The effect of aortic valve replacement on quality of life in symptomatic patients with severe aortic stenosis

M. W. A. van Geldorp · H. J. Heuvelman ·
A. P. Kappetein · J. J. V. Busschbach ·
J. J. M. Takkenberg · A. J. J. C. Bogers

Published online: 13 December 2012
© Springer Media / Bohn Stafleu van Loghum 2012

Abstract

Background Although symptomatic patients with severe aortic stenosis have a high disease burden and guidelines recommend aortic valve replacement, many are treated conservatively. This study describes to what extent quality of life is changed by aortic valve replacement relative to conservative treatment.

Methods This observational study followed 132 symptomatic patients with severe aortic stenosis who were subjected to an SF-36v2TM Health Survey.

Results At baseline 84 patients were treated conservatively, 48 were referred for aortic valve replacement. In the conservatively treated group 15 patients died during a mean follow-up of 18 months (Kaplan-Meier survival was 85 % and 72 % at one and 2 years respectively) and 22 patients crossed over to the surgical group. Of the resulting 70 patients in the surgical group 3 patients died during a mean follow-up of 11 months (survival 95 % at 1 year). Physical functioning, vitality and general health improved significantly 1 year after aortic valve replacement. In conservatively treated patients physical quality of life deteriorated over time while general health, vitality and social

functioning showed a declining trend. Mental health remained stable in both groups.

Conclusions Aortic valve replacement improves physical quality of life, general health and vitality in patients with symptomatic severe aortic stenosis. Besides having a low life expectancy, conservatively treated patients experience deterioration of physical quality of life. Health surveys such as the SF-36v2TM can be valuable tools in monitoring the burden of disease for an individual patient and offer additional help in treatment decisions.

Keywords Aortic valve stenosis · Aortic valve replacement · Quality of life · SF-36

Introduction

Prognosis of symptomatic patients with severe aortic stenosis (AS) is poor when treated conservatively, and according to the American College of Cardiology/American Heart Association and the European Society of Cardiology guidelines patients should be referred for aortic valve replacement (AVR) without delay when they become symptomatic [1–3]. However, in daily practice many symptomatic patients do not receive operative treatment [4–6]. Underestimation of disease burden and the effect of AVR on quality of life (QoL) could in part be responsible for the observed under-treatment, yet there is hardly any literature on this subject [7].

Previously we compared the QoL of patients with severe AS to the general age-matched population and found it is much lower in symptomatic patients: even ‘mild’ symptoms result in both physical and emotional problems which have a major impact on normal daily life and social functioning [8]. The objective of our current study is to investigate if—and to what extent—AVR improves this disease burden, and to

The questions can be answered after the article has been published in print. You have to log in to: www.cvoi.nl.

M. W. A. van Geldorp (✉)
Department of Cardio-thoracic Surgery, Catharina Hospital,
PO Box 1350, 5602 ZA Eindhoven, the Netherlands
e-mail: martijn.v.geldorp@cze.nl

M. W. A. van Geldorp · H. J. Heuvelman · A. P. Kappetein ·
J. J. M. Takkenberg · A. J. J. C. Bogers
Department of Cardio-thoracic Surgery,
Erasmus University Medical Center, Rotterdam, the Netherlands

J. J. V. Busschbach
Department of Medical Psychology and Psychotherapy,
Erasmus University Medical Center, Rotterdam, the Netherlands

compare these outcomes with the QoL of conservatively treated patients during follow-up. This is a novel approach compared with other studies, which only describe subgroups of patients selected for surgery [9–11].

Methods

Patients

This study is part of a recently published multicentre prospective cohort study among patients with severe AS in the Rotterdam area (the Netherlands) between July 2006 and April 2009 [12]. Patients with severe aortic stenosis were recruited from the outpatient clinics of seven local hospitals and were invited to our hospital for several clinical investigations, an echocardiogram and a QoL assessment. Based on patient characteristics and medical history—and for descriptive purposes only—an anticipated operative mortality was calculated using the EuroSCORE model (www.euroscore.org).

After the baseline measurements, patients were followed to register treatment selection, major adverse cardiac events, QoL and survival. Since the design of this study was strictly observational, the investigators did not interfere with treatment selection. Follow-up of the entire patient cohort continued until 1 May 2011.

