ARTIGO ORIGINAL ORIGINAL ARTICLE

AGE IS NOT JUST A NUMBER FOR A RAPID DEPLOYMENT VALVE IN OCTOGENARIANS

Tiago R. Velho*[1, 2], Nuno Carvalho Guerra[1], Hugo Ferreira[1], Rafael Maniés Pereira[1], André Sena[1], Ricardo Ferreira[1], Ângelo Nobre[1]

[1]Cardiothoracic Surgery Department, Hospital de Santa Maria – CHLN, Lisboa, Portugal
[2]Innate Immunity and Inflammation Laboratory, Instituto Gulbenkian de Ciência, Oeiras, Portugal

*Contacto Autor: tiagovelho48@hotmail.com

Abstract

Introduction: *Aortic valve stenosis (AS) is the most common valvular pathology in the elderly and surgery (AVR) remains the gold-standard. However, transcatheter aortic valve replacement (TAVI) has become an emerging alternative to surgery. In a recent survey from the European Society of Cardiology, 9,4% stated that age was the main reason to propose for TAVI.*

Methods: *Single-center retrospective study including 353 patients (149 ≥80 years-old;204 with 60-69 years-old) submitted to AVR between 2013-2016. Primary endpoint was survival. Secondary outcomes included the rate of post-operative complications. Long-term survival was determined by Kaplan-Meier survival analysis. Continuous variables were analyzed with t-test and linear regression and categorical variables with chi-square or Fisher.*

Results: *clinical characteristics were similar between the two groups. Both had similar survival at 30 days, 12 (93,29% 60-69yo vs 91,47% ≥80yo) and 24 months (88,34% 60-69yo vs 86,11% ≥80yo). However, rapid deployment valves (RD) had better survival rates in elderly patients. Cross-clamp time was lower in ≥80yo group, with higher percentage of RD valves (20,1% vs 4.9% in 60-69yo). The rate of post-operative atrial fibrillation was higher in >80yo group (29,06% vs. 17,28%,p=0,0147). In all patients, cross-clamp time was directly related to ventilation time(p=0,025) and chest drainage(p=0,0015).*

Conclusion: *AVR after 80yo is safe. Cross-clamp time is directly correlated with ventilation time and bleeding, with a stronger correlation in patients over 80yo. RD valves reduce cross-clamp times, so their use in elderly may improve surgery outcome. Prospective studies are needed to evaluate if age may be clinical criteria for a RD.*

INTRODUCTION

Aortic valve stenosis is the most common valvular disease in industrialized countries, with an estimated prevalence of 2-7% in patients over 65 years old.[1] The prevalence of valvular disease increases with age, reaching 9.8% over 80 years old.[2] Nowadays, more octogenarians present with aortic stenosis with indication for surgery. The proportion of patients over 80 years old submitted to aortic valve surgery has been increasing in the past decades[3] due to the increasing in global average life expectancy.

Surgical aortic valve replacement (SAVR) remains the gold standard of treatment for aortic valve stenosis in low-intermediate risk patients. However, as age is an important risk factor for mortality and morbility in cardiac surgery[4], and a clear correlation between age, morbidity and mortality has been established, many surgeons hesitate to accept these patients for surgery.[4] According to The Euro Heart Survey, nearly one third of patients with symptomatic severe aortic valve stenosis and age over 80 were denied the standard of care (SAVR). One of the reasons of the refusal was "advanced age".[5]

Elderly patients often have comorbilities that stratify them in high-risk for open cardiac surgery under cardiopulmonary bypass, such as calcified aorta, poor lung function and previous cardiac surgery. However, although studies in this population are limited, SAVR can be performed with acceptable mortality and morbidity in octogenarians.[6]

Recently, transcatheter aortic valve implantation (TAVI) has emerged as an option in high-risk patients.[7] It is now recommended to be performed in high risk patients and some intermediate-risk patients after discussion in heart team. However, in a recent survey from the European Society of Cardiology, 9.4% of the physicians stated that age was the main reason to refer a patient for TAVI instead of surgery (independently from their comorbidities and surgical risk).[8] However, TAVI has also risks and although it allows a quicker recovery, some studies state that the overall quality of life at 6 months does not differ between TAVI and AVR once operability is taken in consideration.[9]

The present study aims to access the outcome of octogenarians patients submitted to SAVR, comparing perioperative outcomes and long-term survival with a similar younger group submitted to the same procedure.

