Risk Factors for Congestive Heart Failure after Aortic Valve Replacement with a Carpentier-Edwards Pericardial Prosthesis in the Elderly

Wilhelm P. Mistiaen[1,2], Philip Van Cauwelaert[3], Philip Muylaert[3], Floris Wuyts[1], Hilde Bortier[1]

[1]University of Antwerp, Antwerp, [2]Dept of Healthcare Sciences, Hogeschool, Antwerpen, Antwerp, [3]Department of Cardiovascular Surgery, General Hospital Middelheim, Antwerp, Belgium

Background and aim of the study: **Congestive heart failure (CHF) after aortic valve replacement (AVR) is an important cause of morbidity. The study aim was to identify preoperative risk factors for CHF.**

Methods: **A total of 500 consecutive patients (271 males, 229 females; median age 73 years; range: 71-77 years) was investigated retrospectively. The AVR was performed using a Carpentier-Edwards pericardial valve, and a total of 348 additional procedures (313 coronary artery bypass grafts; CABG) was carried out. The outcome studied was CHF, during both hospital stay and long-term follow up. Univariate and multivariate statistical analyses were used to investigate 15 risk factors.**

Results: **During the hospital stay, 13 patients developed CHF, with four fatalities. Significant risk factors for CHF included urgent operation (p = 0.031), preoperative atrial fibrillation (AF) (p = 0.031) and NYHA functional class IV (p = 0.05). A logistic regression analysis revealed need for urgent operation (p = 0.034) as the sole factor. During long-term follow up, 43 patients developed CHF, with seven fatalities. Univariate analysis identified seven risk factors with significant effect: valve size <19 mm (p = 0.004), preoperative conduction defects (p = 0.007), chronic postoperative AF (p = 0.013), cross-clamp time >75 min (p = 0.032), NYHA class IV (p = 0.041), coronary artery disease (CAD) (p = 0.043) and additional CABG (p = 0.050). Multivariate analysis identified three risk factors: preoperative conduction defects (p = 0.004), postoperative AF (p = 0.005) and CAD (p = 0.037)**

Conclusion: **Morbidity due to CHF after AVR could be minimized with correct treatment of AF and of conduction defects. Patient age, valve size, cross-clamp time and preoperative severity or symptoms were not independent risk factors. Moreover, small native aortic valve rings should not necessarily be enlarged, the cross-clamp time should be kept to a minimum, and surgery should not be delayed when symptoms have developed.**

The Journal of Heart Valve Disease 2005;14:774-779

Congestive heart failure (CHF) is an important cause of death following aortic valve replacement (AVR), irrespective of the time that has elapsed postoperatively (1). Indeed, CHF is recognized as a serious disorder, with considerable morbidity and mortality (2). As a large proportion of these patients (40-50%) have a normal left ventricular ejection fraction (LVEF) (3-5), this condition is usually referred to as diastolic heart failure, being broadly defined as "…signs and symptoms of congestive heart failure with normal/near normal systolic function" (6). The aim of the present study was to investigate the predictive factors of CHF after AVR in an elderly population with aortic valve disease.

Presented as a poster at the Third Biennial Meeting of the Society for Heart Valve Disease, 17th-20th June 2005, Vancouver Convention and Exhibition Centre, Vancouver, Canada

Address for correspondence:
Wilhelm P. Mistiaen MD, PhD, Dept. of Healthcare Sciences, Hogeschool Antwerpen, J De Boeckstr 10, 2170 Antwerp, Belgium
e-mail: wilhelm.mistiaen@ua.ac.be

Clinical material and methods

Patients

Between 1986 and 2001, a total of 500 consecutive patients (271 males, 229 females; median age 73 years; interquartile range: 71 to 77 years) who each received a Carpentier-Edwards PERIMOUNT™ pericardial valve in the aortic position was investigated retrospectively. Sixty of the patients were aged ≥80 years.

