



## Travel-Related Thrombosis: Is This a Problem?\*

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The association of air travel and venous thromboembolism has been recognized for over 50 years [1]. In the 1970s the growing number of long-haul flights carrying passengers in a cramped sitting position led to the description of the “economy class syndrome” [2]. It has since been found however, that travel-related thrombosis may affect passengers in all airline classes [3].

Until recently there were few studies of this important and common clinical presentation, due in part to the insufficient attention to the problem by aviation authorities and the airline industry [4]. A growing number of reports over the past 7 years has shed light on the epidemiologic and pathophysiologic aspects of travel-related thrombosis. A number of studies demonstrated a history of recent long-haul travel in a significant percentage of patients admitted with a diagnosis of VTE [5-7]. In contrast, reports on passengers in whom severe pulmonary embolism following long-haul flights was diagnosed on arrival to major airports suggest that while the risk increases exponentially with flight duration, the actual prevalence is very low [8,9]. These differences are probably due to the very short catch-up time at airports, one hour at most after landing. It is now well established that VTE can develop up to one month after a long-haul flight, with a particularly increased risk during the first 1–2 weeks after travel [10].

### Problem estimation

The prevalence of VTE following long-haul flights (> 8 hours) has been estimated by a number of studies using Doppler sonography and computed tomography angiograms. The prevalence of sonographically documented deep vein thrombosis within 48 hours of landing ranges from 2 to 10% [11-13], which is comparable to the rate of sonographically documented DVT observed in acutely ill medical patients in the PREVENT trial. Taking into account that about 100 million passengers travel on long-haul flights yearly, this would imply about 5 million asymptomatic DVT cases. By ex-

trapolation from medical and surgical patients, this implies about 500,000 symptomatic DVT and about 20–30,000 fatal pulmonary embolisms yearly. This alarming number is tenfold higher than all lives lost in airplane crashes yearly and is, therefore, a major global health issue.

### Too much sitting or too much clotting?

This is a crucial point in terms of pathophysiologic mechanisms and potential prophylactic interventions [14]. Thrombosis has been described after prolonged sitting in a cramped position [15]. Albeit less common, thrombosis can also be observed in other situations of prolonged sitting such as during travel by trains and motor vehicles [16]. VTE affects more commonly non-aisle passengers, again emphasizing the role of prolonged sitting during long-haul flights. Lack of awareness of the danger contributes to the potential devastating outcome.

It has been suggested that cabin pressure, which is equivalent to hypobaric conditions at 1800–2400 meters altitude, leads to hypoxia and to coagulation activation [17]. Dehydration is common due to cabin microclimate conditions, lack of sufficient water intake and increased alcohol consumption. A recent study in young volunteers demonstrated that indeed too much clotting occurs in air especially in thrombophilic women on oral contraceptives [18].

### Can we identify those at risk?

It is now well established that inherited and acquired factors increase the risk for travel-related thrombosis. The risk is particularly high in long-haul travelers aged over 40 years with co-morbid conditions such as cancer, congestive heart failure, recent surgery or previous VTE, or stroke [3,10]. The risk is also elevated in passengers with varicose veins, obesity or recent trauma. Patients with thrombophilia, pregnant women or women on oral contraceptives or hormone replacement therapy are also at increased risk [13,19]. A recent Australian study demonstrated that one risk factor was found in 84% and two risk factors in 52% of passengers who developed travel-related thrombosis [20]. Thus, assessment of thrombophilic risk factors can help in identifying those at risk.

