Valve sparing aortic root surgery: from revolution to evolution?

Amer Harky[1], Athanasios Antoniou[2], Callum Howard[3], Lara Rimmer[4], Mohammad Usman Ahmad[5], Mohamad Bashir[6]

[1]Department of Cardiothoracic Surgery, Liverpool Heart and Chest, Liverpool, UK; [2]Department of Cardiac Surgery, Barts Heart Centre, St Bartholomew's Hospital, London, UK; [3]Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK; [4]Academic Foundation, East Lancashire Hospitals Trust, Royal Blackburn Hospital, Blackburn, UK; [5]Department of Surgery, Scunthorpe General Hospital, Scunthorpe, UK; [6]Department of Aortovascular Surgery, Manchester Royal Infirmary, Manchester, UK

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Correspondence to: Mohamad Bashir, MD, PhD, MRCS. Department of Aortovascular Surgery, Manchester Royal Infirmary, Manchester, UK. Email: drmbashir@mail.com.

Abstract: Valve sparing aortic root replacement (VSRR) is lucrative option for young patients with aneurysmal disease involving the aortic root while the aortic valve (AV) itself is functionally intact and can be repaired. The benefits of retaining the native AV extends beyond those of avoiding the inconvenience and complications of prolonged exposure to anticoagulants. It includes delaying of need for reoperation related with valvular degeneration of prosthetic valves. Despite these advantages, performance of this procedure has been challenging due to its technical demand and complexity as well as requirement of experienced surgeon to perform the procedure. This review aims to outline the current literature on VSRR and the mid to long-term outcomes in both elective and emergency settings.

Keywords: Aortic root; aortic valve (AV); valve-sparing; root surgery

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Introduction

The aortic root aneurysm achieves its practical significance through three different mechanisms: rupture or dissection of the aneurysm, incompetence of the AV which is primarily caused by anatomical distortion of the aortic root, or through compression to the nearby structures. By definition, a full aortic root replacement (ARR) involves complete replacement of all aortic sinuses and thereafter reimplantation of the coronary arteries buttons to the aortic root prosthesis (1). In certain case, the aortic valve (AV) could be replaced additionally, as demonstrated initially by Bentall-Bono procedure (2), however if the is to be preserved then the procedure known as valve sparing root replacement (VSRR). The VSRR techniques have changed significantly over the last 2–3 decades. This change was mainly led by the gurus of such practice; Magdi Yacoub (3) and Tirone David (4). The goal of these procedures remains to prevent adverse aortic events by replacing the dilated segment of the aorta and at the same time to preserve or restore AV competence, avoiding problems related to valve prostheses. The two most common indications for VSRR include connective tissue disorders, such as Marfan syndrome (MFS) and Loeys-Dietz syndrome, or bicuspid AV. Additionally, there is an increasing number of candidates who are long-term survivors following congenital heart surgeries which are identified through surveillance studies and found to have aortic aneurysms (5).

Anatomical understanding of the aortic root

The aortic root has different entities: among them is AV leaflets, the leaflet attachments, the interleaflet trigones, the sinuses of Valsalva, the sinotubular junction (STJ) and the annulus itself. The hemodynamic and physical distinction between the left ventricle (LV) and the aorta is formed by the aortic leaflets (6,7).

The valve leaflet inserts into the wall of the root forming a thick fibrous structure and even though it is a crown shaped and not circular, yet it is named as the annulus (8). The geometry of the aortic annulus is crucial for a sustainable work of the valve functionality, in addition to the fact that it determines the durability of any aortic root repair.

The Italian anatomist, Antonio Valsalva, named the three bulges off the aortic wall as sinuses of Valsalva; two of them holds the origin of the main coronary arteries and therefore named as left and right coronary sinus while the other one is names as non-coronary sinus. The sinus wall part of the aortic wall, however a thinner structure than the rest of the aortic wall (6,9,10). It is worth to mention that the precise function of the sinuses of Valsalva is unclear, however, there is some evidence suggesting that the vortices in the sinuses are leading to stress reduction on the leaflets and therefore supporting coronary blood flow (9-11). Last not least, the furthest part of the sinuses close to the ascending aorta combined with the commissures itself form a particular tubular structure that is called sinutubular joint (STJ) which in turn separates the aortic root from the ascending aorta. The STJ is smaller than the aortic annulus in young people, however normalizes to normal size in older age (12). The particular importance of the STJ is evident during its aneurysmal dilatation, as this will move the commissures apart and eventually leading to loss of AV leaflet coaptation and development of aortic insufficiency (AI).

The AV leaflets are inserted proximally into the aortic annulus at the aorto-ventricular junction (AVJ) and distally to the STJ. Therefore, functionally, the AV consists of the combination of STJ and AVJ, which all together form the most functional aortic annulus (FAA) and eventually the valve cusps. The integrity of both functional components (the cusps and the FAA) is the basis for good valvular function. In a normal AV, the cusp coaptation can reache the mid-level between the AVJ and the STJ (13) and this is a fundamental principle in VSRR, which has been prescribed by Cameron as the "position of prayer' or by El Khoury as the position in which the patient "is applauding for the reconstruction of the root". Normally, a coaptation level of 2mm is sufficient to provide valve competence in a FAA of normal size; however, a longer coaptation may indicate presence of coaptation reverse which is seen in the event of FAA dilatation. As such, those coaptations and in combination with the individual compliance of the cusps, it explains the significant and the different clinical presentations between the degree of FAA dilatation and the severity of AI (13,14).