Only the aortic valve was replaced in 152 patients, whilst 348 patients underwent a concomitant procedure, including coronary artery bypass graft (CABG; n = 313), a procedure on the ascending aorta (n = 27) or mitral annuloplasty (n = 13). Those patients who

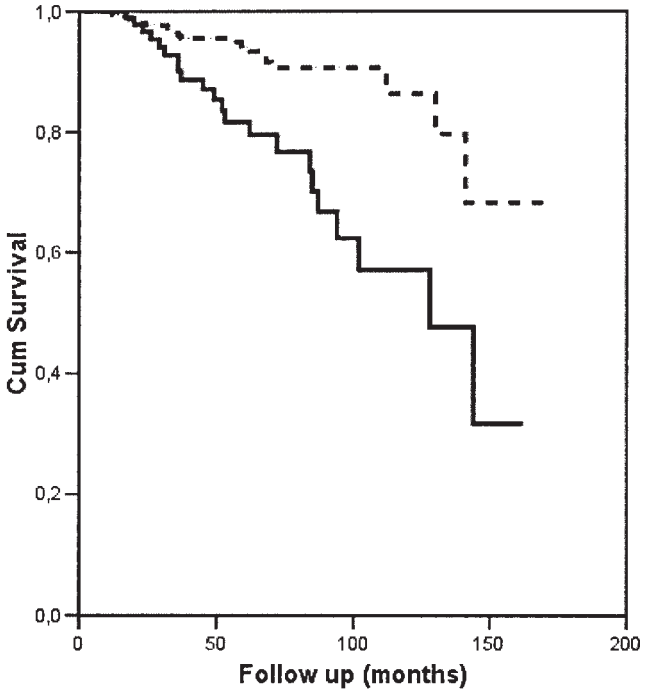

Figure 1: Effect of conduction defects on long-term occurrence of congestive heart failure.

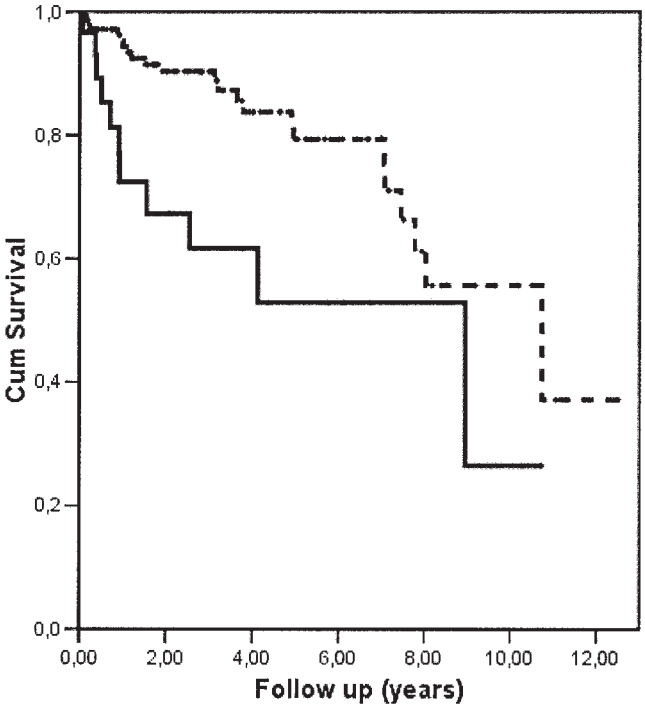

Figure 2: Effect of chronic postoperative atrial fibrillation on long-term occurrence of congestive heart failure.

received a valve in another position, or who received a mechanical valve, were excluded.

Surgical technique

All patients were operated on through a median sternotomy with standard cardiopulmonary bypass, hemodilution and moderate general body hypothermia. Myocardial protection was achieved with orthograde and retrograde administration of a crystalloid cardioplegia solution and topical cooling with sludged ice. The potential risk factors that might influence postoperative CHF were recorded.

Follow up

Follow up was carried out by a questionnaire which was sent to cardiologists. In general, CHF was regarded as a worsening of chronic heart failure or new-onset heart failure precipitated by an acute incident, requiring the administration of diuretics, vasodilators and positive inotropic agents within the hospital. Hospital CHF was defined as the occurrence of the event during the first 30 days after surgery, or in the same hospital period if this exceeded 30 days. Long-term CHF was defined as the occurrence of this event after 30 days postoperatively, or after discharge if the hospital stay exceeded 30 days.

