Aortic Valve Stenosis in Octogenarians: What is the Role of Conventional Aortic Valve Replacement?

Sara Freixo[1], Filipe R. Soares[2], MD; Gonçalo F. Coutinho[2], MD, PhD

1. Faculty of Medicine, University of Coimbra, Portugal
2. Centre of Cardiothoracic Surgery, Coimbra University and Hospital Centre, Portugal

Gonçalo Freitas Coutinho, MD, PhD

Azinhaga de Santa Comba, 3000-548, Coimbra

goncalofcoutinho@gmail.com

Abstract

Background: Transcatheter aortic valve implantation (TAVI) increasingly questions the use of conventional aortic valve replacement (AVR) in high-intermediate risk patients, particularly in octogenarians. Nevertheless, AVR has become less-invasive and surgical outcomes have improved in the last years. In this study, we evaluate the perioperative outcomes, survival and functional status after AVR in octogenarian patients.

Methods: From Jan-2006 to Dec-2016, 2947 patients were submitted to AVR, of whom 385 (13.1%) were octogenarians and constitute the subject of this study. Mean age was 82.1±2.0 years, 57.7% female, and 47.3% were in New York Heart Association (NYHA) class III-IV. Median EuroSCORE-II: 3.6 ± 3.9. Aortic root enlargement was performed in 105 cases (27.1%).

Results: Only one patient died during hospitalization (0.3%) and thirty-day mortality was 0.8% (3 patients). Permanent pacemaker implantation occurred in 3.5%, stroke in 0.8% and acute myocardial infarction in 0.8%. Only 18 patients had peri-prosthetic leak (minimal or mild), no moderate or severe leakage was observed. Mean hospital stay was 8.0±3.2 days. Median follow-up time was 4.4±2.64 years (range: 1-12 years). Survival at 1, 5 and 10 years was 95.1±1.1%, 76.3±2.5% and 41.7±5.3%, respectively, significantly better than the expected survival of the general population (age and gender-matched). Atrial fibrillation (HR:2.428; CI:1.552-3.798, p=0.008), renal failure (HR:1.404; CI:1.037-1.902, p=0.028) and higher NYHA classes (HR:1.464; CI:1.106-1.939, p=0.007) were independent risk factors of late mortality. The majority of subjects (97%) showed a high degree of satisfaction with the surgery and 82.9% were in NYHA class I-II.

Conclusions: Contemporary isolated AVR in octogenarians carries very low mortality and morbidity. In our series, the risk-score calculators overvalued mortality. These results should be viewed as benchmark to which transcatheter procedures should be compared.

Key words: aortic valve stenosis; octogenarians; elderly patients; aortic valve replacement (AVR); transcatheter aortic valve implantation (TAVI).

Resumo

Objetivos: A implantação percutânea da válvula aórtica (TAVI) tem levantado cada vez mais questões quanto ao uso da cirurgia convencional de substituição da válvula aórtica (AVR) em doentes com risco cirúrgico intermédio a elevado, particularmente em octogenários. No entanto, a AVR tornou-se menos invasiva e os resultados cirúrgicos melhoraram nos últimos anos. Neste estudo avaliamos os resultados peri-operatórios, a sobrevida e o estado funcional dos doentes octogenários, submetidos a AVR isolada.

Métodos: De janeiro de 2006 a dezembro de 2016, 2947 doentes foram submetidos a AVR isolada, dos quais 385 (13.1%) eram octogenários e constituem a população deste estudo. A média de idades foi de 82.1 ± 2,0 anos, 57.7% eram mulheres e 47.3% estavam em classe NYHA III-IV. A mediana do EuroSCORE-II foi de 3.6 ± 3.9. O alargamento da raiz da aorta foi realizado em 105 casos (27.1%).

Resultados: Houve apenas um caso de mortalidade intra-hospitalar e a mortalidade total nos primeiros 30 dias foi de 0,8% (2 doentes). Verificou-se a implantação definitiva de pacemaker em 3.5% dos casos, 0.8% tiveram como complicação acidente vascular cerebral e 0,8% enfarte agudo do miocárdio. Não se verificaram casos de regurgitação peri-protésica grave ou moderada e apenas 18 doentes tiveram regurgitação mínima ou ligeira. A média de permanência hospitalar foi de 8,0 ± 3,2 dias. A mediana de tempo de seguimento foi de 4.4±2.64 anos. A sobrevida aos 1, 5 e 10 anos foi de 95.1±1.1%, 76.3±2.5% e 41.7±5.3%, respetivamente, significativamente melhor do que a sobrevivência da população em geral com idade e género correspondentes. A presença de fibrilação auricular (HR:2.428; CI:1.552-3.798, p=0.008), insuficiência renal (HR:1.404; CI:1.037-1.902, p=0.028) e classes de NYHA mais altas (HR:1.464; CI:1.106-1.939, p=0.007) foram fatores de risco independentes de mortalidade tardia. A maioria dos doentes (97%) demonstrou alto grau de satisfação com a cirurgia e 82,9% estavam na classe I-II de NYHA.