MATERIAL AND METHODS

Preoperative demographic, clinical and perioperative data were retrieved retrospectively from the clinical files from our Department. Follow-up data, including major morbidities and date of death were obtained from hospital records and from registries from the national electronic health care database. All patients were submitted to aortic valve replacement surgery between January 2013 and February 2016. All the clinical and follow-up data from patients over 80 years old (≥ 80 yo) were compared to data from patients submitted to the same procedure between 60 and 69 years old (60-69 yo). At 4-6 weeks after the surgery all patients underwent a follow-up assessment.

Statistical analysis

Normally distributed continuous variables are presented as mean and standard deviation (SD). The student t-test was used to compare means. Categorical data is reported as count and percentage, and comparisons were made using Pearson's Chi-square test or the Fisher exact test, depending on the sample analyzed. Overall survival was analyzed by the Kaplan-Meier method. Curves were compared using a log-rank test. A p-value of <0,05 determined statistical significance. Data was analyzed by the GraphPad Prism® software for Macintosh®, version 6.

RESULTS

From January 2013 to December 2016, 353 patients were submitted to aortic valve replacement surgery in our department (204 patients between 60 and 69 years-old and 149 patients with at least 80 years-old). Patients proposed for combined valvular surgery and/ or concomitant coronary artery bypass grafting were not included in this study.

Baseline characteristics of both groups are summarized in Table 1. In the 60-69 yo, patients had a mean

Table 1 Demographic data: comparison between the two groups

	60-70 years old	≥ 80 years old	*p*-value
N	204	149	
Age, years, mean ± SD	65,4 ± 2,787	82,23 ± 1,917	***<0,0001
Male sex, n (%)	123 (60,3)	61 (40,9)	**0,0003
Hypertension, n (%)	173 (84,8)	135 (90,6)	0,1066
Diabetes mellitus, n (%)	72 (35,3)	27 (18,1)	**0,0004
Dyslipidemia, n (%)	143 (70,1)	101 (67,8)	0,6462
Obesity, n (%)	48 (23,5)	13 (8,7)	**0,0003
Atrial fibrillation, n (%)	24 (11,8)	29(19,5)	0,0455
Chronic kidney disease, n (%)	9 (4,4)	14 (9,4)	0,0609
Peripheral vascular disease, n (%)	9 (4,4)	1 (0,7)	*0,0364
Cerebrovascular disease, n (%)	17 (8,3)	10 (6,7)	0,5712
Chronic lung diseas, n (%)	15 (7,4)	15 (10,1)	0,3664
Ischemic cardiopathy, n (%)	9 (4,4)	14 (9,4)	0,0609
LV dysfunction (EF < 50%), n (%)	23 (11,3)	19 (12,8)	0,5882
Hyperuricemia, n (%)	13 (6,4)	6 (4)	0,3348
Thyroid disease, n (%)	7 (3,4)	11 (7,4)	0,0956
OSAS, n (%)	16 (7,8)	4 (2,7)	*0,0384
NYHA I, n (%)	20 (9,8)	9 (6)	0,2417
NYHA II, n (%)	139 (68,1)	102 (68,5)	1,0000
NYHA III, n (%)	44 (21,6)	38 (25,5)	0,2464
NYHA IV, n (%)	1 (0,5)	0 (0)	1,0000

V: left ventricular; OSAS: obstructive sleep apnea syndrom age of 65,4 ± 2,787 years, with the majority being male 123 (60,3%). Younger patients had a higher incidence of diabetes mellitus (p=0,0004) and obesity (p=0,0003). Hypertension was the most prevalent risk factor in both groups, followed by dyslipidemia and diabetes mellitus. In the ≥ 80 yo, patients had a mean age of 82,23 ± 1,917 years, with 40,9% of males (61 patients) [p=0,0003].

