Editorial: Cardiac Resynchronization Therapy as an Alternative to Valve Replacement in High-Risk Patients with a Chronically Decompensated Aortic Stenosis?

Dieter Horstkotte, Cornelia Piper, Jürgen Vogt, Barbara Lamp, Anja Dorszewski

Department of Cardiology, Heart and Diabetes Center North Rhine-Westphalia, Ruhr University Bochum, Germany

The Journal of Heart Valve Disease 2006;15:203-205

In this issue of the journal, Antonini-Canterin and co-workers report on a patient with advanced heart failure due to decompensated valvar aortic stenosis (AS) who underwent cardiac resynchronization therapy (CRT) after being considered unsuitable for aortic valve replacement (AVR) (1). This approach raises several questions.

1. When presenting first in 2000 with AS (residual opening area 0.75 cm^2) and poor left ventricular pump function (left ventricular ejection fraction (LVEF) 35%), the patient already suffered from myocardial maladaption to his chronic left ventricular pressure overload (2,3).

Myocardial adaptation is characterized by an increase in left ventricular muscle mass ('wall thickness') and a decrease in left ventricular diameters, compensating for the increased peak systolic pressure. According to Laplace's law, these adaptation mechanisms ('concentric hypertrophy') maintain normal left ventricular wall stress (3,4). Myocardial maladaption to chronic pressure overload is characterized by afterload mismatch and a significant increase in end-systolic wall stress due to left ventricular enlargement (increase in left ventricular end-diastolic diameter) and a decrease in wall thickness ('eccentric hypertrophy') (3,5).

With respect to the patient reported, there was clearly constant progress over the next 11 months in all parameters indicative of a 'decompensated AS' and a poor prognosis.

2. There is a close correlation between parameters and clinical symptoms indicating left ventricular decompensation and prognosis (3,6-11). Average survival after manifestation of left ventricular enlargement and/or congestive heart failure (12-24 months), angina pectoris despite normal coronary arteries (20-60 months), or syncopes (18-36 months) related to AS has been reported to be in the range of a malignant disease (6,8-11). As in dilated or ischemic cardiomyopathy, the manifestation of a left bundle branch block (LBBB) indicates a further prognostic impairment in patients with myocardially decompensated AS (9,12-14). However, LBBB has not been identified as an independent risk factor for overall survival in AS (9). Although many prognostically relevant parameters are not reported in the reference paper, it is clear that the overall prognosis of the patient was poor, even if undergoing AVR, and his life expectancy without valve replacement was in the range of only 18 to 30 months (6,9,11). The patient survived CRT for 24 months.

3. Valve surgery was not performed because of an expected high perioperative mortality due to a concomitant advanced liver cirrhosis following HCV hepatitis 14 years earlier. As different options for treatment of the AS were considered, liver cirrhosis itself clearly was not the prognostically limiting factor, as is frequently the case in patients with Child-Pugh syndrome classes B and C. Data allowing for risk calculation (e.g. Child-Pugh class, total bilirubin, albumin or albumin-to-globulin ratio, cholinesterase, prothrombin time) are not given.

4. The reported patient very likely was suffering from Child-Pugh class A cirrhosis. In this setting, major complications after open-heart surgery with cardiopulmonary bypass (CPB) have been reported to be 32%, resulting in a significantly prolonged intensive care unit and total hospital stays (15-17). Major complications in this patient group include severe infections (especially sternal wound infections), bleedings, multiple organ failure, and progression of the hepatic dysfunction. Nonetheless, overall early postoperative mortality after CPB surgery reported in four small-cohort studies was only 5%, with another fatality within four months after hospital discharge (15-18). This perioperative morbidity and mortality must be

Address for correspondence:
Dieter Horstkotte MD, PhD, Department of Cardiology, Heart and Diabetes Center North Rhine-Westphalia, Georgstr. 11, 32545 Bad Oeynhausen, Germany
e-mail: akohlstaedt@hdz-nrw.de

weighed against the prognostic benefit. For a disease with an expected mortality rate of 50% within approximately 12 months, and almost 100% within 24 months, a 30% perioperative morbidity and a 6% (or even higher) mortality appeared to be acceptable for both patients and surgeons, and classification of the patient as 'inoperable' may not be justified. One is reminded of the early days of balloon aortic valvotomy (BAV), where larger numbers of patients underwent this procedure because they were considered 'inoperable' (19,20), but later underwent successful valve replacement when the BAV failed (21).

