Aeromedical Concerns in Asymptomatic Aviators with Left Bundle Branch Block

Pei-Chun McGregor; Edwin Valencia Palileo; Jared Travis Haynes; Eddie Dean Davenport

INTRODUCTION: Left bundle branch block (LBBB) is disqualifying for aircrew in the U.S. Air Force (USAF), although outcomes for these patients is limited. We used data from the USAF School of Aerospace Medicine to study this population.

METHODS: A retrospective review was performed on aircrew with LBBB identified using the Central Electrocardiographic Library database. Analysis included baseline participant demographics, cardiac risk factors, and any available cardiovascular results. Critical endpoints were coronary artery disease (CAD), cardiomyopathy (CM) (left ventricular ejection fraction of <50%) and/or clinical heart failure, and death from any cause.

RESULTS: At diagnosis: 271 patients met eligibility; mean age of 40.24 ± 7.39 yr. Of the 147 (54%) patients who had coronary angiography, 7 (2.6%) had aggregate stenosis 50–119% and 5 (1.8%) had aggregate stenosis ≥120%. Two patients underwent percutaneous coronary intervention, with an additional 13 (4.8%) patients demonstrating left ventricular ejection fraction of <50%; 12 were nonischemic. Longitudinal data was available for 177 (65%) patients; median follow-up was 10 yr (range 0–58 yr). During this period, 2 patients developed CAD with aggregate stenosis ≥120% and 5 had myocardial infarction. There were 37 (20%) patients who developed CM. Among 41 deaths, mean age was 75.1 ± 14.1 yr. Nine were premature (<60 yr).

DISCUSSION: Asymptomatic aviators with LBBB had elevated risk for CM (20%). Association with CAD exceeded 10% at 10 yr. Findings support current USAF policy requiring extensive cardiac evaluation and follow-up for LBBB. More prospective research is needed to validate these findings.

KEYWORDS: left bundle branch block, aviators, aircrew, cardiomyopathy, coronary artery disease.

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The management of asymptomatic aviators with left bundle branch block (LBBB) and the potential correlation of this electrocardiographic (ECG) abnormality with underlying cardiovascular (CV) disorders, as well as its prognostic implications in a low-risk population, remains a subject of ongoing debate. Data from the U.S. Air Force School of Aerospace Medicine (USAFSAM) have previously demonstrated that young aviators with LBBB may not have increased risk for CV disease.[15] They argued that while most cohort and longitudinal studies[17] on LBBB have demonstrated poor prognostic outcomes and increased association with CV disorders, those studies focused on sicker and older individuals. Population studies demonstrated a low prevalence for LBBB in young people (<1% at 50 yr of age), and these patients tended to be free from CV risk factors and had better prognosis than their older counterparts (>50 yr of age).[10] Nonetheless, according to the 2018 American College of Cardiology/American Heart Association/Heart Rhythm Society Guideline, individuals with LBBB have a higher probability for associated cardiac disease.[9] All current aeromedical authorities consider new

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LBBB to be initially disqualifying.[8] The object of this analysis is to present a current summary of our observations regarding aviators with LBBB at USAFSAM. We anticipate that these findings will influence both present and forthcoming aeromedical recommendations.

METHODS

Subjects

This retrospective analysis was conducted in accordance with the standards set by the local institutional research board. Confidentiality and privacy for all subjects were rigorously maintained throughout the entire process using such measures as data encryption, deidentification, secure data storage, and limited data access. Authors queried the U.S. Air Force Central Electrocardiographic Library (ECG Library) from its inception in 1957 until 2020. Any aircrew who had at least 1 ECG obtained within the Department of Defense healthcare system documenting LBBB were included in the cohort. All ECGs were reviewed by an independent senior cardiologist. Those not meeting diagnostic LBBB criteria, as outlined below, were excluded. Individuals with CV symptoms were also excluded. Diagnostic LBBB criteria included: 1) QRS ≥120 ms in adults; 2) broad notched or slurred R wave in leads I, aVL, V_5, and V_6 and occasional RS pattern in V_5 and V_6 attributed to displaced transition of QRS complex; 3) absent Q waves in leads I, V_5, and V_6, but a narrow Q wave may be present in aVL; 4) R peak time >60 ms in leads V_5 and V_6 but normal in leads $V_{1\text{-}3}$ and 5) ST and T waves are usually opposite in direction to QRS.[18]

