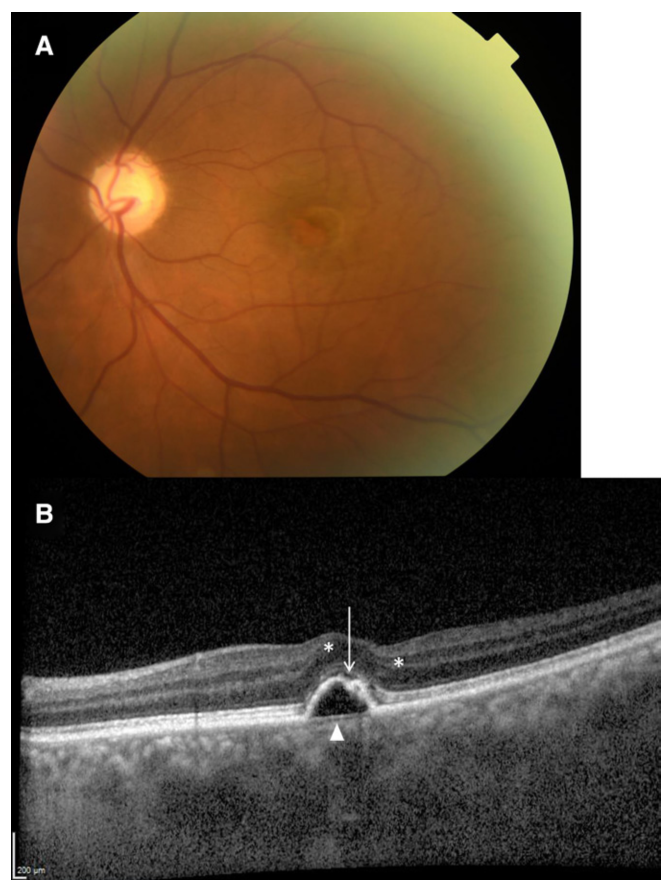

Fig. 2. Findings of the left eye in February 2023, including A) color fundus photograph showing pigment epithelial detachment without drusen, and B) spectral domain optical coherence tomography demonstrating a sliver of subretinal fluid (arrow), subfoveal pigment epithelial detachment (arrowhead), and intraretinal fluid suggestive of neovascularization (asterisks).

neovascular choroidal network. Based on these findings, he was diagnosed with PNV and started on monthly aflibercept IVT treatment for 3 mo before being placed on a treat-and-extend regimen.

Subsequent specialist review in July 2023 showed stable SRF, PED, and intraretinal fluid on OCT **(Fig. 3A)**. During this period, BCVA in the left eye improved to 0.176 LogMAR (20/30 Snellen). However, stereopsis worsened, fluctuating between 60–100 arcsec on Titmus testing. The IVT treatment interval was extended to 10 wk. The flight surgeon extended the flying restriction for an additional 6 mo in July 2023 to allow time for stabilization of the patient's PNV, adding that he should be considered for return to flying duties after: 1) adequate disease control, 2) recovery of visual function, and 3) no complications of treatment.

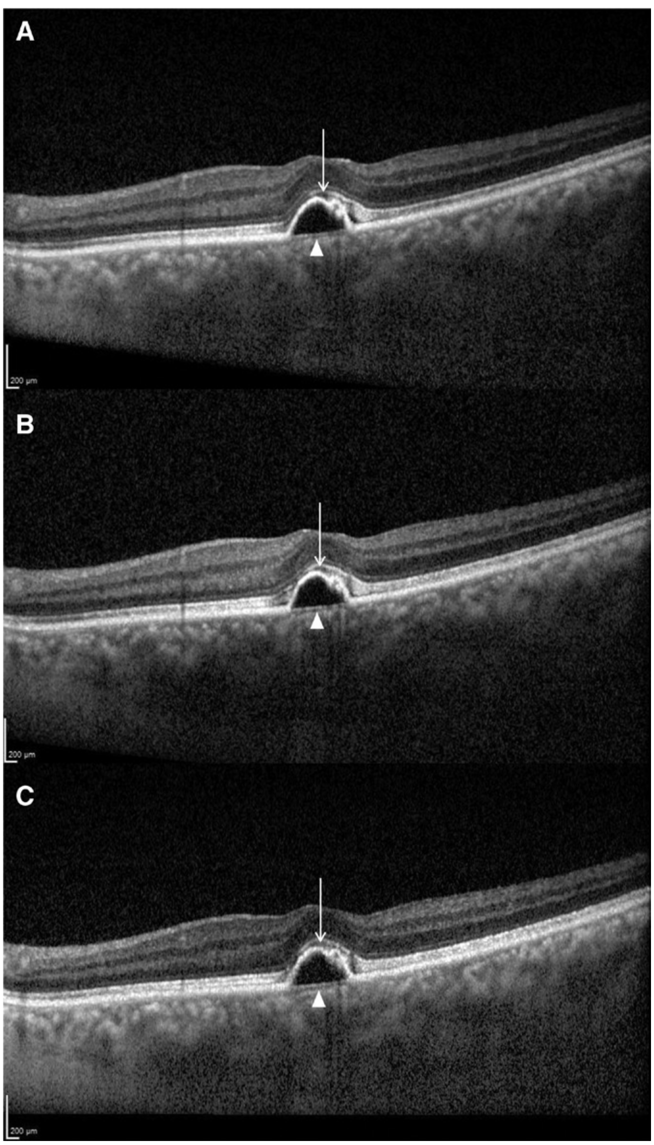

Fig. 3. Spectral domain optical coherence tomography of the left eye in A) July 2023, B) September 2023, and C) December 2023 showing a stable sliver of subretinal fluid (arrow) and subfoveal pigment epithelial detachment (arrowhead).

At the next follow-up with his retina specialist in September 2023, SD-OCT revealed stable findings **(Fig. 3B)**. Given that the SRF remained stable, the IVT interval was extended from 10 wk to 3 mo. The subsequent review in December 2023 revealed stable findings on SD-OCT **(Fig. 3C)** and the aviator continued to remain asymptomatic. LogMAR BCVA tested with new rigid gas permeable contact lenses was 0.04 (20/22 Snellen) in the left eye and 0.02 (20/21 Snellen) in the right eye with monocular testing, and 0.00 (20/20 Snellen) with binocular testing. Stereopsis improved to 40 arcsec on Titmus testing. Humphrey visual fields, Ishihara, Amsler grid, and extraocular movements were normal. Rabin Cone Contrast Test scores were 85 (protan), 90 (deutan), and 90 (tritan) in the left eye, and 95 (protan), 90 (deutan), and 95 (tritan) in the right eye. Slit lamp examination revealed a well-fitted rigid gas permeable contact lens in both eyes, with no complications of keratoconus. His attending retina specialist held off the scheduled IVT on the day of review, swapping him from a treat-and-extend to an as-necessary regimen with plans for an earlier follow-up visit, given that his PNV remained quiescent with good BCVA. The utility of photodynamic therapy (PDT) to achieve disease resolution with the aim of reducing the need for future IVT was discussed with his retina specialist advising against it, in view of possible complications of choroidal ischemia and RPE atrophy.

