## Original research

# Early and long-term outcomes of conventional and valve-sparing aortic root replacement

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#### ABSTRACT Objective To determine the early and long-term

0.5 - 14.5).

outcomes of conventional aortic root (ARR) and valve-

Methods We present prospectively collected data of

609 consecutive patients undergoing elective and urgent

and incidence of postoperative complications. Secondary

aortic root surgery (470 ARR, 139 VSRR) between 2006

and 2020. Primary outcomes were operative mortality

outcomes were long-term survival and requirement for

reintervention. Median follow-up was 7.6 years (range

**Results** 189 patients (31%) had bicuspid aortic valves

and 17 (6.9%) underwent redo procedures. Median

cardiopulmonary bypass of 108 (range 75–296) min.

ischaemic attacks/strokes occurring in 1.1%. In-hospital

received haemofiltration. Intensive care unit and hospital

stay were 1.7 and 7.0 days, respectively. During follow-

up, redo surgery for native aortic valve replacement was

required in 1.4% of the VSRR group. Overall survival was

95.1% at 3 years, 93.1% at 5 years, 91.2% at 7 years

**Conclusions** ARR and VSRR can be performed with

low mortality and morbidity as well as a low rate of

reintervention during the period of long-term follow-

consistent perioperative approach. This series provides

contemporary evidence to balance the risks of aortic

aneurysms and their rupture at diameters of <5.5 cm

up, if performed by an experienced team with a

against the risks and benefits of surgery.

In-hospital mortality was 10 (1.6%), with transient

mortality for VSRR was 0.7%. 12 patients (2.0%)

required a resternotomy for bleeding and 14 (2.3%)

cross-clamp time was 88 (range 54–208) min with

sparing root replacement (VSRR) using a standard

perioperative and operative approach.

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## INTRODUCTION

and 88.6% at 10 years.

Aortic root replacement (ARR) is performed for conditions involving the aortic valve, aortic root and ascending aorta. Some of these conditions include aneurysm formation, dissection, connective tissue disease and infective endocarditis. ARR is classified as major complex surgery by risk stratification methods and European as well as American classifications.<sup>1–3</sup> The reported risks and morbidity of ARR remain significant. The latest return of data to the Society for Cardiothoracic Surgery in Great Britain and Ireland reports an overall mortality for valve-sparing root replacement (VSRR) of 4.6%, with an in-hospital mortality for modified Bentall/ Cabrol procedure being approximately 9.0% for the year 2015–2016.<sup>4</sup> The Society of Thoracic Surgeons (STS) database reporting on 13743 patients<sup>5</sup> showed a mortality for elective and urgent root surgery of 4.2% with only 5% of the sites performing more than 16 ARRs per year with the median number of ARRs per site of 2. A more recent analysis of elective ARR in the STS database reported an in-hospital or 30-day mortality of 2.2% among 24244 patients.<sup>6</sup>

The benefits of surgery have to be balanced against the risk of dissection, endocarditis and future prosthetic valve dysfunction. Guidelines from the American Heart Association for Thoracic Surgery<sup>7</sup> and European Society for Cardiology<sup>8</sup> recommended surgery at a diameter of 5.5 cm for patients without non-connective tissue disease and 5.0 cm for patients with connective tissue disease. These cut-off values correspond to a steep rise in the risk curves with patients presenting with aortic dissection or rupture. Furthermore, the American guidelines regarding bicuspid aortic valve (BAV) aortopathy recommended intervention at 4.5 cm if concomitant valve disease was present.<sup>9 10</sup>

However, evidence from the International Registry of Acute Aortic Dissection highlights that 60% of acute type A dissections occur in ascending aortas of < 5.5 cm, suggesting that the absolute aortic diameter does not represent the only parameter indicating risk of acute aortic events.<sup>11</sup> Using a cross-sectional aortic area/patient height ratio (indexed aortic area) >10 cm<sup>2</sup>/m as a marker of the risk for aortic dissection/rupture, we previously reported that in a population of 187 patients with proximal thoracic aortic aneurysms, 69.5% of aneurysms would not fulfil the current size criteria recommending aortic replacement.<sup>12</sup> Furthermore, 49.0% and 98.5% of subthreshold aneurysms analysed with diameters of 4.5-5.0 cm and 5.0-5.5 cm, respectively, had abnormally high indexed aortic areas, signifying their risk for aortic complications. Similar findings were observed in a pure BAV cohort.13

Therefore, the timing of surgery and knowledge of early and late outcomes of patients who have undergone ARR and VSRR are important in determining future practice. There is evidence suggesting that improvements in outcomes can be achieved in centres with high operative volume.<sup>14–17</sup> We report our experience with patients who underwent elective and urgent ARR and VSRR with a consistent perioperative approach and regular long-term follow-up.



