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Aortic Stenosis: Geriatric Considerations

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1. Introduction

In developed countries, the most frequent heart valve disease is aortic stenosis (AS) (Lung et al., 2003). Approximately, 25% of the population aged over 65 years have aortic valve thickening and some 3% of people older than 75 years have severe AS (Lindroos et al., 1993; Stewart et al., 1997). Its prevalence further increases with age and since life expectancy continues to extend, it is expected that the population of elderly patients with AS will grow in future.

Aortic valve replacement (AVR) is the gold standard treatment of severe and symptomatic AS. The current American College of Cardiology and American Heart Association as well as the European Heart Association Guidelines do not restrict operative treatment in relation to the age of the patient (Bonow et al., 2006; Vahanian, 2007).

Most of the large studies now report of more than 20% of patients undergoing surgery for AS being over the age of 80 years (Charlson et al., 2006). Still, in every day clinical practise, advanced age is considered one of the main reasons to decline surgery.

In the Euro Heart Survey on valvular heart disease (Lung et al, 2003), despite presence of severe and symptomatic AS, aortic valve surgery was refused in as many as 33% of elderly patients (defined as age over 75 years). Advanced age and left ventricular dysfunction were the most striking characteristics of the patients being refused, while comorbidities played a less important role.

The decision to operate an elderly with AS must be carefully considered, and made then when the benefits of the operation, as compared to conventional treatment, outweigh the risk of the intervention.

2. Natural history of aortic stenosis and conventional treatment

Drs. Ross and Braunwald were the first to show that aortic stenosis develops latent over many years, with a near-to-normal survival until the symptoms develop (Ross & Braunwald, 1968). Once the symptoms of angina, dyspnea or syncope develop, the survival declines abruptly. Around 75% of symptomatic patients will expire within 3 years after the onset of symptoms, without valve replacement. The worst prognosis had the patients with global heart failure associated with severe AS, with a median survival of less than one year.

Some other more contemporary studies looked at the survival of patients after being medically or surgically treated for AS. Bouma and coworkers identified three predictive

factors for poor outcome of non-operated patients with aortic stenosis (Bouma et al., 1999). Advanced heart failure (New York Heart Association Class III or IV), associated mitral regurgitation as well as severe left ventricular systolic dysfunction identified patients as high-risk for mortality, with a three-year survival of only 20%. Their study showed a 3-year survival rate of 80% in the group of patients treated operatively versus only 49% in the group of patients treated medically. Still, 41% of these patients with severe symptomatic AVS were treated medically.

A similar survival pattern was observed in the study by Varadarajan and coworkers (Varadarajan et al., 2006). In their hands, surgically treated patients showed improved 1-year, 2-year and 5-year survival rates of 87, 78 and 68%, respectively, as compared with 52, 40 and 22%, respectively, in those managed medically.

With this issue in hand, Pierard and coworkers from Brussels, Belgium have looked at the determinants and their prognostic impact of operative refusal or denial in octogenarians with severe AS (Pierard et al., 2011). Advanced age, a lower transaortic pressure gradient, a larger aortic valve area and presence of diabetes were identified as independent predictors of AVR refusal or denial, which occurred in 40% of all patients with severe and symptomatic AS, and had a profound impact on long-term prognosis, leading in a twofold excess mortality of patients treated without surgery (Pierard et al, 2011).

Nowadays, there is no reason to put into question the decision to perform the operation on an elderly patient with severe AS, since optimal medical treatment remains ineffective when AS becomes symptomatic.

3. Operative treatment of elderly with AVS

Advanced age at the time of the operation has a strong influence upon the perioperative mortality and morbidity. Bridgewater and co-workers, on behalf of the European Association of Cardio-Thoracic Surgery, reported recently that early mortality following isolated AV surgery averaged 1.2% for patients under the age of 56 years, and progresses to 3.7% for patients between 71-75 years, further to 4.1% for patients between 76-80 years of age, and finally to 6.1% for patients older than 80 years (Bridgewater et al, 2010). The same authors also conclude, based on a survey on 40111 operated patients in developed countries that patients older than 80 years stay, on the average, more than 3 days longer than those under 61.

This, however, represents a significant improvement of early results in contemporary aortic valve surgery as compared to outcomes reported two or three decades ago. In a paper published in Circulation in 1994, from the group from Rennes, France, Dr. Logeais and coworkers report of higher early postoperative mortality risk, averaging 6.2% for patients age 60-70 years, and 11.2% for patients older than 70 years of age (Logeais et al, 1994). A better understanding of the role of the preoperative respiratory preparation, improved myocardial protection of otherwise severely hypertrophic myocardium, as well as normothermic cardiopulmonary bypass may be attributed to the improved early postoperative results in the recent studies as compared to those several decades ago.

