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Effects of combined decellularization and cryopreservation procedures on morpho-functional properties of porcine aortic valve allografts

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Heart valve disease is a major public health problem, with surgical valve replacement still representing the leading therapeutic option. In the last 20 years, implantation of cryopreserved human heart valves underwent so progressive increase that current availability of allogeneic valve substitutes is not sufficient to meet clinical demand. However, also valve allografts undergo long-term failure depending on host-versus-graft immune responses and degeneration of resident cells and extracellular matrix components with subsequent priming of mineralization processes. In a previous study, suitably decellularized porcine aortic valves implanted in the pulmonary position in Vietnamese pigs resulted to be permissive of *in vivo* spontaneous repopulation by recipient's cells, showing tissue remodelling and satisfactory hemodynamic performance (1). Using the same animal model, decellularized valve allografts were compared with other ones which were additionally subjected to cryopreservation/thawing before implantation. Previous echocardiographic analysis showed near-normal hemodynamic behaviour for both allograft types. Here, microscopic examination revealed non-uniform outcomes for both treatments, because there was co-presence of native-like and altered regions. In the former, almost complete re-endothelialization and repopulation by cells with features of fibroblasts, myofibroblasts, and smooth muscle cells involved both cusps and aorta walls. Ultrastructural identification of typical canals of collagen fibrillogenesis and elastogenesis-related features revealed actual tissue remodelling to have been occurred. In aorta walls, incipient neo-vascularization and re-innervation of medial and adventitial *tunicae* were also detected. Conversely, altered regions showed fibrin deposits, inflammatory infiltrates, fragmented elastin fibers, and calcific loci in absence of cell repopulation, with these features mainly concerning cryopreserved allografts. In conclusion, cryopreservation was found to limit the favourable outcomes characterizing decellularized allografts, even if hemodynamic performance was not affected. However, both treatments were found to not compromise repopulation by host's cells and tissue renewal. Thus, the obtained preclinical data suggest the feasibility to achieve cryobank-derived self-regenerating and hemodynamically functional allogeneic valve substitutes, after optimization of these two pre-implantation procedures or their mutual compatibility.

References

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Keywords

Decellularized aortic valves; cryopreservation; allograft.

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