Editorial

On rough road of hypoplastic left heart syndrome after Norwood procedure

Chiara Marrone[1], Lorenzo Galletti[2]

[1]Cardiology Department, [2]Cardiac Surgery Department, Hospital Papa Giovanni XXIII, Bergamo, Italy

Correspondence to: Lorenzo Galletti, MD, PhD. Head, Cardiac Surgery Department, Hospital Papa Giovanni XXIII, Piazza OMS 1, 24127 Bergamo, Italy. Email: lgalletti@asst-pg23.it.

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Norwood procedure is the most common surgical treatment strategy for hypoplastic left heart syndrome (HLHS) (1). Although advances in surgical techniques and postoperative care have significantly improved the survival rates after Norwood, a significant proportion of children develop heart failure (HF) at different stages of palliation (1,2). The risk of developing HF in this subset of patients is greatest during infancy and ultimately needs listing for heart transplantation (2). Nowadays, there has been concern regarding the impact of shunt type on the development of HF after Norwood procedure, that is, right ventricle to pulmonary artery shunt (RVPAS) *vs.* modified Blalock-Taussig shunt (MBTS). From the physiopathological point of view, current evidences acknowledge the crucial role of the initial palliative procedures on the future good haemodynamic of patients with single ventricle circulations (3,4). Indeed, allowing for development of the pulmonary vasculature is considered absolutely crucial since the first stage of surgical palliation, as pulmonary vascular resistances (PVR) will become the major determinant for a good long-term result (5). Also, emphasis is placed on protecting the ventricle from extreme loading conditions that can cause structural remodeling and cardiac dysfunction, contributing to the failure of the univentricular circulation (5,6). Therefore, promoting a well-developed pulmonary vascular bed and protecting the single ventricle function represent the most important goals of the initial palliative procedures, particularly Norwood procedure in HLHS patients (4). Despite this fact, substantial gaps in our knowledge of how different surgical Norwood techniques impact the overall survival and morbidities in HLHS patients exist. Most of the previous studies were not randomized and included small sample sizes (7-11). In this scenario, the extension study of the Single Ventricle Reconstruction (SVR II) Trial should be commended for providing a unique opportunity to enhance our understanding of HF after Norwood procedure, representing the first randomized trial comparing at medium follow-up transplant-free survival and morbidity between two different techniques: MBTS and RVPAS (12). The reported study has a number of strengths, related to the valuable structure of the multicentric randomized trials. Firstly, the size of the cohort, with surgical randomization, that is a costly and very precious resource in pediatric clinical practice. Secondly, the all reported deaths had independent adjudication as to cause, which is important considering that most of the HF-related deaths have come from clinical databases with recognized limitations. Finally, the data sets adhere to the "clinical practice" concept, trying to capture what is considered really important for this specific subset of patients. Overall, these characteristics represent an enviable platform of methodological solidity. Newburger and co-workers investigated how the shunt groups relates to transplant-free survival and to interventions and morbidities to age 6 years. Their analysis included 549 HLHS patients followed for a mean follow-up of 7 years, uniformly

enrolled in the RVPAS and MBTS group and splitted into 3 periods based on the stage palliation. The study demonstrated that the RVPAS group had similar transplant-free survival at 6 years; also, the association of RVPAS strategy with morbidity and mortality differently occurred in the 3 stages palliation. Specifically, the RVPAS carries a survival advantage prior to stage II palliation with a greater hazard of catheter interventions until the Fontan procedure. However, after Fontan there is no sustained advantage of the initial surgery either on transplant-free survival or catheter interventions and other morbidities. Such findings highlight a crucial point, that the initial surgery strategy have a prognostic impact on morbidity and mortality predominantly in the first two stages palliation. However, this important finding in the reported study should be considered in light of statistical interpretation, in order to elucidate the reliable effects on survival across the 3 different stages. Since the largest number of events occurred within the II interstage palliation, the analysis may not have been adequately powered to evaluate the impact of the different shunt type after Fontan, thus limiting the interpretation of the issue. Furthermore, an additional limitation, in part acknowledged by the authors, include the short-term follow-up after the Fontan procedure, emphasizing the importance of continued follow-up of this cohort. Importantly, the authors analyzed several risk factors as having a statistically significant impact on death or transplantation in HLHS patients, such as annual surgeon Norwood volume, low birth weight (<2,500 g), higher degree of pre-Norwood tricuspid regurgitation (>2.5 mm jet width), preterm birth (<37 weeks), and combined aortic atresia and preterm birth (all P<0.01). However, a statistically significant interaction with shunt type was only recognized for annual Norwood surgeon volume. Such data, as reported by the authors, underline the crucial role of the surgical single center experience on the Norwood procedure outcomes. It is amazing that the mortality after Norwood procedure varied from 7% to 39% across centers as a consequence of no standardized surgical procedures (13). How might this impact on clinical practice? Theoretically, the choice of the shunt type should be tailored to the center surgeon experience, not to the patient risk profile. Further randomized studies should compare alternative surgeries (hybrid procedure) in high risk patients, taking in consideration the single center surgical experience in both surgical techniques. The authors in this issue also presented important data regarding morbidity of HLHS patients throughout the stage palliation. It is well known from previous studies that the long-term outcomes after Fontan operation performed in patients with univentricular circulations with a low-risk profile show good overall results and most patients enjoy a reasonable quality of life for several decades. However, a functional decline over time is inevitable as PVRs and ventricular filling pressures increase (4). Therefore, the aim of all the therapeutic strategies of univentricular circulation since fetal life should be, again, promoting a well-developed pulmonary vascular bed and protecting the single ventricle function. At this regard, the authors underlined two important points. Firstly, in HLHS patients there was no statistically difference in right ventricular function between the two groups after Fontan. This is an important finding, in contrast with the initial hypothesis and previous published data, since ventriculotomy required for the RVPAS does not seem to be related to development of late ventricular dysfunction, although this result has been obtained only from echocardiographic data. Hence, further studies should confirm this result with other techniques, thus better elucidating the mechanisms involved in the right ventricle remodeling and dysfunction. The second important clinical finding to be commended is the higher incidence of catheter interventions (0.38 *vs.* 0.23/patient-year, P<0.001) including balloon angioplasty (P=0.54), stent (P=0.06) and coiling (P=0.001) observed in the RVPAS group before undergoing Fontan. This difference is not statistically significant; however, we should consider that the potential distortion of pulmonary arteries may predispose to the development of systemic-to pulmonary collaterals that will lead to ventricular overgrowth, eccentric hypertrophy and if excessive, will cause dilation, spherical reconfiguration and dysfunction. This randomized study is of great importance to improve our knowledge in the physiopathology of HLHS patients and to guide the best surgical and therapeutic strategies through the different stage palliation. Continued follow-up of this large, well-characterized cohort of patients will be important, not only to detect any late effects of shunt choice, but also to understand long-term outcomes and how they may impact on management decisions beyond shunt type. As the survival of this high-risk population has surprisingly improved, our focus must now be on improving not only their longevity, but also their quality of life. In that respect, further studies will become increasingly important to address the still considerable burden of disease associated with the Fontan circulation.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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