His disease remained stable and visual function had recovered to an extent that met prescribed visual standards in January 2024. Hence, he was returned to unrestricted flying duties with regular follow-ups with his attending flight surgeon and retina specialist, and daily home Amsler testing. Moreover, a 24-h duties-not-involving-flying (DNIF) period was imposed after each subsequent IVT, if required. DNIF refers to nonflying tasks undertaken by aircrew, such as ground operations. He was also advised to self-monitor for complications following his IVT.

DISCUSSION

PNV is a relatively recently recognized clinical entity of the pachychoroid spectrum, first described as a form of type 1 CNV, occurring over areas of choroidal thickening and choroidal vessel dilatation.[3] Its pathogenesis has not been fully understood and could be related to pachychoroid-induced choriocapillaris ischemia and RPE dysfunction,[3] although it may have a separate angiogenic mechanism from AMD.[4] PNV affects younger patients, lacks drusen, and has lower intraocular vascular endothelial growth factor (VEGF) levels compared to neovascular AMD.[1,5,6] PNV is also distinct from other conditions on the pachychoroid spectrum. Although there are no established diagnostic criteria for PNV, attempts have been made to better define this entity; PNV tends to demonstrate choroidal vascular hyperpermeability on IGCA, as well as RPE anomaly and dilated choroidal vessels below the CNV.[7] In contrast, PCV demonstrates early subretinal hyperfluorescence on IGCA and is also diagnosed by other clinical and angiographic features based on the EVEREST criteria, including abnormal vascular channels supplying the polyps.[8] Nevertheless, PNV has also been described to develop polypoidal lesions and progress into PCV.[9] Multimodal imaging, including fundus examination, SD-OCT, OCT angiography, fluorescein angiography, and ICGA, is used to diagnose PNV and monitor its treatment progress.[7]

In terms of treatment, intravitreal anti-VEGF has demonstrated similar efficacy in addressing central macular thickness and BCVA in both PNV and neovascular AMD.[6] Interestingly, IVT confers significantly greater improvement in subfoveal choroidal thickness,[6] fewer injections (4.2 vs. 4.9, $P = 0.031$), longer treatment-free period (6.1 vs. 4.3 mo, $P = 0.006$), and lower retreatment rate (59.1% vs. 80.9%, $P = 0.018$) after the loading dose in PNV.[10] A hypothesis linking the lower dependence on IVT could be the lower intraocular VEGF concentration in PNV.[5] Regarding choice of anti-VEGF agent, aflibercept was found to be superior to ranibizumab in reducing subfoveal choroidal thickness (−35 μm vs. −9 μm, $P = 0.013$) and achieving SRF resolution (82.6% vs. 51.6%, $P = 0.018$).[11]

Moreover, there appears to be a therapeutic role of PDT, either alone, or adjunctive to anti-VEGF. PDT reduces choroidal thickness by inducing choroidal hypoperfusion. Half-dose PDT alone enables SRF resolution in 96.9% of eyes, with no significant differences compared to IVT.[12] In PNV refractory to loading doses of IVT, adjunctive PDT enabled complete fluid absorption in 85.7–86.7% of cases,[12] and could reduce dependence on IVT in the maintenance phase.[13] Notwithstanding, potential risks of PDT include choroidal ischemia, RPE atrophy, and choroidal neovascularization.

In aviation, optimal visual function is essential. Good visual acuity, stereopsis, color discrimination, ocular alignment, and intact visual fields contribute to safe and effective operation of an aircraft and its onboard systems. As such, strict visual requirements are typically imposed on aircrew, and these are evaluated at annual aircrew medical examinations by both military and civil aviation authorities.

Aeromedical considerations specific to PNV relate to risk of subtle incapacitation from substandard visual acuity, poor contrast sensitivity, poor stereopsis, metamorphopsia, and micropsia. Moreover, complications of PNV, including progression into PCV and development of subretinal hemorrhage (SRH), could cause acute visual incapacitation.

The aviation environment could, conversely, influence the underlying disease process. Hypobaric hypoxia may contribute to the pathogenesis of PNV. Choroidal vessels are unique in that autoregulation is absent and that blood flow does not increase in hypoxemia. Systemic hypoxia causes a fall in choroidal oxygen partial pressure, resulting in reduced oxygen delivery to the outer retina, potentially worsening the preexisting choriocapillaris ischemia and RPE dysfunction present in eyes with pachychoroid, further driving the angiogenesis process.[3] Pachychoroid effects have also been demonstrated on enhanced depth imaging SD-OCT, which showed a reversible increase in central choroidal thickness (baseline = 271 ± 9 μm; altitude = 288 ± 9 μm) following hypobaric exposure to 14,957 ft (4559 m).[14]

Aeromedical considerations of treatment relate to their side effects, expected duration of treatment, and compatibility with flying. IVT could inadvertently introduce air bubbles into the vitreous, which expand during hypobaria as described by Boyle's law. The changes in air meniscus appearance from air expansion could be a source of distraction during flying. The risk of residual air bubbles following IVT is about 11.3%, although most air bubbles (94.9%) resolve by 48 h.[15] Moreover, should the eye's compensatory mechanisms, including choroidal compression, scleral expansion, and accelerated aqueous outflow, fail to accommodate expansion of the intraocular air bubble, raised intraocular pressure could result in ocular discomfort and even visual incapacitation from acute glaucoma and corneal decompensation. Lastly, intraocular air bubbles exert optical effects. Light scatters on the vitreous-air bubble interface and, due to large differences in refractive index between the air and the crystalline lens, the posterior lens becomes strongly refractive. Myopic shift has also been demonstrated following intravitreal gas injection,[16] which could affect visualization of cockpit and radar displays and near target acquisition. Other complications of IVT include endophthalmitis, retinal detachment, and intraocular hemorrhage, which are very rare but potentially visually incapacitating.

