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Surgical aortic valve replacement in the era of transcatheter aortic valve implantation - A review of the UK national database

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ABSTRACT

Objectives - To date the reported outcomes of aortic valve replacement (AVR) are mainly in the settings of trials comparing it with evolving transcatheter aortic valve implantation (TAVI). We set out to examine characteristics and outcomes in people who underwent AVR reflecting a national cohort and therefore 'real world' practice.

Design - Retrospective analysis of prospectively collected data of consecutive people who underwent AVR with or without coronary artery bypass graft (CABG) surgery between April 2013 and March 2018 in the UK. This included elective, urgent and emergency operations. Participants' demographics, pre-operative risk factors, operative data, in-hospital mortality, post-operative complications and effect of the addition of CABG to AVR were analysed.

Setting - 27 (90%) tertiary cardiac surgical centres in the UK submitted their data for analysis.

Participants - 31,277 people with AVR were identified. 19,670 (62.9%) had only AVR and 11,607 (37.1%) had AVR+CABG.

Results - Mortality for isolated AVR was 1.9% (95% CI: 1.6-2.1%) and was 2.4% for AVR+CABG. Mortality by age category for AVR only were: <60 years=2.0%, 60-75 years=1.5%, >75 years=2.2%. For AVR+CABG these were; 2.2%, 1.8% and 3.1%. For different categories of EuroSCORE, mortality for AVR in low risk people was 1.3%, in intermediate risk 1% and for high risk 3.9%. 74.3% of the operations were elective, 24% urgent and 1.7% emergency/salvage. The incidences of re-sternotomy for bleeding and stroke were 3.9% and 1.1% respectively. Multivariable analyses provided no evidence that concomitant CABG influenced outcome. However, urgency of the operation, poor ventricular function, higher EuroSCORE and longer cross clamp and cardiopulmonary bypass times adversely affected outcomes.

Conclusions - Surgical AVR±CABG has low mortality risk and a low level of complications in the UK in people of all ages and risk factors. These results should inform consideration of treatment options in people with aortic valve disease.

Strengths and limitations of this study

- This is a large study of consecutive participants who have undergone aortic valve replacement ± coronary artery bypass graft surgery in the UK, reporting contemporary outcomes.
- This study includes people of all age groups and risks factors, and elective as well as urgent and emergency operations.
- The results are of in-hospital mortality and complications and longer term follow-up data is not available.

BACKGROUND

Aortic valve disease, especially aortic stenosis affects 5% of the population and 3.9% of those between the ages of 70 and 79 and nearly 10% of those above the age of 80.[1] Severe aortic stenosis when untreated has a risk of death of 50% at 2 years.[2] Conventionally the gold standard of treatment has been surgical aortic valve replacement (AVR). However, the role of transcatheter aortic valve implantation (TAVI) has evolved in recent years. TAVI was first introduced in 2002, initially being performed in high risk inoperable patients.[3] The original Placement of Aortic Transcatheter Valves (PARTNER) trial demonstrated a significant reduction in mortality, repeat hospitalisation and cardiac symptoms compared to inoperable patients who had only medical therapy.[4] The original PIVOTAL study also demonstrated significantly higher survival at one year in high risk patients who underwent AVR.[5]

The role of TAVI is being extended to lower risk and younger patients based on recent trials comparing AVR with TAVI.[6,7] Several studies suggest there has been a change in demographics and types of surgical valves used since the advent of TAVI.[8–10] There has been a trend of increased use of tissue valves and a decrease in the use of mechanical valves in recent years.[11] This may be due to the evolution of TAVI practice whereby younger patients can have a TAVI valve with the view that they have another TAVI valve in the future when the tissue valve or TAVI has deteriorated, so called valve-in-valve TAVI.[12,13]

The series in the literature reporting outcomes of AVR are unit based and with small cohorts.[9,14] Also, people with aortic valve disease are given information about the outcomes of AVR which may be out of date and incorrectly extrapolated from smaller studies. There is a lack of contemporary national data to assess the outcomes of AVR (mortality and complications), and to demonstrate the trend in use of prosthetic valves which would inform people with aortic valve disease better. There are some perceived complications of surgery that may be understood by referring general practitioners and cardiologists to be prohibitive risks for surgery.

In order to inform practitioners, people with aortic valve disease and the cardiac surgical community, we set out to examine the results of contemporaneous AVR in a

multi-centre study of UK cardiac surgical units, in the era of TAVI. In addition, we summarise and interpret some of the more recent trials on the management of aortic valve disease.

METHODS

Data

This is an analysis of prospectively collected data of people who underwent AVR +/- coronary artery bypass graft (CABG) surgery between April 2013 and March 2018 in the UK and Republic of Ireland. Anonymised data were submitted to the Society for Cardiothoracic Surgery of Great Britain & Ireland (SCTS) for 27 of the 30 units and then stored in a secure database.

Only participants who had had first time surgery, AVR +/- CABG were included. All participants immaterial of their risk for surgery, people of all age groups and risk factors were included. Those who required other concomitant procedures like replacement of parts of the aorta, aortic root enlargement, other valve procedures and redo surgery were excluded.

Pre-operative risk factors and operative features

Baseline demographic data; significant past medical history such as diabetes, renal dysfunction, hypertension or stroke; predominant aortic valve pathology (stenosis or regurgitation or mixed valve disease) and preoperative left ventricular ejection fraction (LVEF) were collected. Logistic EuroSCORE was collected as well as EuroSCORE II where available. The latter was only used since 2017 and therefore not available for all participants. Logistic EuroSCORE was divided into three categories: <3%, 3-6%, >6%.

LVEF was divided into three categories: good (EF>50%), moderate (EF 30-50%) and poor (EF<30%). Operative data including operative urgency: elective, urgent and emergency/salvage were recorded. Elective was defined as when the person was admitted from home, urgent meaning that the person was admitted with an urgent condition and required surgery during the same hospital admission, emergency and salvage meaning that surgery was required within 24 hours of admission and/or the person was in extremis. Other parameters including cardiopulmonary bypass (CPB) time,

cross clamp (CCT) time, type of valve implanted as well as concomitant CABG surgery performed were also collected.

Postoperative outcomes

Postoperative complication data were collected with the main focus being in-hospital mortality, new stroke, return to theatre for bleeding, deep sternal wound infection and duration of postoperative hospital stay.

Statistical analysis

Once the records for all participants were collated and the data cleaned, each factor was summarised using descriptive methods. Categorical variables are presented as N (%) and continuous variables are presented as median (IQR). New strokes were recoded to be either no stroke or any cerebrovascular accident (transient or permanent). The natural log of post-operative length of stay (days) was used due to positive skewed distribution of this variable. Univariate models were used, logistic regression for binary outcomes and linear regression for continuous outcomes, to assess the impact of the key explanatory variables. In these models, a two-tailed p-value of <0.05 was considered significant. The population analysed included all the participants with data collected, with results checked in the subset who had AVR only (without CABG). Building on this, a multivariable model with all key variables in the model to assess which had the most impact on each of the outcomes was created. Stata/MP 15.1 (StataCorp LLC, Texas, USA) was used for all analyses.

Patient and public involvement

Patients and public were involved in the original design of the database.

Ethics

This data is ordinarily submitted to National Institute of Cardiovascular Outcome Research (NICOR) for which local and national Caldicott guardian approvals have been obtained. The data are validated by the surgical teams and their database

managers/audit officers. For the current study a further approval from the Caldicott Guardian was obtained.

RESULTS

Descriptive analysis

In total 31,277 patients were included. Of these, 19,670 (62.9%) had only AVR and 11,607 (37.1%) had AVR+CABG. There were 14.4% below the age of 60, 46.9% between 60 to 75 and 36.7% older than 75 years with 7.9% missing age data. There were 1.9 times more males than females (10.3% missing).

Regarding pre-operative risk factors, 75.2% had good LVEF, 17.3% had moderate and 4.3% had poor LVEF. 74.3% of the operations were elective, 24% were urgent and 1.7% were emergency or salvage operations.

Logistic EuroSCORE had a median of 1.83 with an IQR of 0.06-6.0. The median EuroSCORE II was 1.95 (IQR 0.67-4.8) albeit with 56.5% with missing data, as this was introduced into the database in 2017. The median CPB time was 104 minutes (IQR 82-135) and CCT was 79 minutes (IQR 61-101).

For valve implant replacement type, 70% had a tissue valve, 12.2% a mechanical valve and 0.2% had homograft or autograft valves. For 17.3% the entry for valve type was unclear. The ratio of mechanical implant to bioprosthetic implant use has remained stable over time.

Overall mortality was 2.4% (95% CI: 2.2-2.6%) and mortality for isolated AVR for all participants was 1.9% (1.6-2.1%). The mortality figures analysed for different age ranges and for categories of EuroSCORE are shown in Table 1.

Overall, 3.9% (3.6% in AVR only) of participants had re-sternotomy for post-operative bleeding or tamponade, 0.04% (0.06% in AVR only) had re-operation for valvular problems (significant paravalvular leak and early endocarditis), 0.7% (0.6% AVR only) had re-operation for other cardiac problems, 0.2% (0.15% for AVR only) had rewiring of sternum for sterile wounds and 0.14% (0.06% for AVR only) had re-wiring of sternum for infection. Transient ischaemic attack occurred in only 0.6% and 1.1% had a stroke (no missing data).

Median post-operative length of stay was 7 days (IQR: 6-11) in those with AVR only and 8 days (IQR: 6-12) in all patients.

The number of bypass grafts was not analysed due to concerns about inconsistent reporting of data describing the number of grafts.

When comparing the two subsets of patients, the characteristics of those with AVR alone were broadly similar to those with AVR+CABG. In AVR alone there were more people aged <60 years (19.3% vs 6.2%), but less people were older than 75 (30.1% vs 43%). A higher proportion of those with AVR+CABG were male (68% vs. 54%). Bypass time was an average of 37 minutes shorter and CCT 27 minutes in the AVR alone group. Amongst those with only AVR the mechanical valve usage was greater, at 16% vs 7%.

Regression analysis

Univariate

Taken in isolation, all pre-operative risk factors were associated with an increased odds of death, as was addition of CABG. The same pattern was observed when analysing the need for re-operation or surgery, with all explanatory variables indicative of a worse outcome without taking into account any others. For new stroke only age, EuroSCORE, operative urgency, ejection fraction, and cumulative bypass and cross clamp times affected a negative outcome (but not gender), as did CABG. All factors predicted a longer postoperative length of stay, including CABG.

As a sensitivity analysis, age categories were also assessed. When included as a continuous variable, age was significant both on its own and in all the multivariable models. All participants were categorised into <60, 60-75 and >75 years of age. Those 60-75 were at a lower odds of death in comparison to those <60 (OR 0.71, 95% CI 0.53-0.95, P=0.021) with no difference in those >75 (OR 1.09, 95% CI 0.82-1.45) in the AVR alone group. These findings were different in the AVR+CABG group, with no significant difference in those 60-75 (OR 0.81, 95% CI 0.64-1.03) but an increased risk in those >75 (OR 1.09, 95% CI 1.12-1.76, P=0.004).

Multivariable Analyses

Analysis of postoperative outcomes using multivariable models including all pre-operative and operative factors are shown in Table 2. This demonstrated that age (OR 1.03 (95% CI 1.02-1.04), P<0.001), moderate ejection fraction (OR 1.48 (95% CI 1.18-1.85), P<0.001), poor ejection fraction (OR 1.90 (95% CI 1.36-2.69), P<0.001), logistic EuroSCORE (OR 1.02 (95% CI 1.02-1.03), P<0.001), urgent operation (OR 1.63 (95% CI 1.30-2.00, P<0.001), emergency surgery (OR 6.87 (95% CI 4.70-10.16), P<0.001) and longer CPB times affected mortality (OR 1.02 (95% CI 1.01-1.02), P<0.001).

When all other variables were taken into account CABG was not significantly associated with an increase in the risk of death (OR 1.15 (95% CI 0.93-1.42), P=0.20).

Older age, (OR 1.01 (95% CI 1.00-1.01), p<0.006), longer CPB time (OR 1.00 (95% CI 1.00-1.01), P<0.001), urgent (OR 1.26 (95% CI 1.08-2.00), P<0.002) and emergency surgery (OR 2.22 (95% CI 1.51-3.26), P<0.001) were significant factors in identifying people requiring return to theatre for bleeding. Again, CABG did not affect the odds of returning to theatre (OR 1.07 (95% CI 0.93-1.24), P=0.33).

Factors affecting stroke were age, (OR 1.02 (95% CI 1.01-1.03), P<0.001), emergency (OR 7.65 (95% CI 5.00-11.70, P<0.001) or salvage surgery (OR 4.38 (95% CI 1.47-13.1) P=0.008), and CPB times (OR 1.00 (95% CI 1.00-1.01), P<0.001). As in the other outcomes, addition of CABG did not affect the outcome (OR 1.12 (95% CI 0.88-1.42), P=0.37).

Age, male gender, moderate and poor ejection fraction, operative urgency, higher logistic EuroSCORE, and cumulative bypass time significantly all affected post-operative length of stay.

DISCUSSION

This study reports contemporary results of AVR and AVR+CABG in the UK, reflecting real world practice, reporting an overall mortality of 1.9% and 2.4% respectively. We have shown a low mortality and complication rate for all comers following surgery in people requiring AVR or AVR+CABG. The complications were low with 3.9% re-sternotomy for bleeding, 0.04% re-operation for valvular problems and 1.1% stroke. Surprisingly, having accounted for other risk factors, addition of CABG did not adversely affect the outcomes.

The strengths of the study include its large number of participants, no exclusion of urgent and emergency/salvage cases, and inclusion of all risk participants. The limitations are that three centres were unable to take part, possible coding errors in using large databases, lack of detailed echocardiographic data on valve annular size and presence or absence of pre-operative infective endocarditis which can adversely affect outcomes. In addition, the results are in-hospital mortality and complications and the database lack longer follow-up information.

Data from the current study are consistent with other large international studies. Data from the US Society of Thoracic Surgeons (STS) database demonstrated in-hospital mortality for isolated AVR of 2.5% and incidence of stroke of 1.5%.[15] A recent analysis of the Japanese Cardiovascular Surgery database which assessed the outcomes of patients undergoing AVR over a 8 year period has demonstrated a similar in-hospital mortality of 2%.[16] They also demonstrated a reduction in mortality over time, despite increasing surgical risk.

We had set out to analyse the results of AVR in the UK to inform practitioners treating people with aortic valve disease and inform people with this condition in an era where other therapies for management of aortic valve disease are evolving with expanding indications. Although the current study did not examine people who received TAVI, we discuss the various trials of AVR and TAVI reported in the context of the literature and compare them with the results of the current study.

In Tables 3-5, the demographics, procedural details and outcomes of the current study are compared with the respective sub-groups of the published trials. Table 5 shows low mortality and complication rate in the participants of this study following surgery in people who required AVR or AVR+CABG. The trials comparing AVR and TAVI have enrolled and classified patients according to the risk of surgery, in particular the more recent trials.[6,7] The most commonly used surgical risk stratification score is the Society of Thoracic Surgery risk score (STS), although this scoring system has been validated in the US population. We have used EuroSCORE and shown that mortality is low in all categories of risk.

There are several recent trials comparing AVR with TAVI. A meta-analysis of six of these trials performed by Barili and colleagues reported that mortality was affected by

the treatment modality with a time-varying effect: TAVI was related to better survival in the first months after implantation whereas, after 40 months, it was a risk factor for all-cause mortality.[17] The NOTION trial, which compared outcomes of patients estimated to have low surgical risk who underwent either TAVI or AVR demonstrated similar early mortality results, with mortality of 2.1% in TAVI group vs 3.7% in the AVR group, p=0.38.[18] The PIVOTAL trial of low risk patients also reported similar results between those who underwent TAVI compared to AVR, with early mortality of 0.5% in TAVI group and 1.3% in AVR.[7] In addition, the 5 year results of the PARTNER 2 study, comparing TAVI vs AVR in intermediate surgical risk demonstrated no significant difference in the incidence of death or stroke at 5 years following AVR or TAVI.[19] The mortality in the intermediate EuroSCORE risk category of the current study was 1.0% for AVR only and 0.9% for AVR+CABG. PARTNER 3 however demonstrated significantly lower mortality in the TAVI group compared to AVR (1% vs 3.3%, P=0.01) at one year.[6] An observational study of 7618 patients comparing AVR with TAVI at 5 years showed however that in a real world population with low and intermediate risk, AVR was associated with lower mortality and major adverse cardiac events, although this was with first generation TAVI devices.[20]

Role of co-existent coronary artery disease and its management

60% of patients with aortic valve disease undergoing AVR and 65% of those undergoing TAVI have coexisting coronary artery disease.[21] In our series, 37% had co-existent coronary artery disease and underwent concomitant CABG. The addition of CABG did not adversely affect outcomes. In PARTNER 2, although both groups had a similar number with coexistent coronary artery disease, 14.5% of the AVR group had concomitant CABG compared to 3.9% of the TAVI group who had percutaneous intervention (Table 4).[22] AVR may therefore be the preferred treatment modality in those with aortic stenosis and multivessel coronary artery disease requiring revascularisation and is the standard of care in those in younger age groups.

