

Impact of Valvular Prosthesis Type on Cardiovascular Outcomes in Patients on Chronic Dialysis

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أثر نوع بدلة الصمام على النتائج القلبية الوعائية لمرضى الغسيل المزمن

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المخلص: يوجد تعارض في البيانات المرشدة إلى إختيار الصمام البديل في مرضى الفشل الكلوي الذين يعالجون بالغسيل الكلوي. قررنا البحث، بعد مراجعة الدراسات المتعلقة المنشورة، عن أفضل بديل للصمام في مرضى الغسيل الكلوي المزمن. مجموعة 9 دراسات إستيعادية قارنت نتائج نوعين من الصمامات، أظهرت نتائج متشابهة وأبرزت أمان إستخدام الصمامات البيولوجية في مرضى الغسيل الكلوي المزمن. لقد تغيرت معايير إختيار الصمامات البديلة عبر الزمن، لفترة طويلة كان يعتقد أن صمامات الأنسجة تخضع للتكلس المبكر بسبب خلل إستقلاب الكالسيوم في مرضى الفشل الكلوي في المراحل المتأخرة. النزف كان أكثر المضاعفات المتعلقة بالصمامات ويمثل أكبر قصور لإستخدام الصمامات الميكانيكية. أوضحت دراستان أن زرع الصمامات الميكانيكية كان له ميزة البقاء لعمر أطول للمرضى. يمكن الإستنتاج بأن جراحين القلب يجب ألا يترددوا في زرع الصمامات البيولوجية لأن تلف هذه الصمامات يعتبر حالات فردية وغير منتشرة في هذه المجموعة من المرضى. إختيار الصمام البديل يجب أن يكون مبني على نفس المعايير المطبقة على المرضى الذين لا يعانون من الفشل الكلوي.

مفتاح الكلمات: غسيل كلوي، بدلات الصمام القلبي، بدلات بيولوجية، بدلات وغرسات، تحليل.

ABSTRACT: There is conflicting evidence guiding valve prosthesis selection in patients with end-stage renal disease on dialysis. We sought to determine, after reviewing the relevant literature, the best valve substitute in patients on chronic dialysis. A total of 9 retrospective studies compared the outcomes of two valves, showing similar results and highlighting the safety of implanting bioprostheses in patients on chronic dialysis. Standards of valve selection have changed over time; it has long been believed that tissue valves undergo premature degeneration due to calcium metabolism derangements in patients with end-stage renal disease. Bleeding was the most common valve-related complication and represented a major drawback of mechanical valves. Two studies demonstrated a survival advantage in favour of mechanical prostheses. It can be concluded that surgeons should not hesitate to implant bioprostheses because singular valve decomposition would be uncommon in this patient population. Prosthesis selection should be based on the same criteria as those used for non-dialysis patients.

Keywords: Renal Dialysis; Heart Valve Prostheses; Bioprostheses; Prostheses and Implants, analysis.

THE BEST VALVE SUBSTITUTE IN PATIENTS on chronic dialysis undergoing valve replacement surgery is still a matter of ongoing debate. When choosing a mechanical valve, the preservation and durability of the biological components of a bioprosthesis should be weighed against the risk of life-threatening bleeding or major thrombo-embolism generally linked to the use of life-long anticoagulants.

Methods

The standards of valve selection have changed over time. It has long been believed that tissue

valves undergo premature degeneration due to the derangements in calcium metabolism in patients with end-stage renal disease. This is based on a report by Lamberti who described two patients with accelerated degeneration of their bioprosthetic valves.¹

In 1998, American College of Cardiology/ American Heart Association (ACC/AHA) guidelines recommended the use of mechanical valves in patients on dialysis. However, 7 retrospective studies from North America and two from Japan specifically compared the outcomes of the two valves and showed similar results,

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highlighting the safety of implanting a bioprosthesis in patients on chronic dialysis.²⁻¹⁰ Recently, accumulating data supporting the very low incidence of rapid tissue valve degeneration in dialysis patients has been taken into consideration, and the 2006 ACC/AHA practice guidelines do not specify the best choice for valve replacement in dialysis patient.

To provide the best evidence to address this issue, a literature review of the most relevant studies was performed using PubMed. The most relevant papers treating this problem are listed and summarised in Table 1.

Results

Lucke *et al.* reviewed 19 consecutive patients with end-stage renal disease from a single institution who had undergone aortic, mitral or aorto-mitral valve replacement.² The mechanical valve patients ($n = 10$) had a significantly higher rate of postoperative cerebrovascular events or bleeding complications than the bioprosthetic patients ($n = 9$). No subsequent reoperations were required for biological valve failure. The overall estimated Kaplan-Meier survival was $42 \pm 14\%$ at 60 months.

Kaplon *et al.*, from the Cleveland Clinic Foundation, found comparable results for both types of valves when reviewing 42 patients on preoperative dialysis undergoing valve replacements;³ 17 received mechanical valves and 25 received a bioprosthesis. Of the 25 fitted with bioprosthetic valves, 4 required reoperation with one admitted for mitral bioprosthesis degeneration. Prosthetic valve-related complications and survival were similar for both mechanical and bioprosthetic valves.