## METHODS

All patients who underwent elective or urgent ARR and VSRR under the care of a surgical team, led by only one consultant cardiac surgeon, between 2006 and 2020, were included in this study; emergency operations such as aortic dissections were excluded. The data were entered in a prospective manner by the database manager and were validated against the national database. The outcome measures studied were operative mortality, in-hospital complications including postoperative bleeding requiring resternotomy, transient ischaemic attack or stroke, requirement for haemofiltration, the use of an intra-aortic balloon pump, peripheral vascular injury and gastrointestinal complications. Operative mortality was defined as death during and after surgery up to 30 days. Neurological deficit lasting less than 24 hours was defined as transient ischaemic attack and that lasting more than 24 hours was defined as a stroke. Gastrointestinal complications were defined when the patient required laparotomy. Other outcomes measured were long-term survival, complications during follow-up including stroke, pacemaker implantations and requirement for reintervention.

Elective surgery was defined as planned surgery, with the patient being admitted form home. Urgent surgery was defined as surgery being performed more than 24 hours after referral with the patient presenting to the emergency department, or when a patient required transfer from a different hospital and could not be discharged without surgery. These definitions are consistent with those used by the Society for Cardiothoracic Surgery in Great Britain and Ireland.<sup>4</sup>

## **Preoperative assessment**

All patients underwent transthoracic echocardiography, CT and/ or MRI. The annulus measurements were made using transthoracic echocardiogram. This was measured in the long-axis view at the hinge point of the aortic valve leaflets in mid-systole. Coronary angiography was performed if the patient was older than 40 years of age. Every patient was discussed at a multidisciplinary team (MDT) meeting comprising of at least one cardiac surgeon, cardiologist, vascular surgeon, radiologist and several trainees from different disciplines. These MDTs were part of the general MDTs in the unit and from 2012 they were designated as aortic MDTs. Patients with known or highly suspected connective tissue disease and those who had aortic root and ascending aneurysms >4.5 cm underwent surgery (the indications used for surgery are shown in figure 1).

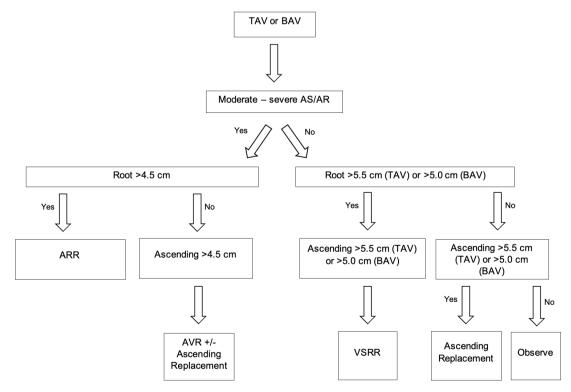
In addition, after 2017 all patients underwent assessment of the cross-sectional aortic area/patient height ratio, <sup>12 13 18 19</sup> which influenced the indication for intervention.

## **Operative technique**

Our operative technique is described in detail.<sup>14 15 20</sup> It is a simple and reproducible technique. Almost no haemostatic material like surgical glue or Teflon is used. Meticulous attention is given to the actual surgical technique. Several parts of the operation are performed by the trainees. The types of valves, type of prosthetic material used for replacement of the ascending aorta, exact type of surgery, any concomitant procedures, cardiopulmonary bypass (CPB), cross-clamp and circulatory arrest times were recorded. For VSRR, the remodelling technique was used.<sup>20 21</sup>

## Anaesthetic protocol and perioperative care

All patients underwent cerebral perfusion monitoring using near-infrared spectroscopy along with a treatment algorithm to manage low values during CPB. Haemoglobin on CPB was maintained above 8g/dL. To assess coagulopathy, thromboelastography and multiplatelet analyser (CobasRoche) for platelet



