RESEARCH LETTERS

Flight-related complications are infrequent in patients with hereditary haemorrhagic telangiectasia/pulmonary arteriovenous malformations, despite low oxygen saturations and anaemia

Individuals with pulmonary arteriovenous malformations (PAVMs) and hereditary haemorrhagic telangiectasia (HHT) commonly have low oxygen saturations and anaemia, two parameters generally used to indicate medical fitness to fly. Using a retrospective questionnaire-based study, the authors examined in-flight complications and predictors in 145 HHT patients (96 with PAVMs) who reported 3950 flights, totalling 18 943 flight hours. Dyspnoea and thrombotic complications were less common than expected, and could not be predicted from sea level oxygen saturations or haemoglobin concentrations. Nosebleeds that can bar individuals from boarding a flight occurred in 13.6% (11.5% to 15.8%) of long-haul flights. The findings should influence preflight advice.

Individuals with pulmonary arteriovenous malformations (PAVMs)¹ and hereditary haemorrhagic telangiectasia (HHT)² commonly have low oxygen saturations and anaemia, parameters that are used in the general population to indicate medical fitness to fly^{3–5} (and online supplementary references). There are very limited published data on flight tolerance for HHT/PAVM patients.

Using the retrospective study methodology reported in full in the online supplementary material, we received 159 replies

from 308 questionnaires sent out to individuals with definite HHT (response rate 51.6%). The average age at the time of reply was 55 years (range 18–90), 12 respondents had not flown and two (pilot and cabin crew) reported more than 10 000 flights. The remaining 145 HHT-affected respondents (96 (66%) with PAVMs) reported 18 943 flight hours over 3950 flights (online supplementary table 1).

The majority (111/145; 77% (95% CI 69.6% to 83.5%)) reported no in-flight or postflight complications. Six (4.1% (0.86% to 7.4%)) reported dyspnoea, two had a deep vein thrombosis and one suffered an ischaemic stroke while flying. The most common in-flight complications were HHT-related nosebleeds (epistaxis). Complications were more frequent during long-haul flights. Many participants listed flights over several decades, but none reported an increase in the frequency or severity of complications as they got older.

For participants with PAVMs who had not reported in-flight dyspnoea, there was a wide range in arterial oxygen saturation (SaO₂) levels (figure 1A). There was no difference in median SaO₂ between those who reported in-flight dyspnoea and those who did not (figure 1B). Flights where dyspnoea was reported did not correspond to times when SaO₂ were lowest for that particular individual (figure 1C). Similarly, there appeared to be no relationship between dyspnoea and either haemoglobin or serum iron (online supplementary figure 1). There was also no relationship between thrombotic complications and oxygen saturations/haemoglobin (online supplementary figure 2) or between in-flight nosebleeds and basal nosebleeds frequency (if at least once per month) or haemoglobin (online supplementary figure 3).

In conclusion, and as discussed in more detail in the online supplementary material, the principal findings of this study were that flying appears safe for the majority of indi-

viduals with PAVMs and HHT despite abnormal oxygen saturations and haemoglobin concentrations. With the exception of nosebleeds, complications, when they occurred, were usually self-limiting. It was difficult to predict who will experience complications, with the best predictor appearing to be previous flight experience. The findings are surprising, and raise difficulties in recommendations for in-flight oxygen and prophylaxis of venous thromboemboli.

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► Additional materials are published online only. To view these files please visit the journal online (<http://thorax.bmj.com/content/67/1.toc>).

Both authors had full access to all of the data in the study, and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Competing interests None.

Ethics approval Ethical approval was obtained from the London-Surrey Borders Research Ethics Committee (NRES 10/H0806/8).

Contributors Both authors designed the study and obtained ethical approval. CLS had reviewed the patients. Questionnaires were sent out and responses tabulated by

Figure 1 Sea level oxygen saturation in 96 participants who flew with pulmonary arteriovenous malformations (PAVMs). (A) Earliest and most recent arterial oxygen saturation (SaO₂) values for PAVM patients who did not report in-flight dyspnoea (improvements were the result of PAVM embolisation). (B) Mean erect oxygen saturations (SaO₂) at sea level for individuals who reported in-flight dyspnoea and those who did not. Horizontal bars denote medians. There was also no difference in earliest or latest SaO₂ (data not shown). (C) Serial SaO₂ in participants who reported dyspnoea over periods of 1–17 years (median 7.5). Circles indicate periods in which flights were reported to cause dyspnoea. The flight causing dyspnoea for participant 107 was the only long-haul flight taken by that individual.

