Prophylactic Splenectomy and Hyposplenism in Spaceflight

Margaret Siu; Dana Levin; Rowena Christiansen; Edward Kelly; Reginald Alouidor; Tovy H. Kamine

BACKGROUND: There is debate whether astronauts traveling to space should undergo a prophylactic splenectomy prior to long duration spaceflight. Risks to the spleen during flight include radiation and trauma. However, splenectomy also carries significant risks.

METHODS: Systematic review of data published over the past 5 decades regarding risks associated with splenectomies and risks associated with irradiation to the spleen from long duration spaceflight were analyzed. A total of 41 articles were reviewed.

RESULTS: Acute risks of splenectomy include intraoperative mortality rate (from hemorrhage) of 3–5%, mortality rate from postoperative complications of 6%, thromboembolic event rate of 10%, and portal vein thrombosis rate of 5–37%. Delayed risks of splenectomy include overwhelming postsplenectomy infection (OPSI) at 0.5% at 5 yr post splenectomy, mortality rate as high as 60% for pneumococcal infections, and development of malignancy with relative risk of 1.53. The risk of hematologic malignancy increases significantly when individuals reach 40 Gy of exposure, much higher than the 0.6 Gy of radiation experienced from a 12-mo round trip to Mars. Lower doses of radiation increase the risk of hyposplenism more so than hematologic malignancy.

CONCLUSION: For protection against hematologic malignancy, the benefits of prophylactic splenectomy do not outweigh the risks. However, there is a possible risk of hyposplenism from long duration spaceflight. It would be beneficial to prophylactically provide vaccines against encapsulated organisms for long duration spaceflight to mitigate the risk of hyposplenism.

KEYWORDS: prophylactic splenectomy, space travel.

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Throughout the duration of human spaceflight, there has been discussion in the literature regarding the benefits of prophylactic appendectomy and cholecystectomy to avoid appendicitis and biliary disease while in space. Appendicitis and cholecystitis are mission critical diagnoses, as they impact the ability to complete the mission for both the patient and other crewmembers.[3,26,29] There is now ongoing debate on the role of prophylactic surgery to avoid these mission critical surgical pathologies.

The spleen is extremely sensitive to trauma and radiation. Unsurprisingly, spaceflight confers risks of both trauma and radiation. Recently, the utility of prophylactic splenectomy to avoid radiation induced lymphoma from long duration spaceflight has also been questioned.[23] While the development of lymphoma following return to Earth is not a mission critical diagnosis, it still carries significant morbidity and mortality for an astronaut and may disqualify them from future missions.[7,38] Thus, a closer analysis must be completed to determine whether prophylactic splenectomy is of use to individuals traveling to space. This article will describe the risks experienced by asplenic individuals, compare those risks with risks of adverse events associated with the spleen during spaceflight, and finally, discuss whether prophylactic splenectomy is of benefit for those traveling on long duration spaceflights.

From the University of Massachusetts Chan Medical School—Baystate Health, Springfield, MA, USA.

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Address correspondence to: Margaret Siu, M.D., Surgery, Baystate Medical Center, 759 Chestnut St., Springfield, MA 01199, USA; margaret.siu@baystatehealth.org.

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METHODS

A systematic review of data published over the past 5 decades regarding risks associated with splenectomies, dosages of radiation leading to adverse effects on the spleen, and radiation risks experienced on long duration spaceflight was completed. Inclusion criteria included articles pertinent to pathology developed postsplenectomy, articles specifically detailing dosages of radiation received by the spleen in everyday situations, and articles reporting radiation experienced during space travel.

RESULTS

Risks in Splenectomy

Hemorrhage is the main risk during a splenectomy and immediately postoperation, varying between 12–30%. Intraoperative mortality rates secondary to hemorrhage is 3–5%. One study shows a mortality rate as high as 30% postoperatively, especially when splenectomy is performed for myeloproliferative disorders.[2,35,39] The risk of mortality following splenectomy not associated with hemorrhage is much lower, as it is with prophylactic splenectomy. Thromboembolic events occur in approximately 10% of postsplenectomy patients, which can include deep vein thrombosis, portal vein thrombosis (PVT), or a pulmonary embolism (PE). Due to the splenic vein's anatomy in relation to the portal vein, the portal vein develops into a prothrombotic state following a splenectomy. One prospective study reveals a 55% chance of PVT in laparoscopic splenectomies. On average, risk of PVT ranges from 5 to 37% postsplenectomy.[8,14,18] PEs have also been associated with splenectomies at a higher rate as compared to other surgeries.[18,22,28] Mortality from PE was associated with a relative risk of 4.53 in splenectomized patients.[22,28] In addition to venous thromboses, splenectomies carry an increased risk for arteriosclerotic disease as well. Myocardial infarction and strokes are more frequently observed following splenectomies in patients over 40 yr of age.[8]

