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Long-term survival after surgical aortic valve replacement in patients aged 80 and over

--Manuscript Draft--

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Author Comments:	Southampton 08.02.2021 To the attention of Matthias Siepe, Editor-in-Chief of European Journal of Cardio-Thoracic Surgery Thierry Carrel, Associate Editor of European Journal of Cardio-Thoracic Surgery Dear Editors, thank you for the time invested in our manuscript. The suggestions from the reviewers were of utmost importance in building up a meaningful discussion. Furthermore, the remarks of the Statistical Reviewer were always punctual and helped in providing a linear stat design and presentation of the results. We went through the last comments and hopefully we are able to provide adequate answers and changes. Whatever the outcome of the submissions, the review process of your Journal represents a valuable occasion of discussion and learning. Best regards Pietro G Malvindi Wessex Cardiothoracic Department University Hospital Southampton
Abstract:	Objectives. Surgical aortic valve replacement can be safely performed in people aged 80 and older with early benefits on both symptomatic and prognostic ground. Whilst new approaches are advocated to treat this elderly and frail population, data on long-term outcomes are not available. Methods. We conducted a retrospective analysis of 1870 patients aged 80 and over who underwent first time surgical aortic valve replacement during the period 2000 – 2019. The Kaplan-Meier method was used to calculate survival and comparisons

among groups was performed by log-rank test. Cox analysis was used to determine independent risk factors for late mortality.
Results. Patients' mean age was 84 years and 53% were male. Isolated aortic valve replacement was performed in 42% of the patients, CABG (n=956), mitral valve (n=94) or aortic surgery (n=69) were associated in the remaining cases. One hundred eighty-one patients (8%) sustained at least one postoperative complication (reopening for bleeding or tamponade 3%, renal replacement therapy 3%, new cerebral stroke 1.5%). In-hospital mortality was 3.2% in the overall population (60/1870) and 2.2% after isolated aortic valve replacement (18/790). Survival was 90%, 66%, 31%, 14% at 1-year, 5-years, 10-years and 15-years, respectively, and was similar to the expected survival of a sex- and age-matched population (log-rank p=0.96). A complicated postoperative course was an independent risk factor for mortality during the follow-up [hazard ratio 1.32 (1.03, 1.68), p=0.026].
Conclusions. Surgical aortic valve replacement can be performed with an acceptable early mortality rate and provides excellent long-term survival in people aged 80 and older.

Response to Reviewers:

Reviewer 1: The revised version of this paper is good. I do not have any more comments.

Reviewer 2: With the additional information provided by the authors, complying with the reviewers' request, now the manuscript becomes a valuable piece of evidence for aortic valve replacement in patients aged 80 years and over.

Reviewer 3: The authors responded well to the reviewers' comments. I agree that this manuscript could represent a benchmark for the forthcoming long-term results of non-surgical treatment of aortic valve.
Now I agree that this manuscript could be accepted for publication in EJCTS.

Answer. We want to thank you for your constructive reviews, they were all fundamental suggestions driving meaningful messages from our numbers and analyses.

Reviewer 4: STATISTICAL REVIEW
The authors took my comments into consideration. As a result of survival analyses with different starting points, readers might be confused. Hence, it is important to formulate the results precisely. Here are my comments:
- As mentioned already in my review of the original version, the starting point of survival should be mentioned in the label of the time axis. According to the Statistical and data reporting guidelines https://emea01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fdoi.org%2F10.1093%2Fejcts%2Fezv168&data=04%7C01%7C%7C7b539a4510a940f0a3b908d8cc1654aa%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C637483743562922721%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=YtkwOCEBfiaXyrbTuyn09GfOyfLgPubd2PoC3qgNkIw%3D&reserved=0, the labels of Kaplan-Meier plots including the central figure should be "Time from surgery (years)" or "Time from discharge (years)" (supplemental figure 1A) instead of "years".
- In the statistical analysis section, the starting points of survival should be mentioned.
- The starting point should be mentioned when it is not obvious. In the section "Long-term outcomes", the starting point is surgery, then it switches to discharge, then goes back to surgery, before it switches to discharge (supplemental figure 1A) and surgery (supplemental figure 1B) again. The authors might change the order of analyses to improve readability. The starting point has to be mentioned after every switch.
- To make figures and tables self contained, the starting point has to be mentioned in the titles or legends.
Answer. We agree with this remark. Summarising, all the KM analyses have the starting point on the date of surgery, while the Cox analysis considers the time from discharge. We have punctually reported the starting point wherever necessary in the main text and legends. Regarding the figures we have opted for three different ways because of different data involved in the KM analysis. Particularly:
-Figure 2: we have followed your suggestion and expanded the x axis legend with "Time from surgery (years);

