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COMMENTARY

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Surgical reconstruction of the right ventricular outflow tract—The clock is still ticking

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The optimal device for heart valve replacement is yet to be developed. If this is certainly true for adult patients with acquired pathologies, the need for better materials is even more pressing in the setting of congenital heart disease, where any valve replacement activates a *ticking clock* towards the next procedure.

In this issue of the *Journal of Cardiac Surgery*, Selcuk et al.[1] report their single-center experience with the BioIntegral Biopulmonic Conduit™, implanted as a right ventricle-to-pulmonary artery conduit in 48 pediatric patients over a period of 13 months.[1] This is a stentless porcine heart valve covered with a 10-cm long porcine pericardial sleeve, and it is available in relatively small sizes (starting from 15 mm). The conduit is initially treated with formaldehyde and glutaraldehyde and then detoxified with the No-React® treatment, with the aim of reducing the risk of endocarditis and structural degeneration.[2]

The No-React® is just one of several different treatments that bioprosthesis producers have developed over the last few decades; all of them released with promises of improved durability, freedom from structural deterioration, and infection. Despite unquestionable innovations in engineering and treatment of the available biomaterials, with the current technology, surgical reconstruction of the right ventricular outflow tract (RVOT) in the pediatric population still exposes patients to a cumulative risk of multiple interventions, morbidity, and potentially mortality.[3]

The study by Selcuk et al. is the first to focus on the use of the BioIntegral Biopulmonic Conduit™ on pediatric patients. The authors' main finding is a high incidence of fever in the early postoperative period (>30%), not previously described in the literature. The pathophysiology of the fever in these patients was not clarified. No clinical or echocardiographic evidence of prosthetic endocarditis was found in those who experienced fever; however, the authors point out that this triggered potentially inappropriate antibiotic use and caused prolonged hospital stay. Furthermore, there seems to be a correlation between fever and early conduit stenosis.

To put these findings into the correct perspective, a few aspects must be mentioned. This is a retrospective, single-center study with no control group and a relatively small number of patients; the indirect evidence that no patient had fever after switching to bovine jugular vein conduit does not come from a statistical analysis and it must be considered at best as speculative. Comparison with the current literature is not straightforward, as the only published paper focusing on the use of this particular conduit on congenital patients is the study from Marianeschi et al. from 2001[4]; all previous papers investigating BioIntegral devices mainly concentrated on midterm rather than short-term results.[5–9] Finally, the median follow-up of 14.5 months is short and a trend towards higher gradients in patients who experienced fever is the only follow-up information provided by the authors.

However, other aspects must also be considered, and the authors' concerns regarding the Biopulmonic Conduit™ performance should not come as a surprise. Even though the literature is highly heterogeneous in terms of the patient population, the device used, and study protocols, a few common key points can be identified. This is not the first study raising questions about early deterioration and early infection of devices treated with the No-React® protocol. Multiple papers focusing on the aortic BioIntegral Bioconduit™ in the adult population or on similar devices implanted in the pulmonary position with a long enough follow-up reported significant rates of adverse valve-related events.[5–9] Moreover, bioprostheses typically degenerate earlier in pediatric patients compared to adult patients, and a similar trend can be expected even in devices undergoing the No-React® treatment. This is even more relevant if we consider that

in the present study, all conduits were implanted in an extra-anatomic position (i.e., in a non-Ross setting), which is a recognized risk factor for early structural deterioration.[10,11] Finally, even if the fever does not always correlate with infection, it always correlates with inflammation, which has been strongly linked to structural deterioration of bioprostheses.[12]

Where do we go from here? Better quality research (both preclinical and clinical) in congenital cardiac surgery is needed: a significant proportion of our clinical practice still derives from single-center experiences and suboptimal observational studies. Outcomes for the available biological conduits for RVOT reconstruction are rather unsatisfactory.[13–15] This, combined with the limited availability of small-size homografts, is the main reason that pushes our interest towards new devices when they become available. However, valve replacement in the pediatric age is the ultimate task for any biomaterial: size, anatomy, and metabolism all plot together against durability. If there are concerns regarding the performance of a biomaterial in the adult population, it is very likely that results in children will be worse.

One may argue that continuing with the current approaches will only provide small improvements. The future is more likely to come from development on the use of biomaterials that act as scaffolds, and which we can repopulate with the patient's own cells. Theoretically, this would be expected to improve durability, but also be the biological substrate for growth, and ultimately reduce morbidity, reoperations, and mortality. Tissue engineering technologies and regenerative medicine have expanded considerably over the last decade, and it may not be long before the translation of this knowledge into clinical practice.

Regretfully till then, after every pediatric RVOT operation, the clock will start ticking.

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CONFLICT OF INTERESTS

The authors have no conflict of interest to declare.

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