Do we really understand what happens to valve allografts?

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Central Message

Helder et al highlight the importance of long-term follow-up examinations.

See Articles page 1156 and 1197.

See Editorial Commentaries page 1165 and 1202.

The article by Helder et al¹ demonstrates that the modes of failure of decellularized aortic valve allografts (DAVAs) do not necessarily differ from standard cryopreserved allograft valves (SCAVs). The authors followed 42 patients who had received a DAVA that was commercially available and decellularization and sterilization had been achieved by a proprietary process (Cryolife Inc, Kennesaw, Ga). The authors found an increase in the rate of reoperation beyond 5 years after implantation.¹ At the time of the study, 37% of survivors had undergone reoperation.

What makes this article interesting is not the comparison with a group of patients who had received SCAV. In fact, the little that we know about the 2 groups suggests that they differ significantly and should not be compared. The interesting finding is that the pathologic analyses of 10 DAVAs revealed scarce recellularization in only a minority of patients, edematous degeneration and calcification in almost all cases, and evidence of adventitial fibrosis and neointimal fibroplasia in all cases. These findings appear not to differ from reports about the modes of failure of SCAV,^{2,3} and the reoperation rates are not low (estimated freedom from reoperation at 10 years was 51%).

Therefore, these data question our expectation that DAVAs are better than normal ones. Where do these expectations come from?

In the 1990s it was shown that implantation of cryopreserved allograft valves elicit a donor-specific cellular and humoral immune response.^{4,5} Given this fact, it appeared logical that decellularization would hamper this response. Several clinical reports supported this hypothesis.⁶⁻⁸ However, little was known about the late fate of DAVAs, especially in the aortic position. In the pulmonary valve position, the available evidence does not suggest that decellularized allografts have lower long-term reoperation rates.^{9,10} In addition, it has not conclusively been demonstrated in clinical settings that the donor-specific immune response against allograft valves is indeed responsible for their degeneration.

Does all that mean that decellularization was a useless idea? I believe we simply do not know.

Decellularization—as briefly discussed by Helder et al¹—can be achieved by different processes. Sterilization and preservation are 2 more steps that necessarily follow. All of these steps can induce damage that might finally result in degeneration and the need for reoperation. Probably these later steps induce damage that is more important than rejection of the relatively small number of viable donor cells found in SCAV. Some recent evidence for this hypothesis comes from the observation that “fresh” DAVAs in the pulmonary position appear to perform better than normal or decellularized cryopreserved allograft valves.¹⁰

Biology is complex and difficult to understand. Measures developed to overcome problems can induce new and unexpected problems that sometimes only manifest late after an operation. Therefore, the central message of the article by Helder et al¹ that “new tissue engineered valves should be studied longer term before use is widespread” has to be fully supported.

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