Conclusões: A AVR isolada convencional em octogenários tem mortalidade e morbidade muito baixas. Na nossa série de doentes, os scores de risco sobrevalorizaram a mortalidade. Estes resultados devem ser vistos como referência e devem ser comparados com os procedimentos percutâneos.

Palavras-chave: estenose da válvula aórtica; octogenários; idosos; cirurgia de substituição da válvula aórtica (AVR); implantação percutânea da válvula aórtica (TAVI).

Introduction

During the last decades, there has been a significant increase in life expectancy which has dramatically changed the characteristics of patients submitted to cardiac surgery. The number of patients over eighty years referred for cardiac surgery has increased, particularly due to aortic valve stenosis which is an age-progressive disease.

Aortic valve replacement (AVR) Is the most common valve surgery performed in octogenarians (1). Simultaneously, the field of cardiac valvular surgery experienced important advancements in technology and perioperative management which allowed interventions in high-risk patients who otherwise would be denied surgery.

However, the decision of the most appropriate type of treatment in elderly patients with aortic stenosis (AS) has been challenging and the choice between surgical or percutaneous treatment has been disputed in recent times.

The European guidelines for management of valvular heart disease (ESC/EACTS) indicate that intervention should be performed in symptomatic patients with severe high-gradient AS or with low-flow, low-gradient and reduced ejection fraction (2). The choice between AVR and transcatheter aortic valve implantation (TAVI) must be based on individual evaluation, considering the risks and benefits of each technique and should be discussed by the Heart Team. Furthermore, guidelines recommend AVR in low surgical risk patients (Euroscore II< 4%) whereas TAVI is recommended in patients who are not suitable for AVR or in those with increased surgical risk (Euroscore > 4%). The choice between AVR and TAVI should be made by the Heart Team, preferring TAVI in elderly patients with suitable transfemoral access (2).

Age has repeatedly been identified as an important risk factor for adverse outcomes, but age alone should not be viewed as a contraindication to AVR (1,3).

It is believed that adequate patient selection and preparation can improve results and reduce operative risk. AVR became less-invasive and the surgical outcomes have improved, even in complex cases, with significant reduction of the operative mortality and morbidity and improved symptoms and quality of life (4,5).

Regardless the risk, AS is a progressive disease and if not treated is associated with a dismal prognosis. Medical treatment does not improve the outcome compared with the natural history of AS, as showed in the PARTNER trial, where elderly high-risk patients who were medically treated, had a 1-year survival of only 50% (4). Nevertheless, multiple series have documented that 30 - 40% of patients with severe AS do not undergo surgery, and the main reasons included advanced age or age-related comorbidities (6,7).

On the other hand, minimally invasive treatments have shown great improvements. TAVI has emerged as an alternative for patients with contraindication to open surgery and as a potential treatment option for patients with high and intermediate surgical risk. However, the long-term results of TAVI are yet to be determined and the high costs of this new technology have limited its widespread use among the world (8). The main objectives of this study are the evaluation of perioperative outcomes, survival and functional status of octogenarians submitted to AVR.

Methods

Patient population and data collection

From January 2006 to December 2016, 2947 patients were submitted to isolated AVR at the Centre of Cardiothoracic Surgery of Coimbra, Portugal, of whom 385 (13.1%) were over eighty years, which constituted our study population. Patients with concomitant valve surgery, coronary artery bypass graft or ascending aorta replacement and those with previous cardiac surgery were excluded.

Patient characteristics, including preoperative echocardiographic findings, are summarized in Supplemental Table 1. Mean age was 82.1 ± 2.0 years (median 82 years; IQR 2 years; range 80 - 90 years), 57.7% were female and 47.3% were in NYHA class III-IV. Although these patients were not presented to a formal Heart Team, since we do not have a formal TAVI program in our institution, all cases were discussed with the referring cardiologist, and a consensus of the best treatment option was always pursued.

The perioperative data, including preoperative clinical and echocardiographic findings, operative reports and early postoperative information were collected from our personal medical records.

Follow-up ended in December 2018, with a median time of 4.4 years (range 1 - 12 years) and patients who were alive at the end of follow-up were invited to respond to a questionnaire (Appendix 1) about the surgery results, current functional New York Heart Association (NYHA) class, medication, occurrence of neurological accidents, hospitalizations, infections and re-operations. The majority of patients (91%) answered the questionnaire by telephone interview.

Mortality and morbidity were reported accordingly to the latest guidelines (9).

All patients agreed to the use of their medical records and follow-up questionnaire data for investigation purposes.

Operative procedure and surgical technique

The operative technique of AVR was standard for all patients and included full median sternotomy, cardiopulmonary bypass (CPB) with moderate hypothermia (28 - 30°C), topical cooling with ice slush and intermittent antegrade cold crystalloid cardioplegia, either in the aortic root or directly in the coronary ostia. Once the aortic valve was excised and the annulus debrided of calcium, valve sizing was performed with the sizers provided

by the manufacturers. All patients received a bioprosthesis. The choice of prosthesis was at the discretion of the surgeon. Prostheses were implanted using simple sutures, hence positioned in an intra-annular fashion.