Procedure

Eligible patients underwent chart review using all available military electronic medical record systems: Armed Forces Health Longitudinal Technology Application, Joint Longitudinal Viewer, Aeromedical Consultation Service Patient Status Worksheet, and Picture Archiving and Communication System, ScImage systems. Baseline characteristics at the time of diagnosis were collected: age, gender, race, weight, body mass index, CV risk factors (hyperlipidemia, hypertension, CV family history, smoking), and history of childhood infections (defined as either measles, mumps, or scarlet fever). Prespecified endpoints were coronary artery disease (CAD), cardiomyopathy (CM), and death. CAD has been strictly defined in aeromedical personnel as presence of any coronary abnormality, including calcifications and/or stenosis, given the high-risk nature of military aviation. Aggregate CAD is a conventional prognostic parameter used in the aeromedical community to estimate the sum of all coronary artery stenosis with established cutoffs at <50% (mild), 50–119% (moderate), and ≥120% (severe) and direct correlation with overall major adverse CV events.[5] CM was defined as a left ventricular ejection fraction (LVEF) of <50%. Deaths were adjudicated by death certificates or documentation in the electronic medical records. Premature deaths were defined as those under the age of 60.

Statistical Analysis

Data analysis was conducted from January 2020 to June 2022 using IBM SPSS 23. Point estimates, mean, and standard deviation were calculated for baseline demographics and preselected CV risk factors. In addition, odds ratio, 95% confidence interval, and *P*-values were calculated using Chi-Square analysis for CAD and CM groups at the time of diagnosis and on the last follow-up.

RESULTS

In total, 307 patients were identified, but 36 were excluded from analysis; 22 did not have LBBB upon ECG review, 1 reported chest pains, and 14 did not have sufficient follow-up data. Of the remaining 271 eligible patients, **Table I** outlines their baseline characteristics. The mean age was 40.2 ± 7.4 yr; 97% were male, 99% were Caucasian, 189 (70%) had a Flying Class II (pilots/navigators) waiver, and 39 (15%) had a Flying Class III (aircrew) waiver. The mean weight was 177 ± 24.3 lbs, with a body mass index of 25.2 ± 2.8 kg · m^{-2}. There were 63 patients (23%) with hyperlipidemia, 55 (20%) with hypertension, 44 (16%) with CV family history, 88 (33%) with a smoking history, and 44 (16%) who had experienced childhood infection. A total of 37 patients met the definition for CAD and 13 for CM. In addition, 244 patients (85%) had normal ECG axis, 35 (12%) had left axis deviation, and 5 (1.8%) had right axis deviation.

A total of 203 patients (203 out of 271, 75%) had noninvasive stress tests performed; 122 had initial treadmill alone, 69 had myocardial perfusion scan, and 11 had treadmill stress echocardiography. Most treadmill tests were reported as clinically normal (86 out of 122, 70.5%) indicating patients had high functional capacity without symptoms, while a portion of the tests (25 out of 122, 20.5%) were deemed uninterpretable. Myocardial perfusion scans predominantly showed abnormal

Table I. Baseline Patient Characteristics at Time of Diagnosis.

DEMOGRAPHIC	LBBB COHORT (*N* = 271)	CAD (*N* = 37)	CM (*N* = 13)
Age, yr	40.24 ± 7.39	42.00 ± 6.37	38.46 ± 6.44
Gender			
Male	264 (97.4)	36 (97.3)	13 (100.0)
Female	7 (2.6)	1 (2.7)	0
Race			
Caucasian	267 (99)	37 (100)	13 (100.0)
Black	4 (1)	0 (0)	0 (0)
Weight, lb	177.05 ± 24.33	183.76 ± 23.73	185.85 ± 23.31
BMI, kg · m^{-2}	25.17 ± 2.83	25.98 ± 2.72	26.18 ± 3.54
Flying Class			
Class II	189 (70)	25 (68)	9 (69)
Class III	39 (15)	9 (24)	3 (23)
HTN	63 (23)	17 (46)	5 (39)
HLP	55 (20)	16 (43)	3 (23)
Family history	44 (16)	13 (35)	1 (8)
Smoking	88 (33)	16 (43)	7 (54)
Childhood infection	44 (16)	3 (8)	1 (8)

LBBB = left bundle branch block; CAD = coronary artery disease; CM = cardiomyopathy; BMI = body mass index; HTN = hypertension; HLP = hyperlipidemia.