**Figure 1** Algorithm for the management of patients with a BAV or TAV with dilatation of the aortic root and/or ascending aorta. AR, aortic regurgitation; ARR, aortic root replacement; AS, aortic stenosis; AVR, aortic valve replacement; BAV, bicuspid aortic valve; TAV, tricuspid aortic valve; VSRR, valve-sparing root replacement.

function were used. Haemostatic blood products were administered in the presence of abnormal tests. Transoesophageal echocardiography was performed for all cases. The routine use of blood products was avoided.

## Follow-up

All patients have been followed up locally. Prior to discharge, a transthoracic echocardiogram was performed. Following discharge, the patient was first seen at 6 weeks, where routine examination, ECG and a chest X-ray were performed. The patient was then seen at 6 months, 1 year and from then on annually, when transthoracic echocardiography, CT or MRI was performed. Particular attention was given to the function of the aortic valve, root anatomy, size and growth of the rest of the aorta.

## Statistical analysis

Continuous variables are expressed as mean±SD and percentage for categorical variables. Median is provided for continuous variables not following normal distribution. The Student's t-test was used as appropriate to assess the difference between aortic annular dimensions, preoperatively and postoperatively, with values of p less than 0.05 as statistically significant. Analyses were performed using SPSS V.24 (IBM Corp). Time-to-event survival analyses for mortality were performed using the logrank test and Kaplan-Meier estimates.

## Patient and public involvement

Patients and the public were not involved in the design of the study.

## RESULTS

Demographic, preoperative and operative data of all patients are shown in tables 1 and 2. In-hospital mortality and perioperative complications for all patients are shown in table 3. The overall in-hospital mortality for the whole cohort was 10 patients (1.6%). The 30-day mortality was the same. Five of the 10 patients had the diagnosis of infective endocarditis, two had had previous surgery, and one had concomitant arch and elephant trunk operation. None of the patients had isolated root surgery.

The operative data and postoperative outcomes of patients who underwent VSRR are shown in table 3. There was one in-hospital death (0.7%) in this subgroup. This was a patient with connective tissue disease and Barlow disease of his mitral valve with severe mitral regurgitation. He had had a previous clam shell incision for a thoracic procedure and had poor lung function. Despite a completely satisfactory repair of his mitral valve and VSRR, his oxygenation at completion of the operation could not be maintained; he required extracorporeal membrane oxygenation and sadly died.

For the VSRR patients, the mean aortic annulus diameter, measured with transthoracic echocardiography, was  $24.3\pm7.1$  mm in the early postoperative period, and  $25.7\pm5.0$  mm (p=0.40) at the time of the last follow-up.

## Follow-up

Overall survival was 95.1% at 3 years, 93.1% at 5 years, 91.2% at 7 years and 88.6% at 10 years (figure 2). The survival curves for mechanical and tissue aortic root replacements are shown. The lowest late survival seen was 81.1% at 10 years in patients who underwent tissue ARR. Table 4 shows the complications that occurred during the

## Table 1 Demographics and preoperative data

	All cases N=609 (%)	ARR N=470 (%)	VSRR N=139 (%)
Clinical baseline characteristics			
Age, years	60 (18–84)	62 (18–84)	51 (18–68)
Male sex	451 (74)	362 (77)	97 (70)
EuroScore 2	3.7±4.3	3.7±4.3	3±2
Smoking	207 (34)	173 (37)	34 (24)
Hypertension	298 (49)	282 (60)	16 (12)
Diabetes mellitus	54 (9)	48 (10)	6 (4)
Chronic pulmonary disease	67 (11)	59 (13)	8 (6)
Prior myocardial infarction	30 (5)	30 (6)	0
Prior stroke/transient ischaemic attack	24 (3.9)	20 (4)	4 (3)
Creatinine >1.5 mg/dL	51 (12)	45 (10)	6 (4)
Connective tissue diseases	138 (23)	48 (10)	90 (65)
Imaging characteristics			
Left ventricular function ejection fraction			
>50%	365 (60)	243 (52)	112 (88)
30%–50%	177 (29)	136 (34)	14 (10)
<30%	67 (11)	64 (14)	3 (2)
Valve morphology			
Tricuspid	420 (69)	283 (60)	137 (99)
Bicuspid	189 (31)	187 (40)	2 (1)
Fusion patterns			
Left-right fusion	144	142	2
Left-none fusion	11	11	0
Right-none fusion	17	17	0
Other	17	17	0
Aortic valve pathology			
Stenosis	432 (71)	432 (92)	0
Regurgitation	104 (17)	38 (8)	66 (47)
Normal	73 (12)	0	73 (53)
Mixed disease	164 (35)	164 (35)	0
Preoperative aortic parameters			
Aortic annulus	24 (17–45)	24 (17–45)	26 (23–31)
Ascending aorta	47 (23–92)	-	-
Aortic arch	30 (16–49)	32 (16–19)	24 (21–36)
Descending aorta	28 (13–80)	28 (13-80)	22 (18–42)