Treatment of coronary artery disease in TAVI patients may require more than one hospital admission and can often result in incomplete revascularisation and its consequent increased morbidity and mortality. A meta-analysis by Sankaramangalam and colleagues, demonstrated that whilst there was no increase in mortality in patients

with coronary artery disease who underwent TAVI at 30 days, there was a significant increase in mortality at one year following TAVI in these patients.[23] The economic costs of readmission after TAVI have been demonstrated to be higher than in those who are readmitted after surgery and so untreated coronary disease which later requires readmission will have cost implications.[24,25] Surgery has the advantage of addressing all the pathology with one operation.

Durability and choice of prosthetic valves

In choosing the technique of treatment for aortic valve disease, life expectancy of the person and durability of the valve need to be considered. Ideally, the prosthetic valve should be durable for the person's lifetime. Both of these are related to person's age. In the UK a 50 year old female has a life expectancy of 34 years and a 70 year old male a life expectancy of 14 years.[26]

The durability of bioprosthetic valves is well documented in the surgical literature and is inversely proportional to person's age. Structural valve deterioration (SVD) has been demonstrated to increase exponentially beyond 10 years following surgery.[27,28] Considering the UK life expectancy [26], a 70 year old male has a 5% risk of re-operation and a 50 year old female has a 30% chance of needing a second operation. Although long term data regarding the durability of TAVI valves is awaited, the 5 year results of the PARTNER 2 trial demonstrated that the incidence of SVD in the TAVI group was significantly higher than in the AVR group.[19] However, a sub-study of the NOTION trial looked at SVD up to 6 years suggested no significant difference between the AVR and TAVI.[29]

The durability of tissue valves in surgery are well documented.[27] Bagur and colleagues have introduced the concept of valve durability: life expectancy ratio.[30] At best, the TAVI valve which is a tissue valve will have the longevity of the best surgical bioprosthetic valves, excluding the deleterious effects of crimping with TAVI valves.[31] A systematic review of observational data by Foroutan and colleagues looking at 8914 patients who underwent TAVI with a follow-up of 1.5 - 5 years showed SVD incidence of 0-1.34 per 100 patient-years with a pooled incidence of 28.08 per 10,000 patient-years.[32] Of those with SVD, 12% underwent re-intervention.

Surgery has the advantage of offering the patient a mechanical or a bioprosthetic valve. The option of a mechanical valve which is only available in surgical AVR should not be overlooked especially in younger people. In the current study, we have shown a fairly consistent ratio of tissue to mechanical valve use. However, the reported literature shows that the number of mechanical valve implantations has reduced in comparison to bioprosthetic valves.[10] Mechanical valves are durable, with one group reporting 6.9% reintervention rate at 15 years versus 12.1% in those who underwent surgery with a bioprosthesis.[33] For this reason, it has been the most commonly considered prosthesis in those under the age of 60, as in our study where 60.2% of participants <60 years had a mechanical valve. Mechanical valves have the disadvantage of requiring anticoagulation, although, newer generations require a lower level of anticoagulation.[34] Whilst mechanical valves are more durable, this has to be balanced against the greater risk of bleeding.[33] At 15 years follow up, Chiang and colleagues also demonstrated no significant difference in survival and stroke between patients who underwent AVR with mechanical vs bioprosthetic valve.[33] Another group demonstrated in the 50-70 year old cohort that survival at 5 years was higher in patients who had undergone AVR with mechanical valve vs bioprosthesis and also demonstrated similar freedom from major bleeding events.[35]

Paravalvular regurgitation and pacemaker implantation

There are several complications associated with TAVI and less with AVR which affect short and long term outcomes. These include paravalvular regurgitation and conduction abnormalities requiring new pacemaker implantation. In the current study less than 0.04% required surgery for paravalvular regurgitation.

In the earlier trials, moderate to severe paravalvular regurgitation was reported in more than 10% of TAVI patients.[4,36] With advances in TAVI technology, this has decreased to approximately 3.5%, however mild paravalvular regurgitation persists in up to 30% of the patients undergoing TAVI compared to 3% in AVR.[6,7] The progression of mild paravalvular regurgitation in AVR has not been studied extensively. In those with mild paravalvular leak, very few are noted to have progression of paravalvular regurgitation.[37] In TAVI patients however, even mild degrees of regurgitation have been shown to have an impact on long term mortality.[38] Padang and colleagues demonstrated

that mild paravalvular leak in both AVR and TAVI patients had no influence on survival in those with high (>8) STS score, however, it was associated with poorer survival in those with lower STS score.[39]

The development of conduction abnormalities and requirement for permanent pacemaker implantation in patients following TAVI and AVR also needs to be considered. New pacemaker was inserted in 1.6% of the participants of the current study. The incidence after AVR is reported between 2 and 7% compared to 6-34% following TAVI.[6,7,40,41] Pacemaker implantation can have deleterious effects on left ventricular function and cause lead induced tricuspid regurgitation resulting in right heart failure, both of which are associated with poor outcomes.[42–44]

Bicuspid aortic valve and aneurysm of the aorta

A significant number of patients requiring AVR have bicuspid aortic valve, which has an incidence of 1-2% in the general population and may present with aortic valve stenosis, regurgitation and ascending aortic aneurysm. The type of native aortic valve is not recorded in the database of our study. Bicuspid aortic valve anatomy, larger annular size, bulky and asymmetric leaflet calcification and dilated ascending aorta all pose technical challenges to TAVI which are not prohibitive risk factors for surgery. BAV may be present in up to 30% of patients undergoing surgical AVR.[45] In fact, associated pathology of aneurysms of the aortic root and ascending aorta can be treated at the time of AVR with little additional risk.[46] People with bicuspid aortic valve disease often present at a younger age than those with tricuspid valve. In GARY (the German Aortic Valve Registry), there was an increased incidence of residual aortic insufficiency in the bicuspid group after TAVI compared to the tricuspid aortic valve group. [47,48]

European guidelines recommend discussing people with aortic valve disease in a multi-disciplinary setting referred to as Heart Team, comprising of a surgeon, a non-interventional and an interventional cardiologist.[49] This will allow the best treatment option to be put forward to the person.

CONCLUSIONS

Surgical AVR with and without CABG has low mortality risk and a low level of complications in the UK in people of all ages and risk factors. Our study provides real world experience of surgical results to improve understanding of the risks of surgery and decision making in a multi-disciplinary team (MDT) setting with Heart Team. The results of this study can be utilised by people with aortic valve disease, referring general practitioners, physicians, surgeons and policy makers. Future studies need to address long term follow-up including factors like quality of life which are currently not collected by the specialist centres.

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Wythenshawe Hospital, Manchester

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Ethical approval: Anonymised data were submitted to the Society for Cardiothoracic Surgery of Great Britain & Ireland (SCTS) for 27 of the 30 units and then stored in a secure database. This data is ordinarily submitted to National Institute of Cardiovascular Outcome Research (NICOR) for which local and national Caldicott guardian approvals have been obtained. A further approval from the Caldicott Guardian was obtained in 2020.

Data sharing: Requests on data sharing can be made by contacting the corresponding author. Data will be shared after review and approval by the authors and terms of collaboration will be reached together with a signed data access agreement.

The corresponding author (MJ) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. The manuscript is read and approved by all authors.

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Tables

Table 1. Mortality (%) for different categories of age and EuroSCORE

Age (years)	AVR	AVR+CABG
<60	2.0	2.2
60-75	1.5	1.8
>75	2.2	3.1
EuroSCORE	**AVR**	**AVR+CABG**
<3%	1.3	2.0
3-6%	1.0	0.9
>6%	3.9	4.4

Table 2. Multivariable modelling of post-operative outcomes using pre-operative and operative factors

Predictor	missing	Category	Hospital mortality		Return to theatre for bleeding		New stroke		Post-operative length of stay (days)	
			Odds ratio	P-value	Odds ratio	P-value	Odds ratio	P-value	Odds ratio	P-value
Age (years)	7.9%	*per unit increase*	1.03 (1.02-1.04)	<0.001	1.01 (1.00-1.01)	0.006	1.02 (1.01-1.03)	0.001	1.00 (1.00-1.00)	<0.001
Gender	10.3%	Female	-		-		-		-	
		Male	0.63 (0.51-0.77)	<0.001	1.18 (1.02-1.36)	0.026	1.02 (0.80-1.29)	0.89	0.94 (0.93-0.96)	<0.001
LVEF	3.1%	Good (>50%)	-		-		-		-	
		Moderate (30-50%)	1.48 (1.18-1.85)	0.001	1.08 (0.91-1.27)	0.38	1.13 (0.86-1.48)	0.38	1.08 (1.06-1.10)	<0.001
		Poor (<30%)	1.90 (1.36-2.69)	<0.001	1.10 (0.82-1.48)	0.53	0.78 (0.44-1.38)	0.40	1.07 (1.03-1.11)	0.001
EuroSCORE Logistic	12.1%	*per unit increase*	1.02 (1.02-1.03)	<0.001	1.01 (1.00-1.01)	0.16	1.00 (0.99-1.02)	0.30	1.01 (1.01-1.01)	<0.001
Operative Urgency	0.02%	1. Elective	-		-		-		-	
		2. Urgent	1.63 (1.30-2.00)	<0.001	1.26 (1.08-2.00)	0.002	1.08 (0.83-1.41)	0.55	1.18 (1.16-1.20)	<0.001
		3. Emergency	6.87 (4.70-10.16)	<0.001	2.22 (1.51-3.26)	<0.001	7.65 (5.00-11.70)	<0.001	1.78 (1.67-1.90)	<0.001
		4. Salvage	11.79 (5.73-24.27)	<0.001	1.51 (0.56-4.02)	0.41	4.38 (1.47-13.1)	0.008	1.25 (1.07-1.46)	0.006
Cumulative Bypass Time (mins)	2.4%	*per unit increase*	1.02 (1.01-1.02)	<0.001	1.00 (1.00-1.01)	<0.001	1.00 (1.00-1.01)	<0.001	1.00 (1.00-1.00)	<0.001
Cumulative Cross Clamp Time (mins)	2.5%	*per unit increase*	0.99 (0.99-0.99)	<0.001	1.00 (1.00-1.00)	0.23	1.00 (0.99-1.00)	0.58	1.00 (1.00-1.00)	0.78
CABG	0%	No	-		-		-		-	
		Yes	1.15 (0.93-1.42)	0.20	1.07 (0.93-1.24)	0.33	1.12 (0.88-1.42)	0.37	1.03 (1.00-1.05)	<0.001

LVEF; left ventricular ejection fraction, CABG; coronary artery bypass graft surgery

Table 3. Baseline characteristics in the current study (UK AVR) versus those in recent trials comparing AVR with TAVI

Characteristic	UK AVR	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT [7]		PIVOTAL [5]		NOTION [18]	
	AVR	AVR	TAVR	AVR	TAVI	AVR	TAVI	AVR	TAVI	AVR	TAVI
	N=31,277	N=1021	N=1011	N=454	N=496	N=678	N=725	N=867	N=390	N=135	N=145
Age (mean±SD)	70.1±11.5	81.7±6.7	81.5±6.7	73.6±6.1	73.3±5.8	73.6±5.9	74.1±5.8	83.2±6.7	83.1±7.1	79 ± 4.7	79.2 ± 4.9
% Male	59	54.8	54.2	71.1	67.5	66.2	64	52.4	53.1	53.8	52.8
BMI (kg/m^2)	28.9±5.5	28.3±6.2	28.6±6.2	30.3±5.1	30.7±5.5	NR	NR	NR	NR	NR	NR
NYHA class III/IV (%)	44.4	76.3	77.3	23.8	31.2	28.4	25.1	86.9	85.7	45.5	48.6
Logistic EuroSCORE (%)	4.3±7.3	NR	NR	1.5±0.9*	1.5±1.2*	NR	NR	18.6±13.1	17.7±13.1	8.9 ± 5.5	8.4 ± 4.0
Diabetes Mellitus (%)	22.2	34.2	37.7	30.2	31.2	30.5	31.4	45.1	34.9	20.7	17.9
Chronic Kidney Disease (%)	3.1	5.2	5.0	0.2	0.2	0.1	0.4	12.8	12.2	0.7	1.4
Hypertension (%)	64.9	NR	NR	NR	NR	82.6	84.8	96.1	95.1	76.3	71.0
Peripheral vascular disease (%)	8.7	32.9	27.9	7.3	6.9	7.5	8.3	41.7	41.1	6.7	4.1
Previous stroke (%)	8.2	31	32.1	5.1	3.4	10.2	11.8	14.0	12.6	16.3	16.6
COPD (%)	13.4	30.0	31.8	6.2	5.1	15.0	18.0	9.8	13.3	11.9	11.7
LV ejection fraction (%)	53.2	55.3±11.9	56.2±10.8	66.2±8.6	65.7±9.0	61.9 ± 7.7	61.7 ± 7.9	NR	NR	NR	NR
Coronary artery disease (%)	37.1	66.5	69.2	28.0	27.7	NR	NR	75.9	75.4	NR	NR
Atrial fibrillation	10.3	35.2	31.0	18.8	15.7	14.5	15.4	45.9	40.9	25.6	27.8
Permanent pacemaker	1.9	12.0	11.7	2.9	2.4	3.8	3.2	21.3	23.3	4.4	3.4

AVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, BMI; body mass index, NYHA; New York Heart Association classification, COPD; chronic obstructive pulmonary disease, NR; not reported

*EuroSCORE II reported only

Table 4. Operative characteristics in the current study (UK AVR) versus those in recent trials comparing AVR with TAVI

Characteristic	UK AVR	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT [7]		DIVOTAL [5]		NOTION [18]	
	AVR N=31,277	AVR N=1021	TAVI N=1011	AVR N=454	TAVI N=496	AVR N=678	TAVI N=725	AVR N= 257	TAVI N= 390	AVR N= 135	TAVI N= 145
Operative urgency											
Elective (%)	74.3	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Urgent (%)	24	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Emergency/Salvage (%)	1.7	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Concomitant CABG (%)	37.1	NR	-	12.8	-	13.6	-	4	-	1	-
Staged PCI	-	-	NR	-	6.5	-	6.9	0.3%			0
Cross clamp time (minutes)	79.0	NR	-	74.3 ± 27.78	-	68.7 ± 29.0	-	74 ± 34	-	NR	NR
Cardiopulmonary bypass time (minutes)	104	NR	-	97.7 ± 33.75	-	93.4 ± 40.2	-	124 ± 45.8	-	NR	NR
Procedure time (minutes)	NR	NR	NR	208.3 ± 62.1	58.6 ± 36.5	276.6 ± 79.5	148.2 ± 55.1	221 ± 84.8	60.4 ± 35.3	177.2 ± 39.8	90.3 ± 38.6

AVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, CABG; coronary artery bypass graft surgery

NR; not reported

Table 5. Outcomes following surgical AVR in the current study (UK AVR) versus those in recent trials comparing AVR with TAVI

Outcome	UK AVR	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT [7]		PIVOTAL [5]		NOTION [18]	
	AVR N=31,277	AVR N=1021	TAVI N=1011	AVR N=454	TAVI N=496	AVR N=678	TAVI N=725	AVR N= 45	TAVI N= 390	AVR N= 135	TAVI N= 145
In-hospital death/30-day mortality (%)	1.9	8.0	6.1	3.3	1.0	1.3	0.5	4.2	3.3	3.7	2.1
Stroke (%)	1.1	6.1	5.5	2.4	0.6	3.4	3.4	6.3	4.9	3.0	1.4
Reoperation for bleeding (%)	3.6	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Post procedure bleeding (%)	-	43.4	10.4	11.9	1.2	7.5	2.4	69.2	41.7	11.3	20.9
Deep sternal wound infection (%)	0.14	NR	-	NR	-	NR	-	NR	-	NR	-
Length of hospital stay (days)	7	NR	-	7.0	3.0	NR	NR	NR	NR	8.9 ± 6.2	12.9 ± 11.6
New pacemaker implantation (%)	1.6	6.9	8.	4.0	6.5	6.1	17.4	7	19.8	1.6	34.1

AVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, CABG; coronary artery bypass graft surgery,

NR; not reported

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	4-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-6
Bias	9	Describe any efforts to address potential sources of bias	4-6
Study size	10	Explain how the study size was arrived at	4-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	6

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7-8
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	7-8
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	NA

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Surgical aortic valve replacement in the era of transcatheter aortic valve implantation - A review of the UK national database

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Surgical aortic valve replacement in the era of transcatheter aortic valve implantation - A review of the UK national database

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ABSTRACT

Objectives - To date the reported outcomes of surgical aortic valve replacement (SAVR) are mainly in the settings of trials comparing it with evolving transcatheter aortic valve implantation (TAVI). We set out to examine characteristics and outcomes in people who underwent AVR reflecting a national cohort and therefore 'real world' practice.