Aortic root enlargement, either trans-annular or supra-annular, by a modification of the Nick's technique previously described (10,11) was performed in near one third of cases (27.1%), in order to implant a larger prosthesis or to safely close the aortotomy. A septal myectomy (below the commissure between the left and right coronary sinuses) was frequently performed, as an additional means to relieve subvalvular obstruction component of hypertrophied ventricles.

The indexed effective orifice area (iEOA) was calculated by dividing the published reference values of the EOA by the patient's body surface area, available for all patients. Prosthesis-patient mismatch (PPM) was defined as an iEOA smaller than 0.85 cm^2/m^2 (moderate: 0.65-0.85 cm^2/m^2; severe: <0.65 cm^2/m^2) (12).

Statistical methodology

Continuous variables are reported as mean ± standard deviation and categorical variables expressed as percentage. The Kaplan-Meier method and Cox regression were used to calculate survival curves and to identify risk factors for long-term mortality. The study population was compared to the general population (age and gender-matched) accordingly with the National Institute of Statistics 2011 census, using the one-sample log-rank test. Statistical significance was defined as a two-tailed probability value <0.05. The data was analysed using the statistical package program Statistical Package for the Social Sciences (SPSS Statistics for MacOS, Version 23.0. Armonk, NY: IBM Corp). Statistical analysis followed the Statistical and data reporting guidelines (13).

Results

Patients' characteristics

The aetiology of the aortic valve lesion was mainly degenerative (351, 91.2%). Other aetiologies included congenital (bicuspid valve) in 25 patients (6.5%), rheumatic in 8 (2.1%) and infectious in 1 patient (0.3%). Preoperatively, sinus rhythm was present in 297 patients (77.1%), atrial fibrillation in 61 (15.8%) and pacemaker rhythm in 24 (6.2%).

The mean gradient measured by transthoracic echography (available in all cases) was 55.3±15.2 mmHg and the mean peak-to-peak gradient measured in the cathlab (when available) was 72.4 ± 24.1 mmHg. The mean diastolic diameter of the LV was 51.3±8.6mm (44.7±8.0mm after surgery). Pulmonary hypertension was registered in 173 patients (71.2%).

The calculated creatinine clearance, using the Cockcroft-Gault equation, was 49.6±15.5%. Applying the National Kidney Foundation (NFK) classification, 90 patients (23.5%) were in renal dysfunction stage 2, 254 (66.3%) in stage 3, 34 (8.9%) in stage 4 and 1 (0.3%) in stage 5. The population included 182 patients (47.3%) in NYHA class III/IV.

Operative data

Aortic root enlargement (trans-annular or supra-annular) was performed in 105 patients (27.1%) and ascending aorta tailoring in 22 (5.7%). Mean cardiopulmonary bypass (CPB) time was 60.1±13.5 minutes (69.5±15.3 minutes if the aortic root was intervened and 56.5±11.0 minutes if it was simple AVR). Mean aortic cross clamp time was 38.2±10.2 minutes (47.0±11.0 minutes with intervention in the aortic root and 34.8±7.7 minutes in isolated AVR). Operative data are summarized in Table 1.

Table 1. Operative data

Variable	Number (%) of Patients*
AVR	258 (66.5)
AVR + tARE	48 (12.4)
AVR + sARE	57 (14.7)
AVR + tailoring	22 (5.7)
Size of valve prosthesis**	21 [range:19-25]
EOA	1.34 ± 0.2
iEOA	0.82 ± 0.1
Mild-Moderate PPM	222 (57.7)
Severe PPM	28 (7.3)
CPB time (min)	60.1 ± 13.5
ACC (min)	38.2 ± 10.2

*For continuous variables, data are shown as: mean ± standard deviation.

** It refers to the median and mode value that in this case are the same.

AVR, aortic valve replacement; tARE, trans-anular aortic root enlargement; sARE, supra-anular aortic root enlargement; EOA, effective orifice area; iEOA, indexed effective orifice area; PPM, prosthesis-patient mismatch; CPB, cardiopulmonary bypass; ACC, aortic cross clamp.

Early mortality and morbidity

Only one patient died during hospitalization (0.3%) and the thirty-day mortality was 0.8% (3 patients). The causes of death after discharge were cerebrovascular accident and cardiorespiratory arrest. Perioperative results are detailed in Table 2. Briefly, inotropic support was required in 42 patients (11.7%) and no patient required mechanical support. Perioperative complete atrioventricular block with permanent pacemaker implantation occurred in 14 cases (3.5%). Supra-ventricular arrhythmias, especially atrial fibrillation, were registered in 142 (36.2%) patients. Perioperative stroke occurred in 3 patients (0.8%) and acute myocardial infarction in another 3 patients (0.8%). There were no cases of moderate or severe peri-prosthetic leak and 18 patients (5.2%) had minimal or mild leak. Fifty two patients (13.8%) suffered from acute kidney injury, mostly transient, but no patient needed substitution therapy. Four patients (1.0%) had significant postoperative bleeding and 3 (0.8%) of them were re-explored. Mean hospital stay was 8.0±3.2 days.

