Commercial Air Travel for Passengers With Cardiovascular Disease: Recommendations for Less Common Conditions, Considerations for Venous Thromboembolism, and General Guidance

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Abstract: The accelerated growth of commercial flights has resulted in a huge upswing of air travelers over the last few decades, including passengers with a wide range of cardiovascular conditions. Notwithstanding the ongoing COVID-19 pandemic that has set back the aviation industry for the next 1-2 years, air travel is expected to rebound fully by 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 updated suite of recommendations for the aeromedical disposition of passenger with uncommon cardiovascular conditions, such as congenital heart diseases, inflammatory cardiac conditions (endocarditis/pericarditis/myocarditis), pulmonary hypertension, and venous thromboembolism. In addition, the article also aims to provide practical general guidance for the aeromedical examiner in

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evaluating, preparing, and optimizing the cardiac status of the patient with cardiovascular ailments for air travel. (Curr Probl Cardiol 2021;46:100782.)

Introduction

Following the earlier 2 parts[1,2] of this review series examining the foundational aerospace principles and evidence undergirding aeromedical fitness for flight for the various common cardiovascular conditions, the final part focuses on less common cardiovascular conditions and considerations for venous thromboembolic risk mitigation and management. In addition, the final section provides an overview and general guidance for the aeromedical examiner in evaluating, preparing, and optimizing the cardiac status of the patient with cardiovascular ailments for air travel.

Congenital Heart Disease

The classification system for congenital heart diseases can be complicated,[3] but for the purpose of aeromedical assessment, they can be broadly dichotomized into either acyanotic or cyanotic. Cyanotic pathologies arise due to right-to-left shunt, either intra- or extracardiac in origin, and results in diversion of deoxygenated blood from the venous to the arterial circulation. Depending on the nature, severity and chronicity of the shunt, there may be complex physiological consequences, such as ventricular remodeling and failure from volume overload, arrhythmias, valvulopathies, paradoxical thromboembolic events, polycythemia with hyperviscosity, and pulmonary hypertension.[3,4]

Eisenmenger syndrome[5,6] represents late stage disease when irreversible pulmonary hypertension develops from an initially left-to-right shunt, which consequently reverses in direction with mixing of desaturated blood with the systemic circulation. This subset of patients is also believed to be prone to in-flight decompensation or medical events when flying due to baseline hypoxemia and a hyperviscous state.[7,8] Shunt thrombosis and systemic thromboembolism from increased thrombogenicity in-flight poses a significant health hazard and thrombophylaxis should be duly considered in this population.[9,10]

Long-term physiological adaptation leads to a rightward shift of the oxygen dissociation curve, with a decreased hemoglobin affinity for oxygen molecules, and patients are still able to maintain a modest degree of functional capacity.[8,9] This attenuates the effects of lower alveolar

oxygen tension in the aircraft cabin while in-flight, and Eisenmenger syndrome patients had been observed to be able to fly safely despite their condition, provided they stay hydrated, avoid alcoholic beverages and minimize in-flight physical activities.[9]

Table 1 summarizes the aeromedical recommendations for congenital cyanotic heart diseases.[7,9-16]

Endocarditis, Pericarditis, and Myocarditis

The spectrum of endocarditis, pericarditis, and myocarditis constitute the 3 commonest entities of cardiac inflammatory reactions arising from infective or immune-mediated insults, or less commonly metabolic/radiation/toxins induced injury, with a multitude of structural and functional consequences.[17-20] Complications can range from persistent septicemia, arrhythmias, distal embolism, severe valvulopathies, direct myocardial injury, and heart failure, to restricted ventricular filling with diminished cardiac output.