	-Figure 3/Central Figure: since there is no surgery date to be considered for the general population, we have opted for expanding the legend of the curve of the surgical population; -Supplemental Figure 1: similar considerations for Figure 3. In this case we have preferred to underline the starting point in the figure legends. Expanding the legends for 4 curves would have had a negative impact on the graph layout. Finally, we welcomed your idea of changing the order of the paragraph in "Long-term outcomes". It sounds more readable. Changes. Page 8 lines 9 and 15 Page 10 lines 22-23 Page 11 lines 3-6 and 15 Page 17 lines 4 and 8 Page 21 line 1 Page 22 line 2 Suppl Page 1 lines 2 and 9 - Supplemental figure 1B: The figure does not show "cumulative risk of mortality" but cumulative survival. Answer. Thank you, corrected. Changes. Suppl Page 1 line 9 - Abstract, results: Text like "0.026; 1.317 (1.033, 1.680)" is incomprehensible. In the results, it might be replaced by something like "p=0.026; HR 1.32, 95% CI 1.03 to 1.68". In the abstract, "(hazard ratio 1.32 (1.03,1.68), P=0.026)" would have only one word more than the incomprehensible text. Note that I would prefer HRs rounded to two decimal places. Answer. Thank you, corrected. Changes. Page 3 line 17 Page 11 lines 17-20 Page 21 Table Page 22 Table
Order of Authors (with Contributor Roles):	Pietro Giorgio Malvindi, MD, PhD (Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Writing – original draft)
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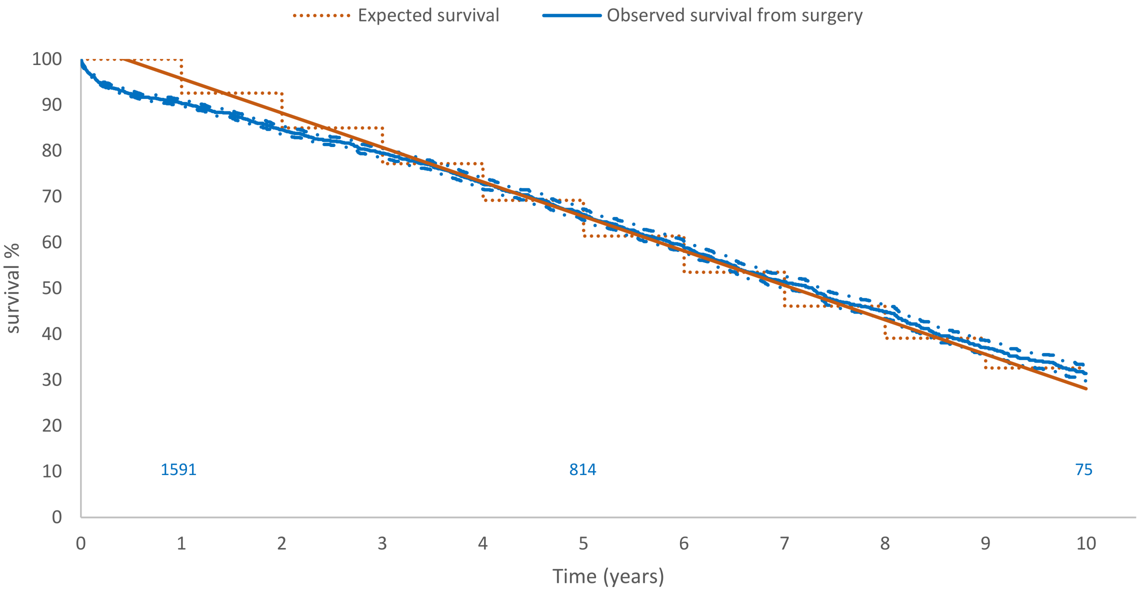
	Suresh Giritharan (Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Writing – review & editing)
	Mariusz Kowalewski (Data curation; Formal analysis; Methodology; Software; Validation; Writing – review & editing)
	Sunil Ohri (Conceptualization; Investigation; Methodology; Project administration; Supervision; Validation; Writing – original draft)

Central image



Title: Long-term Survival After Surgical Aortic Valve Replacement in Patients Aged 80 and Over

Running head: survival after aortic valve replacement

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Word count: 4494

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Visual abstract

Key question: what is the long-term survival of people aged over 80 undergoing aortic valve surgery?

Key findings: survival is 30% at 10-year and similar to the expected survival of an age- and sex-matched population

Take-home message: surgical aortic valve replacement is safe in octogenarian and older patients and provide a good long-term survival

Abstract

Objectives. Surgical aortic valve replacement can be safely performed in people aged 80 and older with early benefits on both symptomatic and prognostic ground. Whilst new approaches are advocated to treat this elderly and frail population, data on long-term outcomes are not available.

Methods. We conducted a retrospective analysis of 1870 patients aged 80 and over who underwent first time surgical aortic valve replacement during the period 2000 – 2019. The Kaplan-Meier method was used to calculate survival and comparisons among groups was performed by log-rank test. Cox analysis was used to determine independent risk factors for late mortality.

Results. Patients' mean age was 84 years and 53% were male. Isolated aortic valve replacement was performed in 42% of the patients, CABG (n=956), mitral valve (n=94) or aortic surgery (n=69) were associated in the remaining cases. One hundred eighty-one patients (8%) sustained at least one postoperative complication (reopening for bleeding or tamponade 3%, renal replacement therapy 3%, new cerebral stroke 1.5%). In-hospital mortality was 3.2% in the overall population (60/1870) and 2.2% after isolated aortic valve replacement (18/790). Survival was 90%, 66%, 31%, 14% at 1-year, 5-years, 10-years and 15-years, respectively, and was similar to the expected survival of a sex- and age-matched population (log-rank p=0.96). A complicated postoperative course was an independent risk factor for mortality during the follow-up [hazard ratio 1.32 (1.03, 1.68), p=0.026].

