Biology and bioresorbable materials in cardiac surgery: why could they be important in the current era of innovations and technology?

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Abstract

In the era of implantable vascular devices and minimally invasive technologies, several aspects of the biological response of cardiovascular structures to surgical procedures and materials seem to be neglected. However, especially in pediatric cardiac surgery, the main mechanisms underlying the most frequently encountered complications are to be found in an inadequate biological adaptation of the heart vascular structures to the conduits and surgical materials used. In particular, inability of the grafts used to follow somatic growth, exuberant scar tissue formation, presence of non-viable tissue at the anastomosis site or impaired tissue viability of the conduits are claimed to be the most significant factors. Biocompatible materials might constitute a useful adjunct in this context as providing at the same time a valid tissue surrogate and a biological support to orientate and improve the physiologically occurring biological processes imposed by surgical corrections or vascular replacements. We explored the use of bioresorbable materials in an experimental model of the Ross procedure and of neopulmonary trunk reconstruction with encouraging results. Reinforcement of a pulmonary autograft with a polydioxanone mesh prevented graft dilation and induced a structural remodeling leading to the formation of a neo-vessel comparable to the native aorta. A similar approach applied to the reconstruction of the pulmonary trunk with pericardium during arterial switch operations, prevented occurrence of subvalvular pulmonary stenosis and warranted the formation of an hemodynamically effective neo-conduit.

Understanding, ameliorating or just exploiting naturally occurring processes through ad hoc designed biocompatible materials might constitute a keystone in several pathological conditions.

Modern cardiac surgery is currently going through a period of profound change due to the introduction of novel technologies and devices with the progressive abandonment of previously established procedures. In the field of congenital cardiac surgery, the recent literature is pointing at the underuse of the Ross procedure¹, while in the pediatric field limitations of the materials and conduits currently used in reconstructive surgery of right ventricular outflow tract (RVOT) and pulmonary artery (PA) are increasingly reported².

For the Ross procedure, is clear that technical difficulties and risks of the procedure, especially if not performed by experienced hands, have conspired against the widespread use of this life-saving operation. Additionally, the advancing technologies of bioprosthesis manufacturing, the reports on their prolonged life together with the increasingly available option of percutaneous valve-in-valve implantation, discouraged the majority of the surgeons to embark in technically challenging operation carrying augmented surgical risk and potential burden on their track records and on the economic management of cardiac units. We think that a parallel miscomprehension of the intrinsic value of this procedure played a role in this situation. As pointed out by Yacoub³ and by the its inventor⁴ the real keystone of this procedure is represented by the possibility to maintain the viability of the aortic valve and preserve the biological activity of the valve leaflets which, as demonstrated recently, warrant an adequate coagulative balance and a favorable tissue homeostasis⁵. When compared to the glutaraldehyde fixed bioprostheses, the active function of a living leaflet would be reflected in prevention of calcific degeneration and avoidance of anticoagulation⁶, but more importantly, when applied to the pediatric or young adult clinical scenario, the advantage of Ross procedure would result in the possibility to provide an aortic root substitute that harmoniously integrates in the vascular system accompanying the progressive somatic growth of the aortic structures. Unfortunately, long-term neoroot dilation with need for re-operation is well described after Ross procedure and represents another major deterrent especially in the surgical management of young patients⁷. This is mainly due to the anatomical and histological features of the native pulmonary artery (PA), which is normally subjected to pulmonary pressures and behaves as a venous conduit. A progressive structural remodeling triggered by the arterial hemodynamic load generally occurs after the early phases of implantation, but if it...
is unsuccessful or inadequate, conduit dilation might happen. Attempts to reinforce the PA using synthetic materials as Dacron or PTFE have been performed but, albeit effective in preventing dilation, the poor elastomechanical properties and the artificial nature of the materials limit the effectiveness of this approach². The potent foreign body reaction associated with their use impairs PA viability, preventing any arterization or vascular remodeling process and eventually resulting in a constraint effect on the growing aorta and in a fibrous degeneration of its wall. Impoverishment of vascular compliance and loss of windkessel effect has been shown to produce in turn detrimental effects on the aorta and the valve leading to regurgitation⁶.

Considering the biological cascade of events triggered by the transposition of the PA in aortic position leading to wall modification and aiming at respecting graft viability and biological features, we explored the possibility to guide and boost the remodeling process through the use of resorbable external reinforcement⁷. The hypothesis at the basis of this strategy relies in the possibility to provide a temporary mechanical support to the PA while guiding and optimizing the process of vascular remodeling through the biological interaction between the resorbable material and the native vessel.

