



# Commercial Air Travel for Passengers With Cardiovascular Disease: Stressors of Flight and Aeromedical Impact

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**Abstract:** The exponential growth of commercial flights has resulted in a sharp rise of air travellers over the last 2 decades, including passengers with a wide range of cardiovascular conditions. Notwithstanding the ongoing COVID-19 pandemic that had set back the aviation industry for the next 1 to 2 years, air travel is expected to rebound fully by 2023-2024. Guidelines and evidence-based recommendations for safe air travel in this group vary, and physicians often encounter situations where opinions and assessments on fitness for flights are sought. This article aims to provide an overview of the stressors of commercial passenger flights with an impact on cardiovascular health for the general cardiologist and family practitioner, when assessing the suitability of such patients for flying fitness. (Curr Probl Cardiol 2021;46:100746.)

## Introduction

**T**he exponential growth of commercial flights, both in terms of accessibility and cost, has resulted in a sharp rise of air travellers over the last 2 decades.<sup>1,2</sup> Notwithstanding the ongoing COVID-19 pandemic that will set back the aviation industry for the next 1 to 2 years, air travel is expected to rebound fully by 2023-2024. Passengers

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with a wide range of cardiovascular conditions, are also rising in parallel, due to a globally aging population and improvements in cardiovascular healthcare. Guidelines and evidence-based recommendations for safe air travel in this group vary,<sup>3,4,5</sup> and physicians attending to such patients often encounter situations where their opinions and assessments on fitness for flights are sought.<sup>6</sup> This review article aims to provide an overview of the stressors of commercial passenger flights with an impact on cardiovascular health, and to summarize the management approach of the various cardiovascular conditions for the general physician.

## **Epidemiology of In-Flight Cardiovascular Emergencies**

The principal concern regarding passengers with chronic cardiovascular conditions undertaking commercial flights is the risk of acute decompensation in-flight, with sudden cardiac arrest or death being the most worrisome outcome.<sup>7</sup> Given the large denominator of air travellers annually, the incidence of such events is exceptionally low. However, due to the heterogeneous nature of the aviation industry and regulatory bodies, and the lack of any centralized or international registry to track the true incidence and nature of in-flight medical emergencies (IMEs) worldwide,<sup>8,9</sup> we are left to extrapolate the risks from studies that are region or airline specific. From a review of 11,920 passenger medical consultations from 317 PubMed indexed articles, a prevalence of 1 in 604 flights of IMEs was observed.<sup>10</sup> Other IMEs estimates ranged from 24 to 130 per 1 million passengers.<sup>11,12</sup> However, these figures most probably underestimate the true prevalence of all IMEs, since minor events, especially those that resolve in-flight and do not require telemedicine consultations or aircraft diversions, are unlikely to be reported or monitored in any registry.<sup>13</sup>

Notably, acute cardiac presentations constituted 7% of all IMEs on commercial flights, with the most frequent reported symptoms related to suspected arrhythmias (sensation of fast, slow or irregular heartbeats) or acute coronary syndromes (chest pain with or without arm/jaw radiation, breathlessness).<sup>9-12,14-20</sup> Based on the above figures, a ballpark incidence of cardiac IMEs of 5 per 1 million passengers can be roughly derived. Clearly, such an estimate guides only generic advice for the air traveller, and further risk stratification needs to be considered for the individual based on his or her overall profile. The attending physician must be mindful to holistically assess the stability of the passenger's existing cardiovascular conditions, in-flight impact on the disease, and pre- and post-travel environments, when conducting the pre-flight assessment. The key

focus is to reduce this remote IME risk to an even lower probability prior to embarkation of air travel.<sup>21</sup>

## **Stressors of Air Travel**

The aviation environment is substantially different from the terrestrial existence that man is accustomed to and physically designed for. Beyond the obvious in-flight milieu subjecting passengers to physiological stressors, peri-flight situations also impose pressures on the mental and physical realm.<sup>22</sup> At the risk of oversimplifying the subject, the 2 main categories of air travel stressors to the cardiovascular system are broadly divided into: (1) Psychological and physical stressors, and (2) physiological stressors.