Data are reported as median (IQR: 25%–75%) for continuous variables and number (%) for categorical variables.

ARR, aortic root replacement; VSRR, valve-sparing root replacement.

follow-up period. Eleven (1.8%) patients underwent redo surgery during the follow-up period. Two (1.4%) patients in the VSRR group required redo surgery with replacement of the aortic valve due to severe aortic regurgitation (AR). One patient developed cusp prolapse and the second patient developed significant dilatation of the aortic annulus during pregnancy resulting in severe AR.

One patient, who had a mechanical ARR, developed a pericardial effusion due to a very high international normalised ratio (INR) (>10) 3 weeks after surgery; this collection was successfully drained but he sadly died within 24 hours of drainage from an arrhythmic episode. This patient was operated on during the COVID-19 pandemic and it seemed that he had great difficulties in obtaining regular INR tests. Overall, follow-up was complete in 92% of patients.

Forty-six patients died during the follow-up period. The causes of death were collected from the medical records and the patient's general practitioners; 35 patients (76%) had died from non-cardiac causes.

Procedure characteristics	All cases N=609 (%)
Classification of intervention	
Elective	493 (81)
Urgent	116 (19)
Redo procedure	17 (2.8)
Procedure type	
ARR only	470 (77)
Tissue valve	298 (63.4)
Mechanical	165 (35.1)
Homograft	7 (1.5)
ARR+concomitant procedure	78 (12.8)
ARR+coronary artery bypass graft surgery	41
ARR+radiofrequency ablation	12
ARR+mitral valve repair	9
ARR+mitral valve replacement	3
ARR+other	2
ARR+arch replacement	9
ARR+arch replacement+elephant trunk	1
ARR+PFO closure	1
VSRR	139 (23)

Data are reported as median (IQR: 25%–75%) for continuous variables and number (%) for categorical variables.

ARR, aortic root replacement; PFO, patent foramen ovale; VSRR, valve-sparing root replacement.

## DISCUSSION

Our results show a low in-hospital mortality and complication rate in patients undergoing elective and urgent ARR and VSRR compared with published series. It compares favourably with larger series in the literature from high-volume centres.<sup>22 23</sup> Follow-up was complete in 92% of patients.

All patients have had follow-up with updated imaging. It is not ethical to randomise patients with aortic root and ascending aortic aneurysms to surgery or observation, but it is hoped that this series provides additional information for the timing of surgery, value and method of follow-up, and short-term as well as long-term complications.

The recent reports that the aorta enlarges abruptly by approximately 0.8 cm or more<sup>24 25</sup> at the time of dissection indicate that the observed aortic diameter at presentation after the acute event is an overestimation of the true diameter. This is because the diameter at the time of dissection recorded on the registry

Table 3         Postoperative outcomes in all patients					
	N (%) N=609	ARR N=470 (%)	VSRR N=139 (%)		
Operative details					
Cross-clamp time, min	88 (54–208)	71 (67–208)	114 (51–169)		
Cardiopulmonary bypass time, min	108 (75–296)	82 (75–296)	136 (78–198)		
Outcome					
Hospital mortality	10 (1.6)	9 (1.9)	1 (0.7)		
Transient ischaemic attack/stroke	7 (1.1)	7 (1.5)	0		
Resternotomy for bleeding	12 (2.0)	11 (2.3)	1 (0.7)		
Haemofiltration	14 (2.3)	14 (3.0)	0		
Intensive care unit stay, days	1.7 (1–17)	1.5 (1–170)	1 (1–3)		
Hospital stay, days	7.0 (4–48)	7 (4–48)	6 (5–7)		
Data are reported as median (IQR: 25%–75%) for continuous variables and number (%) for categorical variables.					