5. In suitable patients, meeting established preselection criteria best identified by adequate hemodynamic (pulse pressure increase) or tissue Doppler imaging response during preimplantation testing (22-26), CRT very effectively results in a reverse remodeling of the left ventricle (27). Major components that contribute to a reverse remodeling are: (i) a decrease in left ventricular dimensions (28-31); (ii) an improvement in myocardial contractility (32); (iii) a prolongation of diastolic filling time; (iv) a reduction in mitral regurgitation (30,33); and (v) an improvement in myocardial energetics (34,35). CRT, however, has no impact on parameters indicative for the prognosis of a severe AS but may contribute to myocardial exhaustion due to an increase in energy consumption. This is despite the fact that patients temporarily may have a symptomatic benefit from this therapy. In the case reported, subjective improvement was not monitored objectively - for example, by spiroergometry.

6. It must be recognized that CRT is not without morbidity and mortality, especially in high-risk patients (36), and it is an experimental - and at best palliative - therapy in patients with advanced AS. On the other hand, AVR - even in a high-risk group of patients with advanced liver dysfunction - has been performed with considerable morbidity and mortality, and is the causal treatment.

References

1. Antonini-Canterin F, Baldessin F, Brieda M, et al. Cardiac resynchronization therapy as an 'alternative' approach to a non-operable severe aortic stenosis with left ventricular dysfunction. J Heart Valve Dis 2006;15:000-000
2. 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
3. Horstkotte D, Piper C, Wiemer M. Schultheiss HP. Diagnostic approach and optimal treatment of aortic valve stenosis. Herz 1998;23:434-440
4. Carabello BA. Aortic stenosis. N Engl J Med 2002;346:677-682
5. Ross J. Afterload mismatch and preload reserve: A conceptual framework for the analysis of ventricular function. Progr Cardiovasc Dis 1970;18:225-264
6. Horstkotte D, Loogen F. The natural history of aortic valve stenosis. Eur Heart J 1988;9(Suppl.E):57-64
7. Carabello BA. Evaluation and management of patients with aortic stenosis. Circulation 2002;105:1746-1750
8. Ross J, Braunwald E. Aortic stenosis. Circulation 1968;38(Suppl.V):61-67
9. Haerten K, Dohn G, Dohn V, Seiptel L, Loogen F. Natural history of patients with severe aortic valve disease under medical therapy. Z Kardiol 1980;69:757-762
10. Matthews BF, Barritt DW, Keen GE, Belsey MG. Preoperative mortality in aortic stenosis. Br Heart J 1974;36:101-103
11. Rapaport E. Natural history of aortic and mitral valve disease. Am J Cardiol 1975;35:221-227
12. Gottipaty VK, Krelis SP, Lu F, et al. The resting electrocardiogram provides a sensitive and inexpensive marker of prognosis in patients with chronic congestive heart failure. J Am Coll Cardiol 1999;33(Suppl.A):145A
13. Padeletti L, Giaccardi M, Turreni F, et al. Influence of QRS prolongation on the natural history of CHF. Eur Heart J 2004;6(Suppl.D):D79-D82
14. Hesse B, Diaz LA, Snader CE, et al. Complete bundle branch block as an independent predictor of all-cause mortality: Report of 7073 patients referred for nuclear exercise testing. Am J Med 2001;110:253-259
15. Hayashida N, Shoujima T, Teshima H, et al. Clinical outcome after cardiac operations in patients with cirrhosis. Ann Thorac Surg 2004;77:500-505
16. Klemperer JD, Ko W, Krieger KH, et al. Cardiac operations in patients with cirrhosis. Ann Thorac Surg 1998;65:85-87
17. Bizouarn P, Ausseur A, Desseigne P, et al. Early and late outcome after elective cardiac surgery in patients with cirrhosis. Ann Thorac Surg 1999;67:1334-1338
18. Kaplan M, Cimen S, Kut MS, Demirtas MM. Cardiac operations for patients with chronic liver disease. Heart Surg Forum 2001;5:60-65
19. Safian RD, Berman AD, Diver DJ, et al. Balloon valvuloplasty in 170 consecutive patients. N Engl J Med 1988;319:125-130
20. Johnson RG, Dhillon JS, Thuru RL, et al. Aortic valve operation following percutaneous balloon aortic valvuloplasty. Ann Thorac Surg 1990;49:740-743
21. Robiczek F. Inappropriate terminology in publications concerning aortic balloon valvuloplasty. Am J Cardiol 1992;69:689-690