Another approach to improve early and long-term survival of elderly patients undergoing AV surgery is to have them undergo surgery in due time. Surgery in octagenarians, as reported by Pipper and coworkers (Pipper, 2009) should not be postponed until chronic myocardial decompensation finally convinces patients, relatives and cardiologists that AV surgery is inevitable, as the preoperative chronic decompensation strongly increases operative mortality and morbidity and negatively impacts long-term survival.

The surgical community worked over the last two decades vigorously to reduce the trauma of the conventional aortic valve operation. Minimally invasive approaches like partial upper sternotomy have replaced the conventional complete median sternotomy when performing AVR in many centres. Aiming for smaller incision, without compromising the quality of the operation and the effectiveness of myocardial protection, improved early outcomes have been reached.

We reported the safety and reliability of AVR via a partial upper sternotomy in 2003 (Dogan et al, 2003). In a prospective randomised trial, we showed that minimally invasive AVR can be performed with only slightly longer operative times, good cosmetic results and improved rib cage stability as well as significantly less blood loss. Furthermore, limited surgical access affected negatively neither the patients' neurological outcome nor the efficacy of myocardial protection.

More recently, the implantation technique for AVR has been also modified, without compromise in hemodynamic performance of the valve substitute, all in order to reduce implantation times, and therefore the myocardium ischemia as well as cardiopulmonary bypass times. We recently reported on the initial clinical experiences with the sutureless, nitinol-stented 3f Enable (Medtronic Inc., Minnesota, USA) aortic valve prosthesis in 32 patients. Implantation time could be significantly reduced down to 9±5 minutes (Martens et al., 2009). The first report of multicenter experience with this particular valve substitute and implantation technique in 140 patients was published in the European Journal of Cardiothoracic Surgery in 2011 (Martens et al., 2011). Reproducibility as well as feasibility and safety with the ATS 3f Enable Bioprosthesis were demonstrated. Valve implantation resulted in excellent hemodynamics and significant clinical improvement. Further comparative studies are underway to prove the clinical benefit using this less-time-consuming implantation technique versus the conventional one.

In the last few years, intensive interest has been put toward the development and perfection of a catheter-delivered valve substitutes for use in patients with aortic stenosis in whom surgical therapy has been rejected (Walther et al, 2007a). Two delivery routes have been used to deploy the valve substitute in such patients.

The transapical route (TAP-AVI – transapical aortic valve implantation), is the one used by the surgeons. By avoiding the sternotomy incision, the cardiopulmonary bypass, aortic crossclamping as well as the cardioplegic cardiac arrest during the procedure, one aims at reduction of perioperative risk in an otherwise high-risk population of patients. The vast majority of patients targeted for this therapy are elderly with multiple severe comorbidities rendering them as high-risk or not suitable for conventional AVR. The mean age of the patients being reported on in the initial multicenter experience was 81 years (Walther et al., 2007b).

We went further on and compared our experience with TAP-AVI versus minimally invasive AVR through partial upper sternotomy in matched population of elderly patients (Zierer et al., JTCVS 2008). Mean age in our collectives were 85 years for the TAP-AVI group and 82 years for the ministernotomy group.

Patient age, preoperative comorbidities and perioperative risk, expressed as logistic EuroSCORE (38%±14% for the TAP-AVI group and 35%±9% for the ministernotomy group) were matched between the groups. Although the TAP-AVI approach was associated with faster postoperative recovery, early and late morbidity and mortality were comparable with those of the surgery group, suggesting that patient age and comorbidities are independent predictors of adverse outcome after AVR, regardless of the surgical approach.

4. Long-term survival of elderly patients after AVR: the issue of left ventricular hypertrophy

The long-term survival after the surgery, although superior to the medical treatment, is still not satisfactory. Reported survival rates in all age groups range between 50% and 66% (David et al, 2001; Hammermeister et al, 2000) and further decrease to 18% at 15 years in patients older than 75 years of age (Jamieson et al., 1994). Several studies have related these poor results after AV surgery with the incomplete regression of the left ventricular hypertrophy (Levy, 1991; Rossi et al, 2000).