Concerns specific to the aviator relate to his reduced BCVA and stereopsis, which could affect missions with high visual demands. The presence of SRF on his initial OCT also indicated active disease, which could lead to suboptimal and fluctuating visual acuity. While PNV could progress into SRH as a complication, he presented with a relatively good BCVA of 0.30 LogMAR (20/40 Snellen) without the presence of polypoidal lesions or SRH on OCT, which were favorable prognostic factors. He was started on aflibercept IVT, which demonstrated good efficacy at controlling disease activity as evidenced by improvement of SRF and intraretinal fluid. A 12-mo treat-and-extend regimen of aflibercept IVT enabled improvements in LogMAR BCVA from 0.50–0.30 in one study (20/63–20/40 Snellen),[10] and from 0.45–0.26 in another (20/56–20/34 Snellen).[11] Following 10 mo of aflibercept, the aviator's LogMAR BCVA showed an even better improvement from 0.30–0.00 (20/40–20/20 Snellen). In terms of achieving remission, after a 3-mo loading dose of aflibercept, studies have demonstrated complete SRF resorption in most eyes (82.6%),[11] and cessation of IVT in 59.1% of eyes.[10] On average, eyes with PNV required 4.2 doses of IVT to achieve treatment-free remission.[10] Comparatively, the aviator required slightly longer duration (5 additional months) and marginally more doses of IVT (0.8 additional doses) to achieve remission.

In terms of treatment-specific considerations, the aviator was swapped from a treat-and-extend IVT regimen to an as-necessary regimen in December 2023. He was returned to unrestricted flying duties in January 2024, with a 24-h DNIF period after each subsequent IVT following deliberation of multiple factors. One, the relatively low frequency of residual air bubbles following IVT, most of which resolve by 48 h. Two, the clinical and optical effects of intraocular gas expansion, which can range from visual distraction to incapacitation.

These effects are likely size dependent and the volume of air bubbles introduced following IVT is also unlikely to be as large as those following pars plana vitrectomy. Three, the time to presentation of other complications, such as endophthalmitis (4.3 ± 3 d, range = 1–15 d),[17] which could guide expected duration of return to flying. Four, the need for IVT retreatment could preclude deployment to austere environments, which lack access to advanced care for IVT-related complications. The aviator was also a nonpilot aircrew with some role redundancy built into his flying duties, and it was felt that a 24-h DNIF period post-IVT would reasonably allow for resolution of significant residual air bubbles and monitoring of complications while minimizing unnecessary delay to flying. In addition to self-monitoring for complications that might present following completion of the DNIF period, the aviator was recommended to inform his attending flight surgeon should there be deployment plans while still on IVT.

While PDT has shown therapeutic efficacy in PNV, it was not considered for the aviator as the risks were assessed to outweigh the benefits. Complications of choroidal ischemia and RPE atrophy could result in permanent visual defects, which would be incompatible with flying. Moreover, the aviator had been responding well to IVT, with stable BCVA and near complete SRF resolution.

At the time of writing, only the U.S. Federal Aviation Administration has articulated guidelines on the aeromedical disposition of aircrew on IVT, and recently considered special issuance for aircrew receiving IVT for the treatment of early and stable exudative AMD.[18] Approved agents include aflibercept, pegaptanib, and ranibizumab. Aircrew require an initial observation of 2 wk, thereafter a 24-h DNIF period after each injection, and self-monitoring for adverse effects. Aircrew experiencing adverse visual changes or side effects are recommended against flying. No other civil or military aviation guidelines are currently available through open source.

Other considerations for aeromedical risk assessment of IVT are vocation- and platform-specific. Visual incapacitation can compromise mission effectiveness regardless of vocation

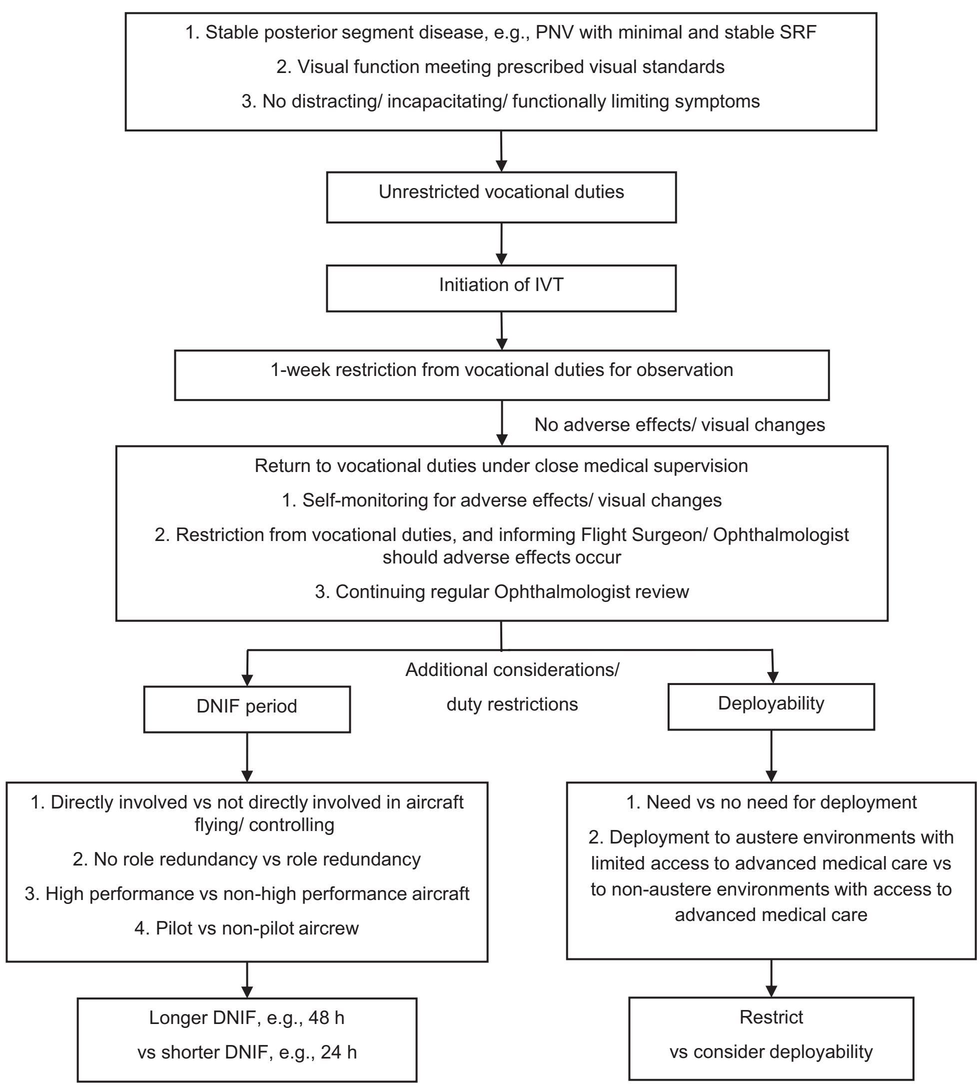

Fig. 4. Aeromedical-decision framework, where the aeromedical disposition of aircrew with posterior segment conditions requiring IVT but meeting the prescribed vision requirements are concerned.