Design - Retrospective analysis of prospectively collected data of consecutive people who underwent SAVR with or without coronary artery bypass graft (CABG) surgery between April 2013 and March 2018 in the UK. This included elective, urgent and emergency operations. Participants' demographics, pre-operative risk factors, operative data, hospital mortality, post-operative complications and effect of the addition of CABG to SAVR were analysed.

Setting - 27 (90%) tertiary cardiac surgical centres in the UK submitted their data for analysis.

Participants - 31,277 people with AVR were identified. 19,670 (62.9%) had only SAVR and 11,607 (37.1%) had AVR+CABG.

Results - Mortality for isolated SAVR was 1.9% (95% CI: 1.6-2.1%) and was 2.4% for AVR+CABG. Mortality by age category for SAVR only were: <60 years=2.0%, 60-75 years=1.5%, >75 years=2.2%. For SAVR+CABG these were; 2.2%, 1.8% and 3.1%. For different categories of EuroSCORE, mortality for SAVR in low risk people was 1.3%, in intermediate risk 1% and for high risk 3.9%. 74.3% of the operations were elective, 24% urgent and 1.7% emergency/salvage. The incidences of re-sternotomy for bleeding and stroke were 3.9% and 1.1% respectively. Multivariable analyses provided no evidence that concomitant CABG influenced outcome. However, urgency of the operation, poor ventricular function, higher EuroSCORE and longer cross clamp and cardiopulmonary bypass times adversely affected outcomes.

Conclusions - Surgical SAVR±CABG has low mortality risk and a low level of complications in the UK in people of all ages and risk factors. These results should inform consideration of treatment options in people with aortic valve disease.

Strengths and limitations of this study

- This is a large study of consecutive participants who have undergone surgical aortic valve replacement ± coronary artery bypass graft surgery in the UK, reporting contemporary outcomes.
- This study includes people of all age groups and risks factors, and elective as well as urgent and emergency operations.
- The results are of in-hospital mortality and complications and longer term follow-up data is not available.

BACKGROUND

Aortic valve disease, especially aortic stenosis affects 5% of the population and 3.9% of those between the ages of 70 and 79 and nearly 10% of those above the age of 80.[1] Severe aortic stenosis when untreated has a risk of death of 50% at 2 years.[2] Conventionally the gold standard of treatment has been surgical aortic valve replacement (SAVR). However, the role of transcatheter aortic valve implantation (TAVI) has evolved in recent years. TAVI was first introduced in 2002, initially being performed in high risk inoperable patients.[3] The original Placement of Aortic Transcatheter Valves (PARTNER) trial demonstrated a significant reduction in mortality, repeat hospitalisation and cardiac symptoms compared to inoperable patients who had only medical therapy.[4] The original PIVOTAL study also demonstrated significantly higher survival at one year in high risk patients who underwent SAVR.[5]

The role of TAVI is being extended to lower risk and younger patients based on recent trials comparing SAVR with TAVI.[6,7] Several studies suggest there has been a change in demographics and types of surgical valves used since the advent of TAVI.[8–10] There has been a trend of increased use of tissue valves and a decrease in the use of mechanical valves in recent years.[11] This may be due to the evolution of TAVI practice whereby younger patients can have a tissue valve with the view that they have a TAVI valve in the future when the tissue valve has deteriorated, so called valve-in-valve.[12,13]

The series in the literature reporting outcomes of SAVR are generally unit based.[9,14] Also, people with aortic valve disease are given information about the outcomes of SAVR which may be out of date and incorrectly extrapolated from smaller studies. There is a lack of contemporary national data to assess the outcomes of SAVR (mortality and complications), and to demonstrate the trend in use of prosthetic valves which would inform people with aortic valve disease better. There are some perceived complications of surgery that may be understood by referring general practitioners and cardiologists to be prohibitive risks for surgery.

In order to inform practitioners, people with aortic valve disease and the cardiac surgical community, we set out to examine the results of contemporaneous SAVR in a multi-centre study of UK cardiac surgical units, in the era of TAVI. In addition, we summarise and interpret some of the more recent trials on the management of aortic valve disease.

METHODS

Data

This is an analysis of prospectively collected data of people who underwent SAVR +/- coronary artery bypass graft (CABG) surgery between April 2013 and March 2018 in the UK and Republic of Ireland. Anonymised data were submitted to the Society for Cardiothoracic Surgery of Great Britain & Ireland (SCTS) for 27 of the 30 units and then stored in a secure database. This period was chosen to reflect fairly contemporary practice and also the data is submitted in March every year. The data is collected by each unit, validated and then submitted to the National Institute of Cardiovascular Outcome Research (NICOR). It took approximately nine months to collect, validate and clean all the data. The outcome measures recorded are based on strict definitions provided by NICOR to provide uniformity.

Only participants who had had first time surgery, SAVR +/- CABG were included. All participants immaterial of their risk for surgery, people of all age groups and risk factors were included. Those who required other concomitant procedures like replacement of parts of the aorta, aortic root enlargement, other valve procedures and redo surgery were excluded.

Pre-operative risk factors and operative features

Baseline demographic data; significant past medical history such as diabetes, renal dysfunction, hypertension or stroke; predominant aortic valve pathology (stenosis or regurgitation or mixed valve disease) and preoperative left ventricular ejection fraction (LVEF) were collected. EuroSCORE is the risk stratification model used in the UK. Logistic EuroSCORE

was collected as well as EuroSCORE II where available. The latter was only used since 2017 and therefore not available for all participants. Logistic EuroSCORE was divided into three categories: <3%, 3-6%, >6%.

LVEF was divided into three categories: good (EF>50%), moderate (EF 30-50%) and poor (EF<30%). Transient ischaemic attack was defined as any neurological symptoms lasting <24 hours. Stroke was defined as new neurological dysfunction persisting >24 hours. Operative data including operative urgency: elective, urgent and emergency/salvage were recorded. Elective was defined as when the person was admitted from home, urgent meaning that the person was admitted with an urgent condition and required surgery during the same hospital admission, emergency and salvage meaning that surgery was required within 24 hours of admission and/or the person was in extremis. Other parameters including cardiopulmonary bypass (CPB) time, cross clamp (CCT) time, type of valve implanted as well as concomitant CABG surgery performed were also collected.

Postoperative outcomes

Postoperative complication data were collected with the main focus being in-hospital mortality, new stroke, return to theatre for bleeding, deep sternal wound infection and duration of postoperative hospital stay.

Statistical analysis

Once the records for all participants were collated and the data cleaned, each factor was summarised using descriptive methods. Categorical variables are presented as N (%) and continuous variables are presented as median (IQR). New strokes were recoded to be either no stroke or any cerebrovascular accident (transient or permanent). The natural log of post-operative length of stay (days) was used due to positive skewed distribution of this variable. Univariate models were used, logistic regression for binary outcomes and linear regression for continuous outcomes, to assess the impact of the key explanatory variables. In these models, a two-tailed p-value of <0.05 was considered significant. The population analysed included all the participants with data collected, with results checked in the subset who had SAVR only (without

CABG). Building on this, a multivariable model with all key variables in the model to assess which had the most impact on each of the outcomes was created. Stata/MP 15.1 (StataCorp LLC, Texas, USA) was used for all analyses. Multiple imputation of missing data was not performed. The missingness was mostly negligible. There was no missing mortality and the data is shown in Table 1.

Patient and public involvement

Patients and public were involved in the original design of the database.

Ethics

This data is ordinarily submitted to National Institute of Cardiovascular Outcome Research (NICOR) for which local and national Caldicott guardian approvals have been obtained. The data are validated by the surgical teams and their database managers/audit officers. For the current study a further approval from the Caldicott Guardian was obtained.

RESULTS

Descriptive analysis

In total 31,277 patients were included. Of these, 19,670 (62.9%) had only SAVR and 11,607 (37.1%) had SAVR+CABG. There were 14.4% below the age of 60, 46.9% between 60 to 75 and 36.7% older than 75 years, with 7.9% missing age data. There were 1.9 times more males than females (10.3% missing).

Regarding pre-operative risk factors, 75.2% had good LVEF, 17.3% had moderate and 4.3% had poor LVEF. 74.3% of the operations were elective, 24% were urgent and 1.7% were emergency or salvage operations.

Logistic EuroSCORE had a median of 1.83 with an IQR of 0.06-6.0. In total, 50% of patients were classified as low risk (<3%), 16% as medium risk (3—6%) and 22% high risk (>6%). 3,792 patients (12.1%) were missing data. The median EuroSCORE II was 1.95 (IQR 0.67-4.8) albeit with 56.5% with missing data, as this was introduced into the database in 2017. The median CPB time was 104 minutes (IQR 82-135) and CCT was 79 minutes (IQR 61-101).

For valve implant replacement type, 70% had a tissue valve, 12.2% a mechanical valve and 0.2% had homograft or autograft valves. For 17.3% the entry for valve type was unclear. The ratio of mechanical implant to bioprosthetic implant use has remained stable over time.

Overall mortality was 2.4% (95% CI: 2.2-2.6%) and mortality for isolated SAVR for all participants was 1.9% (1.6-2.1%). The mortality figures analysed for different age ranges and for categories of EuroSCORE are shown in Table 2.

Overall, 3.9% (3.6% in SAVR only) of participants had re-sternotomy for post-operative bleeding or tamponade, 0.04% (0.06% in SAVR only) had re-operation for valvular problems (significant paravalvular leak and early endocarditis), 0.7% (0.6% SAVR only) had re-operation for other cardiac problems, 0.2% (0.15% for SAVR only) had rewiring of sternum for sterile wounds and 0.14% (0.06% for SAVR only) had re-wiring of sternum for infection. Transient ischaemic attack occurred in only 0.6% and 1.1% had a stroke (no missing data).

Median post-operative length of stay was 7 days (IQR: 6-11) in those with SAVR only and 8 days (IQR: 6-12) in all patients.

The number of bypass grafts was not analysed due to concerns about inconsistent reporting of data describing the number of grafts.

When comparing the two subsets of patients, the characteristics of those with SAVR alone were broadly similar to those with SAVR+CABG. In SAVR alone there were more people aged <60 years (19.3% vs 6.2%), but less people were older than 75 (30.1% vs 43%). A higher proportion of those with SAVR+CABG were male (68% vs. 54%). Bypass time was

an average of 37 minutes shorter and CCT 27 minutes in the SAVR alone group. Amongst those with only SAVR the mechanical valve usage was greater, at 16% vs 7%.

Regression analysis

Univariable

Taken in isolation, all pre-operative risk factors were associated with an increased odds of death, as was addition of CABG. The same pattern was observed when analysing the need for re-operation or surgery, with explanatory variables indicative of a worse outcome without taking into account any others. For new stroke only age, EuroSCORE, operative urgency, ejection fraction, and cumulative bypass and cross clamp times affected a negative outcome (but not gender), as did CABG. All factors predicted a longer postoperative length of stay, including CABG.

As a sensitivity analysis, age categories were also assessed. When included as a continuous variable, age was significant both on its own and in all the multivariable models. All participants were categorised into <60, 60-75 and >75 years of age. Those 60-75 were at a lower odds of death in comparison to those <60 (OR 0.71, 95% CI 0.53-0.95, P=0.021) with no difference in those >75 (OR 1.09, 95% CI 0.82-1.45) in the AVR alone group. These findings were different in the SAVR+CABG group, with no significant difference in those 60-75 (OR 0.81, 95% CI 0.64-1.03) but an increased risk in those >75 (OR 1.09, 95% CI 1.12-1.76, P=0.004).

Multivariable Analyses

Analysis of postoperative outcomes using multivariable models including all pre-operative and operative factors are shown in Table 1. This demonstrated that age (OR 1.03 (95% CI 1.02-1.04), P<0.001), moderate ejection fraction (OR 1.48 (95% CI 1.18-1.85), P<0.001), poor ejection fraction (OR 1.90 (95% CI 1.36-2.69), P<0.001), logistic EuroSCORE (OR 1.02 (95%

CI 1.02-1.03), P<0.001), urgent operation (OR 1.63 (95% CI 1.30-2.00, P<0.001), emergency surgery (OR 6.87 (95% CI 4.70-10.16), P<0.001) and longer CPB times affected mortality (OR 1.02 (95% CI 1.01-1.02), P<0.001).

When all other variables were taken into account CABG was not significantly associated with an increase in the risk of death (OR 1.15 (95% CI 0.93-1.42), P=0.20).

Older age, (OR 1.01 (95% CI 1.00-1.01), p<0.006), longer CPB time (OR 1.00 (95% CI 1.00-1.01), P<0.001), urgent (OR 1.26 (95% CI 1.08-2.00), P<0.002) and emergency surgery (OR 2.22 (95% CI 1.51-3.26), P<0.001) were significant factors in identifying people requiring return to theatre for bleeding. Again, CABG did not affect the odds of returning to theatre (OR 1.07 (95% CI 0.93-1.24), P=0.33).

Factors affecting stroke were age, (OR 1.02 (95% CI 1.01-1.03), P<0.001), emergency (OR 7.65 (95% CI 5.00-11.70, P<0.001) or salvage surgery (OR 4.38 (95% CI 1.47-13.1) P=0.008), and CPB times (OR 1.00 (95% CI 1.00-1.01), P<0.001). As in the other outcomes, addition of CABG did not affect the outcome (OR 1.12 (95% CI 0.88-1.42), P=0.37).

Age, male gender, moderate and poor ejection fraction, operative urgency, higher logistic EuroSCORE, and cumulative bypass time significantly all affected post-operative length of stay.

DISCUSSION

This study reports contemporary results of SAVR and SAVR+CABG in the UK, reflecting real world practice, reporting an overall mortality of 1.9% and 2.4% respectively. We have shown a low mortality and complication rate for all comers following surgery in people requiring SAVR or SAVR+CABG. The complications were low with 3.9% re-sternotomy for bleeding, 0.04% re-operation for valvular problems and 1.1% stroke. Surprisingly, having accounted for other risk factors, addition of CABG did not adversely affect the outcomes.

The strengths of the study include its large number of participants, no exclusion of urgent and emergency/salvage cases, and inclusion of all risk participants. The limitations are that three centres were unable to take part, possible coding

errors in using large databases, lack of detailed echocardiographic data on valve annular size and presence or absence of pre-operative infective endocarditis which can adversely affect outcomes. In addition, the results are in-hospital mortality and complications and the database lack longer follow-up information.

Data from the current study are consistent with other large international studies. Data from the US Society of Thoracic Surgeons (STS) database demonstrated in- hospital mortality for isolated SAVR of 2.5% and incidence of stroke of 1.5%.[15] A recent analysis of the Japanese Cardiovascular Surgery database which assessed the outcome of patients undergoing SAVR over a 8 year period has demonstrated a similar in-hospital mortality of 2%.[16] They also demonstrated a reduction in mortality over time, despite increasing surgical risk. The age of the patients in our study is lower than some of the trials of SAVR and TAVI. This is probably due to the selection criteria in these trials where older patients were selected.

We had set out to analyse the results of SAVR in the UK to inform practitioners treating people with aortic valve disease and inform people with this condition in an era where other therapies for management of aortic valve disease are evolving with expanding indications. Although the current study did not examine people who received TAVI, we discuss the various trials of SAVR and TAVI reported in the context of the literature and compare them with the results of the current study.

In Tables 3-5, the demographics, procedural details and outcomes of the current study are compared with the respective sub-groups of the published trials. Table 5 shows low mortality and complication rate in the participants of this study following surgery in people who required SAVR or SAVR+CABG. The trials comparing AVR and TAVI have enrolled and classified patients according to the risk of surgery, in particular the more recent trials.[6,7] The most commonly used surgical risk stratification score is the Society of Thoracic Surgery risk score (STS), although this scoring system has been validated in the US population. We have used EuroSCORE and shown that mortality is low in all categories of risk.

There are several recent trials comparing SAVR with TAVI. A meta-analysis of six of these trials performed by Barili and colleagues reported that mortality was affected by the treatment modality with a time-varying effect: TAVI was related

to better survival in the first months after implantation whereas, after 40 months, it was a risk factor for all-cause mortality.[17] The NOTION trial, which compared outcomes of patients estimated to have low surgical risk who underwent either TAVI or SAVR demonstrated similar early mortality results, with mortality of 2.1% in TAVI group vs 3.7% in the SAVR group, p=0.38.[18] The PIVOTAL trial of low risk patients also reported similar results between those who underwent TAVI compared to SAVR, with early mortality of 0.5% in TAVI group and 1.3% in SAVR.[7] In addition, the 5 year results of the PARTNER 2 study, comparing TAVI vs SAVR in intermediate surgical risk demonstrated no significant difference in the incidence of death or stroke at 5 years following SAVR or TAVI.[19] The mortality in the intermediate EuroSCORE risk category of the current study was 1.0% for SAVR only and 0.9% for SAVR+CABG. PARTNER 3 however demonstrated significantly lower mortality in the TAVI group compared to SAVR (1% vs 3.3%, P=0.01) at one year.[6] An observational study of 7618 patients comparing SAVR with TAVI at 5 years showed however that in a real world population with low and intermediate risk, SAVR was associated with lower mortality and major adverse cardiac events, although this was with first generation TAVI devices.[20]

Role of co-existent coronary artery disease and its management

60% of patients with aortic valve disease undergoing SAVR and 65% of those undergoing TAVI have coexisting coronary artery disease.[21] In our series, 37% had co-existent coronary artery disease and underwent concomitant CABG. The addition of CABG did not adversely affect outcomes. The US[15] and Japanese[16] series did not look into concomitant CABG. The percentage of concomitant CABG in our series is higher than the trials of SAVR/TAVI. This probably reflects the selection criteria in the latter. In PARTNER 2, although both groups had a similar number with coexistent coronary artery disease, 14.5% of the SAVR group had concomitant CABG compared to 3.9% of the TAVI group who had percutaneous intervention (Table 4).[22] SAVR may therefore be the preferred treatment modality in those with aortic stenosis and multivessel coronary artery disease requiring revascularisation and is the standard of care in those in younger age groups.