The mean predictive logistic European System for Cardiac Operative Risk Evalutation (EuroSCORE II) mortality risk was 1,168 ± 1,157 for 60-69 yo and 1,697 ± 0,75 for ≥ 80 yo (p<0,0001). There were no statistically significant differences concerning other baseline characteristics between the two groups, as described in Table 1.

Aortic stenosis was the main indication for surgery: 84,8% in the 60-69 years old group and 96,6% in the ≥ 80 years old group. In 18 (8,8%) patients in the 60-69 yo group and 4 (2,7%) in the ≥ 80 yo group the indication for surgery was aortic insufficiency, followed by endocarditis in 12 (5,9%) and 1 (0,7%) patient, respectively, and 1 (0,5%) patient with prosthesis dysfunction in the 60-69 yo group, as described in Table 2.

In 175 (85,85%) 60-69 yo patients and 128 (85,9%) ≥ 80 yo patients, surgery was performed electively. In the remaining patients, surgery was performed urgently.

None of the patients submitted to surgery in the elderly group received a mechanical prosthesis, while 57 patients (27,9%) from the younger group received one. Morrow myectomy was concomitantly performed in 20 patients 60-69 yo (9,8%) and in 20 patients (13,4%) ≥ 80 yo (p=0,3110). Surgeons opted for a rapid deployment valve in 10 (4,9%) patients in the 60-69 yo group and in 30 patients (20,1%) in the ≥ 80 yo group (p<0,0001).

The cardiopulmonary bypass time was longer in the 60-69yo group (61,29 ± 2,415) compared with the ≥ 80 yo group (55,27 ± 2,019) (p=0,071). Similarly, the cross clamp time was longer in the younger group (50,93 ± 1,892 *vs* 45,73 ± 1,591, p=0,0432).

The median ventilation time was 11,66 ± 1,898 hours in the 60-69yo group and 10,48 ±1,943 in the ≥ 80 yo group (p<0,6716). Both groups had similar chest tube drainage, intensive care unit and hospital lengths of stay (table 2).

Post-operative complications and their incidence are described in Table 3. Transfusion and hemodynamic support were the most frequent complications in both groups, although both have a higher incidence in the elderly group. Excessive post-operative hemorrhage was more frequent in the 60-69 yo group, although the incidence of re-operation due to excessive hemorrhage was similar: 8 (3,9%) 60-69 yo *vs* 6 (4%) ≥ 80 yo (p=1,00). Atrial fibrillation was more common in the elderly group (30,9% *vs* 17,1%, p=0,0031). Both groups had similar rates of acute kidney injury and stroke. Wound infection

Table 2 **Intraoperative data and clinical outcomes**

	60-70 years old	≥ 80 years old	*p*-value
N	204	149	
Aortic stenosis, n (%)	173 (84,8)	144 (96,6)	***<0,0001
Aortic insufficiency, n (%)	18 (8,8)	4 (2,7)	0,0241
Endocarditis, n (%)	12 (5,9)	1 (0,7)	**0,0094
Aortic prothesis dysfunction, n (%)	1 (0,5)	0 (0)	1,0000
Euroscore, mean ± SD	1,168 ± 1,157	1,697 ± 0,7568	****<0,0001
Biological prothesis, n (%)	147 (72,1)	149 (100)	<0,0001
Mechanical prothesis, n (%)	57 (27,9)	0 (0)	***<0,0001
Rapid depolyment valves, n (%)	10 (4,9)	30 (20,1)	****<0,0001
Morrow Miectomy, n (%)	20 (9,8)	20 (13,4)	0,3110
Elective surgery, n (%)	175 (85,8)	128 (85,9)	1,0000
Urgent surgery, n (%)	29 (14,2)	21, (14,1)	1,0000
Emergent surgery, n (%)	0 (0)	0 (0)	--
Extracorporeal time (min)	61,29 ± 2,415	55,37± 2,019	0,0710
Cross-clamp time (min)	50,93 ± 1,892	45,73 ± 1,591	*0,0432
Ventilator time (h)	11,66 ± 1,898	10,48 ± 1,943	0,6716
Chest tube 24h (cc)	624,8 ± 36,77	689,2 ± 56,65	0,3209
ICU LOS (h)	63,29 ± 4,752	76,99 ± 7,452	0,1059
Hospital LOS (days)	7,46 ± 0,89	8,303 ± 0,46	0,4507