VSRR vs. Bentall: key differences

Historically, the fastest and safest way to repair a diseased aorta would be to replace the entirety of the diseased part with a synthetic conduit. The Bentall Operation, a gold standard of treating a pathological aorta, involves reinserting the coronary ostia after a mechanical or biological prosthetic valve is placed into the aorta, the entire aortic root and valve replaced (15). This has always had its negatives; lifelong anticoagulation for mechanical valves due to a high risk of thromboembolism, or risk of reoperation after biological valve insertion (15,16). Comparably, conserving the native AV is ideal for haemodynamic continuity as well as negating the aforementioned problems of a Bentall (16). In certain patient groups, such as paediatrics, valve replacement brings a risk of long-term follow up complications (17). In the 1990s, the Biological Bentall operation—a biological valve replacement—was one such answer to the problem of anticoagulation (18). In the year of 1989, Tirone David has performed the very first valve-sparing aortic operation; he was faced with a functioning AV (19,20). Yacoub described a valve-sparing root replacement technique, "remodelling", by sewing a polyester graft onto the sinuses (21,22). Remodelling using the graft to suture it to the remaining attachments of the valve leaflets (23). David performed "reimplantation" using a tube graft and reinserting the valve and annulus within it (21). Reimplantation involves preparing and dissecting the aortic root, sizing an appropriate graft, then reimplantation (24). The commissures are reimplanted at the same level of the neo-sinotubular junction (23). A running suture to fix the total graft is then passed from outside the prosthesis, through to the aortic wall, and back again (23). Operatively, aortic cross-clamp times are shorter in Bentall compared to VSRR (25). However, Bentall operations are also prone to haemorrhagic complications; in one meta-analysis, 176 reoperations were required in Bentall group compared to VSRR with 62 bleeding events (25). VSRR is more likely to have significant AI requiring reoperation ($P=0.05$), whereas for Bentall is prosthetic infection (25).

Table 1 Current guidelines for aortic root replacement (2010 ACC/AHA guidelines)

Parameter	Maximum sinus diameter (cm)	Rate of growth (cm/year)
Asymptomatic patients	≥5.5	>0.5
Marfan syndrome	>5.0	>0.5
Loeys-Dietz syndrome	4.0–5.0	
John Hopkins Institution		
Elective patients	>5	>1.0
Marfan syndrome	>5	>1.0
Loeys-Dietz adults	>4	>0.5

Indications or inclusions for VSRR?

The main cohort for VSRR is young patients who suffer connective tissue disorders, this includes but not limited to MFS and Loeys-Dietz syndrome, as mentioned earlier constitutes the basic target-group of patients for VSRR consideration (5). Although MFS is very well described in literature, however, Loeys-Dietz syndrome has been recognized recently only. The common pathology between MFS and Loeys-Dietz patients is the likelihood of development of aortic root aneurysm and thus higher risk of acute aortic syndrome. However, patients with Loeys-Dietz tend to be operated on at an earlier age and with smaller aortic root diameter than MFS patients. Due to high chances of acute aortic syndrome among such cohort, especially in the presence of aortic root aneurysm, elective ARR should be offered when appropriate (26).

According to the 2010 ACCF/AHA guidelines for the diagnosis and management of patients with thoracic aortic disease (27), asymptomatic patients with an ascending aorta with a diameter of 5.5 cm or more or having an annual growth of more than 0.5 cm in an aorta that is less than 5.5 cm in diameter; surgical repair should be considered (COR: I, LOE:C), (*Table 1*). Additionally, patients undergoing AV repair or replacement and have an ascending aorta or aortic root of greater than 4.5 cm should be considered for concomitant repair of the aortic root or replacement of the ascending aorta (COR: I, LOE:C). On the contrary, patients with MFS should undergo repair of the dilated aortic root/ascending aorta at a threshold of an external diameter of 5.0cm, smaller than of the other patients because of the greater tendency for aortic dissection at a smaller diameter (COR: I, LOE:C). Other factors that are considered when the external diameter of the aorta is less than 5.0 cm includes; annual growth of more than 0.5 cm, having family history of previous aortic dissection of an aorta with less than 5.0, or existence of severe AI. On the contrary, presence of Loeys-Dietz syndrome should prompt an earlier elective operation with a smaller aortic diameter (COR: I, LOE:C) (*Table 1*).

The same guidelines (27) also reported that elective aortic replacement is a viable option for MFS patients; however it can also be utilized in patients with other genetic diseases or existence of bicuspid AVs with the ratio of maximal ascending or aortic root area (π r^2) in cm^2 divided by the patient's height in meters exceeds 10 (COR: IIa, LOE:C). furthermore, patients with Loeys-Dietz syndrome or those who have confirmed TGFBR1 or TGFBR2 mutation, it is acceptable to suggest aortic repair when the aortic diameter reaches 4.2 cm or