TABLE 1. Aeromedical recommendations for congenital cyanotic heart diseases

Condition	Elaboration	Aeromedical recommendation(s)
Congenital cyanotic heart diseases (including Eisenmenger syndrome)	NYHA I-II	Fit to fly Consider in-flight oxygen if baseline SpO_2 <80% or significant desaturation with 6-minute walk test[9] Advise not to fly alone
	NYHA III	Fit to fly Consult congenital heart disease cardiologist and aviation medicine specialist Consider medical escort, airport assistance and in-flight supplemental oxygen Consider thromboembolic prophylaxis (low molecular weight heparin, warfarin, direct oral anticoagulants[42], compression stockings etc.)
	NYHA IVa (ambulatory class IV)	Defer non-essential travel If flying required, needs medical escort Consult congenital heart disease cardiologist and aviation medicine specialist Arrange airport assistance and in-flight supplemental oxygen Recommend thromboembolic prophylaxis (low molecular weight heparin, warfarin, direct oral anticoagulants[42], compression stockings etc.)
	General advice	Minimize in-flight physical activities Ensure well hydrated Avoid alcoholic beverages

There are presently no aviation related studies with data on in-flight implications for this group of patients, and existing advisories[21] are aircrew occupational fitness centric and held to more stringent standards than required for commercial flying as passengers, making it challenging to extrapolate for the latter. Aeromedical assessment thus relies on evaluating for symptoms, clinical stability, and the presence or absence of complications. In general, during the acute phase of the condition, commercial flying is strictly prohibited. Post recovery, fitness to resume air travel will be predicated on NYHA functional class status, regardless of the underlying etiology of the insult.

Table 2 lists the aeromedical recommendations for endocarditis, pericarditis, and myocarditis.[21]

Pulmonary Hypertension

Pulmonary hypertension is defined as a mean pulmonary artery pressure $\geq$25 mm Hg at rest, as assessed by invasive right heart catheterization.[22] The development of pulmonary hypertension (PH) may be due to a variety of pathophysiological processes from multiple medical conditions (in isolation or in combination), and usually represents an advanced stage of the underlying disease.[22-25] As chronic lung conditions, left heart diseases, or hematologic/systemic disorders make up the majority of cases of PH, the management strategy usually focuses on treating the underlying condition, rather than PH specific therapy. For aeromedical considerations for flight, such "secondary PH" should then be assessed on the merit of the original disease while acknowledging PH as a late clinical sequela.

Pulmonary arterial hypertension, on the other hand, is a syndrome in which pulmonary arterial obstruction increases pulmonary vascular resistance, which leads to right ventricular failure in the long term.[23] Impaired right-sided systolic function then results in decreased preload to the left heart, and patients will eventually exhibit features of biventricular failure when the condition is clinically advanced.[26]

Rapid constriction of the pulmonary in response to acute exposure to hypoxia, with a consequent rise in pulmonary circulatory pressures, can have deleterious hemodynamic effects on an already strained right heart. If the right ventricle is unable to cope with the sudden increase in afterload, acute decompensation may occur.[27] In contradistinction to the potential adverse hemodynamics, one small study observed that most mildly symptomatic (mainly NYHA I/II) PH passengers were able to tolerate short haul flights of up to 3.6 hours.[28]

TABLE 2. Aeromedical recommendations for endocarditis, pericarditis and myocarditis

Condition	Elaboration	Aeromedical recommendation(s)
Endocarditis (acute)	Uncontrolled sepsis/ arrhythmias	Unfit to fly
	Hemodynamically unstable	Unfit to fly
	Severe valvulopathy (regurgitation, valvular obstruction) with decompensated heart failure	Unfit to fly
	Acute embolic cardiovascular accident from vegetations	Unfit to fly for at least 2 weeks Consult neurologist, cardiologist, and aviation medicine specialist Repeat neurological and cardiac imaging to exclude cerebral hemorrhagic conversion and residual intracardiac vegetations respectively
Endocarditis (old)	Recovered infective endocarditis with fixed and immobile old vegetation, or no vegetations	Unrestricted for flight
Pericarditis (acute)	Uncontrolled symptoms or sepsis (if infective etiology)	Unfit to fly
Pericarditis (chronic)	Mild pericardial effusion (<10 mm circumference)	Unrestricted for flight
	Constrictive pericarditis NYHA I-II	Unrestricted for flight
	Constrictive pericarditis NYHA III	Consider airport assistance and in-flight supplemental oxygen
	Constrictive pericarditis NYHA IVa	Defer non-essential travel Consult cardiologist and aviation medicine specialist Strongly advise airport assistance and in-flight supplemental oxygen
Myocarditis	NYHA I-II	Unrestricted for flight
	NYHA III	Consider airport assistance and in-flight supplemental oxygen
	NYHA IVa	Defer nonessential travel Consult cardiologist and aviation medicine specialist Strongly advise airport assistance and in-flight supplemental oxygen
	Cardiogenic shock Uncontrolled sepsis/ arrhythmias	Unfit to fly
Myopericarditis	Manage as per either pericarditis or myocarditis, whichever is worse	See management for pericarditis or myocarditis