ICU: intensive care unit; LOS: length of stay

Table 3 **Post-operative complications**

	60-70 years old	≥ 80 years old	*p*-value
N	204	149	
Blood or blood product, n (%)	99 (48,5)	92 (61,7)	*0,0173
• Blood	67 (32,8)	80 (53,7)	***0,0001
• Fibrinogen	44 (21,6)	44 (29,5)	0,1053
• Platelets	64 (31,4)	52 (34,9)	0,4936
• FFP	46(22,5)	35 (23,5)	0,8982
Excessive post-op hemorrhage , n (%)	12 (5,9)	6 (4)	0,4744
Reoperation due to tamponade, n (%)	8 (3,9)	6 (4)	1,0000
Atrial fibrillation, n (%)	35 (17,1)	46 (30,9)	**0,0031
Acute kidney failrure, n (%)	44 (21,6)	43 (28,9)	0,1338
Haemodynamic support, n (%)	83 (40,7)	66 (44,3)	0,5143
Stroke, n (%)	2 (1)	1 (0,7)	1,0000
Wound infection, n (%)	6 (3)	0 (0)	0,0414
Discharge, n (%)			
• Other hospital	23 (11,6)	15 (10,4)	0,8619
• Home	175 (88,4)	129 (86,6)	

FFP: fresh frozen plasma

was diagnosed in 6 patients from the 60-69 yo group, while none was diagnosed in the older group (p=0,414).

There were six in-hospital deaths in the 60-69 yo group and 5 in the ≥ 80 yo group. Kaplan-Meier estimates of survival at 1 and 2 years were 93,29% and 88,34% for the 60-69 yo patient, *versus* 91,47% and 86,11% for patients over 80 yo (p=0,5418) [Figure 1]. Considering only the patients over 80 yo, there are no differences in survival at 1 year between the use of conventional valves (91,32%) and rapid deployment valves (91,5%). However, at 2 years, the survival is higher in the rapid deployment group (91,48% *vs* 86,85%) (p=0,5805), although it is not statistically significant [Figure 2]. There are no demographic or peri-operative differences between these groups (data not shown).

Patients between 60 and 69 yo have significant differences in survival at 1 and 2 years when a conventional valve is used (94,61% and 90,34%) *versus* a rapid deployment valve (64% and 48%), respectively (p=0,0002) [Figure 3]. Once again, there are no demographic or peri-operative differences between these groups (data not shown).

To better understand the impact of rapid deployment valves, we correlated cross clamp time with ventilation time, chest tube drainage during the first 24 hours and ICU length of stay. A simple linear regression analysis showed a correlation between cross-clamp time and ventilation time (p=0,02491) and chest tube drainage (p=0,0015), considering all patients. No correlation was observed between cross-clamp time and ICU length of stay for all patients.