and platform. Generally, a higher level of aeromedical risk is tolerated for nonpilot aircrew, who are not directly involved in flying the aircraft. Moreover, role redundancy built into a role could mitigate impact on mission-critical roles by enabling takeover of these duties should visual incapacitation occur. As in this aviator's case, monocular vision loss results in loss of stereoacuity. However, the extent of incapacitation could be mitigated, depending on the visual requirements of his duties and presence of suppression of the worse eye. Conversely, the risk tolerance would be lower for pilots, and may necessitate stricter requirements, such as a longer period of observation following IVT for reassurance of stability, particularly for single-pilot operations (e.g., high performance military aircraft). In commercial large airline operations, aeromedical risks of IVT may be mitigated by the additional safeguard of a copilot.

If the aviator were to operate high performance aircraft, additional factors of high $+G_z$ acceleration should be considered. A single case report described an F-15 pilot who underwent a $+9\ G_z$ centrifuge profile between episodes of CSCR without worsening of visual function or SRF.[19] However, there have been no case precedents of RSAF aircrew flying high performance aircraft while on IVT or having SRF. Future research is needed to explore the relationship between G exposure and intraocular hydrostatic pressure dynamics.

IVT is an effective treatment of PNV and remains the primary therapeutic approach for several other posterior segment conditions, including diabetic macular edema and neovascular AMD. While these tend to affect older patients, it remains relevant in the commercial and private flying license setting in which older aircrew with a higher likelihood of developing such eye conditions, and consequently requiring IVT, operate. It is thus timely for medical personnel and regulatory bodies to gain an understanding of the aeromedical considerations and implications of such a treatment modality.

Based on the aeromedical considerations discussed, we propose an aeromedical decision framework to guide clinical decision-making where aeromedical disposition of aircrew with posterior segment conditions requiring IVT is concerned **(Fig. 4)**. A 1-wk duty restriction could be used following initiation of IVT, for which return to vocational duties thereafter would be considered with appropriate risk mitigation measures. Additional duty restrictions, including a DNIF period and deployability, could be considered based on vocation-, platform-, and task-specific factors.

PNV is a recently described clinical entity belonging to the pachychoroid spectrum. Studies relating to the interaction of disease and treatment within the aviation environment are limited. Nevertheless, a holistic evaluation of the disease characteristics and treatment options, as well as vocation and platform, should continue to guide aeromedical risk assessment in aircrew with pachychoroid disease. Deliberation of compatibility of IVT with flying is essential, given that IVT has been the standard of care for several eye diseases of epidemiological significance. In view of the 1) favorable therapeutic response to IVT, 2) potential for good visual recovery, and 3) low risk of IVT-related complications in the aviation environment, it can be considered reasonable to return certain aircrew with stable posterior segment conditions to flying duties with a suitable DNIF period following each IVT.

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Therapeutic and Diagnostic Perspectives for Advancing Spaceflight Dermatology

Julian Henke; Sana Kamboj; Devon Barrett; Hala Idris; Ameya Gangal; Travis Blalock

INTRODUCTION: As international efforts in space exploration continue, spaceflight dermatology is a critical field for ensuring the health of astronauts. Microgravity, limited hygiene, and radiation uniquely impair skin integrity, contributing to issues such as dermal atrophy, xerosis, and increased infection risk during spaceflight. This commentary highlights practical strategies and potential research avenues for preventing and addressing the array of dermatologic changes during spaceflight. There are multiple promising interventions, including retinoids, vitamin-A derivatives, calcitriol, L-asparaginase, advanced dressings, telemedicine, and immune-system enhancement strategies which may help mitigate skin-thinning, dermatitis, and slow wound-healing. Continued interdisciplinary collaboration, more human data, and real-time data collection will refine and validate strategies, improving skin health in space. Routine consideration of novel dermatologic therapies may benefit spaceflight and overall mission success as humans venture farther into space.

KEYWORDS: microgravity, xerosis, dermal atrophy, wound-healing, teledermatology.

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Space missions pose unique challenges to skin health due a variety of factors: microgravity, low humidity, limited hygiene, and many others, all which have been found to lead to skin-thinning, dermal atrophy, and increased incidence of dermatological symptoms.[1] While multiple reviews of dermatological conditions in spaceflight exist, clear recommendations for the management of such conditions and space dermatoses have not been set forth.[1–3] Such conditions include microgravity-induced skin-thinning, xerosis, and contact dermatitis. Other unique needs include limited diagnostic access and pathogen virulence concerns. Additionally, dermatological disease may impact astronauts' psychological well-being, quality of life, and daily functioning. In this commentary, we summarize spaceflight's impact on skin, current treatments and challenges, and potentially promising countermeasures.

Astronaut clinical studies are scarce, but NASA records from 6-mo International Space Station missions show skin concerns (including dryness, pruritus, and skin irritation) were the most common health complaint, with an incidence over 25 times that of the general public.[4] Animal transcriptomic studies have revealed key space-induced biological changes that may be applicable to human skin health in space. These transcriptomic studies provide novel information related to immune dysfunction, skin health, DNA damage, and repair.[5] These changes have implications for astronaut dermatological health. For example, circulating physiological markers indicated that a more advanced exercise countermeasure reduced the in-flight drop in vitamin D, which is a known mediator of skin health.

