

## Air travel and thrombosis

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Although the first cases of thrombosis following air travel were reported in 1954 by Homans (1), interest has recently heightened. Numerous cases have been reported, but controlled studies are few and contradictory. In a series of patients who had died suddenly at Heathrow Airport, this occurred far more often in the arrival than in the departure area (2). Case-control studies have yielded conflicting results, with two French studies showing a two to fourfold increased risk of travel compared to no travel (3;4), while a Dutch (5) and a British study (6) found no elevated risk. A study of severe pulmonary embolism in travellers showed a 50-fold risk gradient with the distance travelled (7), while two studies using ultrasound measurements to detect asymptomatic clots found these in a significant number of travellers (8;9).

The Multiple Environmental and Genetic Assessment (MEGA) is an ongoing case-control study aimed at assessing interactive effects of genetic and acquired risk factors for venous thrombosis. Cases are consecutive patients with a first objectively confirmed deep-vein thrombosis (DVT) or pulmonary embolism (PE) registered for anticoagulant treatment at six regional Anticoagulation Clinics. Controls are spouses of cases. There are no exclusion criteria.

Cases and controls fill out a detailed questionnaire, are interviewed in-person, and have venous blood drawn. For the current report, we have data on 829 cases and 829 controls. We considered as travel, any travel of more than 4 hours in two months preceding the index data. Factor V Leiden (FVL) and prothrombin 20210A (PT20210A) were measured by standard PCR techniques.

465 (56%) patients had DVT, 341 PE (41%). A prothrombotic mutation (FVL or PT20210A) was present in 19.9% of patients and 7.7% of controls (OR=2.9, CI95 1.9-4.3). 112 (13.5%) of patients had travelled in the preceding two months, for 30 of whom thrombosis was diagnosed within one week after travel. For all modes of travel combined, it increased risk of thrombosis 3-fold (OR=3.1, CI95 1.9-5.1). Plane travel increased risk 6-fold (OR=5.8, CI95 2.0-16.6) and other modes of travel 2-fold (OR 2.2, CI95 1.9-4.3). Individuals with a prothrombotic mutation who travelled by airplane had a 13-fold increased risk compared to individuals without a mutation who did not travel. This joint risk exceeded the sum of the separate risks of flying and mutations.

Prolonged travel by car, autobus and airplane is associated with an increased risk of venous thrombosis, with the highest risk for air travel. Individuals with prothrombotic mutations are at higher risk.

## References

- 1 Homans J Thrombosis of the leg veins due to prolonged sitting *N Engl J Med* 1954,250 148-9
- 2 Sarvesvaran R Sudden natural deaths associated with commercial air travel *Med Sci Law* 1986,26(1) 35-8
- 3 Ferrari E, Chevallier T, Chapelier A, Baudouy M Travel as a risk factor for venous thromboembolic disease a case-control study *Chest* 1999,115(2) 440-4
- 4 Samama MM An epidemiologic study of risk factors for deep vein thrombosis in medical outpatients the Sirius study *Arch Intern Med* 2000,160(22) 3415-20
- 5 Kraaijenhagen RA, Haverkamp D, Koopman MM, Prandoni P, Piovella F, Buller HR Travel and risk of venous thrombosis *Lancet* 2000,356(9240) 1492-3
- 6 Arya R, Barnes JA, Hossain U, Patel RK, Cohen AT Long haul flights and deep vein thrombosis a significant risk only when additional factors are also present *Br J Haematol* 2002,116(3) 653-4
- 7 Lapostolle F, Surget V, Borron SW, Desmazieres M, Sordelet D, Lapandry C et al Severe pulmonary embolism associated with air travel *N Engl J Med* 2001,345(11) 779-83
- 8 Scurr JH, Machin SJ, Bailey-King S, Mackie IJ, McDonald S, Smith PD Frequency and prevention of symptomless deep-vein thrombosis in long haul flights a randomised trial *Lancet* 2001,357(9267) 1485-9
- 9 Cesarone MR, Belcaro G, Nicolaides AN, Incandela L, De S Geroulakos G et al Venous thrombosis from air travel the LONFLIT3 study prevention with aspirin vs low molecular-weight heparin (LMWH) in high-risk subjects a randomized trial *Angiology* 2002,53(1) 1-6