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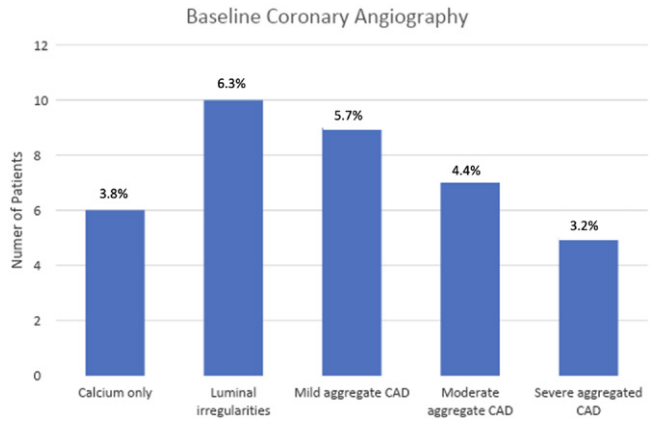

Fig. 1. Distribution of coronary evaluation at baseline. CAD = coronary artery disease.

results, with septal defects observed in the majority (51 out of 69, 74%), in contrast to stress echocardiograms, where the majority (9 out of 11, 81%) were reported normal.

A total of 147 patients (54%) underwent invasive coronary angiography, and 18 (6.6%) had coronary computed tomography angiography (CCTA), 7 of whom also had invasive coronary angiography. Of the 158 patients who had direct coronary evaluation either by invasive coronary angiography or CCTA, we found 6 patients who had only coronary calcification. Luminal irregularities, defined as <20% aggregate stenosis, were found in 10 patients. Mild CAD was defined as aggregate stenosis of 20–49% and was found in 9 patients. Moderate CAD (aggregate ≥50–119% stenosis) was demonstrated in 7 patients, and severe CAD (aggregate stenosis over 120%) was seen in 5 patients (**Fig. 1**). Two patients had percutaneous coronary intervention: one with moderate and the other with severe aggregate CAD. At diagnosis, hyperlipidemia, hypertension, and family history were significant risk factors for CAD, but flying class, smoking, and a history of childhood infection were not (**Table II**). These findings persisted over time during follow-up.

LVEF assessment was obtained in 139 patients (139 out of 271, 51%); using 125 transthoracic echocardiograms, 10 had an invasive left ventriculogram, and 4 with multigated acquisition scan. Among patients with CM, the mean LVEF was 40.8 ± 7.5%. Of these, 12 patients had nonischemic CM and 1 had ischemic CM. Preselected clinical variables were not statistically significant for CM at the time of diagnosis or on follow-up (Table II).

A total of 177 patients (177 out of 271, 65%) with a mean follow-up of 24.5 ± 16.1 yr revealed an additional 30 patients with CAD, but only 16 had corresponding coronary angiography on file. Of these 30, there were 2 with only coronary calcifications, 2 with luminal irregularities, 1 with mild CAD, 2 with severe CAD, 5 with myocardial infarction (MI), 2 with percutaneous coronary intervention, and 1 with coronary artery bypass grafting; none of these were overlapping entities (**Fig. 2**).

CM was identified in 37 patients: 7 nonischemic causes (1 had hypertrophic CM), 6 ischemic CM, and 24 with unclear etiology. Two patients had cardiac MRI documented: one exhibited a reduced LVEF with subepicardial and midepicardial late gadolinium enhancement, while the other underwent the procedure due to a dilated aorta with preserved LVEF and showed no gadolinium enhancement. Six patients later underwent placement of an implantable cardioverter-defibrillator. The percentage of individuals receiving cardiac resynchronization therapy was not specified.

There were 41 confirmed deaths with a mean age of 75.1 ± 14.1 yr. Of the nine premature deaths, one died from MI, one from ventricular fibrillation, one from sudden cardiac arrest, one from cardiac arrest during diagnostic catheterization, one from lung cancer, one from upper gastrointestinal bleed, and two from unknown causes.

Table II. Comparison of Clinical Variables for those with Coronary Artery Disease and Cardiomyopathy at Time of Diagnosis and on Follow-Up.

	TIME OF DIAGNOSIS			TIME OF THE LAST FOLLOW-UP		
VARIABLE	**OR (RR)**	**95% CI**	***P*-VALUE**	**OR (RR)**	**95% CI**	***P*-VALUE**
CAD						
FC II	1.15	[0.93, 1.42]	NA			
FC III	0.59	[0.31, 1.14]	NA			
HTN	3.81	[1.83, 7.95]	0.00	2.81	[1.50, 5.28]	0.00
HLP	3.47	[1.69, 7.16]	0.00	2.36	[1.28, 4.34]	0.00
Family Hx	3.55	[1.64, 7.69]	0.00	2.51	[1.28, 4.96]	0.01
Smoking	1.71	[0.85, 3.48]	0.13	1.72	[0.97, 3.05]	0.06
Childhood infections	0.42	[0.12, 1.42]	0.15	0.63	[0.28, 1.44]	0.27
CM						
FC II	1.11	[0.79, 1.54]	NA			
FC III	0.68	[0.24, 1.88]	NA			
HTN	1.19	[0.32, 4.47]	0.80	1.10	[0.47, 2.56]	0.83
HLP	2.16	[0.68, 6.84]	0.18	0.90	[0.39, 2.08]	0.80
Family Hx	0.42	[0.05, 3.29]	0.39	0.42	[0.12, 1.42]	0.15
Smoking	2.55	[0.83, 7.83]	0.09	1.15	[0.55, 2.38]	0.71
Childhood infections	0.42	[0.05, 3.29]	0.39	0.26	[0.06, 1.13]	0.06