Conclusions. Surgical aortic valve replacement can be performed with an acceptable early mortality rate and provides excellent long-term survival in people aged 80 and older.

Abstract word count: 250

Keywords: aortic valve, aortic valve replacement, aortic valve prosthesis

Introduction

Cardiac surgery has been increasingly performed in octogenarian and older patients during the last decades (1)(2). The initial experiences reported a postoperative mortality up to 17% (3)(4)(5)(6), however, more recent studies reported a progressive reduction of early mortality for these patients (7)(8). Particularly, surgical aortic valve replacement can be nowadays safely performed in patients aged 80 and over with an acceptable in-hospital mortality rate (around 2%) (9)(10)(11) and the provision of improved survival (12) and a satisfactory quality of life at mid-term follow-up (5)(7). Transcatheter techniques have shown similar procedural safety while providing a shorter hospital stay and a quicker recovery (7)(11). These advantages have not translated so far into a better mid-term survival (13), nevertheless, long-term results and the potential impact on the long run of postoperative complications such as acute kidney injury and bleeding, especially in surgical patients (8)(11), or a high incidence of pacemaker implantation and paravalvular regurgitation in patients treated with transcatheter procedures (14)(15), remain undetermined.

No long-term data is available for octogenarian and older patients who underwent surgical aortic valve replacement, for this reason we have reviewed our surgical experience of the last 20 years in order to provide a picture of the survival of this population and to study the risk factors associated with mortality during the follow-up.

Materials and Methods

Ethical statement

Approval was obtained for use of data (Safeguard System approval number SEV/0029, date 24.10.2018). Considering the type of the study involving anonymised and previously collected data, patients' consent was waived.

Population

The internal database of Wessex Cardiothoracic Centre at UHS was searched to identify patients who underwent aortic valve replacement during the period January 2000 – December 2019 using the following criteria.

Inclusion criteria

- Age≥80 years;
- First time sternotomy;
- Associated procedures including CABG, mitral valve surgery, tricuspid valve surgery, aortic surgery;

Exclusion criteria

- Redo procedure (any previous cardiac operation);

A total of 1870 patients fulfilled the criteria.

Study design, data collection and outcomes

This study is a retrospective outcome evaluation from institutional records with prospective data entry collected and used in compliance with institutional data protection and confidentiality policies. The data were collected from the hospital database system, patients records and records of the general practitioners.

The following data were collected:

Preoperative details:

- Age;
- Gender;
- History/diagnosis of systemic hypertension;
- Diabetes Mellitus;
- COPD;
- Smoking history (ex-smoker or active smoker);
- Creatinine>200 µmol/L;
- Previous cerebral stroke;
- Extracardiac arteriopathy;
- Previous acute myocardial infarction;
- NYHA class;
- LVEF;
- Haemodynamic of valve pathology (aortic stenosis, regurgitation);
- Operation status (elective/urgent);
- Logistic EuroSCORE.

Operative data:

- Associated procedures (CABG, MV surgery, TV surgery, aortic surgery);
- Cross-clamp time;
- Cardiopulmonary bypass time.

Postoperative outcomes:

- In-hospital mortality (death before hospital discharge);
- Reopening for bleeding/tamponade;
- Renal replacement therapy/CVVHD;
- New postoperative neurologic deficit (permanent stroke, TIA);
- Deep sternal wound infection;
- Permanent pacemaker implantation (pre-discharge and post-discharge);
- Postoperative hospital length of stay;
- Discharge destination.

Long-term outcomes:

- Survival.

Definitions

The preoperative data collected were as previously defined for EuroSCORE (16). All-cause mortality was considered for survival during the follow-up. Postoperative outcomes (occurred before hospital discharge) were recorded according to the VARC-2 criteria (17). Particularly, new neurologic deficit was coded according to the criteria for "stroke and TIA" (17).

Surgical techniques

All the operations were performed through midline sternotomy. Cardioplegic arrest was achieved with cold blood cardioplegia. Conventional aortic valve prostheses were used in all the cases; a tissue valve was implanted in 99.7% of the patients (1865/1870). Intraoperative TOE has been used routinely in the period 2010 – 2019. All the patients underwent a pre-discharge transthoracic echocardiogram and a clinic follow-up during the first three months since the operation.

Statistical analysis

Continuous variables were presented as mean (SD) or median (1 IQR, 3 IQR). Categorical variables were presented as number (%). Univariable comparisons of preoperative, operative and postoperative variables were performed among the groups using the Student's t-test, Kruskall-Wallis test, or the $\chi 2$ or Fisher's exact test as appropriate.