The loss of the spleen removes the ability to fight encapsulated organisms such as *Streptococcus pneumonia*, *Neisseria meningitides*, and *Hemophilus influenza*. Most cases of overwhelming postsplenectomy infection (OPSI) occur between the second and third year after surgery.[34,36] On average, there is a 0.5% chance of developing OPSI at 5 yr postsplenectomy; however, a 42% chance of OPSI has also been observed in some populations. Mortality rates can be as high as 60% for pneumococcal infections, with higher rates seen in immunodeficient patients. While vaccines specific to *S. pneumonia*, *N. meningitides*, and *H. influenza* are regularly administered to splenectomy patients, other species can also cause OPSI. At times, sepsis and subsequent organ failure develop before vaccines are even able to be given. Other studies show higher rates of death from OPSI the farther an individual is from the operation.[11,34,36]

Due to a lack of immunologic function, splenectomy increases the rate of secondary leukemia.[31] In a retrospective study with 1094 patients, rates of cancer of any type were increased in those without a spleen. Those who developed cancer after splenectomy were also more likely to die from the cancer, with a relative risk of 1.53. While splenectomies may have originally been performed for cancer staging and alleviation of symptoms secondary to lymphomas, postsplenectomy Hodgkin's lymphoma, non-Hodgkin's lymphoma, acute myeloid leukemia, chronic lymphocytic leukemia, and chronic myeloid leukemia are seen in a handful of patients 2 to 5 yr following splenectomy.[22]

Risks to the Spleen from Long Duration Spaceflight

While there is risk to the spleen from trauma in long duration spaceflight, most traumas with high enough impact to cause significant splenic injury are likely to be fatal, as the most common cause of severe splenic injury on Earth is due to high velocity motor vehicle collisions.[17,30] Due to the hematopoietic capabilities of the spleen, the organ itself is relatively more radiosensitive compared to other intraabdominal tissues.[16,25] There is a higher likelihood of the spleen suffering from radiation induced adverse events rather than trauma in long duration spaceflight.

Radiation dosage can be measured in Gray (G_y), which describes the amount of energy that is absorbed based on body mass, and Sievert (Sv), which describes the radiation needed to harm the tissues. For the human spleen, irradiation of 1 Gy is approximately equivalent to 1 Sv.[1,27,40] An individual receives approximately 3 milliSievert (mSv) to 7 mSv to their intraabdominal organs every year from every day, environmental radiation sources.[9,19] A computerized tomography scan of the abdomen and pelvis confers 15 mSv to 31 mSv.[33] In cislunar space, crewmembers may experience radiation of 100 mSv/h during a solar particle event.[4] Solar particle events can deliver as much as 500 mSv/h to internal organs during interplanetary travel.[5] For crewmembers on the International Space Station for 6 mo, the average radiation is approximately 80 mSv.[19] The radiation exposure from a year long trip to Mars is estimated to be 662 mSv.[20]

Up to 72% of patients experienced reduction to tissue volume after experiencing 10 Sv of ionized radiation over 2 wk, or approximately 714 mSv/d.[41] The spleen was noted be reduced to 37% of its original volume with 45 Sv.[37] Irradiation decreases the immune response of the spleen due to both a decrease in mononuclear cells and its prevention of proliferation of surviving mononuclear cells. Cell populations including B lymphocytes, T lymphocytes, monocytes, macrophages, and natural killer cells all declined. For instance, exposure of 8 Sv leads to a decrease of B lymphocytes by a factor of 200. Interestingly, lineages such as natural killer cells are able to regenerate sevenfold the cell count compared to pre-irradiation tissue.[16,21] In a 2017 meta-analysis on the effects of 10 Sv of irradiation to the spleen, 3% experienced neutropenia, 28% experienced anemia, 30% experienced thrombocytopenia, 21% experienced leukopenia, and 8% experienced pancytopenia. In the review, 0.7% resulted in mortality secondary to hemorrhage from thrombocytopenia.[41]