Spaceflight-induced extracellular matrix changes, including reduced fibroblast proliferation and keratinocyte barrier protein expression, lead to microgravity-related impaired skin-healing and dermal atrophy. As a result, although some of the most common skin conditions in space are simple abrasions and rashes, healing this damage can be challenging because of the impacts of space travel on skin structure and function.[3] Retinoids and vitamin-A derivatives may boost collagen synthesis and epidermal turnover both pre- and in flight.[6] In recent causal gene expression relationship studies,

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calcitriol and L-asparaginase have been identified as a significant potential in-flight countermeasure for targeting skin spaceflight dysfunction.[5] Additionally, hydrogels and negative pressure wound dressings could serve as options to mitigate impaired wound-healing by promoting a diffusive environment enhanced for tissue regeneration.[7,8] The swelling ratio of hydrogels and the net negative pressure provided by these dressings may also provide indirect structural benefits. The lack of necessary gravitational force on skin cells may also be counteracted by the increasing stress and strain these hydrogels contribute. These hydrogels and negative pressure dressing may also be helpful in managing peeling, skin infections (in wound contexts), abrasions, and delayed wound-healing. Additionally, platelet-rich plasma may further promote fibroblast-mediated healing and counteract microgravity's effect on wound-healing.[1]

Xerosis, or dry skin, affects over half of International Space Station crewmembers.[3] Given the continued prevalence of xerosis in this population, traditional remedies such as application of moisturizers may not be enough. Contact dermatitis is another space dermatosis and can be induced by electrodes, antiseptic wipes, and no-rinse soap products commonly used by astronauts.[3] It has recently been found that there is a downregulation of Filaggrin through FLG and CASP14 genes in both mice models and astronauts, leading to defects in encoding skin barrier structure, natural moisturizing factors, and microbial defense.[5] These functions have well-known pathological associations with contact dermatitis, atopic dermatitis, and ichthyosis vulgaris. Emollients, barrier creams, corticosteroids, and anti-inflammatory agents have been used for both xerosis and contact dermatitis. However, given the high burden of these conditions for astronauts, the addition of occlusive dressings may combat the established low efficacy of treatments during missions.[9] We recommend a more aggressive combination of emollients, vitamin-A derivatives, and occlusive dressing, as appropriate, especially in particularly sensitive areas. Space hygiene products could also be evaluated and possibly reformulated to exclude common irritants.

Biopsy and histopathology are often not feasible, so minimally invasive diagnostics are preferred. To counteract this, other diagnostic technologies such as dermatoscopy via lens attachments, high-frequency ultrasound, or reflectance confocal microscopy can be considered. Telehealth, remote diagnostic technologies, and artificial-intelligence-based diagnostic models may also help further triage common dermatoses in space, including herpes reactivation or lesions of concern.

Limited hygiene, altered immunity, and delayed repair increase infection risk, especially on longer space missions.[3] The usage of immune-boosting medication, probiotics, lifestyle modification, controlled colonization with *Staphylococcus epidermidis*, allergen desensitization, and/or standardized hygiene protocols may have potential to control the spread of skin infections in space. Optimization of mission infrastructure to mitigate dermatological disease may include increasing mechanisms for surface decontamination and air filtration, along with utilization of less irritating textiles and adhesive materials.

The psychosocial effect of spaceflight on skin extends to crew dynamics, morale, behavior, and sleep. Mitigation of skin physiology and disease during missions can be physically and mentally challenging for astronauts, driving astronauts to adopt coping strategies such as continual sock-wearing for desquamation of feet. Clear, in-depth guidelines are needed to promote mission success, which at a high level would define: 1) screening, monitoring, and prophylactic management; 2) tiered treatment thresholds labeled with standardized hierarchy of evidence; 3) intervention and pharmacological parameters including dosage, frequency, and duration; and 4) escalation pathways from basic self-care to advanced diagnostics.

As international efforts in space exploration continue, spaceflight dermatology is a critical field for ensuring the health of astronauts. Microgravity, limited hygiene, and radiation uniquely impair skin integrity, contributing to issues such as dermal atrophy, xerosis, and increased infection risk during spaceflight.[2,3] This commentary highlights practical strategies and potential research avenues for preventing and addressing the array of dermatological changes during spaceflight. There are multiple promising interventions including retinoids, vitamin-A derivatives, calcitriol, L-asparaginase, advanced dressings, telemedicine, and immune-system enhancement strategies which may help mitigate skin-thinning, dermatitis, and slow wound-healing.[1,10] Novel application of existing dermatological therapies may benefit spaceflight and overall mission success as humans venture farther into space. Continued interdisciplinary collaboration, more human data, and establishing tiered dermatological guidelines will refine and validate strategies to improve skin health in space.

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Letter to the Editor re: Beard Length and the Efficacy of an Aviator Oxygen Mask

Dear Editor:

A recent article by French & Wagner[1] concludes "facial hair of any length has no effect on reducing a contemporary aviator mask effectiveness in maintaining adequate blood oxygenation." Facial hair in aircrew can be an emotive topic, but a sound evidence base is required to challenge established understanding and recommendations.

The study in question was conducted in a normobaric, reduced-oxygen environment using a Collins Sweep-On 2000 mask with the pressure-demand regulator in "normal" (air-mix) mode. As there was no ambient pressure change, the regulator would have mixed oxygen and ambient air in proportions to deliver a ground-level breathing gas mix. The ambient air being mixed contained a reduced oxygen concentration in this experimental setup, so the breathing gas would have contained a fraction of oxygen (FO_2) below that intended by the manufacturer. Combined, these experimental limitations mean that the system was not representative of real-world performance at 30,000-ft (9144 m) pressure altitude.

At lower altitudes, pressure-demand regulators deliver an air-mix with oxygen partial pressure that is greater than sea-level equivalent air. At ground level, a significant inward leak due to poor mask seal may, therefore, not result in an inspired gas mix sufficient to cause hypoxia. Assuming a typical demand regulator delivery performance of FO_2 of 0.35 at ground level, it can be calculated that the inspired gas would remain >0.21 FO_2 despite an inward leak of over 10% from the reduced-oxygen ambient air in this study. Without knowledge of the exact air-mix ratio, particularly considering the nonstandard air-mix, the threshold size of detectable leak cannot be calculated. Civilian standards typically require a minimum FO_2 of 0.95 above 35,000 ft (10668 m).[2] Detection is further affected by the limitations of peripheral oxygen-saturation monitoring[3] and characteristics of the oxyhaemoglobin dissociation curve, which allows peripheral oxygen saturation to be maintained even with an FO_2 below 0.21.

With regard to smoke and fume protection, the authors challenge the need for quantitative fit-testing for protection, instead employing a 5-s static smelling salt exposure. Aircrew masks are required to provide protection during head movement; typical approved qualitative fit tests require specific movements during a total exposure greater than 7 min.[4] Quantitative fit tests assure an inboard leak of no greater than 10%,[4,5] and military mask standards require less than 2% or 5% admixture (UK Ministry of Defense. Certification Specifications for Airworthiness. Part: 01: Fixed Wing Combat Air Systems. Report No. DEF STAN 00-970 Part 13; 2022) (Five Eyes Air Force Interoperability Council. Minimum physiological requirements for aircrew demand breathing systems. Document No. AIR-STD-4039 ED. 1(2); 2020). Only quantitative fit-testing can provide this level of assurance.