Statistical analysis

Statistical analyses were performed using a Kaplan-Meier method to determine which of the potential factors might be of significant prognostic importance. In the multivariate approach, a Cox proportional hazard model was used to directly relate patient characteristics to the risk of long-term CHF. For the hospital CHF, a chi-square and a logistic regression analysis were used.

Results

Among the patient cohort, the median LVEF was 65% (interquartile range: 51 to 77%). Of 478 patients in whom the LVEF was determined, 394 (82.4%) had an LVEF ≥50%. Gender, age, LVEF and 12 other factors were investigated for their effect on CHF. These included: hypertension (n = 349), previous myocardial infarction (n = 61), an episode of preoperative pulmonary edema (n = 80), coronary artery disease (CAD) (n = 325), conduction defect, mostly left-sided (n = 128), pre- and postoperative atrial fibrillation (AF) (n = 83 and 109, respectively), NYHA functional class IV (n = 149), grade III or IV aortic valve regurgitation (n = 77), urgent surgery (n = 12), cross-clamp time >75 min (n = 112), and valve size 19 (n = 22).

The sizes of valves implanted were 19 mm (n = 22), 21 mm (n = 97), 23 mm (n = 168), 25 mm (n = 128), 27 mm (n = 60), and 29 mm (n = 25). Among the patients who received 19 mm valves, two had a dominant valve regurgitation, two had a dominant stenosis with some

J Heart Valve Dis
Vol. 14. No. 6
November 2005

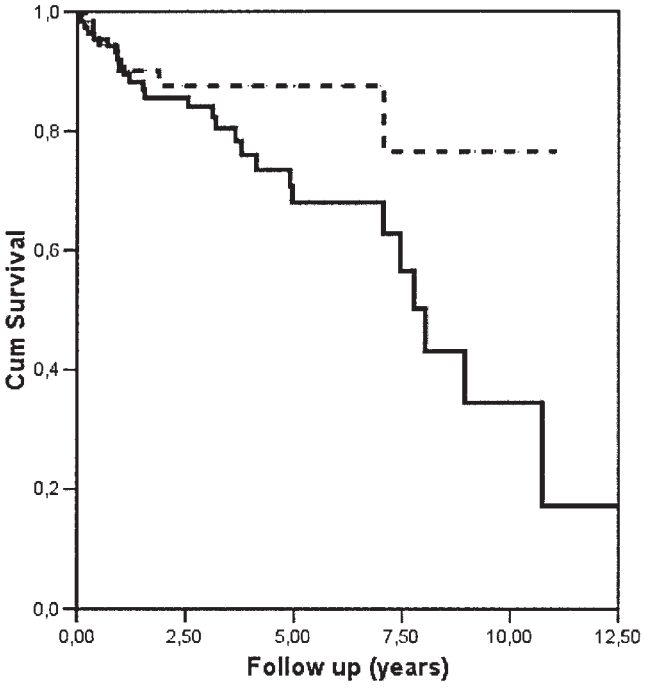

Figure 3: Effect of coronary artery disease on long-term occurrence of congestive heart failure.

regurgitation, and 18 had a pure stenosis. However, this was not statistically significant different from patients with a larger prosthesis size.

Mortality

Nineteen patients died within the first 30 days after surgery, and 13 had an episode of CHF within the hospital, with four fatalities. The significant univariate factors for mortality were urgent operation (2/12 versus 11/488, both fatal; p = 0.031), preoperative AF (5/83 versus 8/417, three fatal; p = 0.034), and grading according to NYHA class IV (8/149 versus 5/231, four fatal; p = 0.05). There was also a trend towards mortality for age over 80 years (4/60 versus 9/440; p = 0.080). Preoperative episode(s) of pulmonary edema, LVEF <50%, previous myocardial infarction, CAD, preoperative conduction defects, hypertension, severe aortic valve regurgitation, cross-clamp time and association of CABG with valve replacement had no significant effect on the occurrence of CHF during the hospital stay.

Data analysis

A logistic regression analysis showed that need for urgent surgery was the only independent predictor for hospital mortality (p = 0.034). The mean follow up was 4.2 years; total follow up was 2,022 patient-years, and a total of 139 patients died. During the follow up, 43 patients had an episode of CHF, with seven fatalities. Postoperative chronic AF was documented in 109 patients. Progression of a pre-existent conduction defect during long-term follow up was observed in 10 patients, and a conduction defect was found in 16 patients in whom the preoperative electrocardiogram was normal.