Table 2. Early outcomes

Variable	Number (%) of Patients*
Hospital mortality	1 (0.3)
Thirty-day mortality (including hospital mortality)	3 (0.8)
Ionotropic support	42 (11.7)
Myocardial infarction	3 (0.8)
Cerebrovascular accident	4 (1.1)
TIA/RIND	1 (0.3)
Stroke	3 (0.8)
Level of renal injury (RIFLE criteria)**	
Risk	86 (22.3)
Injury	23 (6.0)
Failure	3 (0.8)
Acute renal injury	52 (13.8)
Reoperation	5 (1.3)
Bleeding	4 (1.0)
Reoperation for bleeding	3 (0.8)
Mediastinitis	0 (0.0)
Atrial arrythmias	140 (36.4)
Complete A-V block	17 (4.3)
Tansient	3 (0.8)
Pacemaker implantation	14 (3.5)
Peri-prosthetic leak	
Minimal or mild	18 (5.2)
Moderate or severe	0 (0.0)
Prolonged postoperative length of stay***	16 (4.2)
Mean hospital stay (days)	8.0 ± 3.2

*For continuous variables, data is shown as: mean ± standard deviation.

**RIFLE criteria based on serum creatinine.

***Prolonged length of stay was considered more than 15 days.

TIA, transient ischemic attack; RIND, reversible ischemic neurologic deficit.

Late survival and outcomes

One, three, five and ten-year survival was 95.1±1.1%, 87.4±1.7%, 76.3±2.5% and 41.7±5.3% respectively, significantly better than the expected survival of the general population (age and gender-matched) (Figure 1). Several risk factors for late mortality, such as preoperative atrial fibrillation (HR:2.428; CI:1.552-3.798), renal injury (HR:1.404; CI:1.037-1.902) and higher NYHA class (HR:1.464; CI:1.106-1.939) were identified as independent risk factors in the Cox regression multivariable analysis [Table 3].

In the long-term follow-up (Table 4), patients experienced few adverse events, being the most frequent the cerebrovascular accident (31 patients, 8.0%). Infections occurred in 43 patients (11.3%).

There was a significant improvement in the functional status (mean preoperative NYHA= 2.5 vs. mean follow-up NYHA=1.8, P<0.001) and at the follow-up 82.9% of the survivors were in NYHA I-II. A quality of life inquiry was carried out as part of the postoperative evaluation and the majority of patients (97%) showed a high or very high satisfaction level with the surgery results.

Table 3. Risk factors for late mortality after surgery (Multivariable analyses - Cox proportional hazard function).

Variables	HR	95% CI	P-value
Atrial fibrillation	1.985	1.194-3.301	0.008
Renal Failure	1.404	1.037-1.902	0.028
NYHA class	1.461	1.111-1.921	0.007

CI, confidence interval; HR, hazard ratio; NYHA, New York Heart Association.

Table 4. Long-term outcomes

Variable	Number (%) of Patients
Cerebrovascular accident	31 (8.0)
TIA	4 (1.0)
Stroke	27(7.0)
Hospitalization for heart failure	23 (7.6)
Respiratory failure / infection	27 (7.1)
Urinary tract infection	10 (2.6)
Endocarditis	6 (1.6)
Reoperation	0 (0.0)

NYHA (post operatory)	1,8 ± 0.8*
Class I	123 (42.1)
Class II	119 (40.8)
Class III	46 (15.8)
Class IV	4 (1.4)
ACO/AGO medication	210 (62.1)
ASA	145 (37.7)
Warfarin	38 (9.9)
NOACs	26 (6.8)

* mean ± standard deviation.

ASA, acetylsalicylic acid; NOACs, new oral anticoagulants; NYHA, New York Heart Association functional class; TIA, transient ischemic attack;