The current study concerns only the QoL of the symptomatic patients. For observational and analysis purposes we registered symptomatic patients into two groups: an AVR group and a conservatively/medically treated group. Medically treated patients were re-invited to our hospital after six, 12 and 24 months. Patients who were referred for AVR (by their treating cardiologist) were re-invited only once, 1 year after AVR. Patients who were initially treated conservatively but referred for AVR later on, were accounted for in the conservative group and crossed over to the AVR group at the time of operation (and were therefore accounted for in both groups). In the patients who crossed to the AVR group, the measurements of earlier ‘conservative’ visits were carried forward as ‘pre-AVR measurements’. By doing so all AVR patients had recent pre-operative QoL data, instead of data collected at the start of the study.

AVR patients generally underwent conventional AVR through a median sternotomy using extracorporeal circulation, cold crystalloid cardioplegia and mild hypothermia. A minority of AVR patients had a percutaneous valve implantation, using the retrograde transfemoral approach and a Core Valve® device. Transapical valve implantations were performed through a small intercostal incision. All procedures were performed electively.

The study protocol was approved by the institutional ethics committee (MEC 2006-066) and all patients provided written informed consent.

Quality-of-life measurement

The SF-36v2™ Health Survey is a validated and widely used questionnaire originating from the Medical Outcomes Study [13]. The survey consists of 36 multiple-choice health-related questions, grouped into eight multi-item domains measuring quality in different aspects of daily life: ‘Physical Functioning’, physical health related to age- and role-specific activities termed ‘Role Physical’, ‘Bodily Pain’, ‘General Health’, ‘Vitality’, ‘Social Functioning’, personal feelings of performance in age- and role-specific activities termed ‘Role Emotional’, and ‘Mental Health’. The eight domains form two main components: the ‘Physical’ and ‘Mental Component Summary’.

Comparing QoL results of long-term survivors with the results of all patients alive at baseline constitutes a bias since a selection of the healthier patients takes place over time. Therefore patients who died or refused to participate in a certain time interval—either in the AVR or in the conservative group—were withdrawn.

Statistics

For the statistical analyses SPSS 17.0 software was used (SPSS Inc.). Continuous variables with a normal distribution are displayed as means $\pm$ standard deviation (SD). If data were not normally distributed the median and interquartile ranges are given. Categorical variables are displayed as percentages.

Previously, Dutch norms were established by Aaronson et al. using the first version of the SF-36 Health Survey [14]. To allow for useful comparison these raw SF-36 scores have been transformed into norm-based scores from 0 to 100 in which 50 represents the mean score of the general population and 10 points on the scale correspond to 1 SD [15, 16]. A detailed explanation regarding data collection, scoring, interpretation and validation of the SF-36v2™ is given by Ware et al [15].

Paired *t*-test analyses were used to compare QoL outcomes between different points in time within each group. *P* values lower than 0.05 were considered statistically significant.

Survival was explored using Kaplan-Meier analysis in patients who had AVR during follow-up and separately in conservatively treated patients. Because the distinction between the two groups is based on selection, we deliberately chose not to compare baseline characteristics or survival between the two groups and therefore no *p*-values or log-rank tests are given.

Results

Of 191 participating patients with severe AS, 132 were symptomatic and formed the current study group (the flowchart is given in Fig. 1, baseline characteristics in Table 1).

The baseline QoL in the AVR group was slightly worse over all health domains compared with the baseline of the conservative group (Fig. 2). Figure 2 also shows that QoL in both groups was much worse over almost all health domains compared with the general age-matched Dutch population.

Conservative group

Initially 84 symptomatic patients were treated medically. In this group 15 patients died during a mean follow-up of

18 months. A total of 22 patients were referred for AVR after initial conservative treatment; therefore, these patients crossed over to the AVR group (Fig. 1). Sixty-seven patients completed the SF-36v2TM Health Survey after 6 months and 30 after 2 years of conservative treatment. Kaplan-Meier survival in the conservative group was 85 % at 1 year and 72 % at 2 years.

In medically treated patients physical health worsened significantly (Fig. 3b). 'Bodily Pain', 'General Health', 'Vitality' and 'Social Function' only showed a tendency to worsen yet not significant and 'Mental Health' remained stable.