CGM. Both authors obtained further data from primary patient records and analysed the data. The authors co-wrote the manuscript: the table was generated by CGM; figures and statistics by CLS. Both authors approved the final version. CLS is the guarantor of the data.

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Monitoring treatment response in precapillary pulmonary hypertension using non-invasive haemodynamic measurements

Lee *et al* should be commended for showing that non-invasive haemodynamic monitoring using inert gas rebreathing (IGR) might be a valuable tool to detect treatment response in patients with precapillary pulmonary hypertension (PH).¹ Even under resting conditions, haemodynamic parameters may be more sensitive than the 6-minute walk distance. This is especially interesting as it may facilitate frequent therapy monitoring. Although pulmonary blood flow (PBF) equals cardiac output (CO) in the absence of relevant intrapulmonary shunting, it should be noted that a reliable shunt correction algorithm based on the haemoglobin value has already been implemented in the IGR device.² Since using solely PBF significantly increased the measurement bias as compared with the non-invasive gold standard of cardiac MRI, shunt correction should always be applied. A fixed haemoglobin concentration of 14.0 g/dl can be used, if the exact value is not known.³ This seems to be especially important as pulmonary shunting might be altered in PH. In serial measurements, therapeutic effects and changes in CO may also be due to shunting. This may remain undetected when solely

measuring PBF. In analogy to the 6-minute walk distance, IGR measurements require active collaboration, which may limit their application in patients with advanced disease, high WHO functional class or lack of motivation. In these cases, other techniques of measuring CO such as impedance cardiography or continuous-wave Doppler may become potentially valuable, although they are not sufficiently applicable under exercise conditions. There is a rather large variation when compared with IGR or cardiac MRI; however, the reproducibility is high, which is of tremendous importance in serial measurements.^{4–6} Although the overall PBF values in the study at hand were between 3.1 and 6.5 l/min, we would like to mention that there is a significantly worse agreement for IGR in large heterogeneous patient collectives at extreme CO states represented by values between 2–4 and 6.4–9.6 l/min, respectively.⁷ However, this seems to be negligible considering the aims of the study as the reproducibility is not affected. We agree that based on the very promising findings of Lee *et al*, non-invasive haemodynamic measurements in PH justify further studies to improve and monitor specific therapy. IGR seems to be perfectly suitable for measurements during exercise as it is the only non-invasive device to be used under these conditions.

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Authors' response

We would like to thank Trinkmann *et al* for their comments¹ on our paper, 'Use of non-invasive haemodynamic measurements to detect treatment response in precapillary pulmonary hypertension',² and address the point raised regarding shunt correction. We are of the opinion that the in-built shunt correction algorithm in the inert gas rebreathing device may introduce measurement bias, as the assumptions made to correct for shunt flow may not be applicable to patients with pulmonary vascular disease. In the algorithm,³ cardiac output (CO) is derived from pulmonary blood flow (PBF), oxygen content in arterial blood (CaO₂), oxygen content in pulmonary end-capillary blood (CcO₂) and oxygen uptake (VO₂) according to the formula $CO = 1 / (1/PBF + (CaO_2 - CcO_2)/VO_2)$. The oxygen content of arterial blood and pulmonary end-capillary blood is calculated from the formulae $CaO_2 = 0.000139 \times \text{haemoglobin concentration (Hb in g/dl)} \times SaO_2$ and $CcO_2 = 0.000139 \times Hb \times ScO_2$ respectively, where SaO₂ denotes arterial oxygen saturation measured by pulse oximetry and pulmonary end-capillary oxygen saturation (ScO₂) is assumed to be 98%. However, ScO₂ may not reach 98% in patients with pulmonary hypertension due to failure of oxygen equilibration in the alveoli combined with a low mixed venous saturation. As a result of the destruction of pulmonary capillary beds and consequently reduced pulmonary capillary blood volume, red cell transit through pulmonary capillaries is more rapid.⁴ This shortens the time available for oxygen diffusion to complete across the alveolar–capillary membranes, especially as PBF increases in response to exercise. This is compounded by systemic venous blood being more deoxygenated at the start of the equilibration process due to increased peripheral oxygen extraction in a low CO state associated with pulmonary hypertension. These two mechanisms contribute to resting arterial hypoxaemia and exercise desaturation commonly seen in pulmonary hypertension patients. Applying the shunt correction algorithm would overestimate CO, especially for exercise measurements. Therefore, we advocate the use of inert gas rebreathing PBF instead of derived CO in this patient group. As Trinkmann *et al* pointed out, other non-