Treatment of coronary artery disease in TAVI patients may require more than one hospital admission and can often result in incomplete revascularisation and its consequent increased morbidity and mortality. A meta-analysis by Sankaramangalam and colleagues, demonstrated that whilst there was no increase in mortality in patients with coronary artery disease who underwent TAVI at 30 days, there was a significant increase in mortality at one year following TAVI in these patients.[23] The economic costs of readmission after TAVI have been demonstrated to be higher than in those who are readmitted after surgery and so untreated coronary disease which later requires readmission will have cost implications.[24,25] Surgery has the advantage of addressing all the pathology with one operation.

Durability and choice of prosthetic valves

In choosing the technique of treatment for aortic valve disease, life expectancy of the person and durability of the valve need to be considered. Ideally, the prosthetic valve should be durable for the person's lifetime. Both of these are related to person's age. In the UK a 50 year old female has a life expectancy of 34 years and a 70 year old male a life expectancy of 14 years.[26]

The durability of bioprosthetic valves is well documented in the surgical literature and is inversely proportional to person's age. Structural valve deterioration (SVD) has been demonstrated to increase exponentially beyond 10 years following surgery.[27,28] Considering the UK life expectancy [26], a 70 year old male has a 5% risk of re-operation and a 50 year old female has a 30% chance of needing a second operation. Although long term data regarding the durability of TAVI valves is awaited, the 5 year results of the PARTNER 2 trial demonstrated that the incidence of SVD in the TAVI group was significantly higher than in the SAVR group.[19] However, a sub-study of the NOTION trial looked at SVD up to 6 years suggested no significant difference between the SAVR and TAVI.[29]

The durability of tissue valves in surgery are well documented.[27] Bagur and colleagues have introduced the concept of valve durability: life expectancy ratio.[30] More information on durability of TAVI valves is pending, however, there are some

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deleterious effects of crimping with TAVI valves.[31] A systematic review of observational data by Foroutan and colleagues looking at 8914 patients who underwent TAVI with a follow-up of 1.5 - 5 years showed SVD incidence of 0-1.34 per 100 patient-years with a pooled incidence of 28.08 per 10,000 patient-years.[32] Of those with SVD, 12% underwent re-intervention.

Surgery has the advantage of offering the patient a mechanical or a bioprosthetic valve. The option of a mechanical valve which is only available in surgical SAVR should not be overlooked especially in younger people. In the current study, we have shown a fairly consistent ratio of tissue to mechanical valve use. However, the reported literature shows that the number of mechanical valve implantations has reduced in comparison to bioprosthetic valves. Mechanical valves are durable, with one group reporting 6.9% reintervention rate at 15 years versus 12.1% in those who underwent surgery with a bioprosthesis.[33] For this reason, it has been the most commonly considered prosthesis in those under the age of 60, as in our study where 60.2% of participants <60 years had a mechanical valve. Mechanical valves have the disadvantage of requiring anticoagulation, although, newer generations require a lower level of anticoagulation.[34] Whilst mechanical valves are more durable, this has to be balanced against the greater risk of bleeding.[33] At 15 years follow up, Chiang and colleagues also demonstrated no significant difference in survival and stroke between patients who underwent SAVR with mechanical vs bioprosthetic valve.[33] Another group demonstrated in the 50-70 year old cohort that survival at 5 years was higher in patients who had undergone SAVR with mechanical valve vs bioprosthesis and also demonstrated similar freedom from major bleeding events.[35]

Bicuspid aortic valve and aneurysm of the aorta

A significant number of patients requiring SAVR have bicuspid aortic valve, which has an incidence of 1-2% in the general population and may present with aortic valve stenosis, regurgitation and ascending aortic aneurysm. The type of native aortic valve is not recorded in the database of our study. BAV may be present in up to 30% of patients undergoing SAVR.[36] Bicuspid aortic valve anatomy, larger annular size, bulky and asymmetric leaflet calcification and dilated ascending aorta all pose technical challenges to TAVI which are not prohibitive risk factors for surgery. In fact associated pathology of aneurysms of the aortic root and ascending aorta can be treated at the time of SAVR with little additional risk.[37]

European guidelines recommend discussing people with aortic valve disease in a multi-disciplinary setting referred to as Heart Team, comprising of a surgeon, a non-interventional and an interventional cardiologist this will allow the best treatment option to be put forward to the person.

CONCLUSIONS

SAVR with and without CABG has low mortality risk and a low level of complications in the UK in people of all ages and risk factors. Our study provides real world experience of surgical results to improve understanding of the risks of surgery and decision making in a multi-disciplinary team (MDT) setting with Heart Team. The results of this study can be utilised by people with aortic valve disease, referring general practitioners, physicians, surgeons and policy makers. Future studies need to address long term follow-up including factors like quality of life which are currently not collected by the specialist centres.

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2. Rajdeep Bilkhu - thought of the concept, designed the project, planned data collection, collected the data and cleaned it, contribuited significantly to writing major sections of the paper
3. Andrew Embleton-Thirsk – Involved in the design of the study at the outset, of the two main statistician who carried out the statistical work. Attended several meetings to discuss the project, involed in writing all the versions.
4. Hakim-Moulay Dehbi - Involved in the design of the study at the outset, of the two main statistician who carried out the statistical work. Attended several meetings to discuss the project, involed in writing all the versions.
5. Krishna Mani - thought of the concept, designed the project, planned data collection, collected the data and cleaned it, contribuited significantly to writing major sections of the paper, checked the literature contents and references.
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36. Nick Freemantle – Senior statistician who designed the project, defiend the original plan for the study, assisted the other two statistician to analyse the data, took part in several meetings interpreting the data with further analysis, assisted in writing the paper and final analysis.

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Ethical approval: Anonymised data were submitted to the Society for Cardiothoracic Surgery of Great Britain & Ireland (SCTS) for 27 of the 30 units and then stored in a secure database. This data is ordinarily submitted to National Institute of Cardiovascular Outcome Research (NICOR) for which local and national Caldicott guardian approvals have been obtained. A further approval from the Caldicott Guardian was obtained in 2020.

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Data sharing: Requests on data sharing can be made by contacting the corresponding author. Data will be shared after review and approval by the authors and terms of collaboration will be reached together with a signed data access agreement.

The corresponding author (MJ) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. The manuscript is read and approved by all authors.

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Table 1. Multivariable modelling of post-operative outcomes using pre-operative and operative factors

Predictor	missing	Category	Hospital mortality		Return to theatre for bleeding		New stroke		Post-operative length of stay (days)	
			Odds ratio	P-value	Odds ratio	P-value	Odds ratio	P-value	Odds ratio	P-value
Age (years)	7.9%	*per unit increase*	1.03 (1.02-1.04)	<0.001	1.01 (1.00-1.01)	0.006	1.02 (1.01-1.03)	0.001	1.00 (1.00-1.00)	<0.001
Gender	10.3%	Female	-		-		-		-	
		Male	0.63 (0.51-0.77)	<0.001	1.18 (1.02-1.36)	0.026	1.02 (0.80-1.29)	0.89	0.94 (0.93-0.96)	<0.001
LVEF	3.1%	Good (>50%)	-		-		-		-	
		Moderate (30-50%)	1.48 (1.18-1.85)	0.001	1.08 (0.91-1.27)	0.38	1.13 (0.86-1.48)	0.38	1.08 (1.06-1.10)	<0.001
		Poor (<30%)	1.90 (1.36-2.69)	<0.001	1.10 (0.82-1.48)	0.53	0.78 (0.44-1.38)	0.40	1.07 (1.03-1.11)	0.001
EuroSCORE Logistic	12.1%	*per unit increase*	1.02 (1.02-1.03)	<0.001	1.01 (1.00-1.01)	0.16	1.00 (0.99-1.02)	0.30	1.01 (1.01-1.01)	<0.001
Operative Urgency	0.02%	1. Elective	-		-		-		-	
		2. Urgent	1.63 (1.30-2.00)	<0.001	1.26 (1.08-2.00)	0.002	1.08 (0.83-1.41)	0.55	1.18 (1.16-1.20)	<0.001
		3. Emergency	6.87 (4.70-10.16)	<0.001	2.22 (1.51-3.26)	<0.001	7.65 (5.00-11.70)	<0.001	1.78 (1.67-1.90)	<0.001
		4. Salvage	11.79 (5.73-24.27)	<0.001	1.51 (0.56-4.02)	0.41	4.38 (1.47-13.1)	0.008	1.25 (1.07-1.46)	0.006
Cumulative Bypass Time (mins)	2.4%	*per unit increase*	1.02 (1.01-1.02)	<0.001	1.00 (1.00-1.01)	<0.001	1.00 (1.00-1.01)	<0.001	1.00 (1.00-1.00)	<0.001
Cumulative Cross Clamp Time (mins)	2.5%	*per unit increase*	0.99 (0.99-0.99)	<0.001	1.00 (1.00-1.00)	0.23	1.00 (0.99-1.00)	0.58	1.00 (1.00-1.00)	0.78
CABG	0%	No	-		-		-		-	
		Yes	1.15 (0.93-1.42)	0.20	1.07 (0.93-1.24)	0.33	1.12 (0.88-1.42)	0.37	1.03 (1.00-1.05)	<0.001

LVEF; left ventricular ejection fraction, CABG; coronary artery bypass graft surgery

Tables 2. Mortality (%) for different categories of age and EuroSCORE

Euroscore	N (%)	SAVR+CABG (Mortality %)	SAVR (Mortality %)
<3%	15619 (50.0)	2.0	1.3
3-6%	5020 (16.1)	0.9	1.0
>6%	6846 (21.9)	4.4	3.9
Age (years)		**SAVR+CABG**	**SAVR**
<60		2.2	2.0
60-75		1.8	1.5
>75		3.1	2.2

Table 3. Baseline characteristics in the current study (UK SAVR) and those in other national registries and recent trials comparing SAVR with TAVI

Characteristic	UK SAVR	Thourani[15]	Tokuda[16]	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT		PIVOTAL [5]		NOTIO
	SAVR N=31,277	SAVR N=141 905	SAVR N=20 514	SAVR N=1021	TAVR N=1011	SAVR N=454	TAVI N=496	SAVR N=678	TAVI N=725	SAVR N=357	TAVI N=390	SAVR N=135
Age (mean±SD)	70.1±11.5	67.6 ± 13.4	NR	81.7±6.7	81.5±6.7	73.6±6.1	73.3±5.8	73.6±5.9	74.1±5.8	83.2±6.4	83.1±7.1	79 ± 4.7
% Male	59	58	51.1	54.8	54.2	71.1	67.5	66.2	64	52.4	53.1	53.8
BMI (kg/m^2)	28.9±5.5	29.3 ± 6.6	NR	28.3±6.2	28.6±6.2	30.3±5.1	30.7±5.5	NR	NR	NR	NR	NR
NYHA class III/IV (%)	44.4	38.4	15.9	76.3	77.3	23.8	31.2	28.4	25.1	86.9	85.7	45.5
Logistic EuroSCORE (%)	4.3±7.3	NR	NR	NR	NR	1.5±0.9*	1.5±1.2*	NR	NR	18.6±13.0	17.7±13.1	8.9 ± 5.5
Diabetes Mellitus (%)	22.2	25.5	NR	34.2	37.7	30.2	31.2	30.5	31.4	45.4	34.9	20.7
Chronic Kidney Disease (%)	3.1	NR	NR	5.2	5.0	0.2	0.2	0.1	0.4	12.8	12.2	0.7
Hypertension (%)	64.9	NR	NR	NR	NR	NR	NR	82.6	84.8	96.1	95.1	76.3
Peripheral vascular disease (%)	8.7	9.2	NR	32.9	27.9	7.3	6.9	7.5	8.3	41.7	41.1	6.7
Previous stroke (%)	8.2	12.6	0.13	31	32.1	5.1	3.4	10.2	11.8	14.0	12.6	16.3
COPD (%)	13.4	NR	13.6	30.0	31.8	6.2	5.1	15.0	18.0	9.0	13.3	11.9
LV ejection fraction (%)	53.2	54.9 ± 12.9	NR	55.3±11.9	56.2±10.8	66.2±8.6	65.7±9.0	61.9 ± 7.7	61.7 ± 7.9	NR	NR	NR
Coronary artery disease (%)	37.1	NR	NR	66.5	69.2	28.0	27.7	NR	NR	75.9	75.4	NR
Atrial fibrillation	10.3	NR	5.6	35.2	31.0	18.8	15.7	14.5	15.4	45.9	40.9	25.6
Permanent pacemaker	1.9			12.0	11.7	2.9	2.4	3.8	3.2	21.3	23.3	4.4

SAVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, BMI; body mass index, NYHA; New York Heart Association classification, COPD; chronic obstructive pulmonary disease, NR; not reported

*EuroSCORE II reported only

Table 4. Operative characteristics in the current study (UK AVR) and those in other national registries and recent trials comparing SAVR with TAVI

Characteristic	UK SAVR	Thourani[15]	Tokuda[16]	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT		PIVOTAL [5]		NOTION [18]	
	SAVR N=31,277	SAVR N=141 905	SAVR N=20 514	SAVR N=1021	TAVI N=1011	SAVR N=454	TAVI N=496	SAVR N=678	TAVI N=725	SAVR N= 357	TAVI N= 390	SAVR N= 135	TAVI N= 145
Operative urgency													
Elective (%)	74.3	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Urgent (%)	24	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Emergency/Salvage (%)	1.7	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Concomitant CABG (%)	37.1	NR	NR	NR	-	12.8	-	13.6	-	4.8	-	1	-
Staged PCI	-	NR	NR	-	NR	-	6.5	-	-	-	0.3%		0
Cross clamp time (minutes)	79.0	77.0 ± 28.5	NR	NR	-	74.3 ± 27.78	-	68.7 ± 29.0	-	74.0 ± 31.4	-	NR	NR
Cardiopulmonary bypass time (minutes)	104	104.9 ± 39.1	NR	NR	-	97.7 ± 33.75	-	93.4 ± 40.2	-	104.0± 45.8	-	NR	NR
Procedure time (minutes)	NR	NR	NR	NR	NR	208.3 ± 62.1	58.6 ± 36.5	276.6 ± 79.5	148.0 ± 55.7	221 ± 84.8	60.4 ± 35.3	177.2 ± 39.8	90.3 ± 38.6

SAVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, CABG; coronary artery bypass graft surgery

NR; not reported

Table 5. Outcomes following SAVR in the current study (UK AVR) and those in other national registries and recent trials comparing SAVR with TAVI

Outcome	UK SAVR	Thourani[15]	Tokuda[16]	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT [7]		PIVOTAL [5]		NOTION [18]	
	SAVR N=31,277	SAVR N=141 905	SAVR N=20 514	SAVR N=1021	TAVI N=1011	SAVR N=454	TAVI N=496	SAVR N=678	TAVI N=725	SAVR N= 357	TAVI N= 390	SAVR N= 135	TAVI N= 145
In-hospital death/30-day mortality (%)	1.9	2.5	NR	8.0	6.1	3.3	1.0	1.3	0.5	4.5	3.3	3.7	2.1
Stroke (%)	1.1	NR	1.6	6.1	5.5	2.4	0.6	3.4	3.4	6.2	4.9	3.0	1.4
Reoperation for bleeding (%)	3.6	3.9	3	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Post procedure bleeding (%)	-	NR		43.4	10.4	11.9	1.2	7.5	2.4	69.5	41.7	11.3	20.9
Deep sternal wound infection (%)	0.14	0.3	1.1	NR	-	NR	-	NR	-	NR	-	NR	-
Length of hospital stay (days)	7	7.9 ± 7.2	NR	NR	-	7.0	3.0	NR	NR	NR	NR	8.9 ± 6.2	12.9 ± 11.6
New pacemaker implantation (%)	1.6	NR	NR	6.9	8.	4.0	6.5	6.1	17.4	7.1	19.8	1.6	34.1

SAVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, CABG; coronary artery bypass graft surgery

NR; not reported

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	4-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-6
Bias	9	Describe any efforts to address potential sources of bias	4-6
Study size	10	Explain how the study size was arrived at	4-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	6

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7-8
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	7-8
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	NA

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Surgical aortic valve replacement in the era of transcatheter aortic valve implantation - A review of the UK national database

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Surgical aortic valve replacement in the era of transcatheter aortic valve implantation - A review of the UK national database

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ABSTRACT

Objectives - To date the reported outcomes of surgical aortic valve replacement (SAVR) are mainly in the settings of trials comparing it with evolving transcatheter aortic valve implantation (TAVI). We set out to examine characteristics and outcomes in people who underwent SAVR reflecting a national cohort and therefore 'real world' practice.