With regards to in-flight supplemental oxygen for air travelers with PH, proposals for using NYHA functional class, baseline oxygen saturations, pulmonary arterial systolic pressures, or hypoxia challenge testing, have been suggested.[9,27,29,30] Those who are already on long-term oxygen therapy must be advised to arrange in-flight oxygen supplementation before embarkation.

Table 3 lists the aeromedical recommendations for pulmonary hypertension.[9,11,13,27,29]

Venous Thromboembolism

Air travel has been established as a risk factor for deep vein thrombosis (DVT) and venous thromboembolism (VTE) in multiple studies, most notably the landmark WRIGHT project (WHO Research Into Global Hazards of Travel) commissioned by the World Health Organization.[31-33] The final WRIGHT project report, published in 2007, observed that the incidence of VTE increases 2-fold after flights exceeding 4 hours, and linearly rises with prolonged immobility, travel duration, and multiple flights within a short period. Other identified risk factors for VTE events include obesity, extremes of height, oral contraceptives use, and

TABLE 3. Aeromedical recommendations for pulmonary hypertension

Condition	Elaboration	Aeromedical recommendation(s)
Pulmonary hypertension	NYHA I, and Resting SpO_2 $\geq$85%[28]	Fit to fly
	NYHA II, or resting SpO_2 <85%	Fit to fly Advise not to travel alone Consider airport assistance and in-flight supplemental oxygen Consider hypoxia challenge test for borderline cases, in consultation with cardiologist and aviation medicine specialist[43]
	NYHA III, or resting SpO_2 <80%, or PASP >60 mm Hg*	Defer nonessential travel Consult cardiologist and aviation medicine specialist Recommend medical escort, airport assistance and in-flight supplemental oxygen
	NYHA IV or decompensated right heart failure†	Unfit for flight

*Can be derived from echocardiographic Doppler evaluation, not necessarily an invasive right heart study.

†Severe lower extremity edema, ascites (abdominal distension), hepatomegaly/liver dysfunction.

prothrombotic states. While thrombotic risk in association with traditional cardiovascular disease risk factors (such as hypertension, diabetes, and hyperlipidemia) has not been definitively linked,[34,35] it is recognized in heart failure air travelers due to pre-existing circulatory insufficiency aggravated by venous stasis from prolonged immobility in-flight.[7,11,12,14]

A risk-stratified approach is generally prescribed for VTE preventive measures, as illustrated in Table 4.[7,11-14,27,36,37]

TABLE 4. Risk stratified strategy for VTE prevention

Condition	Elaboration	Aeromedical recommendation(s)
Flights <6 h	Short to medium haul flights*	Avoid stasis: intermittent movement around cabin, isometric calf exercises, avoid constrictive clothing around waist and lower extremities, aisle seating if possible Maintain hydration: drink adequately, avoid alcohol and caffeinated drinks
Flights ≥6 h	Low risk No history of DVT/VTE No recent surgery within 4 weeks No other DVT/VTE risk factors† Medium risk Previous history of DVT/VTE Recent major surgery lasting >30 min in the past 2 months but not in the last 4 weeks Known thrombophilia Pregnancy Obesity (BMI >30 kg/m^2)	Avoid stasis and maintain hydration as above Avoid sedatives No smoking (most flights are non-smoking anyway) Avoid stasis and maintain hydration as above Avoid sedatives and smoking Below knee compression stockings
	High risk Recent (within 4 weeks) major surgery under general anesthesia lasting >30 min Previous DVT with known additional risk factor(s) including known cancer Advanced heart failure (EF <20%)	Avoid stasis and maintain hydration as above Avoid sedatives and smoking Below knee compression stockings Prophylactic subcutaneous low molecular weight heparin (enoxaparin) pre-flight ± the following day (usually after arrival at destination), for those not already taking oral anticoagulants

*Long haul flights, as defined by the Centre for Aviation, is typically a long-distance flight of at least 6 hours in duration.[44]

†Risk factors for DVT/VTE9,37: thrombophilic blood disorders; systemic illnesses with coagulopathic states (e.g. severe sepsis); heart failure or recent myocardial infarction; current or history of malignancy; recent major surgery; recent trauma to lower limbs or abdomen; large varicosities in lower extremities; personal or family history of DVT; pregnancy; estrogen hormone therapy, including oral contraception; age above 40; prolonged immobilization (prior to travel); hypovolemic states resulting in increased blood viscosity (e.g. severe diarrhoea/vomiting, extreme fasting).