Left ventricular hypertrophy (LVH), a known complication of aortic stenosis, has been strongly associated with increased risk of sudden death, congestive heart failure, and overall cardiovascular mortality. Incomplete regression of the LVH in patients undergoing AVR has been linked to the obstructive nature of the valve sewing ring and stent, or to patient–prosthesis mismatch, which are being held responsible for persistently elevated transvalvular gradients.

In the late 1980s, stentless valves were introduced with the goal of maximizing the effective orifice area for flow by eliminating the valvular stent and sewing ring, therefore facilitating faster and more complete regression of LVH. Over the next decade, several groups have published their initial results; many of them indicating faster and more complete regression of left ventricular mass after stentless as compared with the stented AVR (Jin et al., 1996, Thomson et al., 1998). However, these advantages have been obtained in the setting of nonrandomized trials. Our team had therefore set forth to determine, if we could measure these early and mid-term postoperative improvements in older patients receiving a stentless versus a stented bioprosthetic aortic valve, in a prospective randomized setting (Risteski et al., 2009).

Between September 1999 and January 2001, 40 patients with severe symptomatic aortic stenosis, over the age of 75 years, were randomly assigned to receive either the stented Perimount (n=20) or the stentless Prima Plus (n=20) bioprosthesis.

The aortic valve was approached through a hockey stick aortotomy. After complete resection of the native aortic valve and debridement of the aortic annulus, accurate sizing was carried out using the respective Carpentier–Edwards sizers for the Prima Plus stentless and the Perimount stented valves.

The Prima Plus stentless valves were implanted in the subcoronary position. The commissures were positioned 120° apart, with the muscular shelf corresponding to the right coronary sinus. Care was taken to suture the base of the valve subannularly, to ensure that the coaptation line of the leaflets was at the height of the native annulus. Single interrupted unpledgeted 4-0 braided polyester sutures were used for the proximal end, and the rims of the valve commissures were sutured to the native aorta using 4-0 polypropylene running sutures. For the Carpentier–Edwards Perimount stented valve implantation, interrupted mattressed pledgeted 2-0 braided polyester sutures were placed circumferentially from below the annulus. The valves were implanted in the supra-annular position, with the valvular stent positioned so as not to interfere with the coronary ostia.

Clinical outcomes, left ventricular mass regression, effective orifice area, ejection fraction and mean gradients were evaluated at discharge, six months, one year and five years after surgery.

Left ventricular mass index (LVMI) was calculated using the formula postulated by Devereux and Reichek, as follows:

$$LVMI\ (g/m^2) = (1.05 \times [(EDD + PWTd + IVSTd)^3 - EDD^3] - 13.6) / BSA$$

where the EDD is the LV end-diastolic diameter (cm), the PWTd is the LV postero-lateral diastolic wall thickness (cm), the IVSTd is the interventricular septum diastolic thickness (cm), and the BSA is the body surface area of the patient (Devereux & Reichek, 1997).

At five years, there were 5/20 (25%) deaths in the stentless group and 6/20 (30%) deaths in the stented group (all non-valve-related). There was one case of endocarditis in each group, early postoperatively. All patients displayed continuous clinical improvement after the operation; at five years, all of the survivors were in New York Heart Association class I or II.

Mean transvalvular gradients (Fig. 1a) have remained consistently low throughout the follow-up with neither clinical nor statistical relevance in the differences between the groups at any of the given time points. Also noted was the lack of significant difference in the follow-up values of the effective orifice areas (Fig. 1b) of both prostheses, although a tendency toward increase of the same in both groups was obvious early in follow-up (at 12 months with regards to 6 months) only to disappear at the 5-year follow-up examination.