Survival probabilities, with time starting on the date of surgery, were calculated using the Kaplan–Meier method. Survival probabilities of a sex and age-matched English population were calculated using Kaplan-Meier method and was based on data available on:

https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/datasets/singleyearlifetablesuk1980to2018.

Log-rank test was used to compare survival curves.

A Cox regression analysis, with time starting on the date of hospital discharge, was performed to determine the hazard ratios (HRs) of long-term survival; a backward stepwise model with a significance of $p < 0.15$ was used. The variables included were gender, age, NYHA III-IV, previous myocardial infarction, diabetes mellitus, hypertension, COPD, history of cerebrovascular accident, extracardiac arteriopathy, LVEF<30%, type of haemodynamic dysfunction (aortic valve stenosis or regurgitation), associated procedures, CPB time, Cross-clamp time, period when operation was performed (2000-2009 or 2010-2019), occurrence or at least one postoperative complication OR single complication, pacemaker implantation.

A p-value of ≤ 0.05 was considered statistically significant.

Statistical analyses were performed using the Stat-View Statistical Software Package 5.0 (SAS Institute, Inc., Cary, NC, USA), NCSS 2001 (Number Cruncher Statistical System, Kaysville, Utah) and Stata/MP version 13 (StataCorp, College Station, Texas 77845 USA).

Results

Preoperative characteristics and operative data

During the period 2000 – 2019, 1870 patients aged 80 and over underwent first time surgical aortic valve replacement.

There was a progressive increase in the number of surgical aortic valve replacement procedures with octogenarian and older patients accounting for almost the 30% of the overall population undergoing aortic valve surgery. Table 1 reports the preoperative characteristics of our population; Figure 1 and Supplemental Table 1 detail about patients' characteristics and number of procedures for every 5-year interval time.

Mean patients' age was 84 (SD: 3) years and among them 53% (987/1870) were male. Logistic EuroSCORE was 13.3% (SD: 7.2%). Forty percent of the patients presented with a NYHA class III-IV; admission with advanced heart failure symptoms was more common at the beginning of our study period (2000 – 2004) with 63% of the patients presenting a marked functional limitation compared with the 31% of the cases in the period 2015 – 2019 ($p<0.001$). Similarly, preoperative creatinine> 200 μmol/L was more common in the early period (7%), while its prevalence declined to 3% in 717 patients operated during 2010-2014 and to 1% in 600 patients operated between 2015 and 2019 (Supplemental Table 1).

Isolated aortic valve replacement was performed in 42% of the patients (790/1870), details of the associated procedures and operative times are reported in Table 2.

Early outcomes

The postoperative course before hospital discharge was complicated in 9.6% of the cases. Reopening for bleeding or tamponade was necessary in 57 patients (3%); a new neurologic deficit was reported in 47 patients (2.5%) and among them 28 suffered a new permanent cerebral stroke (1.5%); 57 patients (3.0%) required renal replacement therapy; a permanent pacemaker was implanted in 78 cases (4.1%) before hospital discharge.

Overall in-hospital mortality was 3.2% (60/1870) at a median time of 11 days (3, 30). In-hospital mortality after isolated aortic valve replacement was 2.2% (18/790) at a median time of 14 days (4, 33). The mortality rate decreased significantly over time from 6% (9/150) in the period 2000 – 2004 to 1.5% (9/600) in the period 2015-2019 (p=0.006). Table 3 and Supplemental Table 1.

In 54% of the cases (977/1810), patients were discharged at home while in the remaining cases a further period of rehabilitation, nursing or medical assistance was required. The overall median postoperative length of stay was 10 (8, 15) days (Table 3 and Supplemental table 1).

During the first 6 months there were further 83 deaths among patients who were discharged from hospital for an overall 6-month mortality of 7.6%.

Long-term outcomes

During a median follow-up of 4.6 (3.5, 11.0) years, there were 907 deaths including in-hospital mortality. The survival probabilities at 1-year, 5-years, 10-years and 15-years from the date of surgery were 90% (SE: 0.7%), 66% (SE: 1.2%), 31% (SE: 1.6%) and 14% (SE: 2.0%), respectively (Figure

2). There was no significant difference in survival between the study population and an age- and sex-matched general English population (log-rank test p=0.96), Figure 3.

The survival for patients who experienced at least one postoperative complication (reopening, new neurologic deficit, renal replacement therapy, deep sternal wound infection) was 71% (SE: 3.7%), 46% (4.2%) and 18% (SE: 4.2%) at 1-year, 5-years and 10-years from the date of surgery, respectively. It was significantly lower (log rank test p=0.002) when compared with the survival of patients who had an uncomplicated postoperative course, 92% (SE: 0.7%) at 1-year, 68% (SE: 1.3%) at 5-years, 33% (SE: 1.7%) at 10-years. Similarly, patients who were operated during the period 2000-2009 showed a significantly lower survival compared with patients who underwent surgery during the period 2010-2019: 10-y survival 27% (SE: 1.9%) vs 41% (SE: 2.5%), respectively (log rank test, p=0.002).

Supplemental Figure 1 provides a graphical view of the impact of the occurrence of postoperative complication(s) and the time of surgery on 10-year survival when compared with the expected survival of an age- and sex-matched general English population.