## **Psychological and Physical Stressors**

Mental stress and psychological duress have been shown to be causally linked to myocardial ischemia in individuals with pre-existing coronary artery disease.<sup>23</sup> The pre- and postflight environments present various stress points, especially for the international traveller. Stricter security clearances, long queues at immigration lines, and tightened infection control measures (due to the recent COVID-19 pandemic) translate to longer wait times and increased anxiety and frustration for passengers. In addition, aerobic stress imposed by the activity of luggage transfer within the airport and transit areas results in a higher physical workload, which may be exacerbated by elevated altitudes or warmer climates at the foreign destinations. These levels of exercise may be beyond what the passenger is accustomed to, and in cardiac patients, may be a trigger for ischemic events. Consequent to the psychological and physical stressors, the body responds with an adrenergic surge and sympathetic activation, resulting in elevated blood pressure and heart rates, further aggravating ischemic stress on the diseased cardiovascular system.

The development of fatigue consequent to acute sleep deprivation with or without circadian disruption is common challenges during transcontinental flights. Early morning departure and arrival timings and multiple time zone crossings are the predominant contributors to such diurnal stress, and may result in an increased risk for acute coronary and arrhythmic events due to adverse effects on the chronobiological regulation of the cardiovascular system.<sup>24,25,26</sup> Contrary to this, another study has shown that sudden death in heart failure was not strongly influenced by circadian sympathetic activation,<sup>27</sup> suggesting that there is no direct increase in cardiac vulnerability secondary to short-term sleep-wake interruption in airline

passengers. However, this trial focused on an advanced heart failure population and may not be representative of the full spectrum of patients with cardiovascular disease. Beyond such contrasting findings, a more pertinent problem faced by passengers with cardiovascular conditions is the time dosing of their medications, especially with abrupt changes in time zones, meals, and wakefulness in transcontinental flights.<sup>22</sup> Certain nonprescription sleep supplements (such as melatonin) consumed by passengers for sleep adjustment have also been observed to interfere or interact with cardiovascular medications,<sup>28,29</sup> and dose titration of the implicated cardiac medications may be required to maintain optimal effects. Some (such as temazepam, zaleplon, etc) may also have direct effects on the cardiovascular system,<sup>30</sup> and discontinuation or avoidance of such pharmacological sleep aids should be strongly advised.

## Physiological and Environmental Stressors

### *Physics of Air Travel and Impact on Cardiovascular Physiology*

To appreciate the physiological stressors experienced during air travel, it is important to understand the basic laws of physics at high altitudes. The 2 main physical laws are: Boyle's law (governing the pressure and volume relationship of gases), and Dalton's law (governing the partial pressure of gases within a shared space). The volume of a gas is also related to its temperature (Charles' law), but such effects are nominal in the commercial flight settings as cabin temperature is artificially and tightly regulated.

Boyle's law<sup>31</sup> defines the relation concerning the compression and expansion of a gas at constant temperature. This **empirical** relation states that the pressure ( $p$ ) of a given quantity of gas varies inversely with its volume ( $v$ ) at constant temperature; that is, in equation form,  $pv = k$ , a constant. Simply put, for any given amount of gas at a constant temperature, the volume is inversely proportional to the pressure. Air containing cavities within the body is thus subjected to volumetric changes from the changing altitudes and accompanying cabin pressures during commercial flights. While this usually has no direct bearing on the heart and circulatory system, it does have consequences for passengers that had recently undergone surgical procedures, where trapped air within the potential spaces of the thorax or pericardium may expand during hypobaric conditions.

