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Deep vein thrombosis and air travel: record linkage study

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Abstract

Objective To investigate the time relations between long haul air travel and venous thromboembolism.

Design Record linkage study using the case crossover approach.

Setting Western Australia.

Participants 5408 patients admitted to hospital with venous thromboembolism and matched with data for arrivals of international flights during 1981-99.

Results The risk of venous thromboembolism is increased for only two weeks after a long haul flight; 46 Australian citizens and 200 non-Australian citizens had an episode of venous thromboembolism during this so called hazard period. The relative risk during this period for Australian citizens was 4.17 (95% confidence interval, 2.94 to 5.40), with 76% of cases (n = 35) attributable to the preceding flight. A "healthy traveller" effect was observed, particularly for Australian citizens.

Conclusions The annual risk of venous thromboembolism is increased by 12% if one long haul flight is taken yearly. The average risk of death from flight related venous thromboembolism is small compared with that from motor vehicle crashes and injuries at work. The individual risk of death from flight related venous thromboembolism for people with certain pre-existing medical conditions is, however, likely to be greater than the average risk of 1 per 2 million for passengers arriving from a flight. Airlines and health authorities should continue to advise passengers on how to minimise risk.

Introduction

Venous thromboembolism after air travel was first recorded in 1954, but the magnitude of risk has not been resolved.^{1 2} Recent small studies have shown relative risks of between 1 and 4 for the condition occurring two to four weeks after a flight, the so called hazard period.^{3 4}

Since 1970, Australia has kept electronic data on arrivals and departures of international travellers. The state of Western Australia uses record linkage under well developed protocols to protect patient privacy.⁵ Most Western Australian residents live in Perth, and flight times from there to other major airports are long. We investigated the relation between international air travel and venous thromboembolism by linking Western Australian hospital data with records on air travel.

Participants and methods

Data included coded personal identifiers, age, sex, arrival and departure dates, and nationality of the traveller (Australian citizen or non-Australian citizen). We used hospital discharge summaries for the period 1981-99 to detect all patients in Western Australia who had been admitted with a principal diagnosis of deep vein thrombosis or pulmonary embolism. These data were used to estimate age and sex specific incidences for venous thromboembolism and expected numbers of venous thromboembolic events, using state-wide incidence.

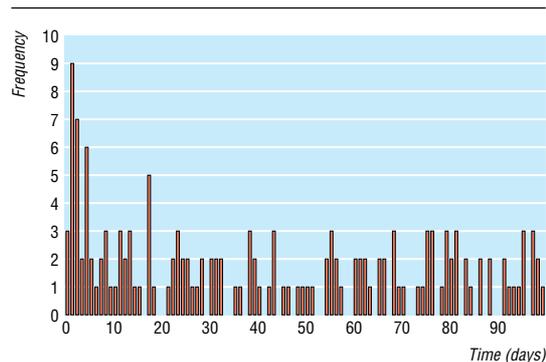
The travel records for all passenger movements to and from Australia during 1981-99 were probabilistically matched to the Western Australian hospital data for the same period.⁶ We thus identified patients with venous thromboembolism who had undertaken international flights, and we recorded the date of patients' first admission for venous thromboembolism and flight dates.

Travellers who had acute venous thromboembolism after leaving Australia would not be admitted to hospital in Western Australia, and so that episode would not be captured in our data. We therefore used information on passengers arriving only. Our main analysis is based on Australian citizens. We did this to minimise bias arising from the fact that travellers not resident in Western Australia often leave the state again within days or weeks of arrival, leading to biased and incomplete data on both hospital admissions and air travel exposure.

Statistical analysis

Our principal analysis looked for evidence of any temporary increase in risk of venous thromboembolism above baseline after arrival from a flight. The method uses the conditional probability distribution of the time from the start of the observation period until the first venous thromboembolic event, given that this event occurred within the observation period. This approach is similar to a case crossover analysis.^{7 8} Because the incidence is low, the risk was estimated as an incidence rate ratio, which gives an approximate relative risk. The incident rate ratio during the hazard period, relative to periods beyond the immediate post flight period, was modelled as a function of age, sex, and time since flight. An appendix on bmj.com describes the analysis in detail.

The estimated incident rate ratio is influenced by the duration of the post flight period selected for analysis. We examined the risk over intervals up to 30



Frequency of venous thromboembolism in Australian citizens (n=153) by days after flight arrival for first 100 days. Day 0 was counted as 0.5 days

days, using a model that allowed different incident rate ratios in three successive periods after travel, and we concluded that most of the excess risk was captured in the two weeks after a flight.