Design - Retrospective analysis of prospectively collected data of consecutive people who underwent SAVR with or without coronary artery bypass graft (CABG) surgery between April 2013 and March 2018 in the UK. This included elective, urgent and emergency operations. Participants' demographics, pre-operative risk factors, operative data, in-hospital mortality, post-operative complications and effect of the addition of CABG to SAVR were analysed.

Setting - 27 (90%) tertiary cardiac surgical centres in the UK submitted their data for analysis.

Participants - 31,277 people with AVR were identified. 19,670 (62.9%) had only SAVR and 11,607 (37.1%) had AVR+CABG.

Results – In-hospital mortality for isolated SAVR was 1.9% (95% CI: 1.6-2.1%) and was 2.4% for AVR+CABG. Mortality by age category for SAVR only were: <60 years=2.0%, 60-75 years=1.5%, >75 years=2.2%. For SAVR+CABG these were; 2.2%, 1.8% and 3.1%. For different categories of EuroSCORE, mortality for SAVR in low risk people was 1.3%, in intermediate risk 1% and for high risk 3.9%. 74.3% of the operations were elective, 24% urgent and 1.7% emergency/salvage. The incidences of re-sternotomy for bleeding and stroke were 3.9% and 1.1% respectively. Multivariable analyses provided no evidence that concomitant CABG influenced outcome. However, urgency of the operation, poor ventricular function, higher EuroSCORE and longer cross clamp and cardiopulmonary bypass times adversely affected outcomes.

Conclusions - Surgical SAVR±CABG has low mortality risk and a low level of complications in the UK in people of all ages and risk factors. These results should inform consideration of treatment options in people with aortic valve disease.

Strengths and limitations of this study

- This is a large study of consecutive participants who have undergone surgical aortic valve replacement ± coronary artery bypass graft surgery in the UK, reporting contemporary outcomes.
- This study includes people of all age groups and risks factors, and elective as well as urgent and emergency operations.
- The results are of in-hospital mortality and complications and longer term follow-up data is not available.

BACKGROUND

Aortic valve disease, especially aortic stenosis affects 5% of the population and 3.9% of those between the ages of 70 and 79 and nearly 10% of those above the age of 80.[1] Severe aortic stenosis when untreated has a risk of death of 50% at 2 years.[2] Conventionally the gold standard of treatment has been surgical aortic valve replacement (SAVR). However, the role of transcatheter aortic valve implantation (TAVI) has evolved in recent years. TAVI was first introduced in 2002, initially being performed in high risk inoperable patients.[3] The original Placement of Aortic Transcatheter Valves (PARTNER) trial demonstrated a significant reduction in mortality, repeat hospitalisation and cardiac symptoms compared to inoperable patients who had only medical therapy.[4] The original PIVOTAL study also demonstrated significantly higher survival at one year in high risk patients who underwent SAVR.[5]

The role of TAVI is being extended to lower risk and younger patients based on recent trials comparing SAVR with TAVI.[6,7] Several studies suggest there has been a change in demographics and types of surgical valves used since the advent of TAVI.[8–10] There has been a trend of increased use of tissue valves and a decrease in the use of mechanical valves in recent years.[11] This may be due to the evolution of TAVI practice whereby younger patients can have a tissue valve with the view that they have a TAVI valve in the future when the tissue valve has deteriorated, so called valve-in-valve.[12,13]

The series in the literature reporting outcomes of SAVR are generally unit based.[9,14] Also, people with aortic valve disease are given information about the outcomes of SAVR which may be out of date and incorrectly extrapolated from smaller studies. There is a lack of contemporary national data to assess the outcomes of SAVR (mortality and complications), and to demonstrate the trend in use of prosthetic valves which would inform people with aortic valve disease better. There are some perceived complications of surgery that may be understood by referring general practitioners and cardiologists to be prohibitive risks for surgery.

In order to inform practitioners, people with aortic valve disease and the cardiac surgical community, we set out to examine the results of contemporaneous SAVR in a multi-centre study of UK cardiac surgical units, in the era of TAVI. In addition, we

summarise and interpret some of the more recent trials on the management of aortic valve disease.

METHODS

Data

This is an analysis of prospectively collected data of people who underwent SAVR +/- coronary artery bypass graft (CABG) surgery between April 2013 and March 2018 in the UK and Republic of Ireland. Anonymised data were submitted to the Society for Cardiothoracic Surgery of Great Britain & Ireland (SCTS) for 27 of the 30 units and then stored in a secure database. This period was chosen to reflect fairly contemporary practice and also the data is submitted in March every year. The data is collected by each unit, validated and then submitted to the National Institute of Cardiovascular Outcome Research (NICOR). It took approximately nine months to collect, validate and clean all the data. The outcome measures recorded are based on strict definitions provided by NICOR to provide uniformity.

Only participants who had had first time surgery, SAVR +/- CABG were included. All participants immaterial of their risk for surgery, people of all age groups and risk factors were included. Those who required other concomitant procedures like replacement of parts of the aorta, aortic root enlargement, other valve procedures and redo surgery were excluded.

Pre-operative risk factors and operative features

Baseline demographic data; significant past medical history such as diabetes, renal dysfunction, hypertension or stroke; predominant aortic valve pathology (stenosis or regurgitation or mixed valve disease) and preoperative left ventricular ejection fraction (LVEF) were collected. EuroSCORE is the risk stratification model used in the UK. Logistic EuroSCORE was collected as well as EuroSCORE II where available. The latter was only used since 2017 and therefore not available for all participants. Logistic EuroSCORE was divided into three categories: <3%, 3-6%, >6%.

LVEF was divided into three categories: good (EF>50%), moderate (EF 30-50%) and poor (EF<30%). Transient ischaemic attack was defined as any neurological

symptoms lasting <24 hours. Stroke was defined as new neurological dysfunction persisting >24 hours. Operative data including operative urgency: elective, urgent and emergency/salvage were recorded. Elective was defined as when the person was admitted from home, urgent meaning that the person was admitted with an urgent condition and required surgery during the same hospital admission, emergency and salvage meaning that surgery was required within 24 hours of admission and/or the person was in extremis. Other parameters including cardiopulmonary bypass (CPB) time, cross clamp (CCT) time, type of valve implanted as well as concomitant CABG surgery performed were also collected.

Postoperative outcomes

Postoperative complication data were collected with the main focus being in-hospital mortality, new stroke, return to theatre for bleeding, deep sternal wound infection and duration of postoperative hospital stay.

Statistical analysis

Once the records for all participants were collated and the data cleaned, each factor was summarised using descriptive methods. Categorical variables are presented as N (%) and continuous variables are presented as median (IQR). New strokes were recoded to be either no stroke or any cerebrovascular accident (transient or permanent). The natural log of post-operative length of stay (days) was used due to positive skewed distribution of this variable. Univariate models were used, logistic regression for binary outcomes and linear regression for continuous outcomes, to assess the impact of the key explanatory variables. In these models, a two-tailed p-value of <0.05 was considered significant. The population analysed included all the participants with data collected, with results checked in the subset who had SAVR only (without CABG). Building on this, a multivariable model with all key variables in the model to assess which had the most impact on each of the outcomes was created. Stata/MP 15.1 (StataCorp LLC, Texas, USA) was used for all analyses. Multiple imputation of missing data was not performed. The missingness was mostly negligible. There was no missing mortality and the data is shown in table 2.

Patient and public involvement

Patients and public were involved in the original design of the database.

Ethics

This data is ordinarily submitted to National Institute of Cardiovascular Outcome Research (NICOR) for which local and national Caldicott guardian approvals have been obtained. The data are validated by the surgical teams and their database managers/audit officers. For the current study a further approval from the Caldicott Guardian was obtained.

RESULTS

Descriptive analysis

In total 31,277 patients were included. Of these, 19,670 (62.9%) had only SAVR and 11,607 (37.1%) had SAVR+CABG. There were 14.4% below the age of 60, 46.9% between 60 to 75 and 36.7% older than 75 years with 7.9% missing age data. There were 1.9 times more males than females (10.3% missing).

Regarding pre-operative risk factors, 75.2% had good LVEF, 17.3% had moderate and 4.3% had poor LVEF. 74.3% of the operations were elective, 24% were urgent and 1.7% were emergency or salvage operations.

Logistic EuroSCORE had a median of 1.83 with an IQR of 0.06-6.0. In total, 50% of patients were classified as low risk (<3%), 16% as medium risk (3—6%) and 22% high risk (>6%). 3,792 patients (12.1%) were missing data. The median EuroSCORE II was 1.95 (IQR 0.67-4.8) albeit with 56.5% with missing data, as this was introduced into the database in 2017. The median CPB time was 104 minutes (IQR 82-135) and CCT was 79 minutes (IQR 61-101).

For valve implant replacement type, 70% had a tissue valve, 12.2% a mechanical valve and 0.2% had homograft or autograft valves. For 17.3% the entry for valve type was unclear. The ratio of mechanical implant to bioprosthetic implant use has remained stable over time.

Overall mortality was 2.4% (95% CI: 2.2-2.6%) and mortality for isolated SAVR for all participants was 1.9% (1.6-2.1%). The mortality figures analysed for different age ranges and for categories of EuroSCORE are shown in Table 1.

Overall, 3.9% (3.6% in SAVR only) of participants had re-sternotomy for post-operative bleeding or tamponade, 0.04% (0.06% in SAVR only) had re-operation for valvular problems (significant paravalvular leak and early endocarditis), 0.7% (0.6% SAVR only) had re-operation for other cardiac problems, 0.2% (0.15% for SAVR only) had rewiring of sternum for sterile wounds and 0.14% (0.06% for SAVR only) had re-wiring of sternum for infection. Transient ischaemic attack occurred in only 0.6% and 1.1% had a stroke (no missing data).

Median post-operative length of stay was 7 days (IQR: 6-11) in those with SAVR only and 8 days (IQR: 6-12) in all patients.

The number of bypass grafts was not analysed due to concerns about inconsistent reporting of data describing the number of grafts.

When comparing the two subsets of patients, the characteristics of those with SAVR alone were broadly similar to those with SAVR+CABG. In SAVR alone there were more people aged <60 years (19.3% vs 6.2%), but less people were older than 75 (30.1% vs 43%). A higher proportion of those with SAVR+CABG were male (68% vs. 54%). Bypass time was an average of 37 minutes shorter and CCT 27 minutes in the SAVR alone group. Amongst those with only SAVR the mechanical valve usage was greater, at 16% vs 7%.

Regression analysis

Univariable

Taken in isolation, all pre-operative risk factors were associated with an increased odds of death, as was addition of CABG. The same pattern was observed when analysing the need for re-operation or surgery, with all explanatory variables indicative of a worse outcome without taking into account any others. For new stroke only age, EuroSCORE, operative urgency, ejection fraction, and cumulative bypass and cross clamp times affected a negative outcome (but not gender), as did CABG. All factors predicted a longer postoperative length of stay, including CABG.

As a sensitivity analysis, age categories were also assessed. When included as a continuous variable, age was significant both on its own and in all the multivariable models. All participants were categorised into <60, 60-75 and >75 years of age. Those 60-75 were at a lower odds of death in comparison to those <60 (OR 0.71, 95% CI 0.53-0.95, P=0.021) with no difference in those >75 (OR 1.09, 95% CI 0.82-1.45) in the AVR alone group. These findings were different in the SAVR+CABG group, with no significant difference in those 60-75 (OR 0.81, 95% CI 0.64-1.03) but an increased risk in those >75 (OR 1.09, 95% CI 1.12-1.76, P=0.004).

Multivariable Analyses

Analysis of postoperative outcomes using multivariable models including all pre-operative and operative factors are shown in Table 2. This demonstrated that age (OR 1.03 (95% CI 1.02-1.04), P<0.001), moderate ejection fraction (OR 1.48 (95% CI 1.18-1.85), P<0.001), poor ejection fraction (OR 1.90 (95% CI 1.36-2.69), P<0.001), logistic EuroSCORE (OR 1.02 (95% CI 1.02-1.03), P<0.001), urgent operation (OR 1.63 (95% CI 1.30-2.00, P<0.001), emergency surgery (OR 6.87 (95% CI 4.70-10.16), P<0.001) and longer CPB times affected mortality (OR 1.02 (95% CI 1.01-1.02), P<0.001).

When all other variables were taken into account CABG was not significantly associated with an increase in the risk of death (OR 1.15 (95% CI 0.93-1.42), P=0.20).

Older age, (OR 1.01 (95% CI 1.00-1.01), p<0.006), longer CPB time (OR 1.00 (95% CI 1.00-1.01), P<0.001), urgent (OR 1.26 (95% CI 1.08-2.00), P<0.002) and emergency surgery (OR 2.22 (95% CI 1.51-3.26), P<0.001) were significant factors in identifying people requiring return to theatre for bleeding. Again, CABG did not affect the odds of returning to theatre (OR 1.07 (95% CI 0.93-1.24), P=0.33).

Factors affecting stroke were age, (OR 1.02 (95% CI 1.01-1.03), P<0.001), emergency (OR 7.65 (95% CI 5.00-11.70, P<0.001) or salvage surgery (OR 4.38 (95% CI 1.47-13.1) P=0.008), and CPB times (OR 1.00 (95% CI 1.00-1.01), P<0.001). As in the other outcomes, addition of CABG did not affect the outcome (OR 1.12 (95% CI 0.88-1.42), P=0.37).

Age, male gender, moderate and poor ejection fraction, operative urgency, higher logistic EuroSCORE, and cumulative bypass time significantly all affected post-operative length of stay.

DISCUSSION

This study reports contemporary results of SAVR and SAVR+CABG in the UK, reflecting real world practice, reporting an overall mortality of 1.9% and 2.4% respectively. We have shown a low mortality and complication rate for all comers following surgery in people requiring SAVR or SAVR+CABG. The complications were low with 3.9% re-sternotomy for bleeding, 0.04% re-operation for valvular problems and 1.1% stroke. Surprisingly, having accounted for other risk factors, addition of CABG did not adversely affect the outcomes.

The strengths of the study include its large number of participants, no exclusion of urgent and emergency/salvage cases, and inclusion of all risk participants. The limitations are that three centres were unable to take part, possible coding errors in using large databases, lack of detailed echocardiographic data on valve annular size and presence or absence of pre-operative infective endocarditis which can adversely affect outcomes. In addition, the results are in-hospital mortality and complications and the database lack longer follow-up information.

Data from the current study are consistent with other large international studies. Data from the US Society of Thoracic Surgeons (STS) database demonstrated in-hospital mortality for isolated SAVR of 2.5% and incidence of stroke of 1.5%.[15] A recent analysis of the Japanese Cardiovascular Surgery database which assessed the outcomes of patients undergoing SAVR over a 8 year period has demonstrated a similar in-hospital mortality of 2%.[16] They also demonstrated a reduction in mortality over time, despite increasing surgical risk. The age of the patients in our study is lower than some of the trials of SAVR and TAVI. This is probably due to the selection criteria in these trials where older patients were selected.

We had set out to analyse the results of SAVR in the UK to inform practitioners treating people with aortic valve disease and inform people with this condition in an era where other therapies for management of aortic valve disease are evolving with

expanding indications. Although the current study did not examine people who received TAVI, we discuss the various trials of SAVR and TAVI reported in the context of the literature and compare them with the results of the current study.

In Tables 3-5, the demographics, procedural details and outcomes of the current study are compared with the respective sub-groups of the published trials. Table 5 shows low mortality and complication rate in the participants of this study following surgery in people who required SAVR or SAVR+CABG. The trials comparing AVR and TAVI have enrolled and classified patients according to the risk of surgery, in particular the more recent trials.[6,7] The most commonly used surgical risk stratification score is the Society of Thoracic Surgery risk score (STS), although this scoring system has been validated in the US population. We have used EuroSCORE and shown that mortality is low in all categories of risk.