A Cox regression, with follow-up starting at the discharge date, was performed to study independent predictors for late mortality in patients who were successfully discharged from hospital. Alongside co-existent preoperative comorbidities (previous myocardial infarction, extracardiac arteriopathy), a complicated postoperative course (p=0.026; HR 1.32, CI 1.03 to 1.68) and surgery in the first 10 years of the study period (p=0.003; HR 1.25, CI 1.08 to 1.46) were independent risk factors for mortality at the long-term (Table 4 and Table 5).

Discussion

Nowadays cardiac surgery can be performed safely in octogenarians and older patients. Several studies reported favourable early and mid-term outcomes across all the spectrum of cardiac diseases and surgical procedures including CABG, aortic valve and aortic surgery, mitral valve surgery and emergency operation (9)(10)(11)(18)(19).

Aortic valve surgery represents one of the most common operations undertaken in people aged over 80 years as, in our experience, they accounted for more than one fourth of the global cases of surgical aortic valve replacement. In these patients, we have found an in-hospital mortality rate of 3.2% over a 20-year period with a progressive and significant reduction of the mortality rate across the years (1.5% in the last period). Our data confirmed recent findings reporting an early mortality rate of 2% in octogenarian and older patients undergoing surgical aortic valve replacement (9)(10)(11). Alongside this evidence of procedural safety, other studies have highlighted that the mid-term survival of elderly patients with aortic valve stenosis is dramatically improved by aortic valve replacement (68% surgery vs. 22% medical therapy at 5-years) (12) and that this longer life-expectancy is characterised by an acceptable quality of life and independent functional status (6).

We have further explored the long-term outcome of these patients and reported a survival rate of 31% at 10-year and 14% at 15-year follow-up. No long-term data from similar surgical populations were available for a comparison, however, we found that the 10-year survival probability of our patients was not different from the survival rate of an English age- and sex-matched population.

Preoperative status and comorbidities play a major role in determining long-term survival. In more recent years, people aged 80 and over underwent surgery in a better functional status and less frequently presented with severe chronic kidney dysfunction and history of previous myocardial infarction, nevertheless the population operated in the last period of observation had a significantly lower mean logistic EuroSCORE value. Reasons for this shift in practice lie probably in an earlier referral driven by a new awareness of the benefits of surgery also in elderly people, the confidence in surgical results and the availability of alternative interventional procedures associated with an established activity of the Heart Valve Team in evaluating frail, high risk and elderly patients. These changes in preoperative management and the possibility of undertaking a cardiac operation before the development of advanced heart failure symptoms, translated in a lower early mortality and a better long-term outcome.

Despite a low perioperative death rate, the first postoperative months were burdened by a significant mortality. This represents a common finding (5)(6)(18) and underlines the vital importance of preserving the already reduced functional reserves of frail and comorbid patients. Prolonged operative times has been extensively associated with perioperative mortality and morbidity in octogenarians undergoing cardiac surgery (3)(8)(20). A complicated postoperative course may also expose these elderly patients to a difficult and prolonged recovery and has been associated with a worse outcome during the first year since surgery with a mortality at 1-year of 67% in patients requiring postoperative dialysis and 35% in patients suffering perioperative cerebral stroke (8). In our experience, any deviation from an uncomplicated postoperative course was significantly associated with a worse survival at long-term follow-up. Particularly, new permanent cerebral injury after surgery was an independent predictor of long-term mortality, as it can affect the postoperative recovery and patients' quality of life and independence.

We recorded a lower in-hospital mortality and a better long-term survival in patients operated during the period 2010-2019. There were no significant technical changes in the intraoperative management of these patients throughout the study period; full sternotomy was the common surgical access and conventional stented prostheses were used. Noteworthy, the last 10 years have been characterised by the establishment and the progressive growing of a transcatheter aortic valve implantation programme.

The implementation of a TAVI programme has been associated with an increase in overall aortic valve intervention and surgical aortic valve replacement activities (21)(22). Similarly to our findings, a French administrative hospital-discharge database showed that the introduction of TAVI procedures translated in an earlier referral with an improved patients' preoperative clinical profile (22).

In French and German nationwide experiences the number of TAVI procedures is now exceeding the surgical activity (22)(23) and this is particularly evident in patients aged over 80 years (22). A less invasive procedure can undoubtedly be associated with a lower degree of postoperative morbidity especially in high-risk elderly patients (11). Transcatheter procedures have been associated with a lower risk of bleeding and postoperative renal failure compared with surgical aortic valve replacement (11) and, according to our findings, this could translate in a potential benefit on survival. However, several observational studies have failed to demonstrate, so far, a difference in early mortality after TAVI vs surgical aortic valve replacement in elderly patients (11)(22)(23). No data are available of mid- and long-term outcomes after transcatheter procedures in low-risk octogenarians and, generally, the impact of prosthesis degeneration and paravalvular regurgitation has not been investigated on the long-term due to the inclusion of cohort of patients with reduced life-expectancy (survival$<$30% at 5-years) (24).

