perceived barriers to PP and the interactions between institutional-level and provider-level barriers.

Although prior work has cited insufficient clinical recognition of patient eligibility for PP as a major barrier to PP uptake (5), barriers at the clinician level can only be overcome after structural barriers have been addressed. Our finding of low uptake of an evidence-based intervention with a mortality benefit at an institutional level (sometimes due to misconceptions) raises multiple questions for future investigation, and suggests that attempts to implement PP among eligible patients will need to include consideration of hospital-level barriers. ■

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Pending Right Heart Failure in Healthy Preterm-Born Subjects?

To the Editor:

We read with great interest the report by Mulchrone and colleagues on impaired right ventricular–pulmonary arterial (RV–PA) coupling in healthy young adults with a history of preterm birth and upper limit of normal of pulmonary vascular resistance (1). The authors estimated RV–PA coupling by the ratio of end-systolic elastance to arterial elastance (Ees/Ea) using a single-beat method applied to high-fidelity measurements of pressures and magnetic resonance imaging of volumes, or simplified either as a ratio of stroke volume to end-systolic volume or as a ratio of the maximum RV pressure (Pmax) to the end-systolic pressure (Pes) minus one. As recently reviewed, the volume-only method avoids the need for a right heart catheterization, whereas the single-beat and pressure-only methods require particular expertise for calculating Pmax by extrapolating the isovolumic portions of the RV pressure curve and a related estimation of Pes (2). Single-beat, pressure-only, and volume-only methods have recently been shown to have acceptable accuracy but limited precision when compared with the gold standard multiple-beat method to assess RV–PA coupling (3).

In the study by Mulchrone and colleagues, the preterm-born subjects had decreased Ees/Ea ratios compared with control subjects, but the magnitude differed considerably depending on the method used. As estimated from numbers in Table 1 and data points in Figure 1 of Reference 1, Ees/Ea decreased by some 50–60% down to 0.8–0.9 when assessed by the single-beat or the pressure-only methods, but only by some 12% when assessed by the volume-only method. Uncoupling of the RV

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from the pulmonary circulation by >50% is associated with increased right heart dimensions and decreased ejection fractions (EFs) to ⩾35%, heralding the transition from maladaptation to failure (4).

The extraordinary RV–PA uncoupling in preterm-born subjects disclosed in the study by Mulchrone and colleagues is probably methodological. The authors applied a recently developed automatic second derivation of rate of pressure rise (dP/dt) (5) instead of a single derivation of dP/dt with manual identification of the end and onset of diastole, which traditionally has been used to determine the isovolumic portions of the RV pressure curve and extrapolate an estimation of Pmax (3, 4). As acknowledged by the authors, the second-derivative approach may reduce variability (i.e., increase precision) but underestimates Pmax by some 13% (5). This would obviously increase Pes, probably in a similar proportion. Calculating the EF from the pressure-only method as 1 − Pes/Pmax with 13–15% corrections of the reported Pmax and Pes in the study by Mulchrone and colleagues would bring it back around the normal value of 60%.

Mulchrone and colleagues claim that there was good agreement between the pressure- and volume-only methods, with a Pearson coefficient of $R^2 = 0.78$ ($P < 0.001$) (1). However, as repeatedly underscored by Bland and Altman, correlation coefficients largely reflect the variability of the subjects being measured, such that if one measurement is always twice as big as the other, they are highly correlated but do not agree (6). The large differences in the means of Ees/Ea obtained by different methods in the preterm-born subjects indicate considerable biases, which would have been disclosed by a correct Bland and Altman analysis.

In conclusion, we believe that preterm-born healthy subjects can be reassured that they are not in a state of pending right heart failure. This discussion also underscores how difficult it is to measure the gold-standard Ees/Ea ratio to assess RV–PA coupling, and the importance of using a rigorous methodology, including the EF, as an indispensable internal control. ■

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Reply to Tello *et al.*

From the Authors:

We appreciate the opportunity to further discuss cardiopulmonary differences between adults born preterm and adults born at term (1). Tello and colleagues raise two important points in their letter that we will address here. First, the "extraordinary" right ventricular–pulmonary arterial (RV–PA) uncoupling in the preterm-born subjects we reported is not the result of our use of the second-derivative approach to the single-beat method (2), as they suggest. The first author of this letter, who is an experienced user of both first- and second-derivative approaches, reanalyzed the hemodynamic data reported by Mulchrone and colleagues and found similar results (Figure 1) that led to a similar conclusion: preterm birth leads to a decrease in the RV–PA end-systolic elastance to arterial elastance ratio (Ees/Ea) that is clinically relevant. With either approach, the decrease is not statistically significant, most likely because of the small sample size.

Second, although data support that uncoupling of the right ventricle from the pulmonary circulation by more than 50% predicts RV failure in pulmonary hypertension (3), preterm birth causes a fundamentally different cardiopulmonary pathology. In particular, preterm birth results in morphologically different ventricles with smaller biventricular chamber size and subtle left ventricular (LV) dysfunction (4, 5). Herein lies a critically important methodological consideration in using RV–PA Ees/Ea to predict RV failure. As elegantly demonstrated decades ago (6, 7), although LV pump function is largely insensitive to RV pump function, the reverse is not true. As we recently showed in a mouse model of pulmonary hypertension secondary to left heart failure, impaired LV function depresses RV–PA Ees/Ea even if the right ventricle itself is in an adaptive, not maladaptive, state of remodeling (8). We anticipate that this is the case in our cohort of preterm-born subjects but must await invasive LV hemodynamic data to prove the point.

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