FCII = flying class II which includes pilots, navigators, and flight surgeons; FCIII = nonrated aircrew such as loadmaster, boom operator, and radio controller; Values are mean ± SD or n (%). BMI = body mass index; CI = confidence interval; HLP = hyperlipidemia; HTN = hypertension; Hx = history; OR = odds ratio; RR = relative risk.

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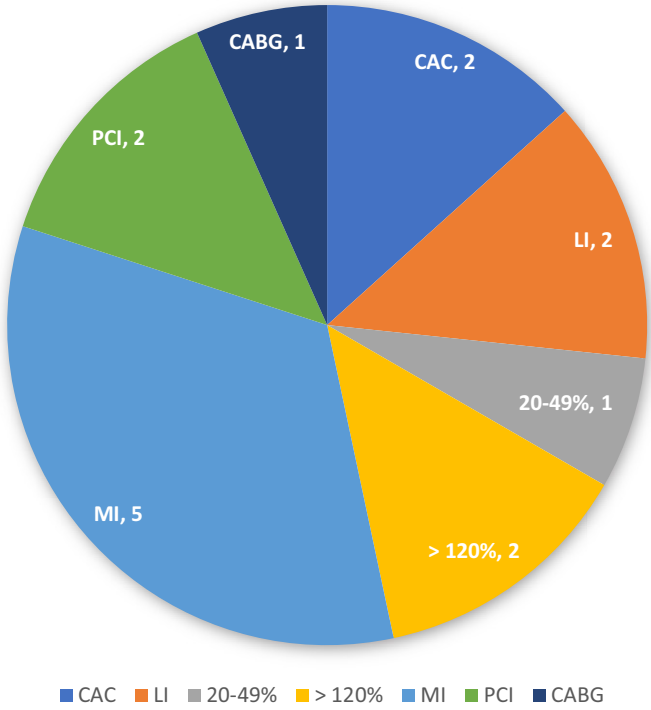

Fig. 2. Distribution of coronary evaluation at follow-up. CABG = coronary artery bypass graft; CAC = coronary artery calcium; MI = myocardial infarction; PCI = percutaneous coronary intervention.

DISCUSSION

The ECG Library was established at USAFSAM in 1957 with the aim to collect and store ECGs on all USAF rated flying personnel and all its applicants for flying or navigator training. The ECG Library now contains well over 1.2 million tracings and allows Aeromedical Consultation Service at USAFSAM to conduct thorough review of ECGs on any flying personnel. In most instances, these aircrew members were asymptomatic, and ECGs were obtained during routine screenings.

LBBB is the result of delayed conduction down the left bundle branch, within its fascicles, Purkinje fibers, or any combination of these. As such, the right ventricular activation occurs first followed by left ventricular endocardium, then midseptal wall, with remainder of the LV activating in a delayed fashion ending in the lateral, basal region.[19] This electrical and mechanical dyssynchrony has been linked to different regional ventricular workloads potentially leading to left ventricular dilation and remodeling.[4] According to longitudinal community-based studies from The Framingham Heart Study, presence of LBBB is associated with increased risk for CAD or heart failure and overall CV mortality, especially in older men (mean age at onset of LBBB was 62 yr).[16,17] Framingham also demonstrated QRS duration to positively correlate with left ventricular mass and dimensions but inversely associate with fractional shortening.[7] Retrospective data from the National Health and Nutrition Examination Survey cohort, with a mean age of 60.5 ± 13.6 yr, found QRS duration in setting of LBBB as an independent predictor of CV mortality (hazard ratio = 2.4, confidence interval = 1.3-4.7, P = 0.009).[2] Other unselected patient data demonstrated similar findings. Participants from the SPPARCS study, a community-based cohort study of those >55 yr old in Sonoma County, CA, overall had 2.5% prevalence of LBBB at baseline. During 6 yr of follow-up, heart failure incidence and CV mortality were higher in those with LBBB than those without LBBB.[1] Additionally, those with underlying CV disorders and LBBB have worse overall outcomes when compared to those with CVD alone.[3]

