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.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The authors are fully committed to the principles of data sharing.

Accepted 5 September 2011
Published Online First 26 September 2011

Thorax 2012;**67**:80–81.
doi:10.1136/thoraxjnl-2011-201027

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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.

Frederik Trinkmann, Dariusch Haghi, Joachim Saur

1st Department of Medicine (Cardiology, Angiology, Pneumology, Intensive Care), Universitätsmedizin Mannheim, Mannheim, Germany

Correspondence to Dr Joachim Saur, I Medizinische Klinik, Universitätsmedizin Mannheim, Theodor-Kutzer-Ufer 1-3, Mannheim D-68167, Germany; joachim.saur@umm.de

Competing interests None.

Contributors FT and JS: writing of the manuscript. DH: thorough revision of the manuscript and scientific advice.

Provenance and peer review Not commissioned; internally peer reviewed.

Accepted 8 August 2011
Published Online First 22 September 2011

Thorax 2012;**67**:81.
doi:10.1136/thoraxjnl-2011-200867

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Authors' response

We would like to thank Trinkmann *et al* for their comments[1] 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 (CaO_2), oxygen content in pulmonary end-capillary blood (CcO_2) and oxygen uptake (VO_2) 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 $CaO_2=0.000139\times$haemoglobin concentration (Hb in g/dl)$\times SaO_2$ and $CcO_2=0.000139\times Hb\times ScO_2$ respectively, where SaO_2 denotes arterial oxygen saturation measured by pulse oximetry and pulmonary end-capillary oxygen saturation (ScO_2) is assumed to be 98%. However, ScO_2 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-