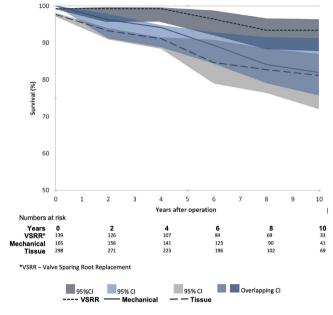


Figure 2 Survival after aortic root and valve-sparing root replacement.

is the post-dissection diameter. In a previous analysis of aortic dimensions in patients presenting with acute type A dissection, we demonstrated aortic diameters of  $4.42\pm0.82$  cm at the midsinus of Valsalva,  $4.05\pm1.18$  cm at the sino-tubular junction and  $5.20\pm1.26$  cm at the mid-ascending aorta.<sup>12</sup> Importantly, these post-dissection diameter measurements do not satisfy current guideline criteria for aortic replacement surgery.

In the current series, 139 patients underwent VSRR, using the remodelling technique with an overall mortality of 0.7% and one death during follow-up. We have recently reported our method and outcomes of aortic root remodelling.<sup>20</sup> None of the patients in the VSRR group had severe AR at the time of surgery. In this subgroup, no patient had aortic stenosis. Our cohort may reflect a selective group of patients who are diagnosed earlier and referred for surgery. This is partly due to the fact that our centre is a national centre for patients with connective tissue disease and therefore patients and their families are under early and regular surveillance and thus diagnosed earlier before the development of severe AR. Given the largely prophylactic nature of this surgery in patients with root dilatation, and the younger age at which surgery is performed, there is an increasing focus on the use of VSRR in the management of these patients, a significant number of whom have connective tissue disease. One of the major criticisms of the remodelling technique of VSRR, in its originally described form, is the lack of annular stabilisation and the concern that the lack of annular stabilisation will result in the incidence of AR in the years following the operation. David and colleagues reported their outcomes and demonstrated that the incidence of AR at 15 years was 7.9%, which was lower after reimplantation than remodelling.<sup>26</sup> In our series, freedom from moderate to severe AR was 98% at a median follow-up of 7.6 years with one hospital mortality and no perioperative stroke. Of note, there was no significant increase in the size of the aortic annulus during follow-up. Therefore, regardless of the technique used, VSRR should continue to be advocated among suitable patients to avoid anticoagulation and to preserve native valve function, particularly given the low incidence of perioperative complications and durability of repaired aortic root.

Thirty-one per cent of patients had bicuspid aortic valve (BAV). Guidelines recommend replacement of the aortic root

## Table 4 Complications during follow-up in all patients

	N (%) N=609	ARR N=470 (%)	VSRR N=139 (%)
Follow-up	7.6 years (0.5–14.5 years)		
Postop DC cardioversion within 1 year	8 (1.3)	5 (1.1)	3 (2.2)
Stroke	4 (0.7)	4 (0.1)	0
Pacemaker placement	5 (0.8)	2 (0.9)	3 (2.2)
Readmitted for drainage of pericardial effusion	1 (0.2)	1 (0.2)	0
Readmission for pleural effusions	4 (0.7)	2 (0.4)	2 (1.4)
Redo surgery for tissue valve failure	3 (0.5)	3 (0.6)	0
Redo surgery for homograft failure	2 (0.3)	2 (0.4)	0
Redo surgery for endocarditis	2 (0.3)	2 (0.4)	0
Redo surgery for arch and descending aneurysm	2 (0.3)	2 (0.4)	0
Redo operation for AV regurgitation	2 (0.3)	0	2 (1.4)

Data are reported as median (IQR: 25%-75%) for continuous variables and number (%) for categorical variables.