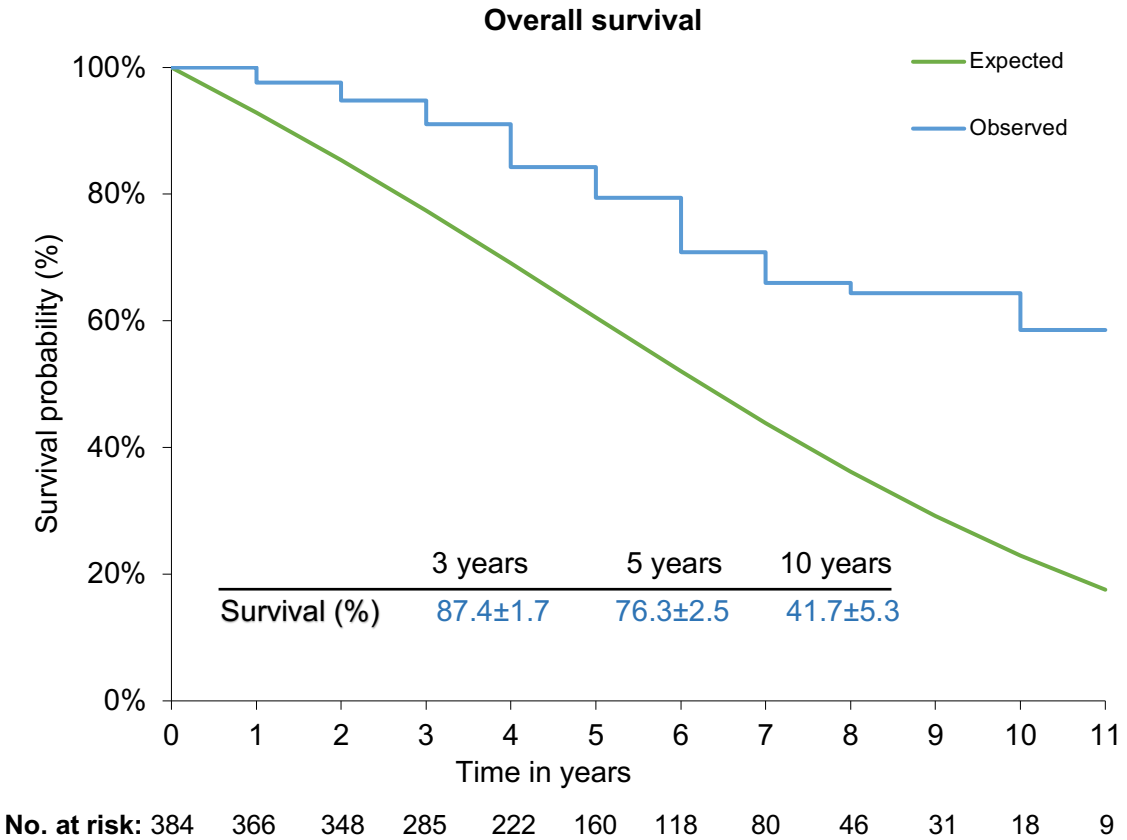

Figure 1, Overall survival of study population (observed) compared with the age- and gender-matched general population (expected: National Institute of Statistics, 2011 census).

Discussion

This study showed that AVR carries low morbidity and mortality in octogenarians and therefore, can be safely performed in severe AS in patients with moderate to high surgical risk. Hence, standard AVR continues to have an essential role in treating patients with aortic valve disease in this setting.

The prognosis of AS is well known: 90% of patients die in 3 years after the symptoms onset and within 2 years if heart failure is present (14). Despite this, approximately one third of patients are not referred to or do not undergo surgery (4,15).

In the last few decades there were demographic changes that culminated in an elderly population due to the increase in average life expectancy. For this reason, the number of octogenarians with degenerative diseases, such as AS, has increased. Age is frequently reported as a very important surgical risk factor, however it does not come alone and age-related comorbidities play an important part in the eligibility for surgery. Long-term survival may be less important in these patients, since in many cases they even have exceeded their life expectancy. The quality of life has a vital importance and we should be able to assess it and balance it in an individual manner, pondering the motivation to live, ability for independent living, frailty index, need for caregiving and the individual benefits of surgery (7,16,17).

During this study, there was no TAVI program in our Centre, hence the vast majority of patients referred for treatment of AS were subjected to AVR. Reflecting this, our study population should be placed in a moderate to high-risk population of patients, with the mean EuroSCORE-II of 3.6 ± 3.9%.

Contemporary AVR and TAVI results

In an era of minimally invasive techniques, TAVI has emerged as an alternative to AVR to treat patients at high risk for surgery. The interest in replacing surgical treatment with TAVI began to appear even in lower-risk patients, especially in the elderly. But what is the current evidence that supports this practice?

There are three comparative randomized clinical trials between TAVI and AVR that compare short and long-term mortality. PARTNER (8), NOTION (18,19) and SURTAVI (20) showed that both interventions have similar mortality outcomes and are associated with their own array of adverse events. While AVR is associated with an increased risk

of acute renal injury, bleeding and new-onset atrial fibrillation, TAVI resulted in more cases of severe regurgitation and permanent pacemaker implantation.

Recently, PARTNER group published a observational study that compares TAVI to AVR in intermediate-risk patients, demonstrating a significant superiority of TAVI and suggesting it as the preferred treatment in this cases (8). However, the European Surgical Community, pointing out several methodologic errors, invalidated direct comparison between treatments and could not support those conclusions (21).

Evidence from the Society of Thoracic Surgeons National Database shows that the operative mortality for isolated AVR has declined to 2.7% in the last decade and is under 1% in many centres (6). However, this data involves all subsets of patients submitted to isolated AVR and not only octogenarians, whom are, naturally, at higher risk for surgery. In a contemporary series of 2,256 patients submitted to AVR, *Di Eusanio et al.* reported that octogenarians had a higher hospital mortality rate in comparison with younger patients (3.7% vs. 1.8%), however the 3 years survival rate is comparable to the life expectancy (3). A multicentric study from the Australasian Society of Cardiac and Thoracic Surgeons documented that isolated AVR in octogenarians achieved excellent outcomes regarding long-term survival comparable to the age-adjusted Australian population, and the 30-day mortality was not significantly higher in these patients (22). *Harris et al.* have also reported very good results, with a 30-day mortality rate of 3.4% (0% in octogenarians under 85 years, probably equivalent to our population) (23). In a prospective cohort study, *Muneretto et al* suggests that TAVI is associated with a higher rate of perioperative complications and decrease survival at 2 years compared with AVR in intermediate to high-risk patients (24).