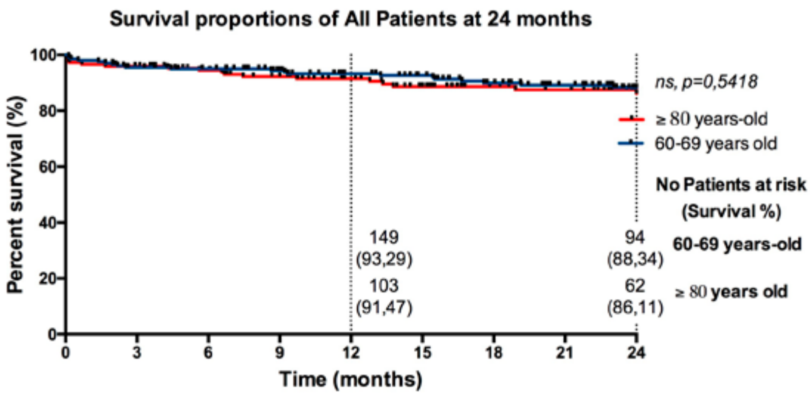

Figure 1 *Survival proportions of all patients at 24 months; ns: non-significant.*

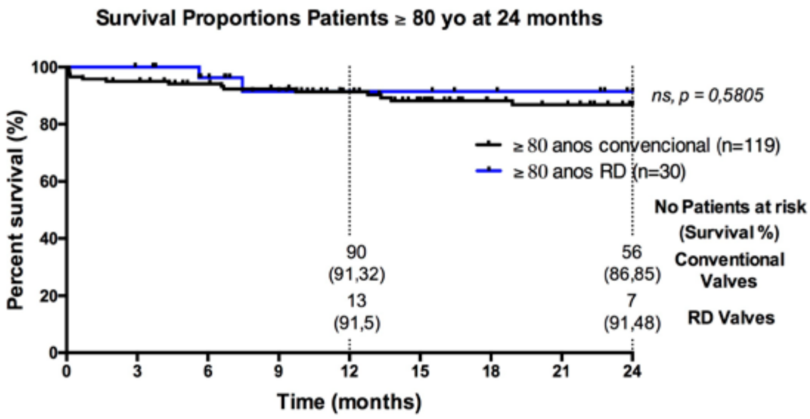

Figure 2 *Survival proportions patients over 80 year-old at 24 months, comparing conventional and rapid deployment valves; RD: rapid-deployment; ns: non-significant.*

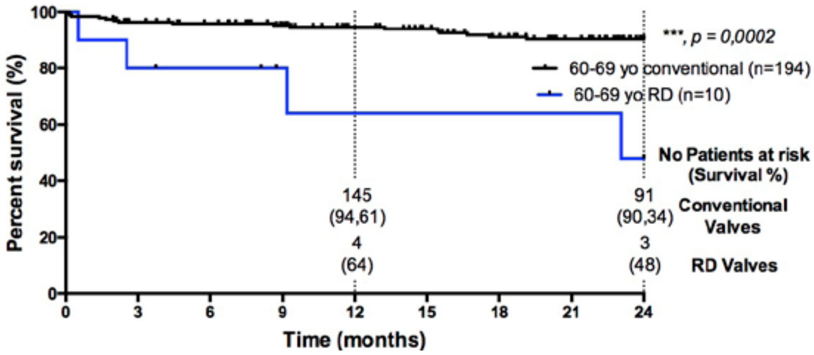

Figure 3 *Survival proportions of patients 60-69 years-old at 24 months, comparing conventional valves with rapid deployment valves; RD: rapid-deployment; ns: non-significant.*

Performing a group sub-analysis, we observed that the cross-clamp time is correlated with ventilation time (p=0,0077), chest tube drainage (p=0,0395) and ICU length of stay (p=0,0493) for patients over 80 yo. On the other hand, in patients 60-69 yo, cross clamp time was only correlated with chest tube drainage (p=0,0063) [Figure 4].

CONCLUSIONS

It is well known that elderly patients have more comorbidities and fragilities that increase the surgical risk. Particularly in cardiac surgery, the assessment of frailty is important since it is associated with the occurrence of major complications, 30-day mortality and extended postoperative length of stay. Frailty is a better predictor for mortality than morbidity.[10] However, the assessment must be individualized as it depends on the patient. Patients with the same age can have different levels of frailty. Its assessment is not yet routinely performed, but it may become useful in our pre-operative routine as the number of patients with advanced age increases.