Studies have shown that there is a proportional relationship between dose of radiation received and cancer risk.[15] However, there continues to be debate on the exact radiation dosage threshold that would induce cancer. Overall, the literature suggests irradiation between 50 mSv to 200 mSv to be carcinogenic.[4,6,32] Leukemia and solid organ malignancy have been observed to be associated with ionized radiation to the spleen. In one study involving 1391 patients, irradiation to the spleen resulted in a relative risk of 5.69 for development of non-Hodgkin's lymphoma compared to those who did not experience splenic radiation as treatment of a prior cancer.[12,13] Other studies reveal a relative risk of 3.67 of acute leukemias, myelodysplastic syndromes, non-Hodgkin's lymphomas, and solid tumors associated with 40 Sv of irradiation to the spleen over a period of several months.[10]

DISCUSSION

We must compare the clinical risks associated with splenectomies to the risks of splenic adverse events that may take place during space travel. **Table I** compares whole body irradiation dosages specific to the human spleen. If we closely evaluate **Table II**, which presents risks associated with radiation, and compare those to risks associated with splenectomies, the radiation threshold needed to induce the listed outcomes are all significantly above what is likely to be experienced on an interplanetary spaceflight. Specifically, malignancy associated with splenic irradiation is noted to have a relative risk between 3.67 and 5.69 compared to those who do not undergo radiation.[10,12,13] However, the dosage in those studies required to cause malignancy is 40 Sv; even a 2-yr round trip to Mars would not reach anywhere close to that level of radiation.

Furthermore, pathologies such as neutropenia, anemia, thrombocytopenia, leukopenia, pancytopenia, and mortality secondary to hemorrhage resulted from radiation doses in the realm of 10 Sv.[20,41] With this data, we can extrapolate that the most likely consequence of radiation from long duration spaceflight outside of low Earth orbit is likely to be mild hyposplenism.

Contrarily, those undergoing splenectomies are at much higher risks for a range of complications. During the perioperative period for instance, deep vein thromobosis (10%) and PVT (5–37%) are common, and mortality can be secondary to hemorrhage (6%) and PE (0.2–0.9%) (see Table II). OPSI rates were noted to be as high as 0.5% at 5 yr following splenectomies, with appropriate vaccination. The overwhelming infectious process is associated with 60% chance of mortality in some studies. While it takes approximately 40 Sv to see development of malignancy, splenectomy itself also garners a relative risk of 1.53 for development of non-Hodgkin's lymphoma. However, we must specify that these reported statistics are based on patients with traumatic injuries, malignancies, or some other pathology requiring a splenectomy. From a clinical perspective, elective splenectomy on a healthy individual would most likely generate lower risks.

Table I. Comparison of Whole-Body Radiation Dosages in MilliSieverts (mSv) Specific to Proton Emission Experienced by Humans.

EXPOSURE	mSv
Yearly from environment*	3–7
CT scan of abdomen and pelvis†	15–31
275 miles above Earth‡	80
Trip to Mars for 12 mo§	662
Solar particle event to internal organ¶	500
Threshold for cancer induction**	200

*Enrici et al.[12], Mohye El-Din[25]; †Smith-Bindman[33]; ‡Mohye El-Din[25]; §Brodsky et al.[7]; ¶Newhall et al.[26]; **Boerma et al.[5], Koeffler et al.[21]

It is also important to discuss the ethics surrounding prophylactic surgery. There are severe ethical issues in requiring individuals in any remote care situation to have prophylactic surgery that is not indicated for any pathology. If the procedure becomes a requirement for selection and an individual is being coerced into the procedure, it suffices as a violation of informed consent. To remove the spleen in anticipation of traumatic splenic injury or development of malignancy is not a standard of care in any civilian clinical setting at this time, and the interplanetary environment should be no exception. We cannot endorse medical or surgical practices that do more harm than good. Performing prophylactic surgery to prevent low incidence diseases is nonproductive. Moreover, a prophylactic splenectomy does not alter the overall surgical capabilities of a spaceflight medical system, which will ultimately have resources to handle surgical emergencies. As spaceflight becomes more accessible and interplanetary spaceflight becomes a reality, hyposplenism may occur; however, prophylactic splenectomy should not be performed.

As a decrease in splenic volume and function is to be expected from long duration spaceflight irradiation, efforts to mitigate this loss of function may be useful. We therefore recommend prophylactic vaccination against encapsulated organisms. Patients are given "post-splenectomy vaccines" in most clinical settings to prevent infection from encapsulated organisms after splenectomy.[24] As such, administration of prophylactic postsplenectomy vaccines may help mitigate potential risks of adverse events secondary to radiation for those embarking on space travel. The specific vaccines necessary are those that prevent infections caused by *S. pneumonia, N. meningitides,* and *H. influenza*, common species leading to OPSI, and should be given prior to long duration spaceflight.