Univariate analysis (Table I) revealed that small valve size (i.e. 19 mm), preoperative conduction defects, chronic postoperative AF, cross-clamp time >75 min, preoperative NYHA class IV, CAD and association of CABG had a significant effect on the occurrence of CHF during long-term follow up. Age, LVEF <50%, previous myocardial infarction, preoperative pulmonary edema, need for urgent surgery, and hypertension had no significant effect. Although patients with pure preoperative aortic valve regurgitation have a lower postoperative survival than those with aortic stenosis, no significant difference was identified in the occurrence of CHF in both groups (p = 0.126). A Cox proportional hazard analysis (Table II) identified three independent significant variables, namely preoperative conduction defects, chronic postoperative AF and CAD.

Table I: Univariate analysis.

Factor	Freedom at 5 years, if present*	Freedom at 5 years, if absent*	p-value
Valve size 19 mm	0.35 ± 0.19	0.77 ± 0.05	0.004
Preoperative CD	0.59 ± 0.10	0.82 ± 0.05	0.007
Chronic postop. AF	0.80 ± 0.06	0.93 ± 0.08	0.013
CCT >75 min	0.34 ± 0.14	0.85 ± 0.06	0.032
NYHA class IV	0.67 ± 0.09	0.85 ± 0.06	0.041
CAD	0.60 ± 0.13	0.82 ± 0.08	0.043
AVR with CABG	0.68 ± 0.06	0.82 ± 0.08	0.050

*Values are mean ± SEM.
AVR: Aortic valve replacement; CABG: Coronary artery bypass graft; CAD: Coronary artery disease; CCT: Cross-clamp time; CD: Conduction defect; postop. AF: Postoperative atrial fibrillation.

Table II: Multivariate analysis.

Factor	Odds ratio	95% CI	p-value
Preoperative CD	1.674	1.730-16.435	0.004
Chronic postop. AF	2.398	1.873-31.250	0.005
CAD	2.041	1.230-98.322	0.037

Abbreviations as Table I.

Discussion

Congestive heart failure after AVR has been an important cause of morbidity and mortality in both the current and previous series (1,3). In the present study, most patients had an LVEF >50% and could be classified as having diastolic heart failure. This was also found in another series (1). Usually, there were also associated factors such as AF, hypertension and CAD (6,7). Impaired left ventricular diastolic function in left ventricular hypertrophy (LVH), which is often present in aortic valve disease, was a primary cause of fatal CHF, irrespective of LVEF (8). In the present series, several associated conditions were predictive for CHF. The management of cardiac failure due to diastolic dysfunction should include the treatment of the associated aggravating pathological conditions (9).

Preoperative conduction defects in the present patients were identified as an independent predictor for CHF after AVR. These were associated with calcification of the mitral valve ring and aortic valve stenosis (10). Even after AVR, some progression of conduction defects was observed in previous (11) and in current series. Perfusion (in the absence of CAD) and wall motion abnormalities were demonstrated in patients with conduction defects such as left bundle branch block. This condition had a profound effect on myocardial activation and ventricular remodeling. There was an association with impaired systolic and diastolic left ventricular function. Whether left bundle branch block was the cause or the consequence of left ventricular dilatation was not clear (12,13). Correction of this condition by biventricular pacing in patients with severe CHF resulted in clinical (14) and hemodynamic improvement (15). The left ventricular volume was reduced and its systolic function increased. These benefits were pacing-dependent and disappeared gradually when pacing was withdrawn (16). The results illustrated the importance of a synchronous myocardial contraction in patients with a decreased ventricular function.

Atrial fibrillation was the second independent predictor for CHF among the present patients. Preoperative AF had a significant effect only on hospital CHF, while chronic postoperative AF had an effect on long-term CHF. Atrial fibrillation was often associated with diastolic heart failure (7). In other series, AF was also seen to be a predictor for CHF after AVR (1,3), though this may be due to loss of the atrial systole and hence left ventricular filling, which was already impaired due to LVH. Approximately 15-30% of patients with systolic heart failure (which was the minority in the present series) were in AF, and the proportion increased with the severity of heart failure. Patients with heart failure and AF had a worse outcome than those in sinus rhythm. Despite the improvement in systolic left ventricular function after treatment with beta-blockers, the exercise capacity, symptoms and survival in those heart failure patients with AF was not improved as much as those in sinus rhythm (2).