There are several recent trials comparing SAVR with TAVI. A meta-analysis of six of these trials performed by Barili and colleagues reported that mortality was affected by the treatment modality with a time-varying effect: TAVI was related to better survival in the first months after implantation whereas, after 40 months, it was a risk factor for all-cause mortality.[17] The NOTION trial, which compared outcomes of patients estimated to have low surgical risk who underwent either TAVI or SAVR demonstrated similar early mortality results, with mortality of 2.1% in TAVI group vs 3.7% in the SAVR group, p=0.38.[18] The PIVOTAL trial of low risk patients also reported similar results between those who underwent TAVI compared to SAVR, with early mortality of 0.5% in TAVI group and 1.3% in SAVR.[7] In addition, the 5 year results of the PARTNER 2 study, comparing TAVI vs SAVR in intermediate surgical risk demonstrated no significant difference in the incidence of death or stroke at 5 years following SAVR or TAVI.[19] The mortality in the intermediate EuroSCORE risk category of the current study was 1.0% for SAVR only and 0.9% for SAVR+CABG. PARTNER 3 however demonstrated significantly lower mortality in the TAVI group compared to SAVR (1% vs 2.5%, P=0.01) at one year.[6] An observational study of 7618 patients comparing SAVR with TAVI at 5 years showed however that in a real world population with low and intermediate risk, SAVR was associated with lower mortality and major adverse cardiac events, although this was with first generation TAVI devices.[20]

Role of co-existent coronary artery disease and its management

60% of patients with aortic valve disease undergoing SAVR and 65% of those undergoing TAVI have coexisting coronary artery disease.[21] In our series, 37% had co-existent coronary artery disease and underwent concomitant CABG. The addition of CABG did not adversely affect outcomes. The US[15] and Japanese[16] series did not look into concomitant CABG. The percentage of concomitant CABG in our series is higher than the trials of SAVR/TAVI. This probably reflects the selection criteria in the latter. In PARTNER 2, although both groups had a similar number with coexistent coronary artery disease, 14.5% of the SAVR group had concomitant CABG compared to 3.9% of the TAVI group who had percutaneous intervention (Table 4).[22] SAVR may therefore be the preferred treatment modality in those with aortic stenosis and multivessel coronary artery disease requiring revascularisation.

Treatment of coronary artery disease in TAVI patients may require more than one hospital admission and can often result in incomplete revascularisation and its consequent increased morbidity and mortality. A meta-analysis by Sankaramangalam and colleagues, demonstrated that whilst there was no increase in mortality in patients with coronary artery disease who underwent TAVI at 30 days, there was a significant increase in mortality at one year following TAVI in these patients.[23] The economic costs of readmission after TAVI have been demonstrated to be higher than in those who are readmitted after surgery and so untreated coronary disease which later requires readmission will have cost implications.[24,25] Surgery has the advantage of addressing all the pathology with one operation.

Durability and choice of prosthetic valves

In choosing the technique of treatment for aortic valve disease, life expectancy of the person and durability of the valve need to be considered. Ideally, the prosthetic valve should be durable for the person's lifetime. Both of these are related to person's age. In the UK a 50 year old female has a life expectancy of 34 years and a 70 year old male a life expectancy of 14 years.[26]

The durability of bioprosthetic valves is well documented in the surgical literature and is inversely proportional to person's age. Structural valve deterioration (SVD) has

been demonstrated to increase exponentially beyond 10 years following surgery.[27,28] Considering the UK life expectancy [26], a 70 year old male has a 5% risk of re-operation and a 50 year old female has a 30% chance of needing a second operation.

Surgery has the advantage of offering the patient a mechanical or a bioprosthetic valve. The option of a mechanical valve which is only available in surgical SAVR should not be overlooked especially in younger people. In the current study, we have shown a fairly consistent ratio of tissue to mechanical valve use. However, the reported literature shows that the number of mechanical valve implantations has reduced in comparison to bioprosthetic valves.[10] Mechanical valves are durable, with one group reporting 6.9% reintervention rate at 15 years versus 12.1% in those who underwent surgery with a bioprosthesis.[29] For this reason, it has been the most commonly considered prosthesis in those under the age of 60, as in our study where 60.2% of participants <60 years had a mechanical valve. Mechanical valves have the disadvantage of requiring anticoagulation, although, newer generations require a lower level of anticoagulation. [30]Whilst mechanical valves are more durable, this has to be balanced against the greater risk of bleeding. [29] At 15 years follow up, Chiang and colleagues also demonstrated no significant difference in survival and stroke between patients who underwent SAVR with mechanical vs bioprosthetic valve.[29] Another group demonstrated in the 50-70 year old cohort that survival at 5 years was higher in patients who had undergone SAVR with mechanical valve vs bioprosthesis and also demonstrated similar freedom from major bleeding events.[31]

Bicuspid aortic valve and aneurysm of the aorta

A significant number of patients requiring SAVR have bicuspid aortic valve, which has an incidence of 1-2% in the general population and may present with aortic valve stenosis, regurgitation and ascending aortic aneurysm. The type of native aortic valve is not recorded in the database of our study. BAV may be present in up to 30% of patients undergoing SAVR.[32] Bicuspid aortic valve anatomy, larger annular size, bulky and asymmetric leaflet calcification and dilated ascending aorta all pose technical challenges to TAVI which are not prohibitive risk factors for surgery. In fact, associated

pathology of aneurysms of the aortic root and ascending aorta can be treated at the time of SAVR with little additional risk.[33]

European guidelines recommend discussing people with aortic valve disease in a multi-disciplinary setting referred to as Heart Team, comprising of a surgeon, a non-interventional and an interventional cardiologist.[34] This will allow the best treatment option to be put forward to the person.

CONCLUSIONS

SAVR with and without CABG has low mortality risk and a low level of complications in the UK in people of all ages and risk factors. Our study provides real world experience of surgical results to improve understanding of the risks of surgery and decision making in a multi-disciplinary team (MDT) setting with Heart Team. The results of this study can be utilised by people with aortic valve disease, referring general practitioners, physicians, surgeons and policy makers. Future studies need to address long term follow-up including factors like quality of life which are currently not collected by the specialist centres.

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each author has cointributed to the various verisons of the manuscipt with constructive comments. Every author has contributed to the interpretation of data. More specifically:

1. Marjan Jahangiri - Thought of the concept, designed the project, plan data collection, identified units, approached each unit, collected and analysed the data. Wrote the first draft and author for subsequesnt versions.
2. Rajdeep Bilkhu - thought of the concept, designed the project, planned data collection, collected the data and cleaned it, contribuited significantly to writing major sections of the paper
3. Andrew Embleton-Thirsk – Involved in the design of the study at the outset, of the two main statistician who carried out the statistical work. Attended several meetings to discuss the project, involed in writing all the versions.
4. Hakim-Moulay Dehbi - Involved in the design of the study at the outset, of the two main statistician who carried out the statistical work. Attended several meetings to discuss the project, involed in writing all the versions.
5. Krishna Mani - thought of the concept, designed the project, planned data collection, collected the data and cleaned it, contribuited significantly to writing major sections of the paper, checked the literature contents and references.
6. Jon Anderson – Planned the project with the first two authors, acquired the data and contributed to several verisons during the wiriing up phase
7. Vassilios Avlonitis - Planned the project with the first two authors, acquired the data and contributed to several verisons during the wirting up phase
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36. Nick Freemantle – Senior statistician who designed the project, defiend the original plan for the study, assisted the other two statistician to analyse the data, took part in several meetings interpreting the data with further analysis,
assisted in writing the paper and final analysis

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Ethical approval: Anonymised data were submitted to the Society for Cardiothoracic Surgery of Great Britain & Ireland (SCTS) for 27 of the 30 units and then stored in a secure database. This data is ordinarily submitted to National Institute of Cardiovascular Outcome Research (NICOR) for which local and national Caldicott guardian approvals have been obtained. A further approval from the Caldicott Guardian was obtained in 2020.

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Data sharing: Requests on data sharing can be made by contacting the corresponding author. Data will be shared after review and approval by the authors and terms of collaboration will be reached together with a signed data access agreement.

The corresponding author (MJ) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. The manuscript is read and approved by all authors.

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Tables 1. Mortality (%) for different categories of age and EuroSCORE

Euroscore	N (%)	SAVR+CABG (Mortality %)	SAVR (Mortality %)
<3%	15619 (50.0)	2.0	1.3
3-6%	5020 (16.1)	0.9	1.0
>6%	6846 (21.9)	4.4	3.9
Age (years)		**SAVR+CABG**	**SAVR**
<60		2.2	2.0
60-75		1.8	1.5
>75		3.1	2.2

Table 2. Multivariable modelling of post-operative outcomes using pre-operative and operative factors

Predictor	missing	Category	Hospital mortality		Return to theatre for bleeding		New stroke		Post-operative length of stay (days)	
			Odds ratio	P-value	Odds ratio	P-value	Odds ratio	P-value	Odds ratio	P-value
Age (years)	7.9%	*per unit increase*	1.03 (1.02-1.04)	<0.001	1.01 (1.00-1.01)	0.006	1.02 (1.01-1.03)	0.001	1.00 (1.00-1.00)	<0.001
Gender	10.3%	Female	-		-		-		-	
		Male	0.63 (0.51-0.77)	<0.001	1.18 (1.02-1.36)	0.026	1.02 (0.80-1.29)	0.89	0.94 (0.93-0.96)	<0.001
LVEF	3.1%	Good (>50%)	-		-		-		-	
		Moderate (30-50%)	1.48 (1.18-1.85)	0.001	1.08 (0.91-1.27)	0.38	1.13 (0.86-1.48)	0.38	1.08 (1.06-1.10)	<0.001
		Poor (<30%)	1.90 (1.36-2.69)	<0.001	1.10 (0.82-1.48)	0.53	0.78 (0.44-1.38)	0.40	1.07 (1.03-1.11)	0.001
EuroSCORE Logistic	12.1%	*per unit increase*	1.02 (1.02-1.03)	<0.001	1.01 (1.00-1.01)	0.16	1.00 (0.99-1.02)	0.30	1.01 (1.01-1.01)	<0.001
Operative Urgency	0.02%	1. Elective	-		-		-		-	
		2. Urgent	1.63 (1.30-2.00)	<0.001	1.26 (1.08-2.00)	0.002	1.08 (0.83-1.41)	0.55	1.18 (1.16-1.20)	<0.001
		3. Emergency	6.87 (4.70-10.16)	<0.001	2.22 (1.51-3.26)	<0.001	7.65 (5.00-11.70)	<0.001	1.78 (1.67-1.90)	<0.001
		4. Salvage	11.79 (5.73-24.27)	<0.001	1.51 (0.56-4.02)	0.41	4.38 (1.47-13.1)	0.008	1.25 (1.07-1.46)	0.006
Cumulative Bypass Time (mins)	2.4%	*per unit increase*	1.02 (1.01-1.02)	<0.001	1.00 (1.00-1.01)	<0.001	1.00 (1.00-1.01)	<0.001	1.00 (1.00-1.00)	<0.001
Cumulative Cross Clamp Time (mins)	2.5%	*per unit increase*	0.99 (0.99-0.99)	<0.001	1.00 (1.00-1.00)	0.23	1.00 (0.99-1.00)	0.58	1.00 (1.00-1.00)	0.78
CABG	0%	No	-		-		-		-	
		Yes	1.15 (0.93-1.42)	0.20	1.07 (0.93-1.24)	0.33	1.12 (0.88-1.42)	0.37	1.03 (1.00-1.05)	<0.001

LVEF; left ventricular ejection fraction, CABG; coronary artery bypass graft surgery

Table 3. Baseline characteristics in the current study (UK SAVR) and those in other national registries and recent trials comparing SAVR with TAVI

Characteristic	UK SAVR	Thourani[15]	Tokuda[16]	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT [7]		PIVOTAL [5]		NOTION
	SAVR N=31,277	SAVR N=141 905	SAVR N=20 514	SAVR N=1021	TAVR N=1011	SAVR N=454	TAVI N=496	SAVR N=678	TAVI N=725	SAVR N=357	TAVI N=390	SAVR N=135
Age (mean±SD)	70.1±11.5	67.6 ± 13.4	NR	81.7±6.7	81.5±6.7	73.6±6.1	73.3±5.8	73.6±5.9	83.1±5.8	83.2±6.4	83.1±7.1	79 ± 4.7
% Male	59	58	51.1	54.8	54.2	71.1	67.5	66.2	52.4	52.4	53.1	53.8
BMI (kg/m^2)	28.9±5.5	29.3 ± 6.6	NR	28.3±6.2	28.6±6.2	30.3±5.1	30.7±5.5	NR	NR	NR	NR	NR
NYHA class III/IV (%)	44.4	38.4	15.9	76.3	77.3	23.8	31.2	28.4	85.1	86.9	85.7	45.5
Logistic EuroSCORE (%)	4.3±7.3	NR	NR	NR	NR	1.5±0.9*	1.5±1.2*	NR	NR	18.6±13.0	17.7±13.1	8.9 ± 5.5
Diabetes Mellitus (%)	22.2	25.5	NR	34.2	37.7	30.2	31.2	30.5	41.4	45.4	34.9	20.7
Chronic Kidney Disease (%)	3.1	NR	NR	5.2	5.0	0.2	0.2	0.1	13.4	12.8	12.2	0.7
Hypertension (%)	64.9	NR	NR	NR	NR	NR	NR	82.6	94.8	96.1	95.1	76.3
Peripheral vascular disease (%)	8.7	9.2	NR	32.9	27.9	7.3	6.9	7.5	40.3	41.7	41.1	6.7
Previous stroke (%)	8.2	12.6	0.13	31	32.1	5.1	3.4	10.2	11.8	14.0	12.6	16.3
COPD (%)	13.4	NR	13.6	30.0	31.8	6.2	5.1	15.0	8.0	9.0	13.3	11.9
LV ejection fraction (%)	53.2	54.9 ± 12.9	NR	55.3±11.9	56.2±10.8	66.2±8.6	65.7±9.0	61.9 ± 7.7	61.7 ± 9.9	NR	NR	NR
Coronary artery disease (%)	37.1	NR	NR	66.5	69.2	28.0	27.7	NR	NR	75.9	75.4	NR
Atrial fibrillation	10.3	NR	5.6	35.2	31.0	18.8	15.7	14.5	40.4	45.9	40.9	25.6
Permanent pacemaker	1.9			12.0	11.7	2.9	2.4	3.8	19.2	21.3	23.3	4.4

SAVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, BMI; body mass index, NYHA; New York Heart Association classification, COPD; chronic obstructive pulmonary disease, NR; not reported

*EuroSCORE II reported only

Table 4. Operative characteristics in the current study (UK AVR) and those in other national registries and recent trials comparing SAVR with TAVI

Characteristic	UK SAVR	Thourani[15]	Tokuda[16]	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT [7]		PIVOTAL [5]		NOTION [18]	
	SAVR N=31,277	SAVR N=141 905	SAVR N=20 514	SAVR N=1021	TAVI N=1011	SAVR N=454	TAVI N=496	SAVR N=678	TAVI N=725	SAVR N= 357	TAVI N= 390	SAVR N= 135	TAVI N= 145
Operative urgency													
Elective (%)	74.3	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Urgent (%)	24	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Emergency/Salvage (%)	1.7	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Concomitant CABG (%)	37.1	NR	NR	NR	-	12.8	-	13.6	-	4.8	-	1	-
Staged PCI	-	NR	NR	-	NR	-	6.5	-	6.5	-	0.3%		0
Cross clamp time (minutes)	79.0	77.0 ± 28.5	NR	NR	-	74.3 ± 27.78	-	68.7 ± 29.0	-	74.0 ± 31.4	-	NR	NR
Cardiopulmonary bypass time (minutes)	104	104.9 ± 39.1	NR	NR	-	97.7 ± 33.75	-	93.4 ± 40.2	-	104.0± 45.8	-	NR	NR
Procedure time (minutes)	NR	NR	NR	NR	NR	208.3 ± 62.1	58.6 ± 36.5	276.6 ± 79.5	218.2 ± 55.	221 ± 84.8	60.4 ± 35.3	177.2 ± 39.8	90.3 ± 38.6

SAVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, CABG; coronary artery bypass graft surgery

NR; not reported

Table 5. Outcomes following SAVR in the current study (UK AVR) and those in other national registries and recent trials comparing SAVR with TAVI

Outcome	UK SAVR	Thourani[15]	Tokuda[16]	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT		PIVOTAL [5]		NOTION [18]	
	SAVR N=31,277	SAVR N=141 905	SAVR N=20 514	SAVR N=1021	TAVI N=1011	SAVR N=454	TAVI N=496	SAVR N=678	TAVI N=725	SAVR N= 357	TAVI N= 390	SAVR N= 135	TAVI N= 145
In-hospital death/30-day mortality (%)	1.9	2.5	NR	8.0	6.1	1.1	0.4	1.3	5.5	4.5	3.3	3.7	2.1
Stroke (%)	1.1	NR	1.6	6.1	5.5	2.4	0.6	3.4	4.4	6.2	4.9	3.0	1.4
Reoperation for bleeding* (%)	3.6	3.9	3	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Post procedure bleeding* (%)	-	NR		43.4	10.4	11.9	1.2	7.5	2.4	69.5	41.7	11.3	20.9
Deep sternal wound infection (%)	0.14	0.3	1.1	NR	-	NR	-	NR		NR	-	NR	-
Length of hospital stay (days)	7	7.9 ± 7.2	NR	NR	-	7.0	3.0	NR	NR	NR	NR	8.9 ± 6.2	12.9 ± 11.6
New pacemaker implantation (%)	1.6	NR	NR	6.9	8.	4.0	6.5	6.1	11.4	7.1	19.8	1.6	34.1

SAVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, CABG; coronary artery bypass graft surgery, NR; not reported

*Reoperation for bleeding and post-operative bleeding were major and required intervention

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	4-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-6
Bias	9	Describe any efforts to address potential sources of bias	4-6
Study size	10	Explain how the study size was arrived at	4-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	6

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7-8
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	7-8
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	NA

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Surgical aortic valve replacement in the era of transcatheter aortic valve implantation - A review of the UK national database

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ABSTRACT

Objectives - To date the reported outcomes of surgical aortic valve replacement (SAVR) are mainly in the settings of trials comparing it with evolving transcatheter aortic valve implantation (TAVI). We set out to examine characteristics and outcomes in people who underwent SAVR reflecting a national cohort and therefore 'real world' practice.