ARR, aortic root replacement; AV, aortic valve; DC, direct current; VSRR, valve-sparing root replacement.

and ascending aorta at the time of aortic valve replacement (AVR) for BAV and when the aorta is >4.5 cm.<sup>9</sup> Despite this, there are no specific guidelines regarding the timing of replacement or at what diameter the aortic arch should be replaced in these patients. Our group analysed the results of patients who underwent replacement of the ascending aorta or ARR over an 11-year period. It was noted that in those patients undergoing proximal aortic surgery for BAV, the aortic arch did not increase in diameter during follow-up. In our experience, prophylactic replacement of the aortic arch in patients with BAV, where the arch is not dilated, is not indicated. Our data suggest that by removing the source of aortic dilatation, that is the aortic valve, and the ascending aorta which is the main part of the aorta affected in patients with BAV, the remaining aorta does not dilate.<sup>20</sup>

In patients who underwent VSRR, only two patients (1.4%) had BAV. The limited number of patients with BAV undergoing VSRR could partly be due to the lack of surveillance and follow-up in patients who are diagnosed with BAV at birth or in their younger years. It is also possible that lack of awareness by referring cardiologists to refer patients with BAV for earlier intervention and valve repair is partly responsible for the low numbers of patients with BAV. Kalogerakos and colleagues at

## Key messages

## What is already known on this subject?

⇒ According to the UK database, aortic root replacement (ARR) and valve-sparing root replacement (VSRR) are performed with a mortality of 9% and 4.6%, respectively. The short-term and long-term outcomes in this population in the UK are not reported.

## What might this study add?

⇒ We report a large series of patients who underwent ARR and VSRR with low mortality and complication rates and a low rate of reintervention at a median follow-up of 7.6 years.

## How might this impact on clinical practice?

⇒ The benefits of elective and urgent root surgery at aortic diameters of >4.5 cm with concomitant aortic valve disease outweigh the risks of complications resulting from untreated aneurysms of the aortic root and ascending aorta.

Yale have recently reported the different natural histories of the aortic root and mid-ascending aorta.<sup>27</sup> The risk curves for the aortic root and mid-ascending aorta revealed hinge points at 5.0 and 5.25 cm, respectively.

In conclusion, we have shown that elective and urgent conventional ARR and VSRR can be performed with a very low in-hospital mortality and morbidity. An experienced team, a standard and consistent perioperative approach, and good collaboration across specialties are key to achieving successful outcomes. Finally, this series provides contemporary evidence of how to balance the risks of aortic aneurysms and the risk of rupture at diameters of < 5.5 cm, against the risks and benefits of surgery.

## Limitations of the study

It would not be ethical to perform a randomised study comparing patients with and without surgery. A matched analysis of patients with the same demographics and aneurysm sizes with and without surgery of the UK national database would be desirable, but this is outside the scope of the current study.

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**Contributors** MJ has been the primary surgeon in charge of the patients, designed the study, cumulated the database, wrote the original drafts and revised subsequent versions. KM has cumulated and cleaned the database and assisted in writing the original and subsequent drafts. MA has assisted in writing the original and subsequent drafts. RA has assisted in writing the original and subsequent drafts. NA has assisted in writing the original and subsequent drafts. RB has assisted in writing the original and subsequent drafts. PQ has contributed significantly to the preoperative and postoperative phases of care. In addition, he has reviewed the data, reviewed several versions of the manuscript and finalised the draft. FS has contributed significantly to the preoperative and postoperative phases of care. In addition, he has reviewed the data, reviewed several versions of the manuscript and finalised the draft. RM has contributed significantly to the preoperative and postoperative phases of care. In addition, he has reviewed the data, reviewed several versions of the manuscript and finalised the draft. RM has contributed significantly to the preoperative and postoperative phases of care. In addition, he has reviewed the data, reviewed several versions of the manuscript and finalised the draft. ME has contributed significantly to the preoperative and postoperative phases of care. In addition, he has reviewed the data, reviewed several versions of the manuscript and finalised the draft. ME has contributed significantly to the preoperative and postoperative phases of care. In addition, he has reviewed the data, reviewed the data, reviewed several versions of the manuscript and finalised the draft. ME has contributed significantly to the preoperative and postoperative phases of care. In addition, he has reviewed the data, reviewed several versions of the manuscript and finalised the draft. MJ is the guarantor.

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