Results

During 1981-99, 4.8 million Australian citizens and 4.6 million non-Australian citizens arrived in Western Australia from an international flight. Over the same period there were 16 205 hospital admissions (13 184 patients) for venous thromboembolism diagnosed by usual clinical criteria in Western Australian hospitals.

Hazard period and risk for Australian citizens

We identified 153 Australian citizens who were admitted to hospital for venous thromboembolism within 100 days of arrival on an international flight. The figure shows the time between arrival and first admission for a venous thromboembolic event for these 153 Australian citizens; 46 events occurred within 14 days of arrival, and 107 events occurred 15-100 days after arrival. The observed number of cases within 14 days of arrival significantly exceeds the number expected under the assumption of a uniform distribution over the 0-100 days after arrival ($\chi^2 = 30.3$, $df = 1$, $P < 0.001$). Table 1 presents the observed and expected numbers of all patients admitted to hospital within the first 100 days of arrival. The observed numbers for Australian citizens are less than those expected from Western Australian population rates, suggesting a "healthy traveller" effect.

The maximum likelihood analysis showed that the incidence rate ratio was increased for Australian citizens within two weeks of arrival, falling from 5.61 (95% confidence interval, 3.94 to 7.97) in week 1 to 2.63 (1.55 to 4.45) in week 2. The increase did not depend significantly on age or sex, and it was not significant in week 3. We estimated that these data correspond to a relative risk of 4.17 (95% confidence interval, 2.94 to 5.40) with 76% of cases (n = 35) attributable to the preceding flight. Our calculations are given on bmj.com. Table 2 gives details of all travellers (Australian citizens and non-Australian citizens) admitted to hospital with venous thromboembolism within two weeks of arrival. Assuming one long haul trip per year, the additional risk due to this exposure amounts to an extra two weeks at $(4.17 - 1) = 3.17$, which corresponds to $3.17 \times 2/52 = 12\%$ extra risk over the entire year.

Observations in non-Australian citizens and mortality

Overall, 200 non-Australian citizens with venous thromboembolism were detected within two weeks of arrival. This significantly exceeds the 105 expected on the basis of Western Australian population rates ($\chi^2 = 85.2$, $df = 1$, $P < 0.001$; table 1). As the exact distribution of length of stay for non-Australian citizens in Western Australia is unknown, it was not possible to completely separate the declining rate for venous thromboembolism over time from bias, owing to the declining denominator for non-Australian citizens over time. We therefore do not show the incident rate ratios for non-Australian citizens.

Five of the 246 patients with venous thromboembolism detected within the hazard period (14 days after arriving) died in hospital. Because our study was based on patients admitted to hospital we could have missed a few cases presenting as sudden death either in flight or soon after arrival.

Discussion

Venous thromboembolism is four times more likely to develop within two weeks of arrival from a long haul flight—the so called hazard period. Although we tried to minimise the effects of possible biases in our study, our results should be generalised with caution. We found a substantial healthy traveller effect among Australian citizens, suggesting that people who undertake

Table 1 Observed and expected numbers of first venous thromboembolism events by time in days since most recent flight arrival

Traveller category	Days since most recent flight arrival				Total
	0-14*	15-30	31-60	61-100	
Australian citizens:					
Observed	46	23	32	52	153
Expected (A)†	102.6	113.2	212.3	283.0	711.1
Expected (B)‡	22.1	24.4	45.7	60.9	153.0
Non-citizens:					
Observed	200	69	78	91	438
Expected (A)§	105.3	116.2	217.9	290.5	729.9
Expected (B)	63.2	69.7	130.7	174.3	438.0

* $\chi^2 = 30.3$, $df = 1$, $P < 0.001$ when patients with venous thromboembolism in first 14 days are compared with expected (B).

†Calculated from total number of arrivals of Australian citizens in Western Australia (4.8 million) and using age and sex specific rates for venous thromboembolism in Western Australian population. These expectations illustrate scale of "healthy traveller" effect.

‡Calculated on assumption that 153 observed venous thromboembolism events of first 100 days are uniformly distributed in time (for example, $153 \times 14.5 / 100.5 = 22.1$). For non-citizens in 0-14 day interval, expectation (A) is biased upwards if anything, whereas expectation (B) is biased downwards because of early departures of visitors from Western Australia. Expectations for citizens are likely to be more robust.