Previously published studies in aviation and nonaviation settings have shown that beards present a significant risk of inward mask leak.[6–8] Only a single unpublished trial (the authors cite a university news article) are in line with French & Wagner's findings. Methodological limitations in both studies mean that inboard ambient air leaks of between 10% and 50% may have gone undetected. This degree of inboard leak would not protect against hypoxia at altitudes in excess of 25,000–30,000 ft (7620–9144 m) or noxious fumes. The evidence presented by this study is not sufficiently robust to support the authors' conclusions, and incorrect application of the reported findings may lead to significant flight safety hazards.

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In Response:

The established "understanding and recommendations" the reviewer references in his opening paragraph derive from the 1980 Federal Aviation Administration (FAA) Advisory Circular. The FAA does not prohibit beards; the Advisory Circular only contends that pilots could be impaired in an emergency if they had beards.

We have two main issues with this established "understanding":

- There are no peer-reviewed studies demonstrating that aviation emergency masks leak enough from beards to impair pilot ability to safely fly the aircraft. Our study showed that bearded pilots do not become hypoxic at altitude while using aviation masks, and thus beards would not compromise their performance.
- The FAA's lack of a definitive stance on disallowing beards leaves airlines in a precarious legal position. If the FAA believes there is evidence that passenger safety is at risk from pilots with beards, it should prohibit beards immediately. The fact that they have not done so means that there must not be sufficient evidence. The lack of a definitive stance by the FAA means that the airlines could be held legally culpable for any incidents where bearded pilot performance might be blamed. This also leaves the FAA culpable for why they have not banned beards if they believe beards could impair pilot performance.

The mask in our normobaric hypoxia chamber combined ambient air with enough oxygen to allow a normoxic mix. The mask operates the same in hypobaric conditions. The reviewer's comment about the mask valves is irrelevant to our study on the mask seal. The air-pressure-filled hoses create a very tight seal leaving indented seal imprints on participants' faces within minutes.

Regarding our participants not smelling ammonia within our test period of about 5 s at chin level while masked, we suggest the reviewer confirm, as we did, that ammonia that close when unmasked will trigger a powerful response in less than 0.5 s.

Regarding the three references that the reviewer claimed document beards causing aviation masks to leak:

- Naber's study was conducted 54 yr ago with outdated mask technology. Moreover, in the conclusion on page 2, the authors admitted that there was "no conclusive evidence that beards cause serious injury."[1]
- Stobbe et al. was a literature review focusing on the methods and findings of 14 Occupational Safety and Health Administration (OSHA) type respirators and included one study with an aviation type mask. This one study was only presented at a 1979 convention in Las Vegas. It only involved four participants tested in nonaviation conditions and was not published in a peer-reviewed journal.[2]
- The reviewer missed the point of Floyd et al.: These authors were making the point that even with OSHA's stringent testing for lethal molecules, some respirators fit adequately on bearded individuals. They suggested OSHA should relax their position on beards because of this.[3]

The author presents assumptions without solid evidence and ignores the issue we addressed with our study, finding that the mask's seal is adequate to protect pilots with beards of any length in a hypoxic environment.

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From the Editor-in-Chief

The research article by French and Wagner published in the April issue of *Aerospace Medicine and Human Performance* has generated quite some interest.[1] Two Letters to the Editor have been received and published, including the one that appears here.[2,3]

As the Editor-in-Chief, I wanted to make a few comments about the process that the article and the two subsequent letters to the editor represent. In essence, the entire point of scientific publication is encapsulated in this. Researchers present the results of their experimental method and the conclusions they've drawn from them in a published article for the wider scientific community to see. Other researchers with different perspectives or experiences can then engage in a critique of that work via the journal's Letter to the Editor process. Each letter is sent to the original authors for their comment, and we always publish the two side-by-side for the benefit of the wider readership.

The beauty of this process is that it fosters academic discussion and debate, which can then generate subsequent experiments taking into account all of the issues raised, which should get nearer to the true answer posed by the original research question. Historically, this has been the entire point of scientific publication: to generate discussion and discourse, highlight design and methodological limitations, challenge conclusions drawn, encourage the design of comprehensive, rigorous follow-on experiments, and ultimately move the body of scientific knowledge and understanding forward.

Richard Feynman, the 1965 Nobel Laureate in Physics, once said, "Scientific knowledge is a body of statements of varying degrees of certainty—some most unsure, some nearly sure, none *absolutely* certain."[4] Out of this uncertainty comes opportunity. The scientific method involves replicating others' studies or finetuning them to compensate for any limitations identified by the original authors or others. No single paper in general represents the sum total of evidence. Indeed, there are exceedingly few instances where a single paper on a topic is the first and last word on any particular matter. Rather, the full understanding of a topic evolves over time, due to continued research and experimentation. Scientific discovery and understanding is an iterative process.

As Editor-in-Chief, I encourage every reader to critically review the articles that we publish. In stimulating debate and discussion, our journal will continue to thrive and the field of aerospace medicine will continue to move forward. That is in everyone's interests. In particular, I encourage any of you interested in the particular topic represented by the original article here and the subsequent letters to the editor to think about how to design an experiment that adequately addresses the question and takes into account the limitations discussed. The results of such experiments are likely to further our understanding on this topic. This is the process by which we move closer to full understanding of any scientific topic, and particularly so in the aerospace medicine field with all its inherent complexities.

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History of the Assured Crew Return Vehicle and Spaceflight Medical Evacuation

Mark R. Campbell

There has always been a concern about spaceflight medical evacuation of an ill or injured crewmember.[1] Besides the possibility of shock due to sepsis or hemorrhage and limited medical care while in transit, there will also exist cardiac deconditioning, loss of plasma volume, and musculoskeletal deconditioning from a long-duration spaceflight. Neurovestibular effects and orthostatic hypotension will also occur upon landing even with well crewmembers. Add to this the reentry G forces experienced and, in some cases, flight termination with a hard landing on Earth causing impact acceleration.[2] G_x reentry forces (chest to back) are tolerated well, but G_z reentry forces (head to foot with decreased brain perfusion) are difficult even in well crewmembers.