Indeed, and as previously described, age has been assumed as a limitation for surgery. Cardiologists have been proposing low-intermediate elderly patients for TAVI instead of surgery based just on age. Even European heart association guidelines use age as a risk factor for referring for TAVI, as age over 75 years old favours TAVI as much as an EuroSCOREII higher than 4%.[11,12]

Age has always been included in risk assessment scores. EuroscoreII includes age as a continuous patient-dependent risk factor. However, EuroscoreII was launched in 2011 with a patient population median age of 64.9 years old. As mean age of patients undergoing cardiac surgery is increasing, the risk model calibration may not be as accurate as it was.[13] In fact, some studies have pointed that risk models, such as EuroscoreII, do not accurately predict mortality nowadays in elderly patients undergoing aortic valve replacement.[14]

Several studies have published data supporting that SAVR can be feasible in elderly patients, with very low mortality and complications rates.

In this study we present the results from our center in octogenarians submitted to SAVR. Patients over 80 yo had similar survival rates at 1 and 2 years to younger patients (60-69 yo), although they had a higher mean EuroscoreII (1,697 *vs* 1,168) with similar comorbidities.

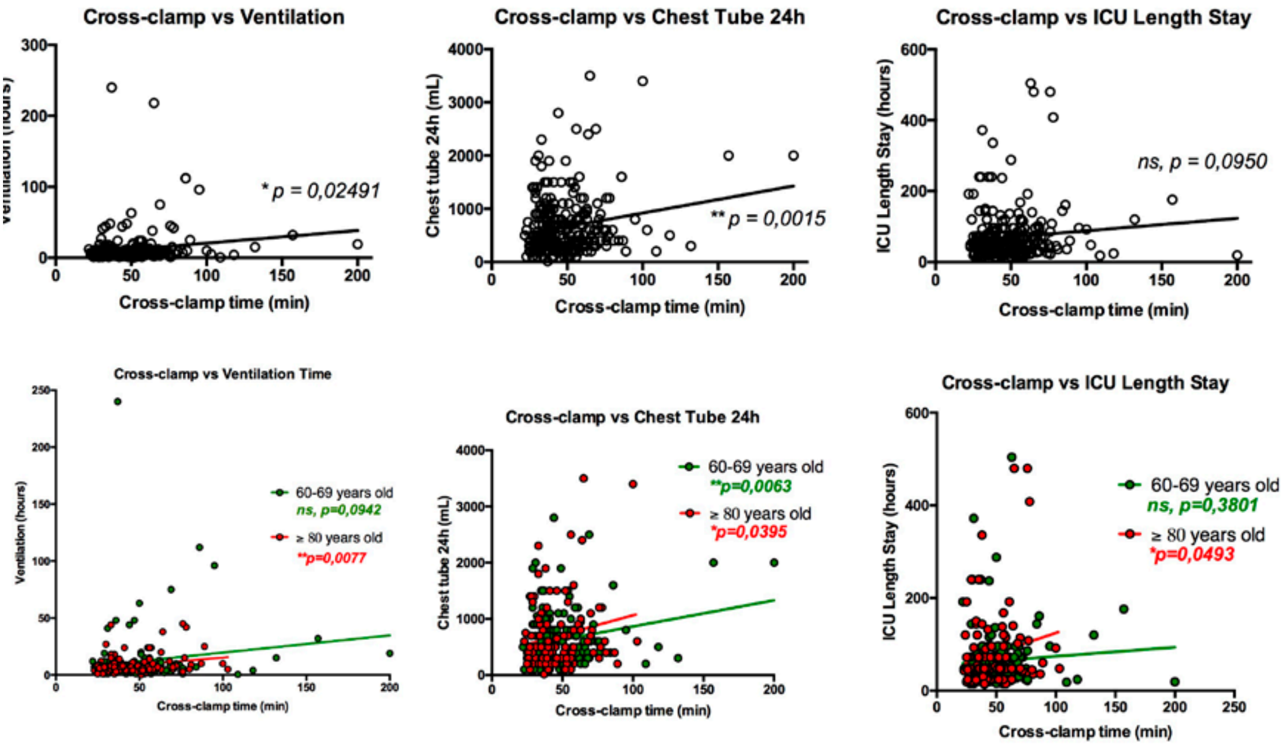

Figure 4 *Cross-clamp time correlation with ventilation time, chest tube drainage and ICU length of stay for all patients; and cross-clamp time correlation with ventilation time, chest tube drainage and ICU length of stay for patients 60-69yo (green) and patients over 80yo (red); ICU: intensive care unit; ns: non-significant; yo: years-old.*