Contrary to the aforementioned studies, population-based data from Atherosclerosis Risk in Communities (ARIC)[12] and Belgian Inter-University Research on Nutrition and Health (BIRNH)[6] did not demonstrate death from coronary heart disease in those with LBBB. Earlier publications on asymptomatic, young Air Force aviators with LBBB have likewise shown no significant increase in CV disease or mortality.[11,13,15]

Our paper represents the most updated aeromedical data since Rotman et al. published their findings in 1975 on USAF flying personnel. Overall, our population was young (average age at diagnosis was 40 yr) and generally healthy, with a minority having smoking, hypertension, hyperlipidemia, and family history as risk factors for CV disease. More than 70% of patients had initial stress testing done, with the majority of these being treadmill alone. We meticulously reviewed all available exercise treadmill test tracings, noting instances of resolved ST-T wave abnormalities at peak exercise, while acknowledging that some remained nondiagnostic. Notably, the designation of "normal" pertains specifically to tests conducted on patients exhibiting exceptionally high functional capacity. In contrast, a large proportion of myocardial perfusion scans were interpreted as abnormal. This is consistent with prior studies demonstrating reduced specificity with myocardial perfusion scans in detecting CAD in those with LBBB given higher false positive septal perfusion defects.[20] Similarly, stress echocardiography may reveal septal wall motion abnormalities affecting overall specificity, but our cohort had mostly (81%) normal results. Admittedly, multislice computed tomography has excellent negative predictive value in excluding CAD,[14] but this technology was not available to our earlier cohort. The noninvasive tests were selected based on the available options at the time of diagnosis. Likewise, while cardiac MRI was not widely accessible for most of our cohort, its availability would have undoubtedly enhanced our diagnostic accuracy.

The initial coronary angiography revealed a total of 12 patients with moderate or severe aggregate CAD, but only 2 required revascularization at time of diagnosis, suggesting most CAD diagnoses at baseline were nonobstructive. Nevertheless, during the follow-up period, there were 5 newly identified cases of MI, an additional 2 instances of stent placements, and 1 coronary artery bypass grafting procedure. Additionally, there were 9 premature deaths, with 5 attributed to cardiac causes. CM was found in 20% of aircrew at some point in the study. These individuals underwent follow-up assessments typically spanning from 1–3 yr. Importantly, no instances of loss of life or

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aircraft occurred while individuals were on flight status within the study. All identified diseases were addressed, treated, and monitored in accordance with the prevailing USAF policy. Patients with CAD also had higher baseline prevalence for hypertension, hyperlipidemia, and family history than patients with LBBB alone. It is possible that these CV risk factors account for CAD rather than LBBB as a marker. When compared to the previously published data from Aeromedical Consultation Service, our data demonstrated higher rates of baseline CM (LVEF < 50%).[18] This discrepancy may be explained by a couple of factors. Firstly, there were only 49% of patients who had any LVEF evaluation performed. Secondly, several different imaging modalities were used limiting overall precision and quality over time. Interestingly, none of the preselected clinical variables were found to impact the development of CM. Aircrew regularly exposed to higher G-forces were also not at higher risk for CAD or CM. Death from sudden cardiac arrest was rare. These findings suggest LBBB may be a preclinical manifestation of underlying myocardial abnormality or perhaps a trigger to developing CM.

A significant limitation is the incompleteness of data, as follow-up was only available in two-thirds of our initial cohort. Given the 63-yr time span of this study, certain imaging modalities were not accessible to earlier cohorts, while guideline recommendations for LBBB workup have also evolved over time. These changes in recordkeeping practices, technology, or diagnostic criteria may potentially affect the consistency and comparability of data over different time periods. Incomplete or missing data, selection bias (inclusion of patients based on availability of medical records), and information bias (accuracy, misinterpretations, or variations of data documentation) may collectively limit the scope, reliability, and generalizability of our findings. For example, we had to exclude Holter data from analysis as we only had data for 51 patients, with none resulting in any significant arrhythmias. Additionally, establishing causation between variables is challenging in retrospective chart reviews; associations identified may not imply causation.

In this retrospective analysis, identification of LBBB in young, asymptomatic, and healthy Caucasian male aviators in the USAF correlated to an elevated risk of CM and a trend toward increased CAD, both at the time of diagnosis and longitudinally, but a low occurrence of sudden death. Current USAF policy of echocardiogram, noninvasive stress testing, and angiography (either invasive or CT coronary angiography) is warranted. Cardiac MRI should also strongly be considered. Follow-up testing every 1–3 yr should be done in all aircrew with LBBB. Further research is advised to validate and elaborate on these findings.

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