22. Lamp B, Vogt J, Schmidt H, Horstkotte D. Impact of cardiopulmonary exercise testing on patient selection for cardiac resynchronisation therapy. Eur Heart J Suppl 2004;6(Suppl.D):D5-D9
23. Faber L, Lamp B, Vogt J, Horstkotte D. Tissue Doppler imaging in patients with congestive heart failure and conduction disorders. Eur Heart J Suppl 2004;6(Suppl.D):D10-D15
24. Breithardt OA, Herbots L, D'Hooge J, et al. Strain rate imaging in CRT candidates. Eur Heart J Suppl 2004;6(Suppl.D):D16-D24
25. Vogt J, Heintze J, Lamp B, Hansky B, Horstkotte D. Standard hemodynamic measurements. Eur Heart J Suppl 2004;6(Suppl.D):D29-D34
26. Steendijk P, Tulner SAF, Wiemer M, et al. Pressure-volume measurements by conductance catheter during cardiac resynchronization therapy. Eur Heart J Suppl 2004;6(Suppl.D):D35-D42
27. Pieske B. Reverse remodelling in heart failure - fact or fiction? Eur Heart J Suppl 2004;6(Suppl.D):D66-D78
28. Abraham WT, Fischer WG, Smith AL, et al. Cardiac resynchronisation in chronic heart failure. N Engl J Med 2002;346:1845-1853
29. Stellbrink C, Breithardt OA, Franke A, et al. Impact of cardiac resynchronisation therapy using hemodynamically optimized pacing on left ventricular remodeling in patients with congestive heart failure and ventricular conduction disturbances. J Am Coll Cardiol 2001;38:1957-1965
30. St. John Sutton M, Pfeffer MA, Plappert T, et al. Quantitative two-dimensional echocardiographic measurements are major predictors of adverse cardiovascular events after myocardial infarction. Circulation 1994;89:68-75
31. Yu CM, Chau E. Sanderson JE, et al. Tissue Doppler echocardiographic evidence for reverse remodeling and improved synchronicity by simultaneously delaying regional contraction after biventricular pacing therapy in heart failure. Circulation 2002;105:438-445
32. Toussaint JF, Lavergne T, Ollitraut J, et al. Biventricular pacing in severe heart failure patients reverses electromechanical dyssynchrony from apex to base. PACE 2000;23(Pt.II):1731-1734
33. Breithardt OA, Sinha AM, Schwammenthal E, et al. Acute effects of cardiac resynchronization therapy on functional mitral regurgitation in advanced systolic heart failure. J Am Coll Cardiol 2003;41:765-770
34. Ukkonen H, Beanlands RS, Burwash IG, et al. Effect of cardiac resynchronisation on myocardial efficiency and regional oxidative metabolism. Circulation 2003;107:28-31
35. Hansky B, Schulte-Eistrup S, Vogt J, et al. Lead selection and implantation technique for biventricular pacing. Eur Heart J Suppl 2004;6(Suppl.D): D112-D116
36. Ellery SM, Paul VE. Complications of biventricular pacing. Eur Heart J Suppl 2004;6(Suppl.D):D117-D121