Herzog *et al.* reviewed the US Renal Data System database. Dialysis patients ($n = 5,858$) hospitalised for heart valve replacement surgery were the subjects of the study.⁴ Tissue valves were used in 881 patients (15%). Aortic valve replacement was performed in 58%, mitral valve replacement in 32%, and combined aortic and mitral valve replacement in 10%. There was no significant difference in survival related to type of valve. The two-year survival rate was $39.7 \pm 3.5\%$ with tissue valves *versus* $39.7 \pm 1.4\%$ for non-tissue valves.

Brinkman *et al.* found that the choice of valve substitute used in dialysis patients did not influence

early and late survival; however, with a mechanical valve there were a six-fold higher incidence of late bleeding or stroke in patients on dialysis.⁵

Chan *et al.* investigated the results of 69 valve replacements in patients with end-stage renal disease.⁶ One case of structural valve deterioration (SVD) occurred in the bioprosthesis group, requiring reoperation at 95 months after surgery. A survival advantage was observed in favour of mechanical prostheses at 5 years. Nevertheless, composites of complications were similar between the two groups.

Toole *et al.* reviewed 50 dialysis patients undergoing left-sided valve replacement.⁷ The tissue valve group had significantly higher Kaplan-Meier freedom from valve-related morbidity and mortality at three years. Freedom from reoperation was not significantly different.

Filsoufi *et al.* analysed data from 155 patients with renal failure who underwent left-sided valve surgery, of whom 108 patients were on chronic dialysis.⁸ Regarding the type of prosthesis, hospital mortality and freedom from reoperation were similar in patients with mechanical and biological valves.

Umezu *et al.* analysed data from 63 consecutive dialysis patients who underwent valvular surgery.⁹ The mechanical group had a higher rate of bleeding events but there was no SVD up to the 5-year follow-up. However, both mechanical and bioprosthetic valve patients had similar survival and event-free rates.

Tanaka *et al.* performed a retrospective review on 73 aortic valve replacements for dialysis patients.¹⁰ No SVD of the bioprosthesis was seen in this series. Valve-related complications were documented in 12 of 44 patients in the mechanical valve group and in 2 of 21 patients in the bioprosthesis group. The all-cause survival rate of patients with bioprosthesis was significantly worse than that of patients with mechanical valves.

Discussion

A major concern of cardiovascular surgical teams when implanting a bioprosthesis in a patient on dialysis is SVD, and many papers have been written on the subject. However, none of the studies have been randomised controlled trials. Only 4 cases of SVD requiring reoperation (at 10–96 months after

Table 1: Literature review comparing the outcomes of bioprosthesis versus mechanical valve replacement in patients with end-stage renal disease on chronic dialysis