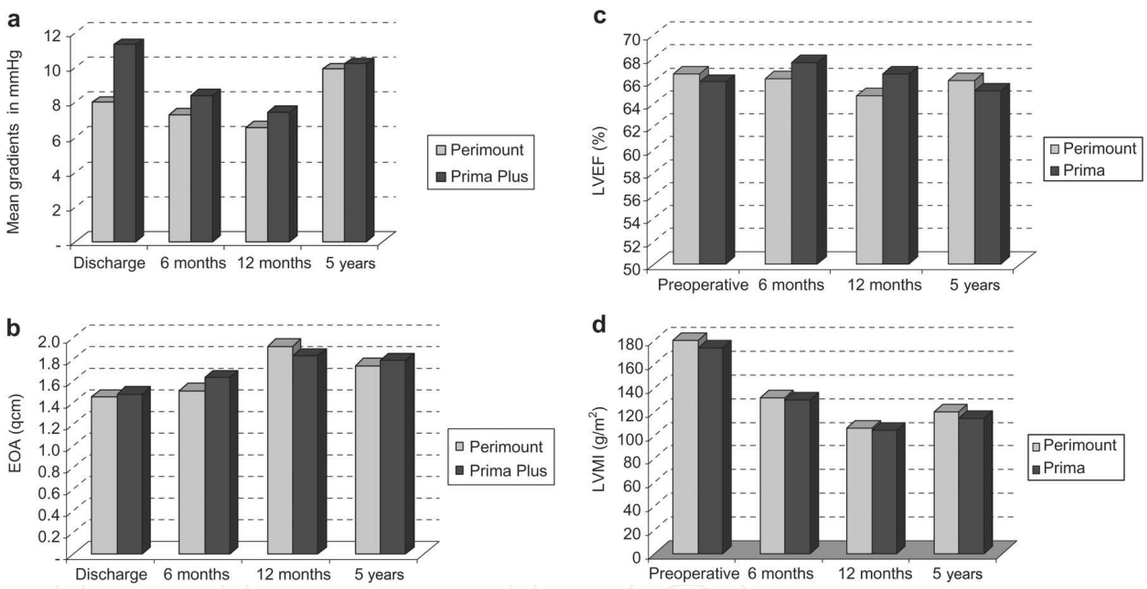

Fig. 1. Hemodynamic results after AVR with Edwards Perimount Stented Valve vs. Prima Plus stentless valve in elderly. (a) Mean transvalvular gradients. (b) Mean effective orifice area (c) Left ventricular ejection fraction (d) Left ventricular mass index.

The left ventricular ejection fraction (Fig. 1c) did not change over the time of follow-up. At 6 and 12 months, as well as at 5 years it did not differ between the groups. The left ventricular mass index (LVMI, Fig. 1d) did display a continuous rate of decrease in the first years after the surgery; however, this tendency was lost after the first year as the mean LVMI at 5 years was almost the same to that at 12 months. Finally, the index failed to reach the normal range in both groups. At all time points, the difference between the groups did not reach statistical significance.

At five years, stentless valves were not superior to the stented valves, with regards to hemodynamic performance, regression of left ventricular mass and clinical outcome. Survival of the patients was not related to the nature of the biologic valve.

Overall, the complexity of stentless valve implantation with its prolonged cross-clamping times might not be justifiable under these circumstances, if as we found, the same results can be achieved with a standard stented bioprosthesis. Our results are in concordance with some other prospective randomized studies that emerged in the meantime (Ali et al., 2007, Perez de Arenaza et al., 2005).

5. Conclusion

There is no scientific reason to put into question the decision to perform the operation on an elderly patient with severe AS, since optimal medical treatment remains ineffective when AS becomes symptomatic. Elderly patient may benefit from one of the available minimally invasive techniques for aortic valve replacement. The regression of the left ventricular hypertrophy as well as the long-term survival after aortic valve replacement is not influence by the nature of the valvular substitute, failing to justify a rather more complex implantation of stentless valve substitute in an elderly patient.

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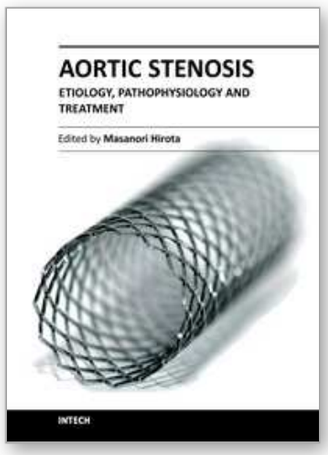

Aortic Stenosis - Etiology, Pathophysiology and Treatment
Edited by Dr. Masanori Hirota

ISBN 978-953-307-660-7
Hard cover, 254 pages
Publisher InTech
Published online 10, October, 2011
Published in print edition October, 2011

Currently, aortic stenosis (AS) is the most prevalent valvular disease in developed countries. Pathological and molecular mechanisms of AS have been investigated in many aspects. And new therapeutic devices such as transcatheter aortic valve implantation have been developed as a less invasive treatment for high-risk patients. Due to advanced prevalent age of AS, further discovery and technology are required to treat elderly patients for longer life expectancy. This book is an effort to present an up-to-date account of existing knowledge, involving recent development in this field. Various opinion leaders described details of established knowledge or newly recognized advances associated with diagnosis, treatment and mechanism. Thus, this book will enable close intercommunication to another field and collaboration technology for new devices. We hope that it will be an important source, not only for clinicians, but also for general practitioners, contributing to development of better therapeutic adjuncts in the future.

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