Design - Retrospective analysis of prospectively collected data of consecutive people who underwent SAVR with or without coronary artery bypass graft (CABG) surgery between April 2013 and March 2018 in the UK. This included elective, urgent and emergency operations. Participants' demographics, pre-operative risk factors, operative data, in-hospital mortality, post-operative complications and effect of the addition of CABG to SAVR were analysed.

Setting - 27 (90%) tertiary cardiac surgical centres in the UK submitted their data for analysis.

Participants - 31,277 people with AVR were identified. 19,670 (62.9%) had only SAVR and 11,607 (37.1%) had AVR+CABG.

Results – In-hospital mortality for isolated SAVR was 1.9% (95% CI: 1.6-2.1%) and was 2.4% for AVR+CABG. Mortality by age category for SAVR only were: <60 years=2.0%, 60-75 years=1.5%, >75 years=2.2%. For SAVR+CABG these were; 2.2%, 1.8% and 3.1%. For different categories of EuroSCORE, mortality for SAVR in low risk people was 1.3%, in intermediate risk 1% and for high risk 3.9%. 74.3% of the operations were elective, 24% urgent and 1.7% emergency/salvage. The incidences of re-sternotomy for bleeding and stroke were 3.9% and 1.1% respectively. Multivariable analyses provided no evidence that concomitant CABG influenced outcome. However, urgency of the operation, poor ventricular function, higher EuroSCORE and longer cross clamp and cardiopulmonary bypass times adversely affected outcomes.

Conclusions - Surgical SAVR±CABG has low mortality risk and a low level of complications in the UK in people of all ages and risk factors. These results should inform consideration of treatment options in people with aortic valve disease.

Strengths and limitations of this study

- This is a large study of consecutive participants who have undergone surgical aortic valve replacement ± coronary artery bypass graft surgery in the UK, reporting contemporary outcomes.
- This study includes people of all age groups and risks factors, and elective as well as urgent and emergency operations.
- The results are of in-hospital mortality and complications and longer term follow-up data is not available.

BACKGROUND

Aortic valve disease, especially aortic stenosis affects 5% of the population and 3.9% of those between the ages of 70 and 79 and nearly 10% of those above the age of 80.[1] Severe aortic stenosis when untreated has a risk of death of 50% at 2 years.[2] Conventionally the gold standard of treatment has been surgical aortic valve replacement (SAVR). However, the role of transcatheter aortic valve implantation (TAVI) has evolved in recent years. TAVI was first introduced in 2002, initially being performed in high risk inoperable patients.[3] The original Placement of Aortic Transcatheter Valves (PARTNER) trial demonstrated a significant reduction in mortality, repeat hospitalisation and cardiac symptoms compared to inoperable patients who had only medical therapy.[4] The original PIVOTAL study also demonstrated significantly higher survival at one year in high risk patients who underwent SAVR.[5]

The role of TAVI is being extended to lower risk and younger patients based on recent trials comparing SAVR with TAVI.[6,7] Several studies suggest there has been a change in demographics and types of surgical valves used since the advent of TAVI.[8–10] There has been a trend of increased use of tissue valves and a decrease in the use of mechanical valves in recent years.[11] This may be due to the evolution of TAVI practice whereby younger patients can have a tissue valve with the view that they have a TAVI valve in the future when the tissue valve has deteriorated, so called valve-in-valve.[12,13]

The series in the literature reporting outcomes of SAVR are generally unit based.[9,14] Also, people with aortic valve disease are given information about the outcomes of SAVR which may be out of date and incorrectly extrapolated from smaller studies. There is a lack of contemporary national data to assess the outcomes of SAVR (mortality and complications), and to demonstrate the trend in use of prosthetic valves which would inform people with aortic valve disease better. There are some perceived complications of surgery that may be understood by referring general practitioners and cardiologists to be prohibitive risks for surgery.

In order to inform practitioners, people with aortic valve disease and the cardiac surgical community, we set out to examine the results of contemporaneous SAVR in a multi-centre study of UK cardiac surgical units, in the era of TAVI. In addition, we

summarise and interpret some of the more recent trials on the management of aortic valve disease.

METHODS

Data

This is an analysis of prospectively collected data of people who underwent SAVR +/- coronary artery bypass graft (CABG) surgery between April 2013 and March 2018 in the UK and Republic of Ireland. Anonymised data were submitted to the Society for Cardiothoracic Surgery of Great Britain & Ireland (SCTS) for 27 of the 30 units and then stored in a secure database. This period was chosen to reflect fairly contemporary practice and also the data is submitted in March every year. The data is collected by each unit, validated and then submitted to the National Institute of Cardiovascular Outcome Research (NICOR). It took approximately nine months to collect, validate and clean all the data. The outcome measures recorded are based on strict definitions provided by NICOR to provide uniformity.

Only participants who had had first time surgery, SAVR +/- CABG were included. All participants immaterial of their risk for surgery, people of all age groups and risk factors were included. Those who required other concomitant procedures like replacement of parts of the aorta, aortic root enlargement, other valve procedures and redo surgery were excluded.

Pre-operative risk factors and operative features

Baseline demographic data; significant past medical history such as diabetes, renal dysfunction, hypertension or stroke; predominant aortic valve pathology (stenosis or regurgitation or mixed valve disease) and preoperative left ventricular ejection fraction (LVEF) were collected. EuroSCORE is the risk stratification model used in the UK. Logistic EuroSCORE was collected as well as EuroSCORE II where available. The latter was only used since 2017 and therefore not available for all participants. Logistic EuroSCORE was divided into three categories: <3%, 3-6%, >6%.

LVEF was divided into three categories: good (EF>50%), moderate (EF 30-50%) and poor (EF<30%). Transient ischaemic attack was defined as any neurological

symptoms lasting <24 hours. Stroke was defined as new neurological dysfunction persisting >24 hours. Operative data including operative urgency: elective, urgent and emergency/salvage were recorded. Elective was defined as when the person was admitted from home, urgent meaning that the person was admitted with an urgent condition and required surgery during the same hospital admission, emergency and salvage meaning that surgery was required within 24 hours of admission and/or the person was in extremis. Other parameters including cardiopulmonary bypass (CPB) time, cross clamp (CCT) time, type of valve implanted as well as concomitant CABG surgery performed were also collected.

Postoperative outcomes

Postoperative complication data were collected with the main focus being in-hospital mortality, new stroke, return to theatre for bleeding, deep sternal wound infection and duration of postoperative hospital stay.

Statistical analysis

Once the records for all participants were collated and the data cleaned, each factor was summarised using descriptive methods. Categorical variables are presented as N (%) and continuous variables are presented as median (IQR). New strokes were recoded to be either no stroke or any cerebrovascular accident (transient or permanent). The natural log of post-operative length of stay (days) was used due to positive skewed distribution of this variable. Univariate models were used, logistic regression for binary outcomes and linear regression for continuous outcomes, to assess the impact of the key explanatory variables. In these models, a two-tailed p-value of <0.05 was considered significant. The population analysed included all the participants with data collected, with results checked in the subset who had SAVR only (without CABG). Building on this, a multivariable model with all key variables in the model to assess which had the most impact on each of the outcomes was created. Stata/MP 15.1 (StataCorp LLC, Texas, USA) was used for all analyses. Multiple imputation of missing data was not performed. The missingness was mostly negligible. There was no missing mortality and the data is shown in table 1.

Patient and public involvement

Patients and public were involved in the original design of the database.

RESULTS

Descriptive analysis

In total 31,277 patients were included. Of these, 19,670 (62.9%) had only SAVR and 11,607 (37.1%) had SAVR+CABG. There were 14.4% below the age of 60, 46.9% between 60 to 75 and 36.7% older than 75 years with 7.9% missing age data. There were 1.9 times more males than females (10.3% missing).

Regarding pre-operative risk factors, 75.2% had good LVEF, 17.3% had moderate and 4.3% had poor LVEF. 74.3% of the operations were elective, 24% were urgent and 1.7% were emergency or salvage operations.

Logistic EuroSCORE had a median of 1.83 with an IQR of 0.06-6.0. In total, 50% of patients were classified as low risk (<3%), 16% as medium risk (3—6%) and 22% high risk (>6%). 3,792 patients (12.1%) were missing data. The median EuroSCORE II was 1.95 (IQR 0.67-4.8) albeit with 56.5% with missing data, as this was introduced into the database in 2017. The median CPB time was 104 minutes (IQR 82-135) and CCT was 79 minutes (IQR 61-101).

For valve implant replacement type, 70% had a tissue valve, 12.2% a mechanical valve and 0.2% had homograft or autograft valves. For 17.3% the entry for valve type was unclear. The ratio of mechanical implant to bioprosthetic implant use has remained stable over time.

Overall mortality was 2.4% (95% CI: 2.2-2.6%) and mortality for isolated SAVR for all participants was 1.9% (1.6-2.1%). The mortality figures analysed for different age ranges and for categories of EuroSCORE are shown in Table 2.

Overall, 3.9% (3.6% in SAVR only) of participants had re-sternotomy for post-operative bleeding or tamponade, 0.04% (0.06% in SAVR only) had re-operation for valvular problems (significant paravalvular leak and early endocarditis), 0.7% (0.6% SAVR only) had re-operation for other cardiac problems, 0.2% (0.15% for SAVR only) had rewiring of sternum for sterile wounds and 0.14% (0.06% for SAVR only) had re-

wiring of sternum for infection. Transient ischaemic attack occurred in only 0.6% and 1.1% had a stroke (no missing data).

Median post-operative length of stay was 7 days (IQR: 6-11) in those with SAVR only and 8 days (IQR: 6-12) in all patients.

The number of bypass grafts was not analysed due to concerns about inconsistent reporting of data describing the number of grafts.

When comparing the two subsets of patients, the characteristics of those with SAVR alone were broadly similar to those with SAVR+CABG. In SAVR alone there were more people aged <60 years (19.3% vs 6.2%), but less people were older than 75 (30.1% vs 43%). A higher proportion of those with SAVR+CABG were male (68% vs. 54%). Bypass time was an average of 37 minutes shorter and CCT 27 minutes in the SAVR alone group. Amongst those with only SAVR the mechanical valve usage was greater, at 16% vs 7%.

Regression analysis

Univariable

Taken in isolation, all pre-operative risk factors were associated with an increased odds of death, as was addition of CABG. The same pattern was observed when analysing the need for re-operation or surgery, with all explanatory variables indicative of a worse outcome without taking into account any others. For new stroke only age, EuroSCORE, operative urgency, ejection fraction, and cumulative bypass and cross clamp times affected a negative outcome (but not gender), as did CABG. All factors predicted a longer postoperative length of stay, including CABG.

As a sensitivity analysis, age categories were also assessed. When included as a continuous variable, age was significant both on its own and in all the multivariable models. All participants were categorised into <60, 60-75 and >75 years of age. Those 60-75 were at a lower odds of death in comparison to those <60 (OR 0.71, 95% CI 0.53-0.95, P=0.021) with no difference in those >75 (OR 1.09, 95% CI 0.82-1.45) in the AVR alone group. These findings were different in the SAVR+CABG group, with no significant difference in those 60-75 (OR 0.81, 95% CI 0.64-1.03) but an increased risk in those >75 (OR 1.09, 95% CI 1.12-1.76, P=0.004).

Multivariable Analyses

Analysis of postoperative outcomes using multivariable models including all pre-operative and operative factors are shown in Table 1. This demonstrated that age (OR 1.03 (95% CI 1.02-1.04), P<0.001), moderate ejection fraction (OR 1.48 (95% CI 1.18-1.85), P<0.001), poor ejection fraction (OR 1.90 (95% CI 1.36-2.69), P<0.001), logistic EuroSCORE (OR 1.02 (95% CI 1.02-1.03), P<0.001), urgent operation (OR 1.63 (95% CI 1.30-2.00, P<0.001), emergency surgery (OR 6.87 (95% CI 4.70-10.16), P<0.001) and longer CPB times affected mortality (OR 1.02 (95% CI 1.01-1.02), P<0.001).

When all other variables were taken into account CABG was not significantly associated with an increase in the risk of death (OR 1.15 (95% CI 0.93-1.42), P=0.20).

Older age, (OR 1.01 (95% CI 1.00-1.01), p<0.006), longer CPB time (OR 1.00 (95% CI 1.00-1.01), P<0.001), urgent (OR 1.26 (95% CI 1.08-2.00), P<0.002) and emergency surgery (OR 2.22 (95% CI 1.51-3.26), P<0.001) were significant factors in identifying people requiring return to theatre for bleeding. Again, CABG did not affect the odds of returning to theatre (OR 1.07 (95% CI 0.93-1.24), P=0.33).

Factors affecting stroke were age, (OR 1.02 (95% CI 1.01-1.03), P<0.001), emergency (OR 7.65 (95% CI 5.00-11.70, P<0.001) or salvage surgery (OR 4.38 (95% CI 1.47-13.1) P=0.008), and CPB times (OR 1.00 (95% CI 1.00-1.01), P<0.001). As in the other outcomes, addition of CABG did not affect the outcome (OR 1.12 (95% CI 0.88-1.42), P=0.37).

Age, male gender, moderate and poor ejection fraction, operative urgency, higher logistic EuroSCORE, and cumulative bypass time significantly all affected post-operative length of stay.

DISCUSSION

This study reports contemporary results of SAVR and SAVR+CABG in the UK, reflecting real world practice, reporting an overall mortality of 1.9% and 2.4% respectively. We have shown a low mortality and complication rate for all comers following surgery in people requiring SAVR or SAVR+CABG. The complications were low with 3.9% re-sternotomy for bleeding, 0.04% re-operation for valvular problems and 1.1% stroke. Surprisingly,

having accounted for other risk factors, addition of CABG did not adversely affect the outcomes.

The strengths of the study include its large number of participants, no exclusion of urgent and emergency/salvage cases, and inclusion of all risk participants. The limitations are that three centres were unable to take part, possible coding errors in using large databases, lack of detailed echocardiographic data on valve annular size and presence or absence of pre-operative infective endocarditis which can adversely affect outcomes. In addition, the results are in-hospital mortality and complications and the database lack longer follow-up information.

Data from the current study are consistent with other large international studies. Data from the US Society of Thoracic Surgeons (STS) database demonstrated in-hospital mortality for isolated SAVR of 2.5% and incidence of stroke of 1.5%.[15] A recent analysis of the Japanese Cardiovascular Surgery database which assessed the outcomes of patients undergoing SAVR over a 8 year period has demonstrated a similar in-hospital mortality of 2%.[16] They also demonstrated a reduction in mortality over time, despite increasing surgical risk. The age of the patients in our study is lower than some of the trials of SAVR and TAVI. This is probably due to the selection criteria in these trials where older patients were selected.

We had set out to analyse the results of SAVR in the UK to inform practitioners treating people with aortic valve disease and inform people with this condition in an era where other therapies for management of aortic valve disease are evolving with expanding indications. Although the current study did not examine people who received TAVI, we discuss the various trials of SAVR and TAVI reported in the context of the literature and compare them with the results of the current study.

In Tables 3-5, the demographics, procedural details and outcomes of the current study are compared with the respective sub-groups of the published trials. Table 5 shows low mortality and complication rate in the participants of this study following surgery in people who required SAVR or SAVR+CABG. The trials comparing AVR and TAVI have enrolled and classified patients according to the risk of surgery, in particular the more recent trials.[6,7] The most commonly used surgical risk stratification score is the Society of Thoracic Surgery risk score (STS), although this scoring system has been validated in

the US population. We have used EuroSCORE and shown that mortality is low in all categories of risk.