Another important issue is the incidence of paravalvular leaks (PVL), consistently observed with TAVI. The documented incidence of moderate to severe PVL in the literature for TAVI patients ranges from 9.6% to 17.3% and for mild leaks is around 22.5%, although the incidence of this complication appears to be reducing after modifications in the design of the prostheses (6). Since it has been shown that patients with clinically relevant PVL have significantly worse survival, this ought to be considered a significant complication (25). But in our series, there was not a single case of moderate-severe PVL and only 18 patients (5.2%) had minimal-mild leakage.

Mortality at 30 days at our centre was also considerably lower, only 0.8%, compared to other trials, with values ranging from 3.7%-8.0% (8,18,20). The reported incidence of perioperative complications in the trials was also slightly higher: stroke (3.0%-6.1% vs. 0.8%); life-threatening bleeding (9.3%-43.4% vs. 0.8%), and pacemaker implantation (4.2%-10.3% vs. 3.5%) (8,18,20).

In almost one third of our patients (27.1%), aortic root enlargement (trans- or supra-anular) was performed which allowed us to implant larger prosthesis and minimize PPM, without compromising operative mortality and morbidity. In our study 7.3% had severe PPM and 57.7% had mild-moderate PPM, which can be considered adequate for these patients, however in this instance, TAVI allows larger orifices areas, comparatively.

Finally, improvement of patients' functional status was evident early after surgery and persisted during follow-up. However, there are patients that will not recover fully, which can partially be due to the natural progression of the underlying cardiac disease and other age-related comorbidities (26). Interestingly, in the opinion questionnaire carried out as part of the postoperative evaluation, 97% of survivors believed that being operated after 80 years of age was the correct choice for them.

Selecting patients: the key issue

In this series, no patient was operated on an urgent/emergency basis, which is known to be an important risk factor for early surgical outcomes. Furthermore, higher NYHA classes were identified as independent risk factors for late mortality. This underlines the importance of operating on elderly patients as early as possible, before an advanced stage of the disease or clinical deterioration (NYHA III-IV) issues (14,15,27). The combination of a physically fragile patient and a poor functional condition is probably the most critical condition with regard poor outcomes. However, the assessment is not always straightforward despite a multitude of existing tests for evaluating patients' functional capacity. Although EuroSCORE-II overestimated the surgical risk in this subset of patients, thus surgical decision and risk assessment should not be solely based on this method (20,23).

Our excellent results translate this natural patient selection but the emphasis has always been more on preparation and optimization of patients for surgery than on simply rejecting the option, which occurred in less than 5% of our referrals. Evidently, not all octogenarians with severe AS are amenable to AVR, but a physically active and highly motivated patient, with isolated AS, good LV function, few comorbidities and without previous cardiac surgery appears to be the perfect candidate for AVR. In our opinion, AVR portends better results than TAVI because overall results (mortality, morbidity, PVL leakage, survival) are excellent and surgical implanted bioprosthesis have confirmed long-term durability which is not the case, yet, of transcatheter prostheses.

Limitations of the study

The inherent selection bias of a retrospective study in a single centre cautions the generalization of the results and conclusions. In this work, we wanted to emphasize the importance of patient selection, but this was made subjectively which is also a limitation. Follow-up data was retrospectively and not prospectively collected, hence reporting bias can also occur. Finally, there are several quality of life questionnaires in clinical practice but none of those was used in the studied population.

Conclusions

Contemporary surgical AVR carries a very low risk of mortality and morbidity, even in octogenarian patients. Our study demonstrates that a vast majority of patients overcome the perioperative period uneventfully and recover good functional capacity after surgery. Preoperative evaluation and optimization (functional, physiologic and respiratory) are major key factors for the success of AVR. Hence, we believe that conventional AVR still has an important role in the treatment of octogenarian patients with AS and no significant co-morbidities.

References

1. Bose, Amal K; Aitchison, James D ; Dark JH. Aortic valve replacement in octogenarians. J Cardiothorac Surg. 2007;2(33).

2. Falk V, Baumgartner H, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Vol. 52, European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery. 2017. 616-664 p.

3. Di Eusanio M, Fortuna D, De Palma R, Dell'Amore A, Lamarra M, Contini GA, et al. Aortic valve replacement: Results and predictors of mortality from a contemporary series of 2256 patients. J Thorac Cardiovasc Surg. 2011;141(4):940–7.

4. Svensson LG, Tuzcu M, Kapadia S, Blackstone EH, Roselli EE, Gillinov AM, et al. A comprehensive review of the PARTNER trial. J Thorac Cardiovasc Surg. 2013;145(3 SUPPL.):S11–6.

5. Brown JM, O'Brien SM, Wu C, Sikora JAH, Griffith BP, Gammie JS. Isolated aortic valve replacement in North America comprising 108,687 patients in 10 years: Changes in risks, valve types, and outcomes in the Society of Thoracic Surgeons National Database. J Thorac Cardiovasc Surg. 2009;137(1):82–90.

6. Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on valvular heart disease. Eur Heart J. 2003;24(13):1231–43.

7. Di Eusanio M, Fortuna D, Cristell D, Pugliese P, Nicolini F, Pacini D, et al. Contemporary outcomes of conventional aortic valve replacement in 638 octogenarians: Insights from an italian regional cardiac surgery registry (RERIC). Eur J Cardio-thoracic Surg. 2012;41(6):1247–53.

8. Thourani VH, Kodali S, Makkar RR, Herrmann HC, Williams M, Babaliaros V, et al. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: A propensity score analysis. Lancet. 2016;387(10034):2218–25.

9. Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeir GL et al. Guidelines for reporting mortality and morbidity after cardiac valve interventions. Eur J Cardiothorac Surg 2008;33:523–8.

10. Nicks R, Cartmill T, Bernstein L. Hypoplasia of the aortic root 1. Thorax. 1970;25(3):339–46.

11. Coutinho GF, Correia PM, Paupério G, de Oliveira F, Antunes MJ. Aortic root enlargement does not increase the surgical risk and short-term patient outcome? Eur J Cardio-thoracic Surg. 2011;40(2):441–7.

12. Pibarot P, Dumesnil JG. Hemodynamic and clinical impact of prosthesis-patient mismatch in the aortic valve position and its prevention. J Am Coll Cardiol. 2000;36(4):1131–41.

13. Hickey GL, Dunning J, Seifert B, Sodeck G, Carr MJ, Burger HU, et al. Statistical and data reporting guidelines for the European Journal of Cardio-Thoracic Surgery and the Interactive CardioVascular and Thoracic Surgery. Eur J Cardio-thoracic Surg. 2015;48(2):180–93.

14. Kolh P, Kerzmann A, Honore C, Comte L, Limet R. Aortic valve surgery in octogenarians: predictive factors for operative and long-term results. Eur J Cardio-thoracic Surg. 2007;31(4):600–6.

15. Holmes DR, MacK MJ, Kaul S, Agnihotri A, Alexander KP, Bailey SR, et al. 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. J Am Coll Cardiol. 2012;59(13):1200–54.

16. Sedrakyan A, Vaccarino V, Pattiel AD, Elefteriades JA, Mattera JA, Roumanis SA, et al. Age does not limit quality of life improvement in cardiac valve surgery. J Am Coll Cardiol. 2003;42(7):1208–14.

17. Sumi M, Ariyoshi T, Miura T, Hashimoto W, Hashizume K, Matsukuma S, et al. Are octogenarians in good condition after cardiac valvular surgery? Ann Thorac Cardiovasc Surg. 2014;20(6):1021–5.

18. Thyregod HGH, Steinbrüchel DA, Ihlemann N, Nissen H, Kjeldsen BJ, Petursson P, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the all-comers NOTION randomized clinical trial. J Am Coll Cardiol. 2015;65(20):2184–94.

19. Søndergaard L, Steinbrüchel DA, Ihlemann N, Nissen H, Kjeldsen BJ, Petursson P, et al. Two-year outcomes in patients with severe aortic valve stenosis randomized to transcatheter versus surgical aortic valve replacement: The all-comers nordic aortic valve intervention randomized clinical trial. Circ Cardiovasc Interv. 2016;9(6):1–9.

20. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, et al. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. N Engl J Med. 2017;376(14):1321–31.

21. Svensson LG, Tuzcu M, Kapadia S, Blackstone EH, Roselli EE, Gillinov AM, et al. The flaws in the detail of an observational study on transcatheter aortic valve

implantation versus surgical aortic valve replacement in intermediate-risks patients. Eur J Cardio-thoracic Surg. 2012;41(4):211–5.

22. Saxena A, Poh CL, Dinh DT, Reid CM, Smith JA, Shardey GC, et al. Early and late outcomes after isolated aortic valve replacement in octogenarians: An Australasian Society of Cardiac and Thoracic Surgeons Cardiac Surgery Database Study. Eur J Cardio-thoracic Surg. 2012;41(1):63–8.

23. Harris RS, Yan TD, Black D, Bannon PG, Bayfield MS, Hendel PN, et al. Outcomes of surgical aortic valve replacement in octogenarians. Hear Lung Circ. 2013;22(8):618–26.

24. Muneretto C, Bisleri G, Moggi A, Di Bacco L, Tespili M, Repossini A, et al. Treating the patients in the “grey-zone” with aortic valve disease: A comparison among conventional surgery, sutureless valves and transcatheter aortic valve replacement. Interact Cardiovasc Thorac Surg. 2015;20(1):90–5.

25. Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, et al. Two-Year Outcomes after Transcatheter or Surgical Aortic-Valve Replacement. N Engl J Med. 2012;366(18):1686–95.

26. Jokinen JJ, Hippelainen MJ, Hanninen T, Turpeinen AK, Hartikainen JEK. Prospective assessment of quality of life of octogenarians after cardiac surgery: factors predicting long-term outcome. Interact Cardiovasc Thorac Surg. 2008;7(5):813–8.