Dalton's law<sup>32</sup> states that the total pressure of a mixture of gases is equal to the sum of the partial pressures of the individual component

gases. The partial pressure is the pressure that each gas would exert if it alone occupied the volume of the mixture at the same temperature. The earth’s atmosphere comprises different gases, predominantly nitrogen, oxygen, and carbon dioxide, with oxygen being most biologically relevant for the maintenance of homeostasis and life. As the altitude increases and atmospheric pressure drops, the partial pressure of oxygen falls in tandem. Hypobaric hypoxia presents the biggest health risk at altitude in unpressurised flights.<sup>33</sup> The development of pressurized aircraft cabins enabled the carriage of passengers and aircrew to altitudes previously considered incompatible, with conventional commercial flights now cruising between 6,000m (20,000 ft) and 13,500 m (44, 000 ft). Aviation regulations stipulate that cabin ambient pressures must not exceed 2438m (8000 ft) at the maximum operating altitude of the airplane,<sup>34,35</sup> which most airliners were found to be able to maintain consistently.<sup>36,37</sup>

At 8000 ft cabin altitude, the approximated partial pressure of oxygen is 16 kPa, while the arterial partial pressure of oxygen (pO<sub>2</sub>) in a healthy individual is between 8 to 9 kPa (Table 1).<sup>38</sup> Juxtaposed against the standard oxygen dissociation curve (of an individual under normal homeostatic conditions and without anemia or other blood dyscrasias), at a cabin pressure altitude of 2438 m (8000 ft), the cabin oxygen partial pressure is 118 mm Hg, arterial pO<sub>2</sub> is 62-67 mm Hg and oxygen saturation is maintained at 90%-93%, which is still at the shallow aspect of the curve. These values arterial pO<sub>2</sub> have been found to be concordant during in-flight measurements with pulse oximeters.<sup>39</sup> Evidently, passengers with pre-existing cardiopulmonary conditions (eg, systolic heart failure, cyanotic heart disease, chronic obstructive lung disease or poorly controlled asthma), especially with abnormal sea level oxygen saturations, are in a precarious position when exposed to even mild hypobaria.<sup>40,41</sup> As such, physicians assessing these passengers for medical clearance for flights must be mindful to evaluate for preconditions fulfilling the criteria for in-flight supplemental oxygen.<sup>7,42-48</sup>

**Table 1.** Relationship between atmospheric pressure, aircraft cabin pO<sub>2</sub>, and arterial pO<sub>2</sub> in healthy subjects (data from Slonim and Hamilton<sup>38</sup>)

Altitude		Atmospheric pressure		Aircraft cabin pO <sub>2</sub>		Arterial pO <sub>2</sub>	
Feet	Meter	mm Hg	kPa	mm Hg	kPa	mm Hg	kPa
0	0	760	101	160	21.3	95-100	12.7-13.4
8000	2438	564	75	118	15.7	62-67	8.2-9

## *Hypoxia and Myocardial Ischemia*

The physiological consequences of hypoxia on the cardiovascular system are myriad, and ranges from vasoactive effects on the coronary, neurological and pulmonary vascular beds, to chronotropic and blood pressure responses, as well as salutary effects on cardiac contractility.<sup>21,48-55</sup> Acute hypoxia induces compensatory mechanisms<sup>56</sup> to counter the hypoxemic state — this includes sinus tachycardia, systemic vasoconstriction, pulmonary vasodilation, and increased minute ventilation. It also stimulates sympathetic activation with resultant increase in cardiac chronotropy and inotropy, and further exacerbates hypertensive response. All these responses converge to increase cardiac workload and place the hypoxic individual at risk of supply-demand mismatch, with potential adverse coronary and arrhythmic events.<sup>57-59</sup> Some of the referenced studies in aviation related papers derived observations from hypoxia during severe sleep apneic episodes, significantly different mechanistically from the hypobaric hypoxia at altitude,<sup>60,61</sup> and care must be taken in interpreting such results in the aviation context. In addition, most of these reported physiological responses do not manifest until marked hypoxemia when arterial pO<sub>2</sub> drops below 40 mm Hg (corresponding to an arterial oxygen saturation <70%),<sup>51,62</sup> which is improbable in a commercial cabin unless acute decompression occurs (secondary to either a breach in cabin integrity, or catastrophic failure of aircraft cabin pressurization systems — both being highly remote occurrences in modern aviation).