AVR patients

Initially 48 patients were referred for AVR within 6 months and during follow-up another 22 patients

Fig. 1 Flowchart

Table 1 Patient characteristics

	Conservative (<i>n</i> =84)	AVR (<i>n</i> =70)
Mean age (years)	73.2 ($\pm$ 10.9)	67.8 ($\pm$ 12.2)
Male gender (%)	61	49
NYHA class (%)		
II	62	45
III	32	45
IV	6	9
Mean NYHA class	2.4 ($\pm$ 0.6)	2.6 ($\pm$ 0.7)
Logistic EuroSCORE	8.2 ($\pm$ 6.3)	6.0 ($\pm$ 6.0)
Echocardiography		
Aortic jet velocity $V_{\max}$ (m/s)	4.1 ($\pm$ 0.7)	4.6 ($\pm$ 0.8)
Peak gradient (mmHg)	68.0 ($\pm$ 23.7)	88.3 ($\pm$ 32.5)
Mean gradient (mmHg)	38.5 ($\pm$ 13.6)	50.8 ($\pm$ 20.1)
Aortic valve area (cm ²)	0.76 ($\pm$ 0.25)	0.74 ($\pm$ 0.31)
Aortic valve/LVOT velocity time integral ratio	4.5 ($\pm$ 1.4)	4.7 ($\pm$ 1.7)
Ejection fraction (%)	52.2 ($\pm$ 12.8)	48.3 ($\pm$ 11.5)
Medical history (%)		
Smoking (current or past)	60.0	53.0
Diabetes mellitus	18.8	15.1
Renal failure/dialysis	11.8/2.4	6.1/0
Hypertension	60.0	43.9
Dyslipidaemia	51.8	48.5
Chronic obstructive pulmonary disease	20.0	19.7
Cerebrovascular accident (infarction/bleeding)	4.7	7.6
Open heart surgery previously	7.1	6.1

LVOT left ventricular outflow tract

Fig. 2 Baseline quality of life of AVR and conservative groups versus general Dutch population

Fig. 3 **a** Quality of life of conservative group: baseline versus 6 months. **b** Quality of life of conservative group: baseline versus 24 months

(Fig. 1). Thirty-day mortality was zero but three patients died within 1 year after AVR. The mean follow-up in the AVR group was 11 months. Kaplan-Meier survival was 95 % at 1 year.

Not only the physical QoL components improved, but also ‘*Vitality*’ and ‘*General Health*’ were significantly better than pre-operatively and approached the scores of the general Dutch population (Fig. 4).

Fig. 4 Quality of life of AVR group: baseline versus 12 months

Discussion

Quality of life in symptomatic patients with severe AS is lower in almost all health domains than in the age-matched general Dutch population, both in patients selected for surgery as well as in conservatively treated patients. In a previous paper we also showed a clear association between New York Heart Association (NYHA) class and the SF-36v2TM outcomes [8].

Conservative group

The conservatively treated patients who survived 2 years showed a slight deterioration of their physical health status after 2 years. Yet the degree of deterioration seems to be less than what might be expected based on the low life expectancy of symptomatic AS patients reported in literature [17, 18]. However, besides a higher mortality also the number of patients who were not capable to complete the subsequent questionnaires is larger in the conservative group compared with the AVR group. The baseline QoL of these withdrawn patients was lower than that of the rest of the group (data not shown). Therefore the observed QoL in our study overestimates the real QoL over time in the total conservative group.

AVR group

Although patients in the conservative group are older, the QoL of the AVR patients seems slightly lower at baseline

(Fig. 2). This is a reflection of clinical practice in which patients with severe symptoms are more likely to be referred for surgery than the ones who have only mild symptoms.

The patients who had AVR and were alive at 1 year follow-up showed a markedly improved QoL after 1 year compared with pre-operatively, except in 'Mental Health'. The improvement is quite large in the physical domains and, although not significant, a positive trend is clearly visible in the 'Bodily Pain' and 'Role Emotional' scales.

We assumed a period of 1 year after AVR would be enough to eliminate most direct postoperative problems and assumed a relatively stable health after that period. It is interesting to see that 'Mental Health' does not improve after AVR, and remains much lower than in the age-matched general population. Whether concentration, memory, emotional or other cognitive problems form the basis of this observation and whether this could be explained by the operation or postoperative recovery remains speculative.

Implications

Whether the improved QoL in operated patients can be extrapolated to the total symptomatic population with severe AS still remains a matter of debate. The gain of surgery in the operated group might be higher than it would be in patients who are currently treated conservatively. In reality, some (elderly) patients are not surgical candidates or simply refuse to be operated upon. From these data it cannot be

determined how the outcomes, both in terms of survival and QoL, would have been if *all* patients had undergone AVR. Therefore projection of the study results to the entire symptomatic patient population is only speculative.

