

Air flight-related thrombosis: reality or hype?

The death of a young woman from a pulmonary embolism soon after her arrival at Heathrow airport on a long-haul flight alerted the public to the issue of air flight-related thrombosis. Despite recent publicity, this issue was first raised in the early 1950s after the report that a doctor developed a deep-vein thrombosis (DVT) following a 14-hour air flight. The initial term 'economy class syndrome' is likely to be a misnomer because it can occur in passengers travelling first/business class, as well as in those travelling by other forms of transport. The common denominator is prolonged lack of mobility with the knee flexed. A similar complication was reported among Londoners sitting in air raid shelters in the Blitz during the Second World War, when a six-fold increase in deaths from pulmonary embolism was observed. More recently, an excess of DVT was seen in Paris during a Metro strike, when passengers had to spend considerably longer periods of time travelling to work by car.

Over the last four decades many case reports and retrospective studies have described venous thromboembolic episodes in persons with a recent history of air travel. However, common to all of these studies is an absence of appropriate control groups. Considering the large number of people who fly, it has been argued that such reports are no more than would be expected over a similar period in patients who had no history of air flight.

In the last two years, three case control studies (from France, Italy and The Netherlands) have addressed the same issue.¹ In the French study, which investigated subjects admitted to a hospital close to an airport in Paris, long-distance travel by air or road was found to be associated with a four-fold excess risk of DVT. The Italian study, performed in a family practice setting, found the risk of DVT in association with prolonged travel to be 2.3. It is possible, however, that both studies could have been flawed because knowledge of long-distance travel could have introduced referral bias. In contrast, the Dutch study, which avoided referral bias by including all patients who were referred for diagnostic leg scanning for suspected DVT, did not find an association between air flight and DVT; however, the number of patients in the study with a history of air travel was very small ($n=17$).

In a large series from France, Lapostolle *et al.*² analysed the frequency of pulmonary embolism among passengers arriving at Charles de Gaulle Airport in Roissy, France. Their study showed clearly that the risk of pulmonary embolism was directly related to the distance travelled, being highest (i.e. five cases per million passengers) for those travelling more than 10 000 km (6200 miles). No cases of pulmonary embolism were seen among passengers travelling for less than six hours. However, it must be appreciated that the study probably failed to detect all episodes of venous thromboembolism because the design would have failed to identify passengers dying from pulmonary embolism before arrival, those whose symptoms developed after leaving the airport, and those with asymptomatic or unrecognised venous thromboembolism.

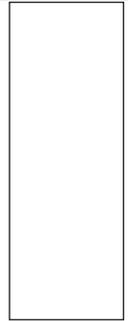
Recently, two studies investigated the problem prospectively and tried to prevent it with the use of graduated elastic stockings. In the study by Scurr *et al.*,³ 200 passengers were randomised to wear either Class 1 below-knee graduated elastic stockings or nothing, and had Doppler scans before and after long-haul flights. The risk of asymptomatic DVT, as detected by Doppler scan, was 10% in the control group but zero among the passengers wearing the stockings. Although stockings appeared to be associated with complete protection against DVT, four (4%) of the subjects wearing stockings developed superficial thrombophlebitis. This study has been criticised because the technicians performing the Doppler scans were able to talk to the passengers while performing the investigations and, in practical terms, may not have been 'blind' in terms of knowing the patient's randomisation group. Furthermore, the DVTs in all the patients were asymptomatic, below the knee and associated with normal D-dimer levels, raising the question that these thromboses were perhaps different from those encountered commonly in clinical practice. Despite these criticisms, the main findings of Scurr's study were confirmed recently by the LONFLIT study, which was performed in two parts.

In LONFLIT 1, patients at low or high risk for DVT were studied by Doppler scanning following air flights of an average of 12 hours. No thromboses were observed in the low-risk group but 4.9% of the high-risk group experienced a leg DVT. High risk was defined as a history of previous DVT, the presence of a coagulation disorder, severe obesity or limited mobility due to bone or joint problems, neoplastic disease in the preceding two years or large varicose veins.

In the LONFLIT 2 study, 833 patients were randomised to a control group or to a group that wore commercially available below-knee graduated elastic stockings, providing a maximum compression of 25mm Hg at the ankle. After an average flight of 12.4 hours, 4.5% of the control group experienced leg thromboses, but the rate in the group using the stockings was nearly 20 times lower, at 0.24%.⁴

While it appears clear that there is an excess of episodes of venous thromboembolism among passengers following long-haul flights, the exact cause remains uncertain. Possible reasons proposed include sitting with the knee flexed for long periods, the short leg space in front of the seat in economy class, dehydration, and the lower atmospheric pressure and humidity in the flight cabin.

Landgraf and colleagues⁵ studied the problem under controlled conditions by simulating 12-hour flights during the day and night, using a Boeing 747 passenger cabin mock-up in the Deutsche Lufthansa facilities at Frankfurt airport. No differences in plasma viscosity or haematocrit were found in the 12 healthy volunteers studied, but the subjects showed a 1150 mL increase in lower leg volume which occurred irrespective of whether they exercised their legs or not. This study, however, failed to simulate the decreases in air pressure or humidity that are experienced during air flight.



In another study from Norway, Bendz and colleagues⁶ examined 20 healthy male volunteers placed in a hypobaric chamber to simulate air-pressure and temperature conditions similar to those encountered in aeroplane cabins. The results showed that markers of coagulation activation increased transiently some two- to eight-fold, suggesting that hypobaric hypoxia may contribute to the increased risk of venous thrombosis.

Understandably, the public is anxious about long haul flight-related thrombosis, especially in view of the recent exaggerated reports in the press. While it is likely that passengers on long-haul flights are at increased risk of venous thromboembolism, this risk is very small in absolute terms, especially in persons without malignancy, thrombophilia, or who are not taking the combined contraceptive pill or sedative medication, and who have not had recent surgery. Based on the information available, it is sensible for passengers to drink plenty of water/soft drinks and avoid/reduce alcohol intake to prevent dehydration, perform passive exercises in the seat, walk about the cabin every hour or two, and wear below-knee elasticated stockings that are now available widely from pharmacists without prescription. The use of an aspirin tablet taken routinely before each leg of a flight has been advocated, but this must be balanced against little, if any, benefit in the prevention of venous thrombosis (in contrast to the clear benefit obtained in arterial thrombosis) and the risk of aspirin-induced gastrointestinal bleeding. Although subcutaneous injections of low-molecular-weight heparin offer the highest degree of protection from venous thromboembolism, at this stage they should be restricted to those who have suffered previous air flight-related thrombosis or who are at a very high risk of thrombosis (e.g. have undergone recent surgery for malignancy). □

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