Research with primates (that were not deconditioned) involving controlled hemorrhage followed by centrifugation to mimic atmospheric reentry forces ($+G_x$) has shown that exposure to reentry acceleration forces[3] has no adverse effects unless the hemorrhage is severe (class III or IV, or 30–50% loss of blood volume) or the forces are excessive (8 G_x instead of 1.8 G_x). Since uninjured but deconditioned crewmembers returning to Earth typically display many of the hypovolemic characteristics of a class I hemorrhage [15% loss of circulating blood volume (750 mL blood loss)] manifested as minimal tachycardia and orthostatic hypotension, a true class I hemorrhage in space may respond more like a class II hemorrhage on return to Earth (i.e., 15–30% blood loss), manifested as tachycardia, tachypnea, and decreased pulse pressure. Therefore, a trauma patient in space is likely to have a decreased ability to tolerate the return to 1 G during a medical evacuation. Although aggressive resuscitation onboard the International Space Station (ISS) before a medical evacuation is initiated would be important, there is a limited ability to provide volume expansion on the ISS as only several liters of crystalloid are available. In the future, lyophilized plasma or "walking donors" might be used.

Designs for crew recovery from disabled manned space vehicles, including the concept of a space "lifeboat," were first proposed as early as 1957.[4] The United States first proposed a permanently manned space station in 1984 that would be serviced by the Space Shuttle every 2 mo. There was a concern that the station could become incapacitated and a Shuttle rescue would not immediately occur. A concept was developed of a "safe haven"—a part of the station that could shelter the crew until a rescue Shuttle arrived.

In 1988, the station concept was better defined to now be multinational and was to be called Space Station Freedom. It was still dependent on servicing by the Space Shuttle every 2 mo. A health maintenance facility was proposed in 1986 that would provide for medical and surgical care of the crew with a surgically capable crew medical officer since medical evacuation might not be available for 45 d. The health maintenance facility was eventually defunded by 1995 as the option of medical evacuation was considered essential.[5]

An Assured Crew Return Vehicle (ACRV) was proposed that could be used for medical evacuation or return of the crew if the Shuttle became incapacitated or if the station needed to be abandoned because it could no longer provide life support.[6] The HL-20 Personnel Launch System (**Fig. 1**) was designed by NASA Langley in 1988 and based upon the U.S. Air Force Dyna Soar and HL-10 lifting body and Soviet BOR-4 spaceplane designs. Langley-funded developmental studies were undertaken by Rockwell International in October 1989 and Lockheed Advanced Development Projects in October 1991. The HL-20 was a lifting body with a desirable 1.5-G vehicle reentry profile and would have been launched by a Titan IV. Langley carried out extensive wind tunnel testing. It would have landed horizontally on a conventional runway. North Carolina State University and North Carolina A&T University built a full-scale mockup that was used to investigate the ergonomics of a medical evacuation. It is now on display in Denver, CO, United States. The projected cost of $2 billion led to early cancelation by 1993.

There were also studies in the ACRV Program involving less expensive ballistic vehicles. The most feasible one was the Station Crew Return Alternative Module (SCRAM), first

This feature is coordinated and edited by Mark Campbell, M.D. It is not peer-reviewed. The AsMA History and Archives Committee sponsors the Focus as a forum to introduce and discuss a variety of topics involving all aspects of aerospace medicine history. Please send your submissions and comments via email to: mcamp@1starnet.com.

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FOCUS ON **AEROSPACE MEDICINE HISTORY,** *continued*

proposed in 1986, which used a Mars Viking heat shield (**Fig. 2**). However, it had a 3.5–8-G_x reentry profile, making it a poor choice for medical evacuation. A full-scale prototype was used in a wave tank to develop procedures for extraction of injured crewmembers after an ocean landing. It is now in Corsicana, TX, United States (**Fig. 3**).

In 1993, Russia was invited to join the partnership and the redesigned station was renamed the International Space Station. The use of the Russian Soyuz as a medical evacuation or escape vehicle had been discussed with the Russians since 1991 and became more acceptable due to the low cost involved. The Soyuz had been used for three minor medical evacuations (actually these were early returns for medical reasons) during the Salyut/Mir Programs. The Soyuz was a very reliable spacecraft, but had several deficiencies as a medical evacuation vehicle. It was extremely cramped, requiring abnormal body positions for crewmembers, had a 3.8-G_x nominal reentry profile (9.0 G_x if ballistic), and terminated in a hard landing. Several injuries had been documented with nominal Soyuz landings. The health medical system used onboard the ISS was now oriented toward stabilization and transport, and NASA flight surgeons and biomedical engineers used the Soyuz simulator in Star City, Russia, to work out medical equipment deployment and medical procedures for a possible medical evacuation. The decision to use the Soyuz for medical evacuation was finalized in 1996 and was considered temporary until a more capable system was developed. Contingency recovery sites were designated in Utah and Australia in addition to the nominal recovery site in Kazakhstan to decrease the definitive medical care time for a medical evacuation to 6–24 h.

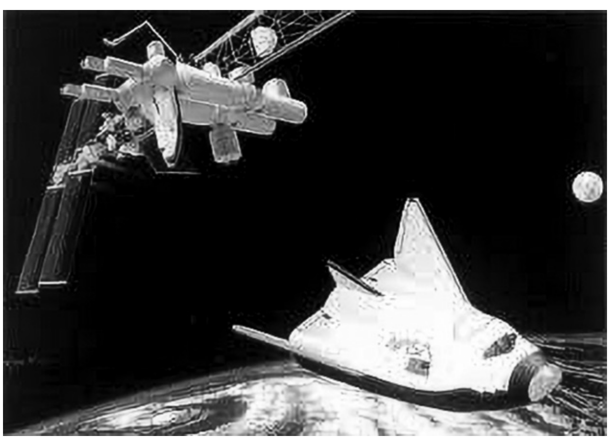

Fig. 1. Conception of the HL-20 ACRV in 1990 (courtesy of NASA).

The French and later European Space Agency (ESA) continued development of the ACRV and had proposals for both lifting bodies derived from the 1975–1992 Hermes project as well as three different ballistic vehicles. Dassault and Aerospatiale had submitted competing proposals for Hermes in 1987 and a full-scale mockup had been constructed. Hermes was canceled in 1992 due to a projected cost of \$4.5 billion. Integrated engineering teams from 1993–1996 that involved ESA and NASA engineers and flight surgeons were meeting regularly to further design work on a lifting body, the ESA Crew Return Vehicle (CRV). Controversy ensued about the requirements for medical evacuation, which dictated supine positioning of crewmembers to experience reentry G forces in the G_x axis and insistence by ESA on vertical positioning of the crew (reentry forces in the less tolerable G_z axis) as they wanted

Fig. 2. SCRAM (ballistic ACRV) as envisioned by NASA in 1993 (courtesy of NASA).

Fig. 3. SCRAM prototype in Corsicana, TX (courtesy of the Corsicana Daily Sun).