One could argue that current treatment selection seems good: in selected patients, QoL generally improves after AVR. Compared with other reports the observed mortality in the conservative group is less high and the presented QoL outcomes in the surviving patients show only a slow and borderline significant worsening over time [17, 18]. On the other hand these findings could be a reflection of a somewhat conservative approach among the studied population.

Timing of surgery in patients with AS is an important and continuing issue of debate. An underestimation of the impact of symptoms on a patient's QoL might be one of the reasons why many symptomatic patients with severe AS are not referred for surgery. Based on our previous study and the current paper, we argue in favour of using QoL surveys in the pre-operative assessment when the choice between surgery or conservative treatment has to be made [8].

Literature

Although other studies describe QoL in cardiac surgery patients [9–11, 19–24], QoL studies by objective surveys such as the SF-36v2TM have, to our knowledge, not been performed in patients who have (symptomatic) AS and in whom the decision to operate or not is yet to be made. Most studies we found did not study QoL in patients with AS, but QoL in patients with AS *who were referred (selected) for surgery*. Some of them describe QoL only in long-term survivors after intervention and do not have a baseline (pre-operative) value. Such analyses constitute a selection bias in which only the healthier patients are subjected to a survey: 'survival of the fittest' [7, 19, 20, 22, 24].

Some studies only concern selective subgroups, others use NYHA classifications as a raw reflection of QoL rather than objective health surveys [19, 23, 24]. The SF-36v2TM Health Survey describes multiple physical and emotional aspects and is therefore a better and more objective reflection of one's (desired) health status than the NYHA classification.

Limitations

For adequate functional and echocardiographic assessment we believed it to be necessary to invite the patients to our hospital each time a QoL assessment was done, resulting in substantial number of patients refusing participation because of a perceived high burden. Often these were the elderly,

more sick patients for whom an extra study trip to the hospital was unfeasible. Therefore, it is likely that we underestimated the magnitude of QoL impairment in the total patient population with symptomatic severe aortic stenosis.

An obvious limitation is the fact that some of the patients—and most likely those with low quality of life—died or refused further cooperation over time which precluded further observations.

Conclusions

AVR offers improved QoL in selected symptomatic patients with severe AS. The beneficial effect is most evident in the physical components, but also general health perception, vitality and emotional aspects improve after AVR to the level of the general age-matched population in contrast to conservatively treated patients.

Besides considering life expectancy and anticipated risks with either conservative or operative treatment, QoL should be taken into account when making treatment decisions in patients with severe AS. A health survey such as the SF-36v2TM could be a valuable tool in monitoring the burden of disease for an individual patient and offer additional help in this decision.

Acknowledgments The authors would like to thank the patients, cardiologists, echo laboratory staff and secretaries of the following hospitals for their kind cooperation: Havenziekenhuis, Rotterdam; St. Franciscus Gasthuis, Rotterdam; IJsselland Hospital, Capelle aan den IJssel; Vlietland Hospital, Vlaarding; Albert Schweitzer Hospital, Dordrecht; Medisch Centrum Rijnmond Zuid, Rotterdam; and Erasmus University Medical Center, Rotterdam.

Disclosures The authors have no disclosures to make.

References

1. Bonow RO, Carabello BA, Kanu C, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *Circulation*. 2006;114(5):e84–231.
2. Vahanian A, Baumgartner H, Bax J, et al. Guidelines on the management of valvular heart disease: The Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology. *Eur Heart J*. 2007;28(2):230–68.
3. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012): The Joint Task Force on the Management of Valvular Heart Disease of the European

- Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2012.
4. Bach DS, Cimino N, Deeb GM. Unoperated patients with severe aortic stenosis. *J Am Coll Cardiol*. 2007;50(20):2018–9.
 5. Iung B, Cachier A, Baron G, et al. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? *Eur Heart J*. 2005;26(24):2714–20.
 6. van Geldorp MW, van Gameren M, Kappetein AP, et al. Therapeutic decisions for patients with symptomatic severe aortic stenosis: room for improvement? *Eur J Cardiothorac Surg*. 2009;35(6):953–7. discussion 7.
 7. Noyez L, de Jager MJ, Markou AL. Quality of life after cardiac surgery: underresearched research. *Interact Cardiovasc Thorac Surg*. 2011;13(5):511–5.
 8. van Geldorp MWA, Heuvelman HJ, Kappetein AP, et al. Quality of life among patients with severe aortic stenosis. *Neth Heart J*. 2013;21. doi:10.1007/s12471-012-0364-9.
 9. Lindsay GM, Hanlon P, Smith LN, et al. Assessment of changes in general health status using the short-form 36 questionnaire 1 year following coronary artery bypass grafting. *Eur J Cardiothorac Surg*. 2000;18(5):557–64.
 10. Rumsfeld JS, Magid DJ, O'Brien M, et al. Changes in health-related quality of life following coronary artery bypass graft surgery. *Ann Thorac Surg*. 2001;72(6):2026–32.
 11. Sedrakyan A, Vaccarino V, Paltiel AD, et al. Age does not limit quality of life improvement in cardiac valve surgery. *J Am Coll Cardiol*. 2003;42(7):1208–14.
 12. Heuvelman HJ, van Geldorp MW, Kappetein AP, et al. Clinical course of patients diagnosed with severe aortic stenosis in the Rotterdam area: insights from the AVARIJN study. *Neth Heart J*. 2012. 10.1007/s12471-012-0309-3.
 13. Ware Jr JE, Gandek B. Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. *J Clin Epidemiol*. 1998;51(11):903–12.
 14. Aaronson NK, Muller M, Cohen PD, et al. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol*. 1998;51(11):1055–68.
 15. Ware Jr JE, Kosinski M, Bjorner JB, et al. User's manual for the SF-36v2 TM health survey. 2nd ed. Lincoln: Quality Metric Incorporated; 2007.
 16. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale: Lawrence Erlbaum Associates; 1988.
 17. Horstkotte D, Loogen F. The natural history of aortic valve stenosis. *Eur Heart J*. 1988;9(Suppl E):57–64.
 18. Varadarajan P, Kapoor N, Bansal RC, et al. Clinical profile and natural history of 453 nonsurgically managed patients with severe aortic stenosis. *Ann Thorac Surg*. 2006;82(6):2111–5.
 19. Sjogren J, Thulin LI. Quality of life in the very elderly after cardiac surgery: a comparison of SF-36 between long-term survivors and an age-matched population. *Gerontology*. 2004;50(6):407–10.
 20. Sundt TM, Bailey MS, Moon MR, et al. Quality of life after aortic valve replacement at the age of >80 years. *Circulation*. 2000;102(19 Suppl 3):III70–4.
 21. Florath I, Albert A, Rosendahl U, et al. Mid term outcome and quality of life after aortic valve replacement in elderly people: mechanical versus stentless biological valves. *Heart*. 2005;91(8):1023–9.
 22. Baberg HT, Dirlich M, Laczkovics A, et al. Determinants of health-related quality of life after aortic valve replacement in six-month survivors of intervention. *J Heart Valve Dis*. 2004;13(6):914–20.
 23. Lam BK, Hendry PJ. Patients over 80 years: quality of life after aortic valve replacement. *Age Ageing*. 2004;33(3):307–9.
 24. Vicchio M, De Santo LS, Della Corte A, et al. Aortic valve replacement with 19-mm bileaflet prostheses in the elderly: left ventricular mass regression and quality of life. *J Heart Valve Dis*. 2008;17(2):216–21.

CVOI E-learning formula!

This is the CVOI e-learning article. The author has prepared 10 questions which are available through the website of the Cardiovascular Educational Institute (CVOI). Please follow the instructions below.

After finishing the questions you will be asked to fill in your name, hospital and e-mail address; then press the button 'verzenden'.

When 6 out of the 10 questions are answered correctly, you acquire 1 accreditation point granted by the Quality Committee of the Netherlands Society of Cardiology (NVVC). The acquired point will be credited to your personal file in the GAIA system. You will also receive an e-mail with all the correct answers.

Over a period of one year 10 e-learning articles will appear in 10 subsequent NHJ editions. In each edition the e-learning article will be recognisable by a special icon. On an annual basis you can collect 10 accreditation points. The accreditation points are credited in the GAIA system by the CVOI.

If you need additional information, please contact the CVOI by e-mail: cvoi@cvoi.org or by phone: 030-2345001.

E.E. van der Wall
Chief editor NHJ

K.B. Schick
Coordinator CVOI