Coronary artery disease and previous myocardial infarction have been identified as predictors of long-term CHF after AVR in some series (1,3). When CABG was associated with AVR, early mortality was reduced but a normal survival could not be anticipated (8). In another series, increased hospital mortality was found among patients requiring concomitant AVR and CABG (17). In the present series, the increase in hospital mortality and CHF was not significant if CABG was associated with AVR. However, in the long term, progression of CAD leads ultimately to a decreased oxygen supply to the heart muscle and to an increased risk for CHF.

Although a small valve size was not an independent predictor for CHF in the present patients, there was an observable effect. A larger size of valve prosthesis was independently associated with freedom from CHF (3) or mortality (17). Prosthesis-patient mismatch predicted increased transprosthesis gradients and CHF; nevertheless, the use of a small aortic valve prosthesis in patients aged over 80 years had no adverse effect on the occurrence of cardiac events, or on mortality after AVR (18).

Stentless valves had excellent effective orifice areas, and consequently very low gradients with good ventricular mass reduction (17) as a result of more normal opening and improved flow dynamics in older patients. In younger patients, a stentless valve could be used (19). There was no demonstration of superior indices with stentless valves, although outcomes were excellent (20). The clinical benefit of a stentless porcine

valve was not due to hemodynamic superiority over stented aortic valves of similar sizes (21).

Among present patients, the cross-clamp time only had an effect in the univariate analysis. Since an increased cross-clamp time could be related to an associated procedure (e.g. CABG), its effect was probably dependent on the presence of CAD. In one study which compared stented and unstented valves, a prolonged cross-clamp was related to the implantation of unstented valves. Nevertheless, a prolonged cross-clamp time was one of the independent predictors for hospital mortality (17) and for hospital complications among octogenarians (22).

Preoperative NYHA class was also predictive of CHF after AVR (3). This factor was associated with left ventricular end-diastolic and end-systolic diameter and LVH. The degree of the latter seemed to be the dominant risk factor for mortality after AVR (23). Most patients in the current series had LVH and were in NYHA class III or IV. As early as 1993 it was clear that, by postponing AVR until the appearance of severe symptoms, a significantly increased mortality from CHF was the rule after AVR for aortic valve stenosis (AS). Impaired diastolic function of the left ventricle, being related to significant residual hypertrophy, was the sole predictor of fatal CHF, irrespective of LVEF (8). Concentric LVH was the primary consequence of acquired aortic stenosis. Latent or manifest myocardial ischemia/hypoxia was a central abnormality in concentric LVH, even in the absence of CAD. Impaired left ventricular diastolic function, due to reduced relaxation of hypertrophied muscle, was the primary cause of congestive failure symptoms. Reduced LVEF developed in succession, and dilation of the ventricle was an end-stage phenomenon. The correlation between structure and function confirmed the hypothesis that the transition from compensated LVH to CHF occurred by fibrosis and myocyte degeneration. Cell loss contributed significantly to the progression of left ventricular systolic dysfunction (24).

In conclusion, CHF after AVR might in some cases be prevented by treatment of associated pathological conditions, including the maintenance or re-establishment of an effective atrial systole in the presence of AF, and ventricular synchronous contraction in the presence of conduction defects. Surgery should not be delayed when symptoms develop. Stentless aortic valve prostheses in the elderly with a small aortic annulus seemed preferable to enlargement of the aortic ring.