Studies have shown that, considering all patients, cardiopulmonary bypass and aortic cross-clamping times are significant and independent risk factors for mortality and morbidity in cardiac surgery.[15] Regarding this fact, technology in cardiac surgery has advanced in the past decades with the development of rapid deployment valves, in order to reduce morbidity and mortality reducing extracorporeal circulation and cross-clamp times.

As elderly patients are more fragile, and usually have more comorbidities, shorter surgeries with reduced extracorporeal circulation and cross-clamping times are more important and may have a major impact comparing to a similar reduction in younger patients. One possible explanation for our good results in patients over 80 yo is that they had a significantly lower cross-clamp time, probably due to the higher use of rapid deployment valves in this group. Moreover, in our study, we have observed that in patients over 80 yo cross clamp time is correlated with post-operative outcomes such as ventilation time, chest tube drainage and ICU length of stay. In these patients, reducing cross clamp time with the use of a rapid deployment valve can actually reduce ventilation time and ICU length of stay and improve the outcome.

When we analyze survival of both groups comparing rapid deployment valves with conventional valves, in the older group both patients have similar survival rates at 1 and 2 years (with a better survival rate with rapid deployment valves, although it is not statistically significant). However, survival rate is significantly lower in patients with 60-69 years old when a rapid deployment valve is used. This may be explained by the use of RD valves in patients with comorbidities that are not included in EuroscoreII, such as renal transplantation or cirrhosis.

Our study has all the limitations inherent to retrospective observational studies. As a single center study our findings are related to our population, and may not be extrapolated to other populations. The limited number of patients and a small age specific group are also limitations of this study. Surgical referral and selection are other two limitations, since the cardiologists refer the majority of patients and many with advanced age are referred for TAVI without a cardiothoracic surgery appointment or heart team discussion. Moreover, follow-up was limited to 24 months and causes of death were unavailable for patients who died outside or were followed outside our institution.

Our results support the safety of aortic valve replacement surgery in the elderly, with a low rate of complications and similar outcomes to younger patients. In elderly patients, frailty assessment may be an important tool to distinguish TAVI and SAVR patients, since age itself does not support any clinical decision. More studies must be performed to evaluate if age is a clinical indication for an aortic rapid deployment valve.

Conflicts of interest

This research received no grant from any public or private institution. Authors have no conflicts of interest to disclose.