27. Litmathe J, Feindt P, Kurt M, Gams E, Boeken U. Aortic valve replacement in octogenarians: outcome and predictors of complications. Hellenic J Cardiol. 2011;52(3):211–5.

Supplemental material

Appendix 1. Follow-up questionnaire

FOLLOW-UP QUESTIONNAIRE

Name: _____ Hospital number: _____
Date of Surgery: ___/___/_____ Phone number: _____

1. How do you feel after surgery?
|__| Worst |__| Similar |__| Better |__| Much better

2. Functional class – Do you feel tired, palpitations or shortness of breath (dyspnea) when you:
|__| Class I – run or make big efforts
|__| Class II – go up a slope (or a flight of stairs)
|__| Class III – make small efforts (daily activities); walk small distances
|__| Class IV – are at rest

3. Current medication:
|__| Warfarin/Acenocoumarol |__| ASA/Clopidrogel |__| NOACs
|__| Diuretics |__| ACE inhibitor/ARBs |__| β-blocker

4. Do you have any device implanted after surgery (pacemaker or ICD)?
|__| Yes. Date of implantation: (__/__/____) |__| No

5. After surgery, did you have any of the following events? When?
|__| Stroke (__/__/____)
|__| Transient ischemic attack (__/__/____)
|__| Myocardial infarction (__/__/____)
|__| Pulmonary thromboembolism (__/__/____)
|__| Hospitalization for congestive heart failure (__/__/____)
|__| Surgical wound infection (__/__/____)
|__| Mediastinitis (__/__/____)
|__| Endocarditis (__/__/____)
|__| Prolonged fever (__/__/____)
|__| Respiratory infection (__/__/____)
|__| Urinary tract infection (__/__/____)
|__| Any hemorrhagic accident (__/__/____)
|__| Acute renal failure (__/__/____)
|__| Cardiac reoperation (__/__/____)
|__| Other complications or events. What? _____(__/__/____)

7. Questionnaire date (__/__/____)
|__| Alive
|__| Death. Date of death (__/__/____) Cause of death: _____

Legend: ASA, acetylsalicylic acid; NOACs, novel oral anticoagulants; ACE inhibitor, angiotensin-converting-enzyme inhibitor; ARBs, angiotensin receptor blockers; ICD, implantable cardioverter defibrillator; LV, left ventricle; LVOT, left ventricle outflow tract; LA, left atrial; PASP, pulmonary artery systolic pressure.

Supplemental Table 1. Preoperative data

Variable	Number (%) of Patients*
Mean age (years)	82.1 ± 2.0 (80-90)
Male gender	163 (42.3)
Body mass index (Kg/m^2)	26.8 ± 3.3
Body surface area (m^2)	1.64 ± 0,16
Hypertension	289 (75.1)
Dyslipidaemia	240 (62.3)
Smoking history	45 (11.7)
Peripheral vascular disease	43 (11.2)
Cerebrovascular disease	33 (8.6)
Diabetes Mellitus	95 (24.7)
COPD	31 (8.1)
Renal failure stage ≥ 3	289 (75.5)
Previous myocardial infarction	14 (3.6)
Previous PCI	21 (5.5)
NYHA	2.5 ± 0,7
Class I	21 (5.5)
Class II	182 (47.3)
Class III	167 (43.4)
Class IV	15 (3.9)
Permanent atrial fibrillation	61 (15.8)
Implanted pacemaker	25 (6.4)
Aortic valve area (cm^2)	0.66 ± 0.2
Systolic/Mean aortic gradient (mmHg)**	72.4 ± 24.1 / 55.3 ± 15.2
Left ventricular function***	62 ± 12
Good (>50%)	278 (83.7)
Moderate (31-50%)	52 (15.7)
Poor (21-30%)	2 (0.6)
PASP (mmHg)	38 ± 11
Pulmonary hypertension	
Moderate (PASP 31-55mmHg)	154 (63.4)
Severe (PASP >55 mmHg)	19 (7.8%)
EuroSCORE II	3.6 ± 3.9 [range:1.0-21.63]

*For continuous variables, data is shown as: mean ± standard deviation.

** Systolic gradient by cardiac catheterization / mean gradient by Doppler

*** According to the EuroSCORE-II LVEF classification.

COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; NYHA, New York Heart Association functional class; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure.

Supplemental Table 2. Univariate analyses for predictors of death.

Variable	***P* Value**
Age	0.025
Etiology	0.050
Atrial fibrillation	0.000
Renal failure	0.052
NYHA class	0.009
Obesity	0.035
Diabetes mellitus	0.098
Arterial hypertension	0.099
COPD	0.043
Previous stroke	0.172
BSA	0.106
PASP	0.129
iEOA	0.071
Aortic cross-clamp (time)	0.192
EuroSCOREII	0.009

BSA, body surface area; COPD, chronic obstructive pulmonary disease; iEOA, indexed effective orifice area; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure

Supplemental Figure 1. Survival curves in different NYHA classes (Cox regression).