There are several recent trials comparing SAVR with TAVI. A meta-analysis of six of these trials performed by Barili and colleagues reported that mortality was affected by the treatment modality with a time-varying effect: TAVI was related to better survival in the first months after implantation whereas, after 40 months, it was a risk factor for all-cause mortality.[17] The NOTION trial, which compared outcomes of patients estimated to have low surgical risk who underwent either TAVI or SAVR demonstrated similar early mortality results, with mortality of 2.1% in TAVI group vs 3.7% in the SAVR group, p=0.38.[18] The PIVOTAL trial of low risk patients also reported similar results between those who underwent TAVI compared to SAVR, with early mortality of 0.5% in TAVI group and 1.3% in SAVR.[7] In addition, the 5 year results of the PARTNER 2 study, comparing TAVI vs SAVR in intermediate surgical risk demonstrated no significant difference in the incidence of death or stroke at 5 years following SAVR or TAVI.[19] The mortality in the intermediate EuroSCORE risk category of the current study was 1.0% for SAVR only and 0.9% for SAVR+CABG. PARTNER 3 however demonstrated significantly lower mortality in the TAVI group compared to SAVR (1% vs 2.5%, P=0.01) at one year.[6] An observational study of 7618 patients comparing SAVR with TAVI at 5 years showed however that in a real world population with low and intermediate risk, SAVR was associated with lower mortality and major adverse cardiac events, although this was with first generation TAVI devices.[20]

Role of co-existent coronary artery disease and its management

60% of patients with aortic valve disease undergoing SAVR and 65% of those undergoing TAVI have coexisting coronary artery disease.[21] In our series, 37% had co-existent coronary artery disease and underwent concomitant CABG. The addition of CABG did not adversely affect outcomes. The US[15] and Japanese[16] series did not look into concomitant CABG. The percentage of concomitant CABG in our series is higher than the trials of SAVR/TAVI. This probably reflects the selection criteria in the latter. In PARTNER 2, although both groups had a similar number with coexistent coronary artery disease, 14.5% of the SAVR group had concomitant CABG compared to 3.9% of the TAVI group who had percutaneous intervention (Table 4).[22] SAVR may therefore be the

preferred treatment modality in those with aortic stenosis and multivessel coronary artery disease requiring revascularisation.

Treatment of coronary artery disease in TAVI patients may require more than one hospital admission and can often result in incomplete revascularisation and its consequent increased morbidity and mortality. A meta-analysis by Sankaramangalam and colleagues, demonstrated that whilst there was no increase in mortality in patients with coronary artery disease who underwent TAVI at 30 days, there was a significant increase in mortality at one year following TAVI in these patients.[23] The economic costs of readmission after TAVI have been demonstrated to be higher than in those who are readmitted after surgery and so untreated coronary disease which later requires readmission will have cost implications.[24,25] Surgery has the advantage of addressing all the pathology with one operation.

Durability and choice of prosthetic valves

In choosing the technique of treatment for aortic valve disease, life expectancy of the person and durability of the valve need to be considered. Ideally, the prosthetic valve should be durable for the person's lifetime. Both of these are related to person's age. In the UK a 50 year old female has a life expectancy of 34 years and a 70 year old male a life expectancy of 14 years.[26]

The durability of bioprosthetic valves is well documented in the surgical literature and is inversely proportional to person's age. Structural valve deterioration (SVD) has been demonstrated to increase exponentially beyond 10 years following surgery.[27,28] Considering the UK life expectancy [26], a 70 year old male has a 5% risk of re-operation and a 50 year old female has a 30% chance of needing a second operation.

Surgery has the advantage of offering the patient a mechanical or a bioprosthetic valve. The option of a mechanical valve which is only available in surgical SAVR should not be overlooked especially in younger people. In the current study, we have shown a fairly consistent ratio of tissue to mechanical valve use. However, the reported literature shows that the number of mechanical valve implantations has reduced in comparison to bioprosthetic valves.[10] Mechanical valves are durable, with one group reporting 6.9% reintervention rate at 15 years versus 12.1% in those who underwent surgery with a

bioprosthesis.[29] For this reason, it has been the most commonly considered prosthesis in those under the age of 60, as in our study where 60.2% of participants <60 years had a mechanical valve. Mechanical valves have the disadvantage of requiring anticoagulation, although, newer generations require a lower level of anticoagulation. [30]Whilst mechanical valves are more durable, this has to be balanced against the greater risk of bleeding. [29] At 15 years follow up, Chiang and colleagues also demonstrated no significant difference in survival and stroke between patients who underwent SAVR with mechanical vs bioprosthetic valve.[29] Another group demonstrated in the 50-70 year old cohort that survival at 5 years was higher in patients who had undergone SAVR with mechanical valve vs bioprosthesis and also demonstrated similar freedom from major bleeding events.[31]

Bicuspid aortic valve and aneurysm of the aorta

A significant number of patients requiring SAVR have bicuspid aortic valve, which has an incidence of 1-2% in the general population and may present with aortic valve stenosis, regurgitation and ascending aortic aneurysm. The type of native aortic valve is not recorded in the database of our study. BAV may be present in up to 30% of patients undergoing SAVR.[32] Bicuspid aortic valve anatomy, larger annular size, bulky and asymmetric leaflet calcification and dilated ascending aorta all pose technical challenges to TAVI which are not prohibitive risk factors for surgery. In fact, associated pathology of aneurysms of the aortic root and ascending aorta can be treated at the time of SAVR with little additional risk.[33]

European guidelines recommend discussing people with aortic valve disease in a multi-disciplinary setting referred to as Heart Team, comprising of a surgeon, a non-interventional and an interventional cardiologist.[34] This will allow the best treatment option to be put forward to the person.

CONCLUSIONS

SAVR with and without CABG has low mortality risk and a low level of complications in the UK in people of all ages and risk factors. Our study provides real world experience of surgical results to improve understanding of the risks of surgery and decision making in a multi-disciplinary team (MDT) setting with Heart Team. The results of this study can be utilised by people with aortic valve disease, referring general practitioners, physicians, surgeons and policy makers. Future studies need to address long term follow-up including factors like quality of life which are currently not collected by the specialist centres.

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each author has cointributed to the various verisons of the manuscipt with constructive comments. Every author has contributed to the interpretation of data. More specifically:

1. Marjan Jahangiri - Thought of the concept, designed the project, plan data collection, identified units, approached each unit, collected and analysed the data. Wrote the first draft and author for subsequesnt versions.
2. Rajdeep Bilkhu - thought of the concept, designed the project, planned data collection, collected the data and cleaned it, contribuited significantly to writing major sections of the paper
3. Andrew Embleton-Thirsk – Involved in the design of the study at the outset, of the two main statistician who carried out the statistical work. Attended several meetings to discuss the project, involed in writing all the versions.

4. Hakim-Moulay Dehbi - Involved in the design of the study at the outset, of the two main statistician who carried out the statistical work. Attended several meetings to discuss the project, involed in writing all the versions.

5. Krishna Mani - thought of the concept, designed the project, planned data collection, collected the data and cleaned it, contribuited significantly to writing major sections of the paper, checked the literature contents and references.

6. Jon Anderson – Planned the project with the first two authors, acquired the data and contributed to several verisons during the wiriing up phase

7. Vassilios Avlonitis - Planned the project with the first two authors, acquired the data and contributed to several verisons during the wirting up phase

8. Max Baghai - Planned the project with the first two authors, acquired the data and contributed to several verisons during the writing up phase

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10. Karen Booth - Planned the project with the first two authors, acquired the data and contributed to several verisons during the writing up phase

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37. Nick Freemantle – Senior statistician who designed the project, defiend the original plan for the study, assisted the other two statistician to analyse the data, took part in several meetings interpreting the data with further analysis,
assisted in writing the paper and final analysis

Competing interests: All authors declare no competing interests.

Ethical approval: Anonymised data were submitted to the Society for Cardiothoracic Surgery of Great Britain & Ireland (SCTS) for 27 of the 30 units and then stored in a secure database. This data is ordinarily submitted to National Institute of Cardiovascular Outcome Research (NICOR) for which local and national Caldicott guardian approvals have been obtained. A further approval from the Caldicott Guardian was obtained in 2020.

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Data sharing: Requests on data sharing can be made by contacting the corresponding author. Data will be shared after review and approval by the authors and terms of collaboration will be reached together with a signed data access agreement.

The corresponding author (MJ) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. The manuscript is read and approved by all authors.

Ethics statement

This data is ordinarily submitted to National Institute of Cardiovascular Outcome Research (NICOR) for which local and national Caldicott guardian approvals have been obtained. The data are validated by the surgical teams and their database managers/audit officers. For the current study a further approval from the Caldicott Guardian was obtained.

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Table 1. Multivariable modelling of post-operative outcomes using pre-operative and operative factors

Predictor	missing	Category	Hospital mortality		Return to theatre for bleeding		New stroke	
			Odds ratio	P-value	Odds ratio	P-value	Odds ratio	P-value
Age (years)	7.9%	*per unit increase*	1.03 (1.02-1.04)	<0.001	1.01 (1.00-1.01)	0.006	1.02 (1.01-1.03)	0.001
Gender	10.3%	Female	-		-		-	
		Male	0.63 (0.51-0.77)	<0.001	1.18 (1.02-1.36)	0.026	1.02 (0.80-1.29)	0.89
LVEF	3.1%	Good (>50%)	-		-		-	
		Moderate (30-50%)	1.48 (1.18-1.85)	0.001	1.08 (0.91-1.27)	0.38	1.13 (0.86-1.48)	0.38
		Poor (<30%)	1.90 (1.36-2.69)	<0.001	1.10 (0.82-1.48)	0.53	0.78 (0.44-1.38)	0.40
EuroSCORE Logistic	12.1%	*per unit increase*	1.02 (1.02-1.03)	<0.001	1.01 (1.00-1.01)	0.16	1.00 (0.99-1.02)	0.30
Operative Urgency	0.02%	1. Elective	-		-		-	
		2. Urgent	1.63 (1.30-2.00)	<0.001	1.26 (1.08-2.00)	0.002	1.08 (0.83-1.41)	0.55
		3. Emergency	6.87 (4.70-10.16)	<0.001	2.22 (1.51-3.26)	<0.001	7.65 (5.00-11.70)	<0.001
		4. Salvage	11.79 (5.73-24.27)	<0.001	1.51 (0.56-4.02)	0.41	4.38 (1.47-13.1)	0.008
Cumulative Bypass Time (mins)	2.4%	*per unit increase*	1.02 (1.01-1.02)	<0.001	1.00 (1.00-1.01)	<0.001	1.00 (1.00-1.01)	<0.001
Cumulative Cross Clamp Time (mins)	2.5%	*per unit increase*	0.99 (0.99-0.99)	<0.001	1.00 (1.00-1.00)	0.23	1.00 (0.99-1.00)	0.58
CABG	0%	No	-		-		-	
		Yes	1.15 (0.93-1.42)	0.20	1.07 (0.93-1.24)	0.33	1.12 (0.88-1.42)	0.37

LVEF; left ventricular ejection fraction, CABG; coronary artery bypass graft surgery

Table 2. Mortality (%) for different categories of age and EuroSCORE

Euroscore	N (%)	SAVR+CABG (Mortality %)	SAVR (Mortality %)
<3%	15619 (50.0)	2.0	1.3
3-6%	5020 (16.1)	0.9	1.0
>6%	6846 (21.9)	4.4	3.9
Age (years)		**SAVR+CABG**	**SAVR**
<60		2.2	2.0
60-75		1.8	1.5
>75		3.1	2.2

Table 3. Baseline characteristics in the current study (UK SAVR) and those in other national registries and recent trials comparing SAVR with TAVI

Characteristic	UK SAVR	Thourani[15]	Tokuda[16]	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT		PIVOTAL [5]		NOTIO
	SAVR N=31,277	SAVR N=141 905	SAVR N=20 514	SAVR N=1021	TAVR N=1011	SAVR N=454	TAVI N=496	SAVR N=678	TAVI N=725	SAVR N=357	TAVI N=390	SAVR N=135
Age (mean±SD)	70.1±11.5	67.6 ± 13.4	NR	81.7±6.7	81.5±6.7	73.6±6.1	73.3±5.8	73.6±5.9	83.1±5.8	83.2±6.4	83.1±7.1	79 ± 4.7
% Male	59	58	51.1	54.8	54.2	71.1	67.5	66.2	64	52.4	53.1	53.8
BMI (kg/m^2)	28.9±5.5	29.3 ± 6.6	NR	28.3±6.2	28.6±6.2	30.3±5.1	30.7±5.5	NR	NR	NR	NR	NR
NYHA class III/IV (%)	44.4	38.4	15.9	76.3	77.3	23.8	31.2	28.4	25.1	86.9	85.7	45.5
Logistic EuroSCORE (%)	4.3±7.3	NR	NR	NR	NR	1.5±0.9*	1.5±1.2*	NR	NR	18.6±13.0	17.7±13.1	8.9 ± 5.5
Diabetes Mellitus (%)	22.2	25.5	NR	34.2	37.7	30.2	31.2	30.5	31.4	45.4	34.9	20.7
Chronic Kidney Disease (%)	3.1	NR	NR	5.2	5.0	0.2	0.2	0.1	0.4	12.8	12.2	0.7
Hypertension (%)	64.9	NR	NR	NR	NR	NR	NR	82.6	84.8	96.1	95.1	76.3
Peripheral vascular disease (%)	8.7	9.2	NR	32.9	27.9	7.3	6.9	7.5	8.3	41.7	41.1	6.7
Previous stroke (%)	8.2	12.6	0.13	31	32.1	5.1	3.4	10.2	11.8	14.0	12.6	16.3
COPD (%)	13.4	NR	13.6	30.0	31.8	6.2	5.1	15.0	18.0	9.0	13.3	11.9
LV ejection fraction (%)	53.2	54.9 ± 12.9	NR	55.3±11.9	56.2±10.8	66.2±8.6	65.7±9.0	61.9 ± 7.7	61.7 ± 7.9	NR	NR	NR
Coronary artery disease (%)	37.1	NR	NR	66.5	69.2	28.0	27.7	NR	NR	75.9	75.4	NR
Atrial fibrillation	10.3	NR	5.6	35.2	31.0	18.8	15.7	14.5	15.4	45.9	40.9	25.6
Permanent pacemaker	1.9			12.0	11.7	2.9	2.4	3.8	3.2	21.3	23.3	4.4

SAVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, BMI; body mass index, NYHA; New York Heart Association classification, COPD; chronic obstructive pulmonary disease, NR; not reported

*EuroSCORE II reported only

Table 4. Operative characteristics in the current study (UK AVR) and those in other national registries and recent trials comparing SAVR with TAVI

Characteristic	UK SAVR	Thourani[15]	Tokuda[16]	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT		PIVOTAL [5]		NOTION [18]	
	SAVR N=31,277	SAVR N=141 905	SAVR N=20 514	SAVR N=1021	TAVI N=1011	SAVR N=454	TAVI N=496	SAVR N=678	TAVI N=725	SAVR N= 357	TAVI N= 390	SAVR N= 135	TAVI N= 145
Operative urgency													
Elective (%)	74.3	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Urgent (%)	24	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Emergency/Salvage (%)	1.7	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Concomitant CABG (%)	37.1	NR	NR	NR	-	12.8	-	13.6	-	4.8	-	1	-
Staged PCI	-	NR	NR	-	NR	-	6.5	-	-	-	0.3%		0
Cross clamp time (minutes)	79.0	77.0 ± 28.5	NR	NR	-	74.3 ± 27.78	-	68.7 ± 29.0	-	74.0 ± 31.4	-	NR	NR
Cardiopulmonary bypass time (minutes)	104	104.9 ± 39.1	NR	NR	-	97.7 ± 33.75	-	93.4 ± 40.2	-	104.0± 45.8	-	NR	NR
Procedure time (minutes)	NR	NR	NR	NR	NR	208.3 ± 62.1	58.6 ± 36.5	276.6 ± 79.5	148.2 ± 55.7	221 ± 84.8	60.4 ± 35.3	177.2 ± 39.8	90.3 ± 38.6

SAVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, CABG; coronary artery bypass graft surgery

NR; not reported

Table 5. Outcomes following SAVR in the current study (UK AVR) and those in other national registries and recent trials comparing SAVR with TAVI

Outcome	UK SAVR	Thourani[15]	Tokuda[16]	PARTNER 2A [22]		PARTNER 3 [6]		EVOLUT [7]		PIVOTAL [5]		NOTION [18]	
	SAVR N=31,277	SAVR N=141 905	SAVR N=20 514	SAVR N=1021	TAVI N=1011	SAVR N=454	TAVI N=496	SAVR N=678	TAVI N=725	SAVR N= 357	TAVI N= 390	SAVR N= 135	TAVI N= 145
In-hospital death/30-day mortality (%)	1.9	2.5	NR	8.0	6.1	1.1	0.4	1.3	0.5	4.5	3.3	3.7	2.1
Stroke (%)	1.1	NR	1.6	6.1	5.5	2.4	0.6	3.4	3.4	6.2	4.9	3.0	1.4
Reoperation for bleeding* (%)	3.6	3.9	3	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Post procedure bleeding* (%)	-	NR		43.4	10.4	11.9	1.2	7.5	2.4	69.5	41.7	11.3	20.9
Deep sternal wound infection (%)	0.14	0.3	1.1	NR	-	NR	-	NR	-	NR	-	NR	-
Length of hospital stay (days)	7	7.9 ± 7.2	NR	NR	-	7.0	3.0	NR	NR	NR	NR	8.9 ± 6.2	12.9 ± 11.6
New pacemaker implantation (%)	1.6	NR	NR	6.9	8.	4.0	6.5	6.1	17.4	7.1	19.8	1.6	34.1

SAVR; surgical aortic valve replacement, TAVI; transcatheter aortic valve implantation, CABG; coronary artery bypass graft surgery, NR; not reported

*Reoperation for bleeding and post-operative bleeding were major and required intervention

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	4-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-6
Bias	9	Describe any efforts to address potential sources of bias	4-6
Study size	10	Explain how the study size was arrived at	4-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	6

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7-8
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	7-8
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	NA

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.