REFERENCES

1. B. Iung and A. Vahanian, "Epidemiology of acquired valvular heart disease," Can. J. Cardiol., 2014.
2. G. W. Eveborn, H. Schirmer, G. Heggelund, and P. Lunde, "The evolving epidemiology of valvular aortic stenosis . The Tromsø Study," pp. 396–400, 2013.
3. D. Mozaffarian, E. J. Benjamin, A. S. Go, D. K. Arnett, M. J. Blaha, M. Cushman, S. R. Das, S. de Ferranti, J.-P. Després, H. J. Fullerton, V. J. Howard, M. D. Huffman, C. R. Isasi, M. C. Jiménez, S. E. Judd, B. M. Kissela, J. H. Lichtman, L. D. Lisabeth, S. Liu, R. H. Mackey, D. J. Magid, D. K. McGuire, E. R. Mohler, C. S. Moy, P. Muntner, M. E. Mussolino, K. Nasir, R. W. Neumar, G. Nichol, L. Palaniappan, D. K. Pandey, M. J. Reeves, C. J. Rodriguez, W. Rosamond, P. D. Sorlie, J. Stein, A. Towfighi, T. N. Turan, S. S. Virani, D. Woo, R. W. Yeh, and M. B. Turner, Heart Disease and Stroke Statistics-2016 Update, vol. 133, no. 4. 2016.
4. F. Nicolini, A. Agostinelli, A. Vezzani, T. Manca, F. Benassi, A. Molardi, and T. Gherli, "The evolution of cardiovascular surgery in elderly patient: A review of current options and outcomes," Biomed Res. Int., vol. 2014, 2014.
5. B. Iung, G. Baron, E. G. Butchart, F. Delahaye, C. Gohlke--Bärwolf, O. W. Levang, P. Tornos, J. L. Vanoverschelde, F. Vermeer, E. Boersma, P. Ravaud, and A. Vahanian, "A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on valvular heart disease," Eur. Heart J., vol. 24, no. 13, pp. 1231–1243, 2003.
6. E. Ho, M. N. Mathur, P. W. Brady, D. Marshman, R. J. Brereton, D. E. Ross, R. Bhindi, and P. S. Hansen, "Surgical aortic valve replacement in very elderly patients aged 80 years and over: Evaluation of early clinical outcomes," Hear. Lung Circ., vol. 23, no. 3, pp. 242–248, 2014.
7. V. Falk, H. Baumgartner, J. J. Bax, M. De Bonis, C. Hamm, P. J. Holm, B. Iung, P. Lancellotti, E. Lansac, D. R. Muñoz, R. Rosenhek, J. Sjögren, P. Tornos Mas, A. Vahanian, T. Walther, O. Wendler, S. Windecker, and J. L. Zamorano, 2017 ESC/EACTS Guidelines for the management of valvular heart disease, vol. 52, no. 4. 2017.
8. G. Practitioners, "TAVI SURVEY Performed by the ESC Council for Cardiology Practice."
9. P. J. Tully, P. Roshan, G. D. Rice, A. Sinhal, J. S. Bennetts, and R. A. Baker, "Change in quality of life after transcatheter aortic valve implantation and aortic valve replacement surgery in Australian patients aged ≥ 75 years: The effects of EuroSCORE and patient operability," J. Geriatr. Cardiol., vol. 12, no. 1, pp. 30–36, 2015.
10. G. Esses, E. Andreopoulos, H. M. Lin, S. Arya, and S. Deiner, "A Comparison of Three Frailty Indices in Predicting Morbidity and Mortality after On-Pump Aortic Valve Replacement," Anesth. Analg., vol. 126, no. 1, pp. 39-45, 2018.
11. T. Cahill, M. Chen, K. Hatashida, A. Latib, T. Modine, N. Piazza, S. Redwood, L. Sondergaard, and B. Prendergast, "Transcatheter aortic valve implantation-current status and future perspectives," Eur. Heart J., vol. 39, no. 28, pp. 2625–2634, 2018.
12. A. Khosravi and O. Wendler, "TAVI 2018: from guidelines to practice," E-Journal Cardiol. Pract., vol. 15, no. 29, 2018.
13. M. Poullis, M. Pullan, J. Chalmers, and N. Mediratta, "The validity of the original EuroSCORE and EuroSCORE II in patients over the age of seventy," Interact. Cardiovasc. Thorac. Surg., vol. 20, no. 2, pp. 172–177, 2015.
14. S. Leontyev, T. Walther, M. A. Borger, S. Lehmann, A. K. Funkat, A. Rastan, J. Kempfert, V. Falk, and F. W. Mohr, "Aortic Valve Replacement in Octogenarians: Utility of Risk Stratification With EuroSCORE," Ann. Thorac. Surg., vol. 87, no. 5, pp. 1440-1445, 2009.
15. N. Al-Sarraf, L. Thalib, A. Hughes, M. Houlihan, M. Tolan, V. Young, and E. McGovern, "Cross-clamp time is an independent predictor of mortality and morbidity in low- and high--risk cardiac patients," Int. J. Surg., vol. 9, no. 1, pp. 104–109, 2011.