

Air travel and the risk of thromboembolism

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Abstract Almost two billion people use commercial aircraft annually. Long-haul flights are taken by over 300 million people. A serious complication of long-distance travel (or prolonged time of flight) is thromboembolism. The real incidence of the problem is difficult to evaluate since there is no consensus about the diagnostic tests or limitation of time after landing connected to the VTE complication. A direct relation between VTE incidence and long-distance flights has been documented. The risk for DVT is 3–12% in a long-haul flight. The pathophysiologic changes that increase VTE risk at flight are stasis (sitting in crowded condition), hypoxia in the airplane cabin, and dehydration. Individual risk factors for air travel-related VTE include age over 40 years, gender (female), women who use oral contraceptives, varicose veins in lower limbs, obesity and genetic thrombophilia. Prevention measures include environmental protection such as keeping the pressure inside the airplane cabinet in hypobaric condition, avoiding dehydration and prolonged sitting. For individuals at increased risk, venous blood stasis can be reduced by wearing elastic stockings and prophylactic use of low-molecular-weight heparin.

Keywords Air travel · Thromboembolism

Introduction

Annually, almost two billion people travel by commercial aircraft (short- and long-haul flights) [1], and over 300 million people travel long-haul flights [2]. The major health problems related to flying are cabin hypoxia, transmission of infectious diseases, fear and anxiety, jet lag and thromboembolic events (VTE) [1]. This review will highlight the problem in terms of the VTE incidence in long distance flights and the specific population whose risk is increased. Some recommendations regarding prevention of this complication will be discussed [1, 3].

Epidemiology

There are three main difficulties in assessing the incidence of VTE related to flying.

First, several large studies are based on medical records [3, 5, 6] and not on imaging or confirmed diagnostic tests for VTE [2, 8].

Second, there is no consensus on the time frame, after the flight, regarding the definition of travel-related VTE (Table 1). Some studies included VTE on the day of landing, while others included all VTE up to 1 month after a long-distance flight [5, 6, 8].

Indeed, while most episodes occur within the first 2 weeks, with a median of 4 days, the risk is prolonged up to 4 weeks after landing [2, 14]. Third, measured outcomes of the studies differ. A number of trials include deep vein thrombosis (DVT), several consider only pulmonary embolism (PE) and some (Table 2) encompass all cases of

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Table 1 Studies based on medical records and timing of DVT/PE after landing post a long-distance flight

Author	Study type/included subjects	Cases	Time interval for VTE screening after air travel
Lapostolle [5]	Study cohort: all travellers arriving in the airport	Documented PE	1 day (Day of landing)
Perez –Rodriguez [6]	Study cohort: all travellers arriving in the airport	Documented PE	1 day (Day of landing)
Kelman [8]	Case control study: passengers who were hospitalized after air travel	Documented PE	1–14 days
	Population based study: volunteers planning a long-distance flight	10% symptomless DVT	48 h
Hughes [11] (NZAIT study)	Population based study: volunteers planning a long-distance flight	D-Dimer as screening for VTE U/S to confirm DVT Angiography to confirm PE	3–90 days
Martinelli [13]	Case control study/consecutive patients attending thrombosis centre for thrombophilia screening after at least first DVT	Documented DVT	1–30 days
Cannegieter [14] (MEGA study)	Case control study/consecutive patients attending thrombosis centre for thrombophilia screening after at least first DVT	Documented DVT	1–8 weeks

Table 2 Specific type of venous thromboembolism: DVT or PTE after long-distance flight

Author	Type of VTE	Incidence (length/duration of flight)	Odds ratio
Lapostolle [5]	PTE	1.5/1,000,000 (>5,000 km)	–
		4.8/1,000,000 (>10,000 km)	
Lapostolle [25]	PTE	0.61/1,000,000 (>10,000 km) for women	–
		0.2/1,000,000 (>10,000 km) for men	
Perez-Rodrigues [6]	PTE	0.25/1,000,000 (6–8 h)	–
		1.65/1,000,000 (>8 h)	
Kelman [8]	DVT	Relative risk 4.17%	2.94–5.40
Schwarz [9]	DVT + PE	2.8% (\geq 8 h)	1.46–5.49

venous thromboembolism [3, 4]. VTE incidence increases when the time from landing is included in the study, and it directly correlates to the flight duration [3, 4]. Studies focusing on VTE developed upon arrival in major airports reveal its direct relation to the flight length or duration [3, 4].

The risk of PE post air travel is $0.5/1 \times 10^6$ on the day of landing [5, 6] and rises to $27/1 \times 10^6$ VTE (DVT or PE) during the first 14 days after landing [9]. Fatal PE was not observed in over 1 million passengers of transatlantic flights or in any of the 1341 patients diagnosed with PE shortly after landing [7].

The estimation is 1.1 VTE per million person-days, which is in close proximity to the frequency of DVT in the healthy population (1.9–5.2 per million person-days). If the diagnosis is based on ultrasonographic studies (which demonstrate asymptomatic, mostly distal clots), the risk of

DVT is increased to 3–12% for long distance flights [10, 11].

This discrepancy between the high rates of asymptomatic clot and the very low rates of symptomatic events upon arrival in major airports is due to several factors. The first is the time frame: 1 h versus 4 weeks, which can explain the 50–100-fold difference. Second, asymptomatic DVT is 5–20-fold more common than symptomatic events. Thus, there is a 250–2000-fold difference.