On these bases, in our practice, advanced age alone does not represent a sufficient factor to favour a transcatheter procedure over conventional surgery. In our experience, a better preoperative functional status and the careful selection of surgical candidates, while offering transcatheter procedures to higher-risk patients, were the two most important factors that ultimately led to a reduced incidence of postoperative complications, lower early mortality, better late outcomes and the opportunity to offer an interventional treatment (conventional surgery OR transcatheter procedure) to a wider population of elderly patients.

Within the limitations of a single-centre retrospective evaluation, we have reported in a large population an historical view of long-term outcomes of patients aged 80 and older who underwent surgical aortic valve replacement. This evidence represents a reliable picture of the contemporary surgical outcomes of aortic valve surgery in elderly patients and could represent a benchmark for the forthcoming long-term results of non-surgical interventional treatment of aortic valve disease.

Conclusions

Conventional surgical aortic valve replacement during the last 20 years provided a safe and successful treatment for aortic valve disease in elderly patients with an in-hospital mortality that in more recent years was for both isolated and combined procedures below 2%. An early surgical referral before the development of advanced signs of heart failure and the availability of alternative interventional procedures and a careful patients' selection, contributed to a progressive and significant reduction of postoperative complications and periprocedural mortality, and led to an improved long-term survival.

Conflict of interest: none declared

Funding statement: no fund

Authors contribution:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work;
2. Drafting the work or revising it critically for important intellectual content;
3. Final approval of the version to be published;
4. Agreement to be accountable for his/her contributions of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved.

PGM: 1-2-3-4

SL: 1-2-3-4

SG: 1-2-3-4

MK: 1-2-3-4

SKO: 1-2-3-4

Figures

Figure 1. Trend in aortic valve replacement in patients aged 80 years and over during the period 2000 – 2019.

Figure 2. Kaplan-Meier survival curve, with starting point on the date of surgery, for the overall population who underwent surgical aortic valve replacement.

Figure 3. Survival curves of study population patients aged [80 – 90] years and of an age- and sex-matched general English population (log-rank test p=0.96) At 10-year follow-up, observed survival was 33% (SE: 1.6%) and expected survival 33% (SE: 1.1%). Time from surgery was considered for the observed survival.

[https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/datasets/singleyearlifetablesuk1980to2018].

Tables

Table 1. Preoperative characteristics

Variables	Mean (SD) or Number (%)
Number of patients	1870
Gender M/F	987/883 (53%/47%)
Age (y)	84 (SD: 3)
Previous myocardial infarction	151 (8%)
NYHA class III-IV	739 (40%)
Diabetes Mellitus	178 (9%)
Hypertension	1223 (65%)
Smoking history	1015 (54%)
COPD	243 (13%)
Creatinine>200 µmol/L	51 (3%)
Cerebral stroke	187 (10%)
Extracardiac arteriopathy	125 (7%)
Aortic valve stenosis	1764 (94%)
LVEF<30%	94 (5%)
Acute infective endocarditis	12 (1%)
Emergency/salvage operation	46 (2%)
Logistic EuroSCORE %	13.3 (SD: 7.2)

Table 2. Operative data

Variables	Mean (SD) or Number (%)
Isolated Aortic Valve replacement	790 (42%)
Associated CABG • Mean number of grafts	956 (51%) • 1.96 (SD: 0.93)
Associated Mitral Valve surgery • Mitral Valve repair • Mitral Valve replacement	94 (5%) • 52 (3%) • 42 (2%)
Associated Tricuspid Valve repair	28 (2%)
Associated aortic surgery	69 (4%)
CPB times (minutes)	101 (SD: 40)
Crossclamp times (minutes)	73 (SD: 28)

Table 3. Postoperative data

Variables	Median [IQR] or Number (%)
Complications	181/1870 (9.6%)
Re-opening for bleeding or tamponade	57 (3.0%)
Continuous veno-venous haemodialysis	57 (3.0%)
Neurologic deficit	47 (2.5%)
• Permanent cerebral stroke	• 28 (1.5%)
• Transient ischaemic attack	• 19 (1.0%)
Deep Sternal Wound Infection	9 (0.5%)
Permanent pacemaker implantation	123 (6.5%)
• Pre discharge	• 78 (4.1%)
• Post discharge	• 45 (2.4%)
Length of stay (days)	10 (8, 15)
Discharge destination	
Home/Rehabilitation	977 (54%) / 833 (46%)
In-Hospital Mortality	
Overall	3.2% (60/1870)
Isolated Aortic Valve replacement	2.2% (18/790)
Follow-up (years)	4.6 (3.5, 11.0)

Table 4. Predictors of late mortality among survivors by Multivariable Cox analysis with time starting on discharge date and backward stepwise variables selection [Schoenfeld test p=0.38].