## *Hypoxia and Electrophysiology*

There is a paucity of well-designed randomized trials to evaluate arrhythmic risks in humans in a hypobaric environment, and most studies inferring increased arrhythmic risks at high altitudes are usually conducted at barometric pressures much lower (such as during extreme mountaineering) than that within commercial aircraft cabins, or were conducted in animals, and may not be directly applicable to the aviation context.<sup>63-65</sup> Arrhythmias are postulated to be triggered by sympathetic nervous system activation in susceptible passengers, especially those with underlying structural heart disease,<sup>66</sup> and commercial flying presents multiple precipitants (hypoxia, tachycardia, hyperventilation, missed medications, etc) for such scenarios. Two volunteer-based studies<sup>67,68</sup> from the Netherlands demonstrated a linear correlation between increasing altitudes and ventricular and supraventricular ectopy, in a population of healthy middle-aged and elderly men (50-64 years old). The investigators also observed that these findings did not extend to sustained or

hemodynamically significant ventricular arrhythmias. Extrapolating this data, it is reasonable to expect passengers with cardiomyopathies, especially those more than 50 years old, to be more predisposed to arrhythmias during commercial flights, even though the absolute risk increment is probably nominal.

## *Aviation Environment and Electrophysiology*

In terms of environmental interactions with cardiac implantable electronic devices (“CIEDs” – comprising pacemakers, defibrillators, loop recorders) in the aircraft cabin, insufficient large-scale studies currently exist. From a smaller trial conducted in the early 2000s, pacemakers (each embedded within an artificial thorax) were exposed to the cockpit environs of a single engine fixed wing aircraft to assess for electromagnetic interference (EMI) by the avionics system on device function, with all found to be working normally during and after the test flight.<sup>69</sup> A follow-up study looking at implantable cardioverter defibrillators function under comparable circumstances was conducted by the same group in 2017, with similar findings.<sup>70</sup> Nine mountaineers who scaled Mount Everest base camp (up to 5600 m) were implanted with subpectoral loop recorders as part of a study to assess altitude related arrhythmias, with all the loop recorders explanted in working condition.<sup>63</sup>

Another study subjected 13 patients with implantable pacemakers to a simulated altitude of 4000 m in a hypobaric chamber, with pacemaker interrogation and arterial blood gas analyses performed at predetermined altitudes.<sup>71</sup> The investigators reported that ascent to 4000 m resulted in arterial desaturation ( $79\% \pm 2.5\%$ ) but without affecting pacemaker stimulation thresholds or strength-duration curve (a measure of pacing threshold to stimulus pulse duration). Given that conventional aircraft cabin altitudes do not exceed 2438 m (8000 ft), this provides sufficient support that pacemakers will likely operate safely within the aircraft confines, an opinion shared by similar studies and expert consensus papers.<sup>72,73</sup>

In contradistinction, it is the preflight ground conditions that subject passengers with CIEDs to risk of device malfunction. The EMI from airport security scanners are known to cause inhibition of pacing on occasions,<sup>74,80</sup> which would be disastrous for a patient who is pacing dependent. However, such occurrences are rare and larger studies refute any significant EMI on CIEDs for either handheld or walk-through metal detectors of airport security systems.<sup>75,76,77</sup> It must be noted that exposures to such EMI are usually brief, and passengers with CIEDs must be cautioned to inform security personnel of their devices to avoid

prolonged contact with the security equipment,<sup>78,79</sup> and to avoid unnecessary stress from the inadvertent alarm trigger when the security devices detect the metallic CIEDs.<sup>79,80,81</sup>