§ $\chi^2 = 85.2$, $df = 1$, $P < 0.001$ when patients with venous thromboembolism in first 14 days are compared with expected (A).

Table 2 Characteristics of 246 travellers (Australian citizens and non-Australian citizens) admitted to hospital with venous thromboembolism within 14 days of arrival from an international flight for study period 1981-99

Age group	No of patients with venous thromboembolism	Total No of people arriving	Rate per 100 000 people arriving*
0-14	0	1118070	0.00
15-19	2	834 355	0.24
20-24	4	950 621	0.42
25-29	4	909 289	0.44
30-34	4	910 372	0.44
35-39	7	924 062	0.76
40-44	22	870 695	2.53
45-49	31	717 674	4.32
50-54	40	570 198	7.02
55-59	25	308 846	8.09
60-64	30	457 647	6.56
65-69	29	336 319	8.62
70-74	27	200 015	13.50
≥75	21	149 679	14.03
All	246	9 257 842	2.66

140 patients had deep vein thrombosis and 106 had pulmonary embolism. Five deaths occurred in hospital. *Rates are reasonable approximation as only 16% of patients had more than one venous thromboembolism event and it would be expected that few would have had multiple flight related events.

What is already known on this topic

Venous thromboembolism has been suggested to be up to four times more likely to develop within two to four weeks of a flight (the "hazard period")

The incidence of pulmonary embolism is greater among passengers travelling more than 10 000 km

What this study adds

The risk of venous thromboembolism is highest within two weeks of a long haul flight

The annual risk of venous thromboembolism is increased by 12% in those undertaking one long haul flight a year

international travel are more healthy and less likely to develop spontaneous venous thromboembolism than those who do not travel. Presumably, people with risk factors are less likely to fly (see bmj.com).

Of 4.8 million Australian citizens arriving in Western Australia during 1981-99, 46 developed venous thromboembolism within 14 days. This corresponds to an absolute rate of around 9.6 patients with venous thromboembolism per million people arriving, of which 7.3 per million would be attributable to the preceding flight. Of around 4.6 million non-Australian citizens arriving in Western Australia, there were 200 patients with venous thromboembolism in the hazard period, with an estimated 33 cases per million people arriving attributable to the preceding flight (data not shown). This higher estimate for the absolute risk for non-Australian citizens is not due to differences in age and sex, as the distributions for arrivals of Australian and non-Australian citizens were similar. The greater risk in non-Australian citizens could be due to longer flights from Europe, in contrast to the generally shorter flights of Western Australian residents, who more often visit South East Asia.⁹ The study data did not, however, allow us to test the effect of flight duration on the risk of venous thromboembolism. It is also possible that non-Australian citizens with an incentive to visit Western

Australia are less healthy on average than Australian citizens who choose to leave Western Australia for tourist or business purposes. Other selective biases could apply—for example, the threshold for hospital admission in Australian citizens with a family doctor could be higher than for visitors, who might present directly to a hospital emergency department.

We found a 12% increase in annual risk for venous thromboembolism for a traveller undertaking one long flight yearly. However, as citizens who travel seem more healthy than non-travellers, the absolute risk for an average traveller will be less than that estimated from rates in a population that includes non-travellers as well as travellers. If venous thromboembolism risks apparently caused by air travel to Western Australia are extrapolated nationally, around 27 venous thromboembolism episodes per million people arriving would be expected, or about 250 episodes in 2003. Most of these episodes would be in non-Australian citizens. We found that around five deaths per year from pulmonary embolism could be attributable to international flights terminating in Australia, which would correspond to a death rate of 1 per 2 million people arriving. These results are generally consistent with other reports.^{3 4 9-11}

Although the average risk of venous thromboembolism is small, prospective passengers with certain medical conditions are likely to have a higher than average risk of flight related venous thromboembolism because of the underlying risk (see bmj.com). Airlines and health authorities should continue to advise passengers on ways to minimise that risk. Further studies of predisposing factors and causal mechanisms are needed, as are evaluations of the preventive measures already introduced by airlines and health authorities.^{2 12} Future research should also define the healthy traveller effect and better quantify risk in relation to duration of travel.

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Competing interests: None declared.

Ethical approval: The research protocol was approved by the ethics committee of the Commonwealth Department of Health and Ageing, the human research ethics committee at the University of Western Australia, and the Confidentiality of Health Information Committee of the Western Australian Department of Health.

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