Approximately 275,000 patients receive a heart valve replacement annually. Their choices and the choices of their surgeons are limited to either a metal valve replacement or a preserved (typically allogeneic or xenogeneic) tissue valve replacement. These patients are then subject to the morbidity associated with anticoagulation when mechanical valves are used or the limited durability of a biological prosthesis with the prospect of replacement surgery. An off-the-shelf heart valve with the durability of metal valves and the biocompatibility of biological valves would likely receive immediate and widespread acceptance.

See p 2783

Metal heart valves have experienced a series of transformations since the Lucite ball valve and the silicone caged ball valve of the 1950s and 1960s. Thromboembolic complications with these valves led to the development of a variety of disk valves including the Björk-Shiley, the Lillehei-Kaster, and the St. Jude bileaflet valve. Superior hemodynamic characteristics were possible with these disk valve designs as compared with the caged ball valves, but the need for life-long anticoagulation still existed.

The field of regenerative medicine has invested significant resources to create blood vessels, functional myocardium, and heart valves, but these efforts have yet to be translated into the clinical setting. Early attempts to engineer a heart valve leaflet from synthetic resorbable polymers seeded with endothelial cells and fibroblasts showed promise, but problems with calcification and deformation during remodeling were seen.1,2

The first successful translation of a regenerative medicine approach to reconstruction of the pulmonary artery and vena cava was recently reported by Shi’noka in a series of 44 patients.3 These investigators seeded degradable scaffold manufactured from a resorbable synthetic biomaterial. The cell-scaffold construct was cultured for several weeks in vitro followed by implantation into the pulmonic valve location of sheep and observed for 8 months. The morphological remodeling that occurred in these tissue-engineered heart valves showed the organization of 3 distinct layers essentially equivalent to the zona ventricularis, the zona spongiosa, and the zona fibrosa. There was a confluent endothelial covering on the valve surfaces, and although the valves were thicker than a native valve, they showed near-normal coaptation with minimal change in mean gradients from the time of implantation to the time of harvest. There are still numerous hurdles to overcome before such technology will be used in human patients, but proof-of-concept has been demonstrated in the present study.

Perhaps the most significant aspect of the work reported herein was the constructive remodeling that occurred in the tissue-engineered valve after implantation. The cells present within and on the surface of the leaflets assumed a site-appropriate phenotype. The viability of these cells suggests that they will retain the capacity to repair and remodel over time, and to metabolize calcium and avoid the long-term problems of mineralization.

Although proof-of-concept has been shown with the study by Sutherland and associates, there are several practical limitations that still exist. There appears to be a minimum of 6 to 8 weeks’ lag time from the harvesting and isolation of autologous mesenchymal stem cells until the time of implantation with this approach. The potential for calcification over time has not been fully evaluated, and although the present approach shows promise for the low-pressure right-side location within the heart, it remains to be shown whether such an approach would work in the more challenging left side of the heart.

In summary, the learned principles of regenerative medicine are beginning to be applied successfully and are a step closer to human clinical applications. We now understand that if the appropriate mixture of cells, substrates, and environment are provided, then the in vivo self-assembly of functional tissue structures is possible. The result of such a process in the present report is not the perfect recapitulation of development of a normal heart valve but rather an acceptable biological substitute that can become integrated into host tissues, will likely continue to remodel with time, and will not require lifelong anticoagulation. If the results of this study can be consistently repeated and translated into the human host, then the first major advancement in several decades for heart valve replacement will be possible.
References


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