Hybrid versus Norwood: “Fifty shades of grey”

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The article by Malik and colleagues¹ in this issue of the *Journal* is an elegantly constructed analysis of a difficult problem in our specialty. The authors have used instrumental variable techniques, popularized in the field of economics, to investigate whether the hybrid procedure is superior to the traditional Norwood procedure for infants with hypoplastic left heart syndrome. The authors found that the use of the hybrid procedure, when analyzed with instrumental variable methodology, reduced the odds of mortality and renal failure, and decreased the index hospital length of stay by 20 days compared with the Norwood procedure. The outcomes of both procedures were equivalent regarding these outcomes when analyzed using more conventional propensity score methods. Unfortunately, because the provocative results favoring the hybrid procedure were supported *only* by an emerging and often misunderstood analytic technique, the present study only leads to further obfuscation of any clarity in an already muddy comparison.

Although a full discussion of the theory, assumptions, and appropriate application of instrumental variable methods is the subject of an upcoming statistical techniques article in the *Journal* and therefore beyond the scope of this editorial, some introductory comments are pertinent. Our recent article² describing the current patterns of use for the hybrid procedure revealed that neonates undergoing the hybrid had a higher prevalence of preoperative risk factors than neonates undergoing the Norwood procedure. These high-risk neonates, before the advent of the hybrid, which is ostensibly a less-invasive procedure than the Norwood, may have been excluded from any possible intervention. Our prior analysis also demonstrated a clear institutional bias, that is, centers with higher Norwood mortality generally favored the hybrid procedure.² Given these inherent inequities, the application of analytic methods designed to control for such informative biases is paramount. Outside of a randomized trial, which controls for bias through the process of randomization, 2 statistical approaches can be used to eliminate or reduce selection and allocation bias: propensity scores and instrumental

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Central Message

Comparison of hybrid versus Norwood is problematic, and the current study may only further confuse the issue.

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variables. Both methods aim, in different ways, at producing comparable groups with respect to important characteristics. Although most readers are more familiar with propensity scores or propensity matching to “balance” groups under comparison, an instrumental variable approach is more appropriate when important confounding variables are not known or observed. The instrumental variable method requires the identification of a variable, known as an instrument, that is associated with the exposure (or treatment) of interest but does not directly affect the outcome. Therefore, the instrument is related to the outcome only through the exposure (or treatment) of interest. Inclusion of the instrument as a substitute for the treatment assignment in traditional multivariable models can be used to purge the treatment variable of its association with any influential omitted variables.

The authors used variation in physician practice patterns at tertiary care children's hospitals as the instrumental variable and defined the individual center annual hybrid rate as their instrument. Characterization of variations in health-care practices as instrumental variables has been used frequently in previous studies, and these reports have added considerably to our knowledge of the heretofore underestimated impact of allocation and selection bias in observational studies.³

In the study by Malik and colleagues,¹ 3654 neonates were identified from 39 hospitals participating in the Pediatric Health Information System. Of these, 3412 (93%) underwent the Norwood and 242 (7%) underwent the hybrid. The majority of hybrid procedures were performed at 5 hospitals, and 8 hospitals did not perform any hybrid

procedures. A major limitation is the skewed distribution of hybrid procedures. That only 5 centers performed hybrids at any meaningful rate, suggesting that perhaps patient mix and levels of care are inconsistent among the sampled hospitals, calls into question whether the second assumption of the instrumental variable method (whether the instrument is not correlated with unobserved variables that affect outcome) is actually satisfied. Moreover, the validity of the results is reduced because the authors did not include important surgeon and center-level factors or consider the potential interaction of these factors in their analysis. It could be, as has been shown in numerous studies, that outcomes with the hybrid or the Norwood are contingent on these unmeasured confounders. Although I agree that instrumental variable methodology is ideally suited to address the aims of the study by Malik and colleagues¹ and am pleased to see these techniques make their debut in the congenital heart surgery realm, it is unfortunate and disconcerting that the propensity models generated opposing results. Chris Caldarone⁴ articulated in his recent commentary, *W(h)ither the Hybrid? Up the "Slope of Enlightenment,"* "It is clear that the hybrid innovation is an important tool in our clinical armamentarium for managing patients with single ventricle physiology. We simply need to figure out how best to use it." It appears now we also need to figure out how to study it.

So, what are we to infer from this study? Malik and colleagues¹ state "...the hybrid approach may represent an improvement over the Norwood in neonatal and longer-term outcomes." Is this really the case? Should all centers, even those with arguably excellent Norwood survival and proven durability abandon this technique and convert to

hybrid procedures? Or should centers with superior results with either strategy continue to refine, develop, and extrapolate those techniques? It is a difficult question with no current answer. What is clear is that wider application of surgical innovation, especially in high-risk populations, must be initiated cautiously. Historically, the enthusiasm for new surgical technology has often outpaced solid evidence of its benefits. Although the hybrid may offer advantages in select circumstances, we have not made much progress in elucidating these circumstances. Moreover, rapid adoption before such clarity and efficacy have been established is fiscally irresponsible and could adversely affect the fate of our most fragile patients. As Charles Wilson⁵ eloquently stated in his treatise regarding the wisdom of adopting new surgical technology, "In the final analysis, a surgeon's skill and ability to perform a procedure well is unimportant, in fact irrelevant, if the procedure should not be done in the first place."

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