Variables	**p; HR (95% lower, 95% upper)**
Gender male	0.001; 1.26 (1.09, 1.43)
Age (y)	<0.001; 1.07 (1.05, 1.10)
NYHA III-IV	0.14; 1.11 (0.97, 1.28)
Previous MI	0.001; 1.43 (1.15, 1.78)
Extracardiac arteriopathy	<0.001; 1.68 (1.31, 2.14)
CPB time (minutes)	0.008; 1.006 (1.001, 1.010)
Crossclamp time (minutes)	0.008; 0.992 (0.986, 0.998)
Operation date	
(2010 – 2019 reference)	
2000 – 2009	0.003; 1.26 (1.08, 1.46)
Postoperative complication(s)	0.026; 1.32 (1.03, 1.68)

Table 5. Predictors of late mortality among survivors by Multivariable Cox analysis with time starting on discharge date and backward stepwise variables selection including each complication individually [Schoenfeld test p=0.57].

Variables	**p; HR (95% lower, 95% upper)**
Age (y)	<0.001; 1.08 (1.05, 1.10)
Gender male	0.001; 1.27 (1.10, 1.47)
NYHA III-IV	0.12; 1.19 (0.97, 1.29)
Previous MI	<0.001; 1.45 (1.16, 1.80)
Extracardiac arteriopathy	<0.001; 1.69 (1.33, 2.16)
LVEF<30%	0.12; 1.25 (0.94, 1.66)
CPB time (minutes)	0.016; 1.005 (1.001 – 1.010)
Crossclamp time (minutes)	0.011; 0.992 (0.986, 0.998)
Operation date (2010 – 2019 reference) 2000 – 2009	 0.037; 1.25 (1.08, 1.45)
Postoperative cerebral stroke	<0.001; 2.75 (1.69, 4.46)
Renal replacement therapy	0.075; 1.65 (0.95, 2.87)

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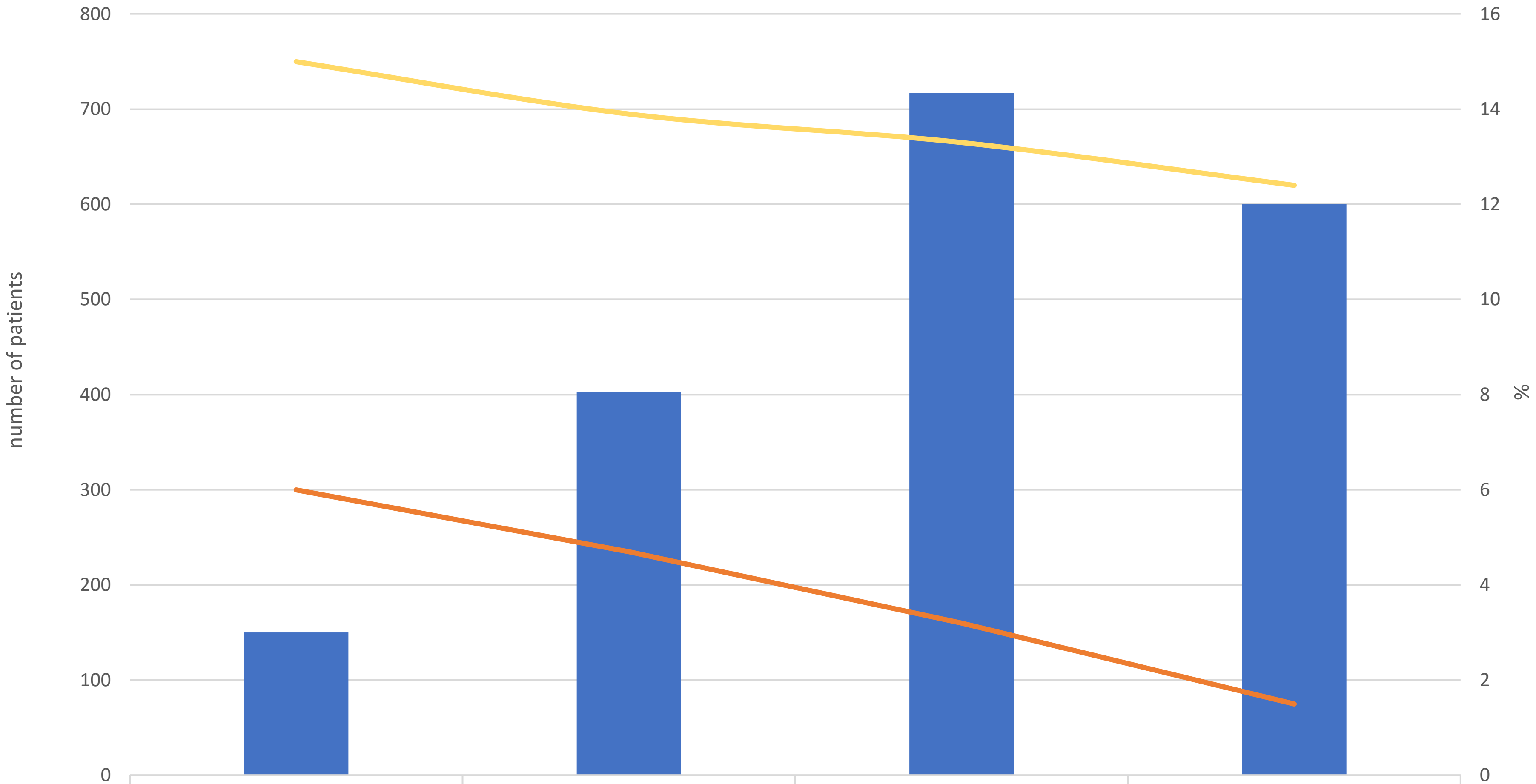
Figure 1



