The investigation of a study

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See related article on pages 358-66.

Aortic reconstruction, especially in the context of single-ventricle physiology, is possibly the most important aspect of the repair, yet outcomes are still not ideal, and there is no uniformity in opinion regarding what constitutes the optimal technique. Focused investigation of postoperative aortic arch geometry and arch angles has yielded some insight as to mechanisms of postoperative recoarctation or compression of the bronchial or pulmonary arterial trees. A recent PubMed literature search with the key words *aortic arch geometry and pediatric* yielded 101 results. Admittedly, there are few reports that include such anatomic study after Norwood reconstruction.

Accordingly, Hasegawa and colleagues¹ in this issue of the *Journal* have expanded our understanding as to how postoperative geometry may influence outcomes. Hasegawa and colleagues¹ report the results of a retrospective review of 36 patients who underwent a Norwood procedure followed by a multidetector computed tomographic scan at their institution during a 15-year period. Hasegawa and colleagues¹ aimed to understand whether arch geometry was correlated with recoarctation or pulmonary artery or bronchial compression and whether the technique of arch angle augmentation was associated with improved rates of the aforementioned outcomes.

Despite the excellent results reported by Hasegawa and colleagues¹ and the potential utility of the described technique, the focus of this commentary is to “study a study,” thereby highlighting those methodologic concerns that diminish the gravity of the results and undermine the data themselves.

The first critical limitation of this study is the failure to exclude critical patient subgroups that ought to be excluded, including those managed with hybrid strategies (application of bilateral pulmonary artery bands and either prostaglandin infusion or ductal stenting) and patients

undergoing biventricular conversion (ie, Yasui reconstruction). Although the primary end point as articulated by Hasegawa and colleagues¹ was pulmonary artery compression by the aorta rather than pulmonary artery stenosis per se, what are the sensitivity and specificity of computed tomography to discriminate between these entities? That 20 of the 36 patients in this study underwent initial hybrid palliation followed by a Norwood operation is a significant issue. Moreover, the status of the left ventricular outflow tract among patients with Yasui reconstruction (n = 9 in this study) is another important concern. Important gradients across the subaortic region may have influenced the growth or flow dynamics across the reconstructed aorta and contributed to later obstruction or compression. Despite the claim of Hasegawa and colleagues¹ that postoperative left ventricular outflow tract gradients were minimal among their cohort, the inclusion of these patients confounds the analysis considerably and hampers interpretation of the data. As an extension of this argument, maintaining anatomic homogeneity when investigating the unknown forces of “flow” and pressure would be helpful. This study included patients with aortic atresia and those with forward flow across the aorta–pulmonary artery amalgamation—different anatomic circumstances that can have unclear implications regarding the selected end points.

The second critical issue is attrition bias. Among the 52 patients undergoing arch reconstructions, evaluable computed tomographic scans were not performed in 16 because of in-hospital death. No additional data are provided as to the types of arch reconstruction performed among these patients. Hypothetically, if all of these patients had undergone aortic arch angle augmentation and died, the conclusions of the study would be drastically different. A formal sensitivity analysis, or at a minimum disclosure of the relationship of the deceased subjects with respect to the predictor and outcome variables, would be of great importance. Moreover, death should be compared and analyzed between groups. It is the hardest and most significant of outcomes, and in a cohort with substantial mortality, consideration of mortality is vital.

The third issue is era effect. Hasegawa and colleagues¹ state that surgeon variability was accounted for within their analysis and did not emerge as a risk factor. On inspection, however, surgeon was uniformly correlated with era, as surgeon M.Y. performed all Norwood reconstructions before 2005 and surgeon Y.O. performed the more contemporary

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Disclosures: Authors have nothing to disclose with regard to commercial support. Received for publication May 19, 2015; accepted for publication May 21, 2015; available ahead of print June 16, 2015.

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J Thorac Cardiovasc Surg 2015;150:367-8

0022-5223/\$36.00

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<http://dx.doi.org/10.1016/j.jtcvs.2015.05.054>

Norwood reconstructions. Surgeon Y.O. appears to prefer the patch technique. As one might predict, Norwood outcomes improved with time at the institution of Hasegawa and colleagues,¹ from 43% in-hospital mortality to 14% in-hospital mortality. The era effect alone could certainly lead to an important bias in terms of the conclusions favoring the patch technique. In light of the small numbers of patients, inclusion of an explanatory variable within a multivariable model does not exclude the potential for confounding.

The fourth issue is the lack of preoperative imaging data to confirm that postoperative differences in arch anatomy did not exist a priori. Hasegawa and colleagues¹ need to make a compelling argument that aortopulmonary space measurements did not differ between populations before surgical intervention. Ascertainment of even 2 or 3 preoperative imaging studies in patients would allay concerns that these are real postoperative discrepancies between the groups.

Fifth, the issue of statistical power cannot be ignored. The statistical models are overfitted. Hasegawa and colleagues¹ have included at least 13 variables in their multivariable model for reintervention or reoperation for bronchomalacia or branch pulmonary artery stenosis. Although it is not explicitly stated, if all these were considered, the models are overparameterized, as they have only 7 total events in these 2 categories. Furthermore, there is no detail regarding the type of selection used for variable inclusion, other than that the threshold was a *P* value less than .1. Although re-coarctation was ostensibly considered as one of their primary end points, neither univariable nor multivariable models were fitted for this event.

Finally, the use of suboptimal control populations and the lack of blinded observers ascertaining imaging measurements (which introduces the potential for reporter bias) are minor detractions that are often seen in retrospective studies. Although it is laudable that Hasegawa and colleagues¹ included a control group, the validity of this control group is questionable, because they appear to be patients with congenital heart disease, although the morphology of the congenital defect is not further defined. A better choice would have been age-matched healthy control patients without concomitant congenital heart disease.

In summary, the report by Hasegawa and colleagues¹ highlights the critical importance of final aortic geometry in Norwood-type aortic reconstructions. Residual or recurrent systemic arterial obstruction remains problematic in these patients, but we are reminded here that there are additional considerations of significant clinical importance. The described technique for improved aortic geometry may ultimately prove useful in avoiding these issues; unfortunately, however, methodologic issues have eclipsed the validity of their conclusions. This is often how progress must begin. Early concerns, observations, and considerations are seldom definitively resolved with retrospective reviews. But Hasegawa and colleagues¹ have brought forward the salient issues, and the stage is now set for more rigorous inquiry.

Reference

1. Hasegawa T, Oshima Y, Maruo A, Matsuhisa H, Tanaka A, Noda R, et al. Aortic arch geometry after the Norwood procedure: efficacy of arch angle augmentation for creating a sufficient aortopulmonary space. *J Thorac Cardiovasc Surg*. 2015; 150:358-66.