Venovenous extracorporeal membrane oxygenation for patients with single-ventricle anatomy: A registry report

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The article by Aydin and colleagues¹ in this issue of the *Journal* uses the Extracorporeal Life Support (ELSO) registry to describe the growing experience with use of venovenous extracorporeal membrane oxygenation (VV-ECMO) for patients with single-ventricle anatomy (SVA) and pure oxygenation/ventilation impairment. As an investigator who has clearly used registry data frequently over the past 14 years, some may argue that my comments vis-à-vis this article are ironic at best and blatantly hypocritical at worst. This justifiable skepticism notwithstanding, my opinions represent a wealth of lessons learned and an escalating concern that inadequate, incomplete, or biased data, which seem to be increasingly represented in the cardiac surgery literature, may compromise the rigor of contemporary investigation and undermine the validity and import of conclusions reached. A PubMed query² revealed more than 15,288 citations for cardiac registry reports, 59% (n = 8933) of which were published in the last 5 years. A PubMed search³ using the combined terms “descriptive,” “database,” and “registry” reveals 263 citations. It is within this lens, or conceptual framework, that I offer the following critique.

The descriptive nature of the study, necessitated by the lack of adequate granularity within the chosen dataset, hampers the articulation of a well-defined hypothesis investigating an important knowledge gap in our field. For example, the critical question that I and other reviewers wanted the authors¹ to address is whether VV-ECMO can be deployed rationally (or at all) among patients with SVA with cardiac failure so that those requiring venoarterial ECMO support could be differentiated outright. The present study reported that among 89 patients with SVA undergoing VV-ECMO within the ELSO database between 1999 and 2012, 30 (32%) required support for a cardiac indication. Recipients (N = 4) of extracorporeal cardiopulmonary resuscitation were excluded. Unfortunately, although survival was equivalent for those patients with respiratory indications (51%) or cardiac indications (53%), there is

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Central Message

Descriptive reports using registries are increasing. Although descriptive analyses can be a formative step, they should be used judiciously and followed by hypothesis-driven investigation.

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no information provided in the article regarding the nature of the cardiac indications. A recently developed cardiac addendum to the existing ELSO registry that ostensibly includes echocardiographic systemic ventricular function, cardiac catheterization data, and so forth is available. However, this addendum reportedly contained data on only 20% of the study patients, and therefore these data were not included. Moreover, because the registry, as one would expect, contains only de-identified data, there is no mechanism to trace these patients to their respective institutions in the hope of ascertaining additional critical information. Although these limitations are understandable at first and we are tempted to placidly accept them as unsurmountable or beyond the scope of the initial study, one viable option that could significantly improve the article by Aydin and colleagues¹ would be the inclusion of relevant data and outcomes within one (or better, within all) of the authors' centers. Indeed, that one of the co-authors (R.T.) has published several reports of patients with SVA supported by ECMO underscores the inherent feasibility of such an approach.⁴⁻⁶

The lack of data within the ELSO registry within the time-frame studied further compromises the ability of the

authors¹ to investigate another critical issue, the timing of ECMO support, both in its relationship to a preceding cardiac procedure and within the context of the entire hospitalization. For example, were these patients immediately postpericardiotomy, were they lingering on a ward, or were they readmitted weeks after their cardiac operation? Nearly every article that investigates outcomes among patients with SVA requiring ECMO support (including the present study) concludes that *timely* institution of mechanical support is a key principle in improving survival and reducing morbidity.^{7,8} Without knowledge of the context of ECMO deployment, these questions remain unanswered. Moreover, the authors are unable to address the efficacy and utility of relevant, yet contentious, processes of care, such as mandatory in-house extracorporeal cardiopulmonary resuscitation systems; ongoing, regular training (so-called mock codes) for personnel regarding potentially challenging cannulation strategies; mobile ECMO units; and simulation programs for residents and fellows. It is disappointing indeed that additional insight is not provided by the current effort of these highly qualified investigators. At the risk of redundant rhetoric, the inclusion of available institutional clinical data regarding these variables would have supplemented the authors' study significantly.

The statistical analysis used in this article is fairly traditional. Aydin and colleagues¹ have avoided the pitfall of dichotomizing continuous predictor variables along arbitrary thresholds that may simplify interpretation but limit the generalizability and utility of the statistical information should these thresholds subsequently change over time. The authors also have specified the incremental increase in the odds of mortality associated with changes (either positive or negative) in these continuous predictor variables. It is critical for the reader to understand the magnitude of risk and its direction associated with even small fluctuations within the continuous variables. For example, it is interesting and somewhat counterintuitive that the odds of death increase by 1.16 with an increase in mean arterial blood pressure by 1 mm Hg.

In the final lexicon, what can we glean from Aydin and colleagues?¹ Description is an important formative step. There is certainly value in understanding the prevalence of a particular lesion and the outcomes of various treatment strategies to correct these lesions. A registry report provides an opportunity to chronicle limitations (as the authors have nicely done) and therefore iteratively improve the data within the registry. The Society of Thoracic Surgeons Congenital Heart Surgery Database has done this successfully with both consensus and empirically derived database upgrades and the addition of modules designed to focus on specific aspects (ie, anesthesia, perfusion, quality of care processes) that affect surgical outcomes in patients with congenital heart disease. The United

Network Organ Sharing database, in part related to our article that described the deficiencies of coding for congenital heart disease among transplant recipients, has made several additions to their registry.⁹ However, it is now time to transcend these initial steps and invest in the pursuit of the more difficult, yet critically important questions that restrict forward progress in our field. This investment must be concerted and broad-based. Our scientific journals should increasingly insist that a study is hypothesis-driven and that the limitations elucidated by the authors are *reasonable* and not simply a convenient rationale for avoiding *feasible* additional data collection or more sophisticated analyses. Potential fruitful avenues on which to focus resources include (1) supporting research infrastructure and dedicated time for interested investigators in our hospitals; (2) using biostatistical input throughout conceptualization, design, and analysis of study data; (3) developing new dataset linkages and exploiting available linkages, which will further streamline the integration of clinical data with existing registry data; and (4) generating incentivized collaboration and increased use of focused consortia to facilitate sharing of scarce or costly resources.

Critics of the descriptive article perhaps can be somewhat mollified by the promise that such initial reports will lead to more guided investigation. Indeed, the authors¹ mention the availability of more detailed cardiac data within the ELSO registry, which, along with harnessing the aforementioned ideas, may yet give us the answers. Let's hold these authors, and all others, to this promise.

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