Addendum to Guidelines on travel-related venous thrombosis (British Journal of Haematology. 2010; 152:31-34)

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Role of risk factors in the development of thrombosis

There is limited evidence that patients with prior venous thromboembolism (VTE) are more susceptible to air travel related VTE. A case-control study using data from the MEGA follow-up study did not show a higher risk for recurrent VTE with long-haul air travel (>4 hours) or long-duration travel by car, bus, or train.[1] This finding was not explained by preventative measures taken during travel, as these were equally distributed between cases and controls. The confidence intervals for the odds ratios reported for the travel vs non-travel groups however were wide.

One study showed that a cumulative flying time of >12h is associated with a similar risk of VTE within the subsequent 4 weeks as long-haul air travel in which one or more flight legs is longer than 4h.[2] The study also showed that risk factors such as surgery in the preceding 4 weeks (OR 32.21 CI 16.36-63.41), previous VTE (OR 9.23 CI 5.85-14.56), BMI >30 (OR 2.67 CI 1.94- 3.66) or BMI 25-30 (OR 1.54 CI 1.17-2.05) increased the risk of VTE associated with air travel.

A cohort study showed that several VTE risk factors (e.g., cancer, plaster casts, hormone replacement therapy, oral contraceptives, and pregnancy) increase the risk of air travel–related VTE.[3] This showed pregnant women who travelled by air had an odds ratio (OR) for VTE of 14.3 (95% CI, 1.7-121.0) compared with an OR of 4.3 (95%, 0.9-19.8) associated with pregnancy alone.[4] Women using oral contraceptives who travelled by air had an 8.2-fold (95% CI, 2.3-28.7) elevated risk for VTE

compared with non-travellers not on contraceptives, whereas the risk with oral contraceptives alone was increased 2.5-fold (95% CI, 0.9-7.0). A limitation of this study was the relatively small number of cases with a combination of air travel and the studied risk factor, thus explaining the very wide confidence intervals. The authors concluded that the risk of travel-related VTE is most increased in travellers who have recently undergone surgery, those with a malignant disease and pregnant women, and that preventative measures might be considered in these groups.

The RCOG published an opinion paper on air travel and pregnancy in which they advise all pregnant women to wear graduated compression stockings (GCS) for flights lasting >4hrs.[5] They advise an individualised risk assessment for VTE and that women with additional risk factors for VTE should be considered for prophylaxis with low molecular weight heparin (LMWH), with the duration dependant on clinical judgement.

Two separate retrospective cohort studies assessed the risk of VTE in total joint arthroplasty patients and found no association between preoperative or postoperative air travel and VTE risk.[6,7] However, findings might be biased if travellers took measures to reduce their VTE risk, and studies might not have been sufficiently powered to detect associations.

Strategies for prevention of travel associated VTE

As outlined in the guideline, the effectiveness of a short course of pharmacological prophylaxis in the prevention of travel related thrombosis is not supported by good data and is not routinely recommended.

To date there are no studies evaluating the use of direct oral anticoagulants (DOACs) in this setting.

A 2016 Cochrane review included 9 RCTs with 2637 participants in trials where GCS were worn on both legs during air travel of more than 5 hours.[8] The follow up period

was from immediately to 48 hours post flight. Asymptomatic DVT occurred in 50 participants. 3/50 wore stockings and 47/50 did not [OR 0.10, 95% CI 0.04–0.25] P<0.001). The study concluded that the findings provided evidence of a substantial reduction in asymptomatic DVT in airline passengers wearing stockings. There were no symptomatic DVT, PE or deaths in these trials, therefore, the impact of wearing stockings could not be evaluated for these events.

A case–control study to evaluate the impact of flight-related behaviour on the risk of VTE after air travel selected 80 patients with VTE and 108 controls from the MEGA study who had travelled more than 4 hours by air within the prior 8 weeks.[9] Window seating compared to aisle seating increased the risk two-fold (OR 2.2; 95% CI 1.1–4.4), possibly related to ease of mobilising. However, there was no evidence of increased risk with alcohol consumption (OR 1.1; 95% CI: 0.5–2.4). Wearing GCS did not appear to have any effect. There are no studies specifically evaluating the effect of either regular mobilisation or calf muscle exercise on prevention of VTE in long-distance travel.

Flying business class may be associated with a lower VTE risk (OR 0.7; 95% CI: 0.2–1.8) but the wide confidence interval reduces any certainty of effect. It is recognised that the risk of VTE caused by reduced movement on long distance flights outweighs that relating to seating class.[10]

Defining risk groups

Risk Group	Examples of risk factors for VTE	Suggested intervention for travel < 4 hrs	Suggested intervention for travel > 4 hrs
Low	None of the risk factors listed below	None	None
High	Any of the following single risk factors: • Surgery in previous 4 weeks • Active cancer • Previous unprovoked VTE no longer on anticoagulants • Previous travel related VTE • Up to 6 weeks postpartum • Severe immobility e.g lower limb immobilisation Or 2 or more combined risk factors including: • BMI>30	None	Prophylactic pharmacological thromboprophylaxis with or without graduated compression stockings

	• Pregnancy • Hormonal treatment		

If thromboprophylaxis is indicated, as per the table above, expert consensus provided by the taskforce members is to administer thromboprophylaxis 2-4hrs before each flight of >4hours.

Neither LMWH nor DOACs have a specific license for thromboprophylaxis in this setting. However, prophylactic LMWH has been used for this indication for many years, therefore providing a significant amount of experience with this agent compared with DOACs.

Recommendations

- **In long-distance (>4 hours) travellers without risk factors for VTE, we do not recommend using graduated compression stockings or pharmacological thromboprophylaxis (1C).**

- **For individuals in the high-risk group consider using pharmacological thromboprophylaxis with or without graduated compression stockings for long-distance (>4 hours) travel (2C).**

References

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