[#]Risk factors for DVT/VTE[11,37]: thrombophilic blood disorders; systemic illnesses with coagulopathic states (eg, severe sepsis); heart failure or recent myocardial infarction; current or history of malignancy; recent major surgery; recent trauma to lower limbs or abdomen; large varicosities in lower extremities; personal or family history of DVT; pregnancy; estrogen hormone therapy, including oral contraception; age above 40; prolonged immobilization (prior to travel); hypovolemic states resulting in increased blood viscosity (eg, severe diarrhea/vomiting, extreme fasting)

Preflight Evaluation and General Advice

Airlines reserve the rights to deny passengers deemed medically unfit to fly.[36,38,39] A dynamic tension exists—is the passenger "fit to fly unless otherwise proven," or "unfit to fly unless otherwise proven"? From a safety perspective, for any traveler with pre-existing cardiovascular conditions, the burden of proof resides with the attending physician to determine that he or she is clinically stable, and risk mitigated before embarking on air travel.

Besides the evaluation for fitness to fly status (referencing the matrices in the earlier sections), the physician should also be the provider of traveling advice, covering potential blind spots in the pre-, post-, and in-flight phases of the journey. This would also include appropriate adjustments of multidose chronic medications across different time zones, particularly for ultralong-haul flights with multiple time zone crossings. As a general rule of thumb, slight under-dosing or even omission may be advisable to prevent potential toxic side effects from supratherapeutic levels (from shortened dosing intervals), and is generally acceptable given the short duration of dosing adjustments (usually over 24-36 hours). Further customization of drug scheduling is advised if there are extended transit points or lay-overs in between the journey. Attention should be paid to the half-lives of the affected medications, impact of excessive or missed dosing, and the influence of circadian changes and meal timings.

A brief summary of the guidance for the medical examiner, and the air traveler with cardiovascular disease, is suggested in Table 5.[11,13,14,27,37,40]

Conclusion

Airlines have a duty of care for passengers to ensure they are medically safe to fly, not just for their personal health and safety, but also to avoid potential in-flight medical emergencies that cannot be managed on board and require aircraft diversion, incurring significant costs and inconvenience for the rest of the passengers.[40,41] To an even greater extent, it is incumbent

Table 5. Medical guidance for air travelers with cardiovascular disease

Domain	Elaboration	Recommendation(s)
Preflight evaluation and preparation	Comprehensive history and physical examination	- Measure baseline oxygen saturation by pulse oximeter - 12-lead ECG - Chest X-ray (postdevice implantation) - Check INR if on warfarin (at least 24-48 h predeparture)
	Medical prescriptions, reports, and investigations	- Hand carry relevant documents for immigration and security clearances at airport - Provide latest copy of 12-lead ECG with and without pacing - Assist with airlines MEDIF forms where required*
	Post cardiac implantable electronic devices (pacemakers, ICD, loop recorders etc.) or left ventricular assist device procedures	- Provide device or equipment card to patient - Provide latest copy of device interrogation report/print-out - Liaise ahead with device or equipment management capable clinic, and manufacturer representative at travel destination - Inform security personnel to avoid placing handheld metal detectors over CIEDs - Minimize dwell time near metal detectors - Airport and in-flight assistance with luggage, especially during stowing and unloading from overhead cabins
	Itinerary planning and airport ground assistance	- Allow adequate intervals between connecting flights, and cater time buffers for delays at immigration/security, to avoid rush and stress - Arrange with airport ground staff in advance for assistance at departure and arrival airports: transfer and intra-facilities conveyance (buggy, wheelchair, fast lane), luggage assistance etc.
	Aeromedical fitness for flight	- Determine suitability for solo vs accompanied vs medically escorted air travel - Consult attending cardiologist and/or aviation medicine specialist for special/difficult cases
In-flight precautions	General advice	- Arrange for mobility devices (wheelchair, electric carts), special diet, seat requests (near toilet, non-smoking zone, aisle), or in-flight supplemental oxygen with airline in advance - Arrange for medical escort and clearance for on-board carriage of medical equipment in advance - Inform flight attendant whenever feeling unwell - Maintain hydration and avoid prolonged immobility - Avoid alcohol and caffeinated beverages
	Remedial actions for impending cardiac events	- Ischemic chest pain: inform flight attendant, rest in seat, sublingual nitroglycerin - Neurocardiogenic syncope: inform flight attendant, rest in seat (recline if possible), cross legs, hydrate - Paroxysmal supraventricular tachycardia: inform flight attendant, Valsalva maneuver
	Medications quantum and type	- Provide latest prescription to patient (with information on drug allergies) - Hand carry adequate supply of medications to last for flight and up to 3-5 days after (in the event of diversions