Comprehensively assessing these risks, our recommendation is that astronauts can safely pursue long duration space travel outside of low Earth orbit without the need of prophylactic splenectomy. The use of prophylactic surgery to prevent the possibility of splenic trauma and radiation induced malignancies, which overall are of low incidence, is not an appropriate method of preparing for spaceflight and prevention of hyposplenism—the potential benefits do not outweigh the significant risks. However, the risks of hyposplenism from radiation during long duration interplanetary spaceflight are real and may be best mitigated by prophylactic vaccination against encapsulated organisms.

Table II. Acute and Delayed Risks Associated with Splenectomy and Risks Associated with Splenic Irradiation.

SPLENECTOMY RISKS	PERCENT RISK	REFERENCES
Acute Risks Associated with Splenectomy		
Splenic injury in blunt traumatic injury	23.8%	Hsieh et al.,[17] Reiff et al.[30]
Mortality associated with splenic injury from blunt trauma	33%	Hsieh et al.,[17] Reiff et al.[30]
Mortality associated with intraoperative hemorrhage during splenectomy	3–5%	Weledji,[39] Targarona,[35] Asoglu et al.[2]
Mortality associated with post splenectomy hemorrhage	6%	Weledji,[39] Targarona,[35] Asoglu et al.[2]
Deep vein thrombosis post splenectomy	10%	Ha & Arrendondo,[14] Ikeda et al.,[18] Crary & Buchanan[8]
Portal vein thrombosis post splenectomy	5–37%	Ha & Arrendondo,[14] Ikeda et al.,[18] Crary & Buchanan[8]
Mortality associated with pulmonary embolism post splenectomy	0.9%	Pimpl et al.,[28] Ha & Arrendondo,[14] Kristinsson et al.[22]
Delayed Risks Associated with Splenectomy		
Overwhelming postsplenectomy infection (OPSI) at 5 yr	0.5%	Weledji,[39] Kristinsson et al.,[22] Edgren et al.,[11] Tahir et al.[34]
Mortality associated with OPSI	60%	Weledji,[39] Kristinsson et al.,[22] Edgren et al.[11]
Malignancy associated with splenectomy*	RR 1.53†	Weledji,[39] Kristinsson et al,[22] Edgren et al,[11] Rodeghiero & Ruggeri[31]

RISKS TO THE SPLEEN FROM POTENTIAL RADIATION DURING SPACE TRAVEL	PERCENT RISK	RADIATION NEEDED	REFERENCES
Tissue volume reduction	72%	10 Sv	Trip et al.,[37] Harrington et al.,[16] Zaorsky et al.[41]
Neutropenia	3%	10 Sv	Harrington et al.,[16] Zaorsky et al.,[41] Koeffler et al.[21]
Anemia	28%	10 Sv	Harrington et al.,[16] Zaorsky et al.,[41] Koeffler et al.[21]
Thrombocytopenia	30%	10 Sv	Harrington et al.,[16] Zaorsky et al.,[41] Koeffler et al.[21]
Leukopenia	21%	10 Sv	Harrington et al.,[16] Zaorsky et al.,[41] Koeffler et al.[21]
Pancytopenia	8%	10 Sv	Harrington et al.,[16] Zaorsky et al.,[41] Koeffler et al.[21]
Mortality associated with hemorrhage from thrombocytopenia	0.7%	10 Sv	Harrington et al.,[16] Zaorsky et al.,[41] Koeffler et al.[21]
Acute leukemia, myelodysplastic syndromes, non-Hodgkin's lymphoma, solid tumors	RR 3.67–5.69*	40 Sv	Gilbert,[13] Enrici et al.,[12] Dietrich et al.[10]

*Malignancy associated with splenectomy was mostly determined as non-Hodgkin's lymphoma.
†Relative risk is compared to individuals without splenectomies or those who did not undergo intraabdominal radiation as treatment for other cancers.

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Authors and Affiliations: Margaret Siu, M.D., Department of Surgery, and Edward Kelly, M.D., FACS, Reginald Alouidor, M.D., FACS, and Tovy H. Kamine, M.D., FACS, Division of Trauma/Critical Care and Acute Care Surgery, Baystate Medical Center, UMASS Chan Medical School, Springfield, MA, USA; Dana Levin, M.D., M.P.H., NASA Johnson Space Center, Houston, TX, and Department of Emergency Medicine, Columbia University Irving Medical Center, New York, NY, USA; and Rowena Christiansen, M.Emerg. Health., M.B.B.S., The University of Melbourne, Parkville, Victoria, Australia.

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