Fig. 4. X-38 CRV in drop tests in 1998 (courtesy of NASA).

the ability to pilot the spacecraft. The $1.7 billion cost and eventual acceptance of the Soyuz as a rescue vehicle led to cancellation in 1996.

Following cancellation of the ESA CRV, the United States and ESA began development of the X-38 CRV. The design was dedicated to medical evacuation with supine positioning (reentry forces in the G_x axis), automated return (in fact it did not have any windows but did have a manual override), lifting body design with reentry forces on the vehicle of <2.0 G, and a parafoil landing. The landing was a nonprecision desert landing that did not require a pilot or a runway. This is important, as the longest Shuttle flight (and therefore the longest that a pilot has been in space before piloting a vehicle on return) was only 17.5 d. How a pilot would perform on longer missions was speculative. A full-scale mockup was used in parabolic flight to study ingress and egress of medical transport and to optimize medical equipment deployment. Two 80% scale test vehicles were used in drop tests from a B-52 at Dryden Flight Research Center in 1998–1999 to validate flying characteristics (**Fig. 4**). They are now on display in museums in Oregon and Nebraska. A full-scale prototype that was to be launched on the Shuttle to the International Space Station for unmanned testing/demonstration was being constructed in-house at Johnson Space Center. It was 90% complete when the program was canceled in 2002 as the cost was projected at $1.1 billion.

The SpaceX Crew Dragon (operational since 2019) can now be used for medical evacuation and, although ballistic, has far more interior space than the Soyuz. Currently in development, the Starliner (ballistic) and Dream Chaser (lifting body) spacecraft are also being studied for medical evacuation configurations. Sierra Space Corporation began development of the Dream Chaser, which was directly derived from the HL-20 and the X-38, in 2004. It will be launched vertically on a Vulcan Centaur, has manned and cargo versions, has only a 1.5-G vehicle reentry profile, and terminates with a horizontal runway landing that can be automated.

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OCTOBER 2000

Laser threats (Federal Aviation Administration, Civil Aerospace Medical Institute, Oklahoma City, OK): "Laser pointers have been used by teachers and lecturers for years to highlight key areas on charts and screens during visual presentations. When used in a responsible manner, laser pointers are not considered to be hazardous. However, as the availability of such devices has increased, so have reports of their misuse. The Food and Drug Administration (FDA) issued a warning in December 1997 on the possibility of eye injury to children from handheld laser pointers. In October 1998, the American Academy of Ophthalmology upgraded an earlier caution to a warning, stating that laser pointers can be hazardous and should be kept away from children, after two reports of eye injuries involving young girls (age 11 and 13 yr). Of particular concern was the promotion of laser products as children's toys, such as those that can project cartoon figures and line drawings. Additionally, there have been reports involving the misuse of laser pointers (e.g., arrests made after police interpreted the red beam to be a laser-sighted weapon, spectators aiming laser lights at athletes during sporting events, cars illuminated on highways, and numerous incidents involving the illumination of aircraft)."[1]

OCTOBER 1975

Personality in isolation (Submarine Development Group One, San Diego, CA): "The current shortage of fossil fuels has made it necessary to draw on large reserves located in environments which are difficult and dangerous to explore. Perhaps the most abundant of these reserves are those which lie beneath the oceans. The exploration and development of these suboceanic resources is heavily dependent on a technology which is still in its infancy but which a recent article declared was 'a research technology whose time had come' - Deep Submergence Vehicles or DSVs . The DSV mediates the transfer of critical sensorimotor and problem-solving skills between those who operate and observe from DSVs and the hostile ocean environment. Because DSV technology has progressed slowly over the last several decades, this performance transfer is limited, and much remains to be done to overcome performance degradations and to protect DSV personnel against the hazards of undersea exploration. Among the factors which are involved in poor performance and unsafe operating conditions are: cramped and poorly arranged spaces; poor observation and lifting facilities; limited propulsion, ballast and manipulator control; inadequate life support, especially for emergency situations; and the absence of an organized and dependable rescue capability …

"The personality and developmental characteristics of U.S. Navy Deep Submergence Vehicle (DSV) personnel, including operators and crews, were documented and compared to the characteristics of U.S. Navy divers. The results show that DSV operators (DSV Oprs) had a significantly less asocial developmental pattern than divers, while developmental experiences of DSV crews (DSV Crs) were similar to those of divers. Personality measures (EPPS) indicate that both DSV Oprs and DSV Crs are presently more sociable as adults than divers and would probably be more effective in situations involving small group interaction. The modifications which have occurred in the behavior of DSV Crs may be related to experience in the highly interpersonal DSV situation. The findings also show that DSV Oprs prefer to take fewer risks than divers, while the DSV Crs are more like divers in risk-taking behavior."[2]

OCTOBER 1950

Cosmic radiation (U.S. Naval School of Aviation Medicine, Pensacola, FL): "The fact that the intensity of cosmic radiation increases rapidly from its small value at sea level to higher altitudes raises the question of a possible hazard to health in flight at extreme altitudes. Among the abundant experimental data on cosmic radiation are only a few which can be used for an evaluation in terms of the actual biological dosage at different altitudes. This biological dosage rate increases from its sea level value of 0.1 milliroentgens per day to a maximum of 15 mr./day at 70,000 feet altitude in northern latitudes. Beyond this altitude the dosage rate decreases due to the decrease in the number of collision processes of the primaries with the air molecules.

"For a full criticism of these dosage values it has to be realized that the ionization from cosmic radiation is produced largely by particles of a higher specific ionization than x-rays and beta particles. The milliroentgen equivalent-man values therefore will be markedly higher than the equivalent physical values. Present knowledge does not yet permit one to give a reliable numerical value for this conversion factor.

"Beyond 70,000 feet altitude the situation is completely different. A new component has been discovered in these regions, the heavy nuclei rays. They have a relatively small penetrating power and do not occur therefore below 70,000 feet. They consist of atomic nuclei of higher atomic numbers which are stripped of all their orbital electrons. They carry the tremendous amount of kinetic energy of more than 2 billion electron-volts per atomic number. Their specific ionization is much higher than any other hitherto observed value. The mechanism of absorption in matter is of the same type as that of alpha particles but magnified by a factor of 1,000. Their range in living tissue reaches values of 10 centimeters in comparison of 50 microns for alpha particles. An estimation of their possible biological action indicates that they might represent a serious hazard to health."[3]

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This column is prepared each month by Walter Dalitsch III, M.D., M.P.H. Most of the articles mentioned here were printed over the years in the official journal of the Aerospace Medical Association. These are available for download at https://asma.kglmeridian.com/.

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