The quest for a durable bioengineered tissue for the treatment of valvular heart disease

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In this issue of the *Journal*, Brizard and colleagues¹ report the results of their use of a new engineered treatment of bovine pericardium in valve surgery. In this study, the investigators replaced the posterior leaflet of the mitral valve, as well as one of the leaflets of the pulmonary valve, with CardioCel (Admedus Ltd, Perth, Australia), a chemically engineered bovine pericardium, and compared the engineered tissue with glutaraldehyde-treated autologous pericardium in a juvenile sheep model.

Brizard and colleagues¹ report that the use of the CardioCel bovine patch in a widely used and challenging growing lamb model resulted in durable valve repair in both the mitral and the pulmonary positions for as long as 7 months after the procedure. In their hands, the mechanical properties of the patch were preserved. Interestingly, the treated bovine pericardium exhibited controlled healing without significant calcification and demonstrated better performance than did the autologous pericardium.

In the search for a durable valve prosthesis that will yield stable results and very little deterioration over time, Brizard and colleagues¹ have made a valuable contribution. The challenges presented by this quest are especially daunting in pediatric populations. Unlike valve surgery in adults, repairs of congenital valve deformities require very small valve sizes, which are not currently commercially available. Adding to the conundrum that is inherent in the use of existing mechanical and biological prostheses in pediatric patients is the failure of these devices to grow, repair, and remodel.² It is therefore possible that tissue-engineered heart valves and patches offer a promising solution to these challenges. Brizard and colleagues¹ add important information to what is currently known about the behavior of the CardioCel bovine patch in comparison with that of autologous pericardium.

An interesting question posed by this study is whether the control used here is the ideal one. It is probably not, but

Brizard and colleagues¹ are clear that autologous pericardium is readily available and is being widely used. The long-term success of any patch used in this context is necessarily related to the amount of calcium deposits, the healing process, and tissue strength and growth. Previous studies have identified several major variables that are associated with tissue calcification, degeneration, and lack of microenvironment for host progenitor cell migration in tissue implants—namely, cellular antigens, circulating calcium ions, phospholipids present in the native tissue, and glutaraldehyde processing. The CardioCel Patch is the result of a chemically engineered, multistep ADAPT treatment (Admedus, Perth, Australia) involving multiple factors that could interfere with the prosthetic's viability. Other bioengineered materials currently being studied use processes such as lyophilization,³ which has shown promising results in reducing inflammation. Another proposed approach is the use of decellularized valves and patches with the promise of normal remodeling and growth,⁴ such as extracellular matrix and its potential for tissue regeneration.⁵

A previous publication⁶ has reported promising clinical outcomes obtained by magnetic resonance imaging and echocardiography with the use of the CardioCel patch in 30 patients. The results of Brizard and colleagues,¹ together with those of other recent publications reporting positive results with extracellular matrix,⁷ provide hope for a breakthrough in the field of bioengineering to further improve the treatment of heart valve disease. The key bioengineering challenge is to determine how biologic, structural, and mechanical factors interact and function in vivo. The understanding of these factors will prove critical to the development of a clinically viable tissue-engineered heart valve.

References

1. Brizard CP, Brink J, Horton SB, Edwards GA, Galati JC, Neethling WM. New engineering treatment of bovine pericardium confers outstanding resistance to calcification in mitral and pulmonary implantations in a juvenile sheep model. *J Thorac Cardiovasc Surg*. 2014;148:3194-201.
2. Saleeb SF, Newburger JW, Geva T, Baird CW, Gauvreau K, Padera RF, et al. Accelerated degeneration of a bovine pericardial bioprosthetic aortic valve in children and young adults. *Circulation*. 2014;130:51-60.
3. Maizato MJ, Taniguchi FP, Ambar RF, Pitombo RN, Leimer AA, Cestari IA, et al. Behavior of lyophilized biological valves in a chronic animal model. *Artif Organs*. 2013;37:958-64.
4. Iop L, Bonetti A, Naso F, Rizzo S, Cagnin S, Bianco R, et al. Decellularized allogeneic heart valves demonstrate self-regeneration potential after a long-term preclinical evaluation. *PLoS One*. 2014;9:e99593.
5. Rabkin E, Hoerstrup SP, Aikawa M, Mayer JE Jr, Schoen FJ. Evolution of cell phenotype and extracellular matrix in tissue-engineered heart valves during in-vitro maturation and in-vivo remodeling. *J Heart Valve Dis*. 2002;11:308-14; discussion 314.

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6. Neethling WM, Strange G, Firth L, Smit FE. Evaluation of a tissue-engineered bovine pericardial patch in paediatric patients with congenital cardiac anomalies: initial experience with the ADAPT-treated CardioCel® patch. *Interact Cardiovasc Thorac Surg*. 2013;17:698-702.
7. Gerdisch MW, Shea RJ, Barron MD. Clinical experience with CorMatrix extracellular matrix in the surgical treatment of mitral valve disease. *J Thorac Cardiovasc Surg*. 2014;148:1370-8.