

## The Saudi clinical practice guideline for the prophylaxis of venous thromboembolism in long-distance travelers

*To the Editor*

I read with great interest the paper published by Al-Hameed et al<sup>1</sup> entitled “The Saudi clinical practice guideline for the prophylaxis of venous thromboembolism (VTE) in long-distance travelers. While I really congratulate the authors for this great systematic work addressing a very controversial and challenging topic, I have few points to address. While the author did mention estrogen use as one of the risk factors for VTE among travellers, we need to point out that hormonal therapy used to treat cancers are also important. In particular, tamoxifen therapy, used in the active treatment or in the prevention of breast cancer, is reported to increase the risk of deep venous thrombosis (DVT) and pulmonary embolism (PE), especially in elderly and during the first 2 years of therapy,<sup>2</sup> and such risk might be higher during travel. Such risk, however, appeared to be lower, albeit not negligible, with the aromatase inhibitors; a group of hormonal therapy drugs widely used in postmenopausal women with hormone receptor-positive breast cancer.

We also need to stress the word “active” cancer used correctly by the authors. Prior history of cancer does not necessarily add to the risk of VTE. Active cancers include those who are currently on active treatment such as hormonal therapy or chemotherapy or those with wide spread metastatic disease.

The authors used the fact that KSA is the land of the Two Holy Mosques and as such is the destination of high number of travelers from many distant countries, as an argument for the need of these “tailored” guidelines. The emphasis all through the guidelines was that of air travel, but we need to mention here that large number of travelers enter and leave KSA, for Omrah and Hajj, using land transportation, a journey that usually take a lot more than 8 hours as discussed in the guidelines. Risk of VTE is not restricted to air travel alone.<sup>3</sup> Travellers using land transportation do not have the chance to move around and ambulate; the value of which, we agree with authors, is questioned in air-travel, but might be of value here. An emphasis on

this mode of travel would have an added value and distinctions of these guidelines.

Dehydration can be an added risk factor for VTE during air or land travel. In-flight consumption of alcoholic drinks and other diuretics such as tea and coffee, and the low humidity of the aircraft cabin all may contribute to dehydration and add to the risk of VTE, especially in elderly.<sup>4</sup> To add to this problem, the peak of travel to and from KSA is during the month of Ramadan. Though breaking fasting while travelling is allowed, and even encouraged, still many argue and keep fasting adding to their dehydration. We feel that addressing this point is extremely important when discussing VTE risk and ways that can add to preventive measures.

Though the authors, and many other international guidelines and studies, used the 8-hours mark, it is also extremely important when assessing traveller’s risk for VTE to consider the time spent during the trip. Many of air-travel plans nowadays include connecting flights and some layover time. Such total travel time need to be considered, especially so when considering prophylactic measures in high risk travelers.

Last, it is interesting to mention that the link between air travel and the development of DVT and subsequent PE was first suggested in 1954 by a report describing DVT in a doctor after a 14-hour flight!<sup>5</sup>

Once again, I really congratulate the authors for their great intension and inordinate product

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### *Reply from the Author*

We would like to welcome and thank Dr. Hikmat Abdel-Razeq’s comments on “The Saudi clinical practice guideline for the prophylaxis of venous thromboembolism in long-distance travelers”.<sup>1</sup> In general we agree with most of his comments and elaborations. The main points raised were: 1) hormonal treatment for breast cancer as a risk factor for venous thromboembolism (VTE) in travelers; 2) generalizability of guideline to non-air travel; 3) dehydration associated with fasting during travel; and 4) considering the total travel time including layover.

Firstly, we agree that hormonal therapy for breast cancer therapy is a risk factor for VTE,<sup>6</sup> and that individuals on such therapy are high-risk travelers. Hence, the guideline applies to them as it applies to individuals with any other risk factor for VTE.

Secondly, long-distance non-air travel, whether by car, bus, train or ship, is a VTE risk factor, especially when associated with prolonged immobility and/or other VTE risk factors.<sup>7</sup> However, this guideline was intended for air travelers and so its recommendations did not address non-air travel. It may be reasonable to extrapolate the recommendations from this guideline to long-distance non-air travel. Nevertheless, research on this topic is desperately needed to make specific recommendations.

Thirdly, fasting may exacerbate travel-associated dehydration and theoretically increase VTE risk during travel. Though, the data on the relationship between Ramadan fasting and VTE are scarce. Lai et al<sup>8</sup> found no thrombosis events in 32 patients on warfarin who fasted Ramadan. Nonetheless, recommending to break Ramadan fasting is reasonable for high-risk patients in accordance with the Quranic license. We believe that research on the impact of religious practices on health is much needed.

Fourthly, the travel time is an important determinant of VTE risk. In the guideline,<sup>1</sup> long-distance travel was defined as air travel requiring more than 8 hours, as suggested by multiple studies. However, VTE risk may be higher than normal with shorter travel duration (namely, 4-6hours).<sup>9</sup> We agree with Dr. Abdel-Razeq that the total travel time including layover should be considered when assessing VTE risk and the need for thromboprophylaxis measures.

Observational studies and clinical trials are needed to answer many questions related to travel, thrombosis and thromboprophylaxis.

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