(*continued*)

Table 5. (*continued*)

Domain	Elaboration	Recommendation(s)
		to destinations with poor medical support, loss of luggage etc.) - Hand carry emergency medications (eg, nitroglycerin for ischemic heart disease, pill-in-the pocket antiarrhythmics for paroxysmal atrial fibrillation) - Prophylactic medications for infectious diseases (eg, anti-malarials) may interact with cardiac medications—cross check with cardiologist and pharmacy when prescribing such drugs
	Medications scheduling This loosely references the insulin adjustment matrix for multiple time zone crossings as a guide.[11] Slight under-dosing is recommended to prevent toxic effects and is acceptable given short duration of dosing adjustments (usually over 24-36h). Further customization is advised if there are extended transits or lay-overs in between. Exceptions to these recommendations include patients who are at very high risk for adverse events even with single omission or delay of medications (for eg, a patient with metallic mitral valve replacement with sub-therapeutic INR and history of valve thrombosis). Such cases should be discussed with the attending cardiologist on a case-by-case basis and drug regimens during transcontinental flight customized accordingly.	Time zone difference <6 hours at destination: - Adhere to usual dosing time of medications as departure location - Gradually adjust to destination timings within the first 24-48h on arrival Time zone difference ≥6 hours at destination (either eastward or westward travel): - Once a day dosing → Departure day = usual pre-flight dose before boarding, subsequent doses to adjust to in-flight meal timings depending on departure time → First day at destination (for first dose after landing) = half dose, or consider omitting if last consumed dose in-flight is within 6-8 h → Second day at destination = usual dose - Twice a day dosing → Departure day = usual pre-flight doses before boarding, subsequent doses to adjust to in-flight meal timings depending on departure time → First day at destination (for first dose after landing) = half dose or consider omitting if last consumed dose in-flight is within 6-8 h; (for second dose after landing, if applicable to destination time) = half dose → Second day at destination = usual two doses - Thrice a day dosing → Departure day = usual pre-flight doses before boarding, subsequent doses to adjust to in-flight meal timings depending on departure time → First day at destination (for first dose after landing) = half dose or consider omitting if last consumed dose in-flight is within 6-8 h; (for second dose after landing, if applicable to destination time) = half dose; (for third dose after landing, if applicable to destination time) = usual dose → Second day at destination = usual three doses
	DVT/VTE prophylaxis	See section on DVT/VTE

*MEDIF is the name given to the forms used by airlines to manage passengers requiring special assistance and medical clearance. It has 2 attachments: "Attachment A" (Information Sheet for Passengers Requiring Special Assistance) and "Attachment B" (Information Sheet for Passengers requiring medical clearance).[13,45]

on physicians assessing fitness for flight for patients with cardiovascular disorders to ensure that thorough and comprehensive assessments are carried out, to ensure any identified risks are eliminated or diminished to the lowest possible levels, and to discourage travel plans if such a state cannot be achieved. This set of guidelines aims to inform the medical examiner of the potential interactions between the air travel environment and the various cardiovascular conditions. When faced with a complex situation beyond the scope of this guideline, the examiner should confer with the relevant medical specialists involved in the care of the patient, in order to reach a well-deliberated consensus decision on flying fitness.

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