References

1. Verheul HA, Van den Brink RB, Bouma BJ, et al. Analysis of risk factors for excess mortality after aortic valve replacement. J Am Coll Cardiol 1995;26:1280-1286
2. Fung JW, Yu CM, Kum LC, Yip GW, Sanderson JE. Role of beta-blocker therapy in heart failure and atrial fibrillation. Card Electrophysiol Rev 2003;7:236-242
3. Ruel M, Rubens FD, Masters RG, et al. Late incidence and predictors of persistent or recurrent heart failure in patients with aortic prosthetic valves. J Thorac Cardiovasc Surg 2004;127: 149-159
4. Burlew BS. Diastolic dysfunction in the elderly - the interstitial issue. Am J Geriatr Cardiol 2004;13:29-38
5. Hogg K, Swedberg K, McMurray J. Heart failure with preserved left ventricular systolic function: Epidemiology, clinical characteristics, and prognosis. J Am Coll Cardiol 2004;43:317-327
6. Chen HH, Lainchbury JG, Senni M, Bailey KR, Redfield MM. Diastolic heart failure in the community: Clinical profile, natural history, therapy, and impact of proposed diagnostic criteria. J Card Fail 2002;8:279-287
7. Courtois M, Ludbrook PA, Kovacs SJ. Unsolved problems in diastole. Cardiol Clin 2000;18:653-667
8. Lund O. Valve replacement for aortic stenosis: The curative potential of early operation. Scand J Cardiovasc Surg Suppl 1993;40:1-137
9. Millaire A. Insuffisance cardiaque diastolique. Modalites therapeutiques. [Diastolic cardiac failure: therapeutic modalities]. Arch Mal Coeur Vaiss 1998;91:1365-1369
10. Adler Y, Fink N, Spector D, Wiser I, Sagie A. Mitral annulus calcification - a window to diffuse atherosclerosis of the vascular system. Atherosclerosis 2001;155:1-8
11. Habicht JM, Scherr P, Zerkowski HR, Hoffmann A. Late conduction defects following aortic valve replacement. J Heart Valve Dis 2000;9:629-632
12. Littmann L, Symanski JD. Hemodynamic implications of left bundle branch block. J Electrocardiol 2000;33(Suppl.):115-121
13. Bavelaar Croon CD, Wahba FF, Van Hecke MV, et al. Perfusion and functional abnormalities outside the septal region in patients with left bundle branch block assessed with gated SPECT. Q J Nucl Med 2001;45:108-114
14. Sciagra R, Giaccardi M, Porciani MC, et al. Myocardial perfusion imaging using gated SPECT in heart failure patients undergoing cardiac resynchronization therapy. J Nucl Med 2004;45:164-168
15. Blanc JJ, Etienne Y, Gilard M, et al. Evaluation of different ventricular pacing sites in patients with severe heart failure: Results of an acute hemodynamic study. Circulation 1997;96:3273-3277
16. Yu CM. New insight into left ventricular reverse

remodeling after biventricular pacing therapy for heart failure. Congest Heart Fail 2003;9:279-283; quiz 284-285
17. Luciani GB, Casali G, Auriemma S, Santini F, Mazzucco A. Survival after stentless and stented xenograft aortic valve replacement: A concurrent, controlled trial. Ann Thorac Surg 2002;74:1443-1449
18. Medalion B, Lytle BW, McCarthy PM, et al. Aortic valve replacement for octogenarians: Are small valves bad? Ann Thorac Surg 1998;66:699-705; discussion 705-706
19. Petracek MR. Assessing options for the small aortic root. J Heart Valve Dis 2002;11(Suppl.1):S50-S55
20. Cohen G, Christakis GT, Joyner CD, et al. Are stentless valves hemodynamically superior to stented valves? Ann Thorac Surg 2002;73:767-775; discussion 775-778
21. Rao V, Christakis GT, Sever J, et al. A novel comparison of stentless versus stented valves in the small aortic root. J Thorac Cardiovasc Surg 1999;117:431-436; discussion 436-438
22. Gatti G, Cardu G, Lusa AM, Pugliese P. Predictors of postoperative complications in high-risk octogenarians undergoing cardiac operations. Ann Thorac Surg 2002;74:671-677
23. Lund O, Nielsen TT, Emmertsen K, Pilegaard H, Knudsen M, Magnussen K. M-mode echocardiography in aortic stenosis. Clinical correlates and prognostic significance after valve replacement. Scand Cardiovasc J 1997;31:17-23
24. Hein S, Arnon E, Kostin S, et al. Progression from compensated hypertrophy to failure in the pressure-overloaded human heart: structural deterioration and compensatory mechanisms. Circulation 2003;107:984-991