A biocompatible device designed to minimize radial tension and based on the combination of a single-layer polyglactin (PG) (early resorbability material) strengthened by an interlaced polydioxanone (PDS) (late resorbability material) was used in an experimental model of Ross procedure in growing lambs as reinforcement of the PA⁸. The device, embracing PA outer aspect, prevented aneurysmal dilation of the neo-aorta while allowing a harmonic growth of the PA. Surprisingly, the resorbable materials triggered a process of histoarchitectural rearrangement at the medial and adventitial side of the vessel in absence of a strong inflammatory infiltrates. Over time new matrix deposition was observed and a shift towards an elastic remodeling of the PA⁹. In a separate set of experimental studies biologically reinforced PA showed 6 months after implantation a medial thickening with highly organized fibromuscular cells mixed to abundant neo-formed connectival tissue could be detected. Interestingly, MMP-9 was found to be overexpressed in this group, indicating an ongoing matrix remodeling process. Specific analysis of extracellular matrix revealed the presence of high amount of elastic fibers, reliably deposited by fibromuscular cells, and absent in the control group, while collagen appeared to be more organized and dense with a compact distribution in the "elastic zone" of the vessel.¹⁰

We might reliably speculate that the temporary interaction between the bioresorbable reinforcement and the PA might have orchestrated a complex process of vascular remodeling based on a balance between inflammation and extracellular matrix production. After biomaterial resorption, a "neovessel" exhibiting characteristics similar to those of the aorta but still biologically alive and capable of growth was obtained. This system would therefore facilitate the creation in vivo of a PA with morphostructural features enabling it to both face the hemodynamic load of the arterial system and guarantee an harmonious increase in size during the somatic growth¹¹. Even if in need of more confirmatory results, the possibility to guide and improve the physiologically occurring processes of graft biological remodeling and reaction to foreign materials through the use of biocompatible external reinforcements which respect tissue growth, might constitute a innovative avenue to solve some of the drawbacks of Ross procedure.

Similarly, in pediatric surgery, the disadvantages inherent in currently available valve conduits concerning low durability, inability to match the somatic growth and early valve dysfunction¹², demand alternative materials to allow efficient cardiac structures reconstruction. Additionally, biological conduits cannot be applied during reconstruction of RVTO in neonates with simple transposition of the great arteries (sTGA) undergoing arterial switch operation (ASO). In these conditions autologous pericardium to reconstruct the neopulmonary trunk (NPT) is generally considered the best option even if harnessed by long-term drawbacks, especially concerning supravalvular pulmonary stenosis (SPS). Also in the case of SPS, the main mechanisms underlying this complication need to be found in the inadequate biological adaptation of the heart vascular structures to the conduits and surgical materials used. Scar tissue formation and the presence of non-viable tissue at the anastomosis site¹³, impaired tissue viability of NPT and its inability to follow somatic growth are claimed to be the most significant factors¹⁴. Applying similar concepts, we thought to augment the biological properties of the autologous pericardium used to reconstruct NPT through the use of biocompatible materials able to confer increased resistance to dilation but also promoting its harmonious integration with cardiac structures and preventing progression to SPS. In a model of NPT reconstruction in growing lambs a bioreabsorbable mesh composed by PDS was wrapped around the pericardium neopulmonary artery. The mesh did not impair the viability and physiological somatic growth of the neopulmonary artery as testified by formation of an intact endothelial lining on the inner surface of the graft and by the consensual increase in diameter over time. While animals treated with non-reinforced NPT underwent SPS during time, animals treated with PDS reinforcement showed at the end of the resorption period of the bioprosthesis a phenomenon of histoarchitectural remodeling within the neopulmonary wall, leading to the formation of a trilaminar structure, similar to native vessels. This process was accompanied by a minimal inflammatory reaction and avoided formation of fibrotic tissue, which is considered among the determinants of SPS as causing neonital hyperplasia and hemodynamic abnormalities.

In conclusion, there is an increasingly emerging need to reconsider biological adaptive mechanisms and the response of cardiovascular structures to surgical procedures. Understanding, ameliorating or just exploiting naturally occurring processes through ad hoc designed biocompatible materials might constitute a keystone in several pathological conditions.

Statement of ethical publishing: The authors state that they adhere to the statement of ethical publishing of the International Cardiovascular Forum Journal¹⁶.

Disclosures:
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