American Heart Association.
Circulation
Manuscript Submission and Peer Review System

Disclaimer: The manuscript and its contents are confidential, intended for journal review purposes only, and not to be further disclosed.

URL: http://circ-submit.aha-journals.org

Title: Response to Letter Regarding Article "Immediate and Midterm Cardiac Remodelling Following Surgical Pulmonary Valve Replacement in Adults with Repaired Tetralogy of Fallot: A Prospective Cardiovascular Magnetic Resonance and Clinical Study."

Manuscript number: CIRCULATIONAHA/2018/033771

Author(s): Sonya Babu-Narayan, Royal Brompton Hospital
Ee Ling Heng, Royal Brompton Hospital
Gerhard-Paul Diller, Royal Brompton Hospital
Michael Gatzoulis, Royal Brompton Hospital

Disclaimer: The manuscript and its contents are confidential, intended for journal review purposes only, and not to be further disclosed.

Response to Letter Regarding Article: Immediate and Midterm Cardiac Remodeling After Surgical Pulmonary Valve Replacement in Adults With Repaired Tetralogy of Fallot

Ee Ling Heng MBBS BSc MRCP PhD[1, 2], Gerhard-Paul Diller MD PhD[3], Michael A Gatzoulis MD PhD FESC[1, 2], Sonya V Babu-Narayan MBBS BSc FRCP PhD FESC[1, 2]

[1]Adult Congenital Heart Disease Centre, Royal Brompton Hospital, London, UK. [2]NIHR Cardiovascular Biomedical Research Unit, Royal Brompton & Harefield NHS Foundation Trust and Imperial College London, UK. [3] University Hospital of Münster, Division of Adult Congenital and Valvular Heart Disease, Department of Cardiovascular Medicine, Münster, Germany

***Corresponding Author:**

Dr Sonya V Babu-Narayan, MBBS BSc FRCP PhD FESC

Department of Adult Congenital Heart Disease

National Heart & Lung Institute, Imperial College London

Royal Brompton Hospital, Sydney Street, London SW3 6NP

Phone: 0207 351 8803, Fax: 0207 351 8816

Email: s.babu-narayan@rbht.nhs.uk

Disclaimer: The manuscript and its contents are confidential, intended for journal review purposes only, and not to be further disclosed.

Word Count: 396 words

In Response:

We thank the authors for their interest in our recent publication in which we reported on significant right heart structural reverse remodelling seen in the immediate post-surgical pulmonary valve replacement (PVR) period in patients with repaired Tetralogy of Fallot (rTOF), which was followed by further time-related biological remodelling exemplified by further reduction in RVESVi.[1] Patients put forth for PVR following multidisciplinary review were opportunistically and serially approached by the research team (SVB-N) for study inclusion if they fulfilled the study inclusion criteria. The study cohort patients did not differ from the rest of the patients with TOF undergoing surgical PVR during this period in terms of clinically relevant co-variates of age, gender, symptomatology, QRS duration on ECG as well as biventricular volumes and function as assessed by CMR. The relevant data illustrating this is presented in Supplementary Table 3, online supplement.[1]

We acknowledge that specific right ventricular (RV) volumetric thresholds (RVEDVi≥150ml/m^2, RVESVi≥80ml/m^2) were being gradually adopted for asymptomatic patients during the study period, which may have influenced the timing of PVRs and therefore limit the applicability of our results to patients with severely dilated RVs at the extremes of the volumetric spectrum. We had therefore compared the study patients to non-study TOF patients undergoing PVR in Supplementary Table 3 and showed that there was no evidence of excluding patients at volumetric extremes. In addition, we feel our study cohort is likely representative of the typical patients with TOF in contemporary clinical practice who are largely asymptomatic and undergo elective PVR surgery with similar volumetric thresholds applied at other tertiary institutions.[2, 3] Therefore, clinicians should be able to contextualise our results as appropriate to their own patient cohort.

We welcome the authors' comments with regards to the potential utility of joint modelling and dynamic predictive models towards customised, patient specific care. Whilst such models are conceptually appealing, we remain mindful of the complex interactions between

Disclaimer: The manuscript and its contents are confidential, intended for journal review purposes only, and not to be further disclosed.

myocardial, electromechanical and neurohormonal factors that are increasingly recognised to be implicated in adverse outcomes for this patient population. These factors are more challenging than temporal haemodynamic changes to meaningfully incorporate into such models. The application of such models to our current, modest study cohort size may be viewed as speculative, but we support the ambition of extending risk prediction models in future prospective collaborative studies towards optimising cardiac remodelling and clinical outcomes following PVR in this expanding patient population.

Sources of Funding

Dr Heng (FS/13/76/30477) and Dr Babu-Narayan (FS/11/38/28864) are supported by the British Heart Foundation) and the National Institute for Health Research Cardiovascular Biomedical Research Unit of the Royal Brompton & Harefield National Health Service Foundation Trust and Imperial College London.

Disclosures

The authors report no conflict of interest.

Disclaimer: The manuscript and its contents are confidential, intended for journal review purposes only, and not to be further disclosed.

References

1. Heng EL, Gatzoulis MA, Uebing A, Sethia B, Uemura H, Smith GC, Diller GP, McCarthy KP, Ho SY, Li W, Wright P, Spadotto V, Kilner PJ, Oldershaw P, Pennell DJ, Shore DF, Babu-Narayan SV. Immediate and Midterm Cardiac Remodelling After Surgical Pulmonary Valve Replacement in Adults With Repaired Tetralogy of Fallot: A Prospective Cardiovascular Magnetic Resonance and Clinical Study. Circulation 2017;136(8):1703-1713
2. Frigiola A, Tsang V, Bull C, Coats L, Khambadkone S, Derrick G, Mist B, Walker F, van Doorn C, Bonhoeffer P, Taylor AM. Biventricular response after pulmonary valve replacement for right ventricular outflow tract dysfunction: is age a predictor of outcome? Circulation 2008; 118(14 Suppl):S182-190
3. Ferraz Cavalcanti PE, Sa MP, Santos CA, Esmeraldo IM, de Escobar RR, de Menezes AM, de Azevedo OM Jr, de Vasconcelos Silva FP, Lins RF, Lima Rde C. Pulmonary valve replacement after operative repair of tetralogy of Fallot: meta-analysis and meta-regression of 3,118 patients from 48 studies. J Am Coll Cardiol 2013; 62(23):2227-2243

Disclaimer: The manuscript and its contents are confidential, intended for journal review purposes only, and not to be further disclosed.