	2000-2004	2005-2009	2010-2014	2015-2019
number of patients	150	403	717	600
in-hospital mortality (%)	6	4,7	3,2	1,5
LogES (%)	15	13,9	13,3	12,4

Figure 2

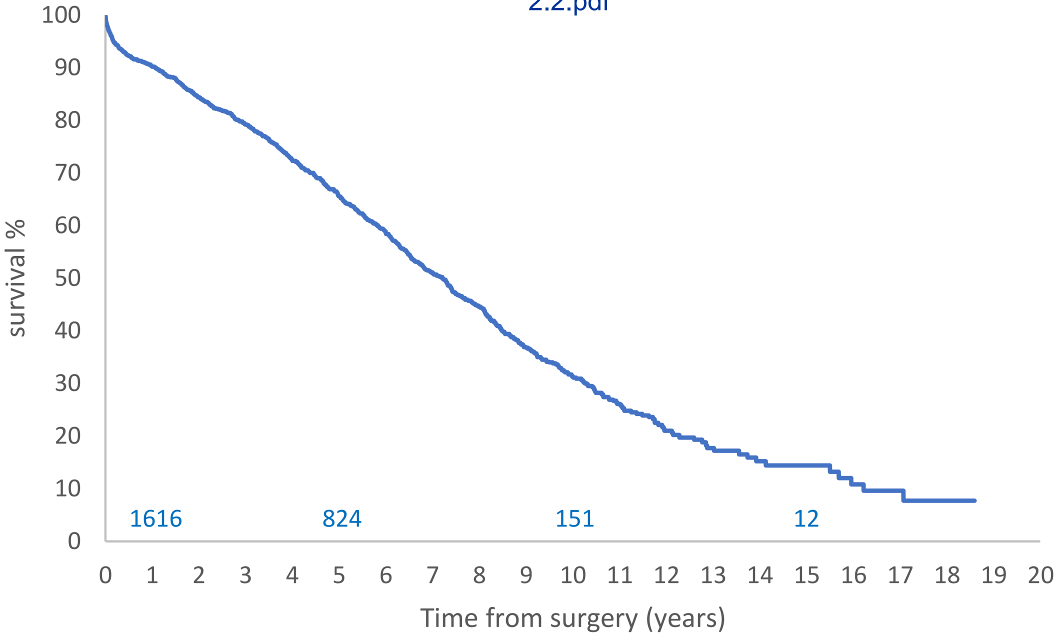

100
90
80
70
60
50
40
30
20
10
0
survival %
1616
824
151
12
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Time from surgery (years)

Figure 3

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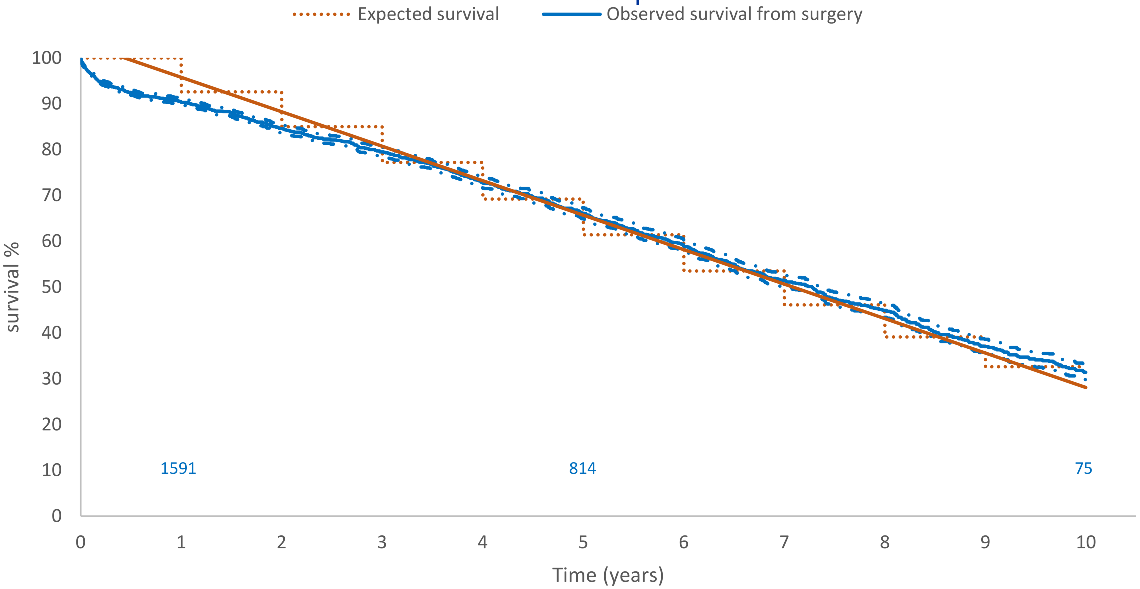

Supplementary Figure 1

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