Morphologie (2017) 101, 77—87

Disponible en ligne sur
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com

MORPHOLOGIE
Bulletin de l'Association des Morphologistes

ORIGINAL ARTICLE

Microstructural alterations owing to handling of bovine pericardium to manufacture bioprosthetic heart valves: A potential risk for cusp dehiscence

Modifications microstructurales causées par la manipulation du péricarde bovin pour monter des bioprothèses valvulaires : une cause potentielle de déhiscence cuspide

J. Mao[a], Y. Wang[a], E. Philippe[a], T. Cianciulli[b], I. Vesely[c], D. How[d], J.-M. Bourget[a], L. Germain[a], Z. Zhang[a], R. Guidoin[a,*]

[a] *Department of Surgery, Faculty of Medicine, Laval University and Axe médecine régénérative, centre de recherches du CHU, Ferdinand-Vandry Building, Room 4873, 2325, rue de l'Université, Québec G1V 0A6, QC, Canada*
[b] *Department of Cardiology, Hospital of the Government of the City of Buenos Aires ''Prof. Cosme Argerich'', Pi y Margall 780, C1155AHB Ciudad Autónoma de Buenos Aires, Argentina*
[c] *Cardiology, School of Medicine, University of Colorado Denver, Denver (CO) 80045, USA*
[d] *Peninsula School of Medicine and Dentistry, Plymouth University, PL4 8AA, Plymouth, UK*

Available online 22 April 2017

KEYWORDS
Bovine pericardium valve;
Heart valve bioprosthesis;
Compression;
Collagen waviness

Summary
Introduction. — Cross-linking and anti-calcification of prosthetic heart valves have been continuously improved to prevent degeneration and calcification. However, non-calcific structural deteriorations such as cuspal dehiscences along the stent still require further analysis.
Material and method. — Based upon the previous analysis of an explanted valve after 7 years, a fresh commercial aortic valve was embedded in poly(methyl methacrylate) (PMMA) and cut into slices to ensure the detailed observation of the assembly and material structures. A pericardial patch embossed to provide the adequate shape of the cusps was investigated after paraffin embedding and appropriate staining. The microstructural damages that occurred during manufacturing process were identified and evaluated by light microscopy, polarized microscopy, scanning electron microscopy (SEM) and transmission electron microscopy (TEM).

* Corresponding author.
E-mail address: robert.guidoin@fmed.ulaval.ca (R. Guidoin).

http://dx.doi.org/10.1016/j.morpho.2017.03.003

Results. — The wavy collagen bundles, the key structure of the pericardium patch, were damaged to a great extent at suture sites along the stent and in the compressed areas around the stent post. The fixation of the embossed pericardium patch along the plots of the stent aggravated the microstructural modifications. The damages mainly appeared as the elimination of collagen bundle waviness and delamination between the bundles.
Conclusion. — Considering the modes of failure of the explant, the damages to the collagen bundles may identify the vulnerable sites that play an important role in the cusp dehiscence of heart valve implants. Such information is important to the manufacturers. Recommendations to prevent in vivo cusp dehiscence can therefore be formulated.

MOTS CLÉS
Valve en péricarde ;
Bioprothèse cardiaque ;
Compression ;
Ondulation du collagène

Résumé
Introduction. — Les méthodes de réticulation et de traitement anticalcique des valves cardiaques prothétiques se sont constamment améliorées concernant la prévention de la dégénérescence et de la calcification des tissus. Toutefois, les détériorations structurales en absence de calcification telles que les déchirures des cuspides le long de l'armature, requièrent des études supplémentaires.
Matériel et méthode. — Suite à l'analyse antérieure d'une valve explantée 7 années après sa mise en place, une valve commerciale fraîchement fabriquée fut enrobée dans le polyméthylméthacrylate (PMMA) et coupée en lames fines afin d'observer les structures et les matériaux assemblés. Un feuillet de péricarde après embossage pour former les cuspides fut également étudié après enrobage dans la paraffine et colorations multiples. Les modifications microstructurales qui sont survenues pendant la fabrication des valves furent identifiées et évaluées en microscopie optique, incluant la microscopie en lumière polarisée, en microscopie électronique à balayage (MEB) et en microscopie électronique à transmission (MET).
Résultats. — Les faisceaux ondulés de collagène qui constituent la structure essentielle du péricarde bovin étaient très sévèrement comprimés et même délaminés dans les zones au contact de l'armature. La fixation du feuillet embossé sur l'armature a entraîné une certaine aggravation des modifications microstructurales. Les dommages se sont manifestés par l'élimination des ondulations dans les faisceaux de collagène et les délaminations entre les faisceaux.
Conclusion. — En considérant les différents modes d'échec d'un implant, les modifications structurales des faisceaux de collagène précisent les sites de vulnérabilité dans une valve cardiaque en ce qui concerne les déchirures des cuspides. Ces informations sont importantes pour les fabricants et permettent de formuler des recommandations importantes pour la prévention de la déhiscence des cuspides in vivo.

Introduction

Presently more than 300,000 patients benefit from heart valve replacement worldwide every year [1—3]. Two types of valves are commercially available: mechanical valves, the durability of which is well established, and bioprosthetic valves that do not require mandatory anticoagulation and the durability of which has dramatically increased during the last decades [4—6]. Among the various bioprosthetic heart valves, the chemically processed porcine valves and bovine pericardium valves are given preference in clinical applications. In the last 10 years, the percentage of mechanical prosthetic valves used for aortic replacement has declined from 70% to 30%, and the indications to give preference to bioprostheses are becoming less restrictive [7,8]. The porcine aortic valves firstly transplanted to human by Binet et al. were treated with iodine salts, which did not guarantee the long-term durability [9]. Then glutaraldehyde was introduced as the cross-linking agent of choice to fix biological tissues [10] and its monopoly is still undisputed despite various attempts with alternative chemical fixatives using epoxy compounds, diphenylphosphoryl azide, acyl azides, cyanamide, diisocyanates, carbodiimide to name a few [11,12]. Glutaraldehyde reduces, and possibly eliminates, antigenicity and preserves the physical characteristics of the collagen networks but it induces calcification [13]. Ionescu et al. introduced the concept of bovine pericardium processed with the similar cross-link treatment, eventually leading to an equal or greater hemodynamics and durability compared to the porcine valve [14—16]. Over the years, the tissue processing technology for both porcine aortic valves and bovine pericardium valves has continuously been improved, together with the revised designs and the strict quality control by manufacturers. Chemically processed bovine pericardium compares favorably to porcine valves in long-term follow-up [17]. Regretfully, adverse events, i.e., tearing and calcification, have not been completely eradicated and are still identified as the Achilles' heel of these bioprostheses [18,19].