Risk assessment for VTE in flights

Overall, the risk of VTE is increased twofold in long-distance flights (>8 h). The risk is 18% higher for each 2-h increase in travel duration, and it is even 26% higher (per 2 h) when limited exclusively to air travel [4]. The realistic

risk of symptomatic event is 1/600 for flights over 4 h and 1/500 for flights over 12 h in travellers over 50 years of age [2, 20, 21].

At least seven risk factors have been identified for VTE related to flying or travelling by car, train or bus [3]:

1. The length of the travel—in prolonged flights (over 6 h), the risk is increased by 2.3-fold in comparison with shorter flights [4, 5]. A summary of nine studies, including 126 VTE cases associated with air travel, indicates six risk factors [3, 8–10].
2. Age over 40 years (45% of 126 DVT cases) [3].
3. Women who use oral contraceptive drugs (OC) or hormone replacement therapy (HRT) (31% of 126 cases) or 2.4-fold increased risk [3, 12, 13].
4. Lower limb varicose veins (19% of 126 cases) [3].
5. Obesity (BMI > 30) [3].
6. Genetic thrombophilia (6% of 126 cases) [3]. Elevated levels of coagulation factors II and VIII [19].
7. Other risk factors, e.g. tall stature, short stature, etc. (7% of 126 cases) [3, 14].

The risk is equal for those who fly in economy class or business class [9].

The MEGA study [14] finds an eightfold increased risk for DVT for travellers by bus, car or train who carried the mutation factor V Leiden, and an even higher risk (12-fold) for air travellers.

In women, the combination of long-distance travel and OC use increases the risk of DVT by about 20-fold [2, 14, 21]. Importantly, a stronger correlation is observed between air flight and OC use in the MEGA study, which indicates a 40-fold increased risk for VTE. Martinelli et al. [12] studied the combined effect of travelling and thrombophilia, and found a 16-fold increased risk for air travel and VTE, and only a 1.7-fold increased risk without thrombophilia.

Lapostolle et al. [25] have recently published a large cohort study that confirms the hypothesis that female gender is an independent risk factor for pulmonary embolism after long-distance flight. The risk for women is three times higher in comparison with men (0.61 female vs. 0.2 male per million passengers).

Pathogenesis of VTE in air travel

To prevent hypoxic conditions in the passenger cabins, commercial aircraft would need to keep inside cabin air pressure similar to that on the ground, albeit cruising at an altitude of 6–12 km [1, 2]. Hypoxia related to the inside cabin pressure is equivalent to an oxygen saturation of approximately 72 mmHg. The interior air pressure in most commercial aircraft is similar to living at heights of

1800–2400 m. Most modern aircraft are designed to support a vast pressure difference between the exterior and interior environments. Maintaining ideal air pressure difference between the interior and exterior compartments would demand a huge amount of fuel, thereby adding weight to the aircraft. Hypoxic conditions are dangerous, especially for patients with cardiovascular or chronic lung diseases [1, 3, 15], and probably play a role in activating the coagulation system during air travel [15, 16]. Air travel for at least 8 h significantly increases pro-coagulant activity in 17% of healthy persons, and particularly in those harbouring thrombophilia or in women who use hormonal contraceptives or replacement therapy [2, 14].

Sitting conditions in the economy class are crowded, without enough room for stretching legs or standing/walking liberally. Most passengers remain seated for many hours, increasing venous stasis and procoagulant activity. In the LONFLIT study, immobilisation was linked to 75% cases of venous thromboembolism after long distance flights [12].

Sitting without moving significantly increases procoagulant activity in a hypobaric chamber mimicking cabin conditions [16, 17]. Prolonged standing also increases procoagulant activity in young healthy individuals [18].

Dehydration during flight may increase the risk of hypercoagulability by inducing haemoconcentration and hyperviscosity. Contributing factors are low cabin humidity (8–12%) that leads to fluid loss, reduced fluid intake and consumption of coffee and alcohol that induce diuresis [20].

Prevention of air travel VTE

Preventive measures against VTE during flights can be described in two categories, individual prophylaxis and environmental protection:

1. Environmental protection includes keeping the inside cabin air pressure at hypobaric conditions (1.8–2.5 km altitude); avoiding dehydration by supplying adequate humidity via the airconditioning units and encouraging passenger to drink water or light non-alcoholic drinks; improving sitting position and space between rows, so that leg stretching, movements and easy walking in the aisles are possible. Likewise, oxygen support may be useful in patients with COPD or CHF [13].
2. Individual prophylaxis includes general recommendations for all travellers and specific measures for high-risk passengers. The general rules are to avoid prolonged sitting, to exercise calf muscles while sitting; short walking in the aisle every 2–3 h [22], to drink ample amounts of water and to avoid alcohol consumption [23].

Venous blood stasis prevention can be achieved by wearing graduated elastic stockings, which have been demonstrated to reduce VTE incidence by almost 90% in standard risk patients [21–24]. Pharmacological prophylaxis is reserved for high-risk patients. Anti-aggregating agents (aspirin, clopidogrel) have not been proven to reduce VTE incidence in high-risk patients. Enoxaparin, an LMWH, at a dose of 1 mg/kg 2–4 h prior to long-haul flights significantly decreases VTE incidence from 4.8 to 0% [2, 22, 23].

Conclusion

The burden of air travel-induced risk of VTE is expected to increase, as air travel is becoming more accessible. Even healthy individuals are at risk for VTE during long flights (>8 h), and its incidence appears to be especially high among the subjects with identified VTE risk factors. Healthy passengers do not require pharmacological protective agents, but are encouraged to avoid immobility and dehydration. Travellers at high risk are advised to use mechanical or pharmacological prophylactic modes, especially prior to long flights.

Conflict of interest None.

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