## *Hypoxia and Systolic Heart Failure*

Passengers with heart failure with reduced ejection fraction (HFREF), defined as a left ventricular ejection fraction  $<40\%$ ,<sup>82,83</sup> presents an at-risk group for IMEs during commercial flights.<sup>21,84,85</sup> Hypoxia has deleterious effects on HFREF, but large populations trials of heart failure patients under hypobaric conditions presently do not exist. Hobkirk et al<sup>86</sup> showed that in a small group of patients with HFREF and NYHA functional class II (74%) or III (26%) statuses, inducing isocapnic hypoxia (via inspiration of 15% oxygen) did not cause worsening of baseline symptoms despite reductions in arterial oxygen tension (to  $86\% \pm 4\%$ ). However, it must be noted that this small study was conducted for a very short duration (1 hour), and the author proposed that further research was required to assess the hemodynamic and echocardiographic responses to longer durations of hypoxia in a larger sample size of heart failure passengers. In another retrospective survey-based study,<sup>87</sup> HFREF passengers of various underlying etiologies (ischemic, dilated, hypertensive or valvular) responded favorably on tolerating the in-flight phase of air travel. In fact, the main negative experiences were from ground destinations related activities, such as the carriage of luggage across airport terminals, than the flights themselves (25% vs 9% of respondents). Even at increased workloads under experimental conditions, stable HFREF patients with more advanced disease (NYHA III and IV) were able to complete cardiopulmonary exercise tests uneventfully when exposed to an altitude equivalent to 3000 m (9842 ft).<sup>88</sup> In the Ideal Cabin Environment (ICE) project,<sup>89</sup> conducted under the auspices of the European Commission, volunteers with stable HFREF (all NYHA II functional status) were subjected to a 7-hour simulated flight. The mean oxygen saturation at 8000 ft cabin altitude was measured at 91%, but none of the subjects reported new or worsening symptoms.

In general, current evidence indicates that passengers with stable HFREF, regardless of functional class, are likely able to tolerate conventional commercial flights with in-flight physical levels commensurate with their activities of daily living.

Standalone right heart failure (defined as right ventricular fractional area change of  $<35\%$ ,<sup>90,91</sup> traditionally derived from echocardiographic evaluation), and heart failure with preserved ejection fraction (“HFPEF”



– left ventricular ejection fraction >50%), are less common entities, and literature on safety of commercial flights in such a niche population is scarce. More research needs to be conducted in this realm to assess the effects of commercial flights on such conditions before firmer recommendations can be made.

## *Hypoxia and Thrombogenicity*

From a cardiovascular standpoint, the chief concern of hypoxia induced procoagulable state is the formation of occlusive coronary thrombus in already atherosclerotic segments, or deep vein thrombosis (DVT) with risk of embolic events (pulmonary embolism from peripheral DVT, or systemic embolism if right-to-left shunt is present).<sup>4,21,46,50,79,85</sup> Both transient and chronic exposure to extreme altitudes (>5000 m) have been shown to result in increased activation of clotting factors,<sup>92,93</sup> with increased release of thromboxane and prostacyclin, and elevated levels of factor VIII and D-dimer. However, such in-vivo findings did not translate to real-world clinical consequences,<sup>94</sup> including 2 small studies of healthy volunteers in simulated flights.<sup>95,96</sup> A more sizeable trial<sup>97</sup> involving 73 subjects in a hypobaric chamber recreating the cabin environment of a long haul flight (8 hours) at an altitude of 2438 m (8000 ft) did not demonstrate any significant differences in prothrombotic states of mild hypoxia on low risk, healthy individuals.

In summary, majority of commercial air travellers exposed to hypobaria in-flight do not appear to be at increased risk of cardiovascular events despite mildly reduced arterial oxygen content, including myocardial ischemia, acute decompensation of heart failure, or significant cardiac dysrhythmias. In addition, passengers with CIEDs are also unlikely to experience device malfunctions during the flying phase of travel. These assertions are adequately supported by current evidence-based studies for short to medium range flights (up to 8 hours), but data regarding flight risks for super long-haul flights (duration >12 hours) in the modern era of high endurance aircraft are presently lacking.<sup>21,98</sup>

## **Conclusion**

Knowledge of the aviation environment and its attendant physiological consequences, as well as commercial flying associated stressors, underpins the decision-making process for the clinician in certifying any passengers fit for flight prior to their air travel. This review has summarized the key aerospace principles and evidence relevant for the attending physician to

develop an understanding of the various factors that will impact cardiovascular health for the patient undertaking commercial flights.

## Author Contribution

KOH Choong Hou contributes fully and independently in the crafting of this manuscript.

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