Author and study period Overall patients	Aortic/ Mitral/ Aorto- mitral	Number or % ; Mean age in years	Mean follow-up	B failure	Bleeding and thrombo- embolic events	Overall survival	Comments and conclusions
Herzog, <i>et al.</i> ¹ 1978–1998 5,858	3,398/ 1,875/585	B: 881 ; N/R M: 4,977 ; N/R	18.8 ± 22.5 months	N/R	N/R	At 2-years B: 39.7 ± 3.5% / M: 9.7 ± 1.4% P = 0.7	Little insight into the actual cause of adverse survival of dialysis patients after VR. Decision on VR type based on claims data. Current practice guidelines of use of B heart valves in haemodialysis patients should be rescinded.
Lucke, <i>et al.</i> ² 1979–1994 19	12/15/2	B: 9 ; 56.5 M: 10 ; 56.6	32 ± 53 months	1 aortic after 156 months (not requiring reoperation)	B: none M: all	At 12 months: 60% ± 12% At 60 months: 42% ± 14%	Relatively short follow-up period. Follow-up completed in 78%. Preference should be given to B valve instead of M valve prostheses.
Brinkman, <i>et al.</i> ⁵ 1985–2000 72 (74 VR)	55/37/0 3 tricuspid	B: 29 ; 62.2 ± 13 M: 43 ; 3.4 ± 13	N/R	1 mitral failure after 54 months; 1 aortic failure after 15 months	Stroke B: 4 / M: 8 Bleeding B: 1 / M: 13	At 3 months: 72.8% At 1 year: 60.5% At 6 years: 15.9%	Long-term follow-up available in only 46 patients. B valves are the valve substitute of choice.
Chan, <i>et al.</i> ⁶ 1985–2000 69	40/22/0 7 multiple	B: 47 ; 64.7 ± 14 M: 22 ; 55.5 ± 12	B: 68.4 patient-y M: 60.4 patient-y	1 mitral failure after 95 months	5-year F from V/R compl. B: 82.8 ± 8.1% / M: 76.4 ± 12% P = 0.58	At 5 years B: 21.9 ± 7.1% / M: 52 ± 12.9% P = 0.0299	The study encompasses data from 4 hospitals over 27 years. Variability such as surgical technique can influence outcomes.
Kaplon, <i>et al.</i> ³ 1986–1998 42	27/11/4	B: 25 ; 59 ± 15 M: 17 ; 54 ± 18	B: 2.3 ± 1.2 years M: 3.4 ± 2.5 years	1 mitral failure after 10 months 3 for allograft endocarditis	Stroke B: 1 / M: 2 5-year F from haemorrhage B: 81% / M: 76% P = 0.5	At 3 years B: 36% / M: 50% At 5 years B: 27% / M: 33% P = 0.3	Follow-up was 100%. Surgeons should not hesitate to implant B valves.
Umez, <i>et al.</i> ⁹ 1990–2007 63 (64 VR)	44/13/7	B: 22 ; 61.5 ± 7.7 M: 37 ; 56.5 ± 9.4	49 months	None	Bleeding B: 5 / M: 13	Survival rate at midterm B = M P = 0.87 Event-free rate at midterm B = M P = 0.27	Follow-up was accomplished in 95.2%. Prosthesis selection should be based on patient's profile as well as criteria for non-dialysis patients.
Toole, <i>et al.</i> ⁷ 1991–2004 50 (60 VR)	31/29	B: 33 ; 53 M: 17 ; 51	B: 21.4 ± 18 months M: 19.4 ± 21 months	1 failure after 11 months hyper-PTH	3-year F from V/R MBD B: 74 ± 9% / M: 42 ± 16% P = 0.043	3-year F from V/R MBD and MRT B: 69.9 ± 9% / M: 37 ± 14% P = 0.037	No standardised protocols used for prosthesis choice; data subject to individual surgeon biases. Also, number of M valve recipients was small. Unacceptably high rates of compl. and death with M valves.
Tanaka, <i>et al.</i> ¹⁰ 1995–2007 73	73/0/0	B: 22 ; 73.4 ± 4.2 M: 51 ; 61.5 ± 7.9	42 ± 31 months	None	Bleeding B: 1 / M: 6 Stroke B: 1 / M: 4	5-year all-cause survival rate M better than B P = 0.001 5-year V/R survival rate B = M P = 0.202	Concomitant procedures performed in 49% of cases. The advantage in the all-cause survival in favour of the M valve group is difficult to interpret, because the patients who received B were significantly older. Regarding aortic VR, dialysis patients can be treated just like non-dialysis patients.
Filsoufi, <i>et al.</i> ⁸ 1998–2006 G 1: 47 NDDRF G 2: 108 dialysis	N/R	B: 41% ; 67 ± 12 M: 32% ; 55 ± 14	3.9 ± 2.5 years	None	5-year F from reoperation B: 51 ± 10% / M: 55 ± 8% P = 0.75	At 5 years B: 42.4 ± 11% / M: 55 ± 8% P = 0.44	Clinical outcomes limited to major post-operative MBD and MRT. No information on late compl., QoL, or cause of death during follow-up. Bs

B = bioprosthesis; M = mechanical; VR = valve replacement; N/R = not recorded; patient-y = patient-year; F = freedom; V/R = valve-related; compl. = complications; Hyper-PTH = hyperparathyroidism; MBD = mitral bioprosthesis; MRT = mortality; G = group; NDDRF = non-dialysis-dependent renal failure; QoL = quality of life.

the initial valve replacement surgery) were identified from the 9 retrospective studies.^{2–10} Of note, the mean follow-up of each study was relatively short; therefore, definite conclusions about the long-term performance of tissue valves in this patient population cannot be drawn.

Bleeding was the most common valve-related complication, representing a major drawback of mechanical valves. Thromboembolic events were reported in 35 patients, of whom 31 received mechanical prostheses. A total of 7 of the 9 studies did not demonstrate a survival difference according to prosthesis type. The remaining two studies demonstrated a survival advantage in favour of mechanical prostheses.^{6,10} However, patients who received bioprosthetic valves were older and more likely to have had a previous myocardial infarction or to have received concomitant coronary artery bypass grafting.

Recently, Chan *et al.* performed a systematic review and meta-analysis of valve replacement in patients on dialysis.¹¹ In 9 studies published from 1997 to 2010, no difference in survival was observed between the valve types (bioprosthesis *versus* mechanical prosthesis; hazard ratio 1.3, 95% CI 1.0–1.9, $P = 0.09$). However, bioprosthetic valves were associated with fewer valve-related complications compared with mechanical prostheses (odds ratio 0.4, 95% CI 0.2–0.7, $P = 0.002$). They concluded that there was no survival difference following valve replacement with either bioprosthesis or mechanical prosthesis in patients on dialysis.

More recently, Pai *et al.* published their review on the same subject. They found 8 relevant retrospective studies and concluded that there was no significant difference in the results and survival between patients receiving a mechanical and those receiving a bioprosthetic valve.¹² However, bleeding complications were more common with mechanical valves.

Conclusion

It can be concluded that dialysis patients after cardiac valve replacement suffer poor midterm and long-term survival rates. Therefore, due to the limited life expectancy of these patients, physicians should not hesitate to implant bioprosthetic valves because SVD will be uncommon in this patient

population. Prosthesis selection should be based on the same criteria used for non-dialysis patients.

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