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VTE = venous thromboembolism  
DVT = deep vein thrombosis

However, even passengers with low to moderate risk can develop travel-related thrombosis. In the study by Lapostolle et al. [8], over 90% of the patients who develop pulmonary embolism had only moderate risk (age over 40 years, varicose veins, or hormonal therapy), and the NZATT study demonstrated a prevalence of 1% VTE that necessitated anticoagulation in passengers with low to moderate risk [21]. This can be explained by too much flying [14]. Indeed, one long-haul flight increases the annual risk of VTE by 12% [10]. The risk is further increased following consecutive long-haul flights and potentially following a number of adjacent shorter flights. Data from the Leiden group presented at the recent Air Travel and Health Symposium in Eilat, Israel, demonstrate that the risk is increased four- and eightfold following 8 and 12 hours, flights respectively. It is expected that over the age of 50 a 12 hour flight will result in a VTE clinical event rate of 1/500 passengers. Tall (> 190 cm) and short (< 160 cm) travelers are at greater risk.

### Preventive measures

Knowledge is of utmost importance in public health issues. Passengers should be informed of the potential risks and should be encouraged and guided to exercise regularly, to take short walks in the aisle and to avoid dehydration and alcohol intake. In-flight education of passengers on the problem and precaution measures including ample water intake, limit of alcoholic drinks, and regular exercise are highly advisable. A recent study on the effect of flight-related behavior on risk for venous thrombosis found that while excessive alcohol intake increased the risk, ample non-alcoholic fluid intake did not reduce the risk [22].

In general, prophylaxis includes physical measures and antithrombotic drugs. If indeed, prolonged immobilization is the main risk factor, elastic stockings, which have proved to be beneficial in patients with standard risk – by reducing the rate of DVT from 12% to 0% in the study by Scurr et al. [11], and from 5% to 0.24% in the LONFLIT investigators study [23] – should be advised. A recent Cochrane review evaluated available randomized trials on the prevention of symptomless travel-related thrombosis by means of elastic stockings [24]. A significant risk reduction of symptomless DVT was observed in the elastic stocking group. However, seven of the nine trials included low or medium risk passengers and only two high risk travelers. The role of various mechanical devices that can prevent stasis and increase circulation is currently under investigation in this setting. The Dutch group evaluated in healthy volunteers the effect of an innovative intermittent mechanical calf compression device designed for prevention of travelers' thrombosis [25]. The results showed that the device increases venous blood flow but does not significantly affect thrombin generation and fibrinolytic parameters. Antithrombotic prophylaxis has been evaluated by limited small-scale studies.

The LONFLIT III study demonstrated in high risk long-haul flight passengers that while aspirin at a dose of 400 mg taken 12 hours before the flight and for the next 3 days did not prevent DVT, the low molecular weight heparin enoxaparin at a dose of 1 mg/kg 2–4 hours prior to a long-haul flight significantly reduced

the prevalence of DVT from 4.8% to 0% by Doppler sonography [23]. Interestingly, coagulation activation could be abrogated by injection of LMWH prior to exposure to a hypobaric chamber simulating cabin pressure [24]. Of note, in the NZATT study, 17% of participants wore elastic stockings and 31% took aspirin. However, despite these measures, several individuals developed VTE [21]. In another study by the LONFLIT investigators, an oral profibrinolytic agent proved to be useful in preventing DVT in high risk long-haul flight passengers [25].

Thus it can be concluded that while the value of low dose aspirin is limited in this setting, prospective studies with LMWH and new anticoagulants in predefined high risk groups, such as passengers with thrombophilia or women on hormonal therapy, are highly warranted. In the meantime, passengers with risk factors should be advised on an individual basis on the potential risk of long-haul flights and the available prophylactic measures.

The Aerospace Medical Association (AsMA) recently published guidelines for prevention of travel-related DVT [29]. For moderate risk the AsMA guidelines suggest aspirin with or without graduated compression stocking. The high risk group is defined as previous VTE, known thrombophilia, major surgery within 6 weeks, previous stroke, malignancy, and family history of VTE. For this group, LMWH or heparin prophylaxis may be recommended by the passengers' physicians. International health organizations, aviation authorities and the airline industry should cooperate with researchers and the health industry to support these timely studies on a potentially preventable disease with a global impact.

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LMWH = low molecular weight heparin

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