Hypoplastic left heart syndrome, which occurs in 1 per 5000 live births, refers to a family of cardiac defects that are characterized by hypoplasia of the structures making up the left side of the circulation, including the mitral and aortic valves, the left atrium and left ventricle, and the aorta. Infants with this syndrome typically undergo a 3-stage surgical palliation. Without this surgery, the defect is lethal. Since the report of the first Norwood procedure for hypoplastic left heart syndrome by Dr William Norwood in 1981, results from treatment of hypoplastic left heart syndrome have improved considerably. In a large single-center report, operative mortality associated with the first-stage procedure was reduced from 59% to 19% between 1990 and 2001. Nonetheless, the complete palliative sequence entails 3 surgeries and has considerable interstage mortality, so the overall survival for patients with hypoplastic left heart syndrome remains poor.

The primary study outcome was the rate of death or cardiac transplantation at 12 months compared between the 2 shunt patterns. The results of this trial, which were published in 2010, showed that the RVPA shunt offered greater survival at 12 months (74% for RVPA versus 64% for MBT).

Interestingly, when transplantation-free survival was compared between groups using all available follow-up data rather than truncating at 12 months, the survival advantage of the RVPA shunt was no longer seen, complicating the interpretation of the study results.

Over the following years, a number of secondary analyses from the Single Ventricle Reconstruction Trial have been published, illuminating additional aspects of a highly complex disease and treatment. Importantly, a detailed analysis of mortality from the initial trial demonstrated that 54% of deaths occurred during the initial operation and associated hospital stay, whereas 33% of deaths occurred after hospital discharge while the patient was awaiting the second-stage operation (interstage mortality). The second-stage operation and subsequent follow-up accounted for the remaining 14% of deaths.

The hospital mortality rate during the stage 1 operation was 16% and was not related to shunt type. However, interstage mortality between stages 1 and 2 was 6% for the RVPA shunt and 18% for the MBT group, for an odds ratio of 3.4 for MBT compared with RVPA. Thus, the major survival advantage of the RVPA shunt was attributable to interstage mortality rather than to procedural mortality. Further analyses demonstrated a complex relationship between anatomic subtype, other innate patient risk factors, and the risk associated with each shunt type. For example, patients who were full term at surgery and had aortic atresia were more likely to benefit from the RVPA shunt, whereas preterm infants with a hypoplastic but patent aortic valve benefited from the MBT shunt.

In this study, the RVPA shunt and MBT shunt were compared. The primary study outcome was the rate of death or cardiac transplantation at 12 months compared between the 2 shunt groups. The results of this trial, which were published in 2010, showed that the RVPA shunt offered greater survival at 12 months (74% for RVPA versus 64% for MBT).

Newburger and colleagues have taken an important additional step with the current publication of survival outcomes at 3 years in this same cohort. In showing overall equivalence of survival between the RVPA and MBT groups at 3 years, the authors confirm the trend raised in the initial trial publication and demonstrate the complex time dependence of survival benefit between the surgical approaches. In the early phase, encompassing both surgical mortality and the first interstage interval, the hazard ratio favored the RVPA shunt, whereas after 12 months, the MBT was favored in terms of both survival and morbidity (as represented by excess interventions). This evolution of risks over time is consistent with the theoretical framework described in the initial study design whereby...
the RVPA shunt is associated with more favorable postoperative physiology but poses problems of pulmonary artery growth and right ventricular function, possibly as a result of the right ventriculotomy. The results of the present study are also consistent with an alternative hypothesis that the innate patient risk profile is not altered materially by the choice of shunt. In this explanation, the decrease in right ventricular function described by Newburger and colleagues is a manifestation of survival of a marginal patient cohort with the RVPA shunt, whereas the MBT shunt did not afford this group the same short-term survival. As this marginal cohort undergoes attrition, persisting equality of the remaining cohort would be expected. Conversely, if the ventriculotomy or other aspects of the RVPA shunt are problematic, that should be evident after additional time elapses through further divergence of the cohorts. Additional longitudinal studies of this cohort may help elucidate these issues and will be invaluable for these and for other reasons.

A cohort of this size, with surgical randomization, is a costly and very precious resource that should be fully utilized, as is being done with the multiple analyses emerging from the primary trial. At the same time, a cautionary note is needed. None of these secondary analyses were part of the primary study power calculation, and there is potential for both over-powered and under-powered results of the present study. Moreover, the MBT shunt and RVPA shunt are variants of a single-shunt strategy. Additional longitudinal studies of this cohort may be valuable for these and for other reasons. The results of the present study are also consistent with an alternative hypothesis that the innate patient risk profile is not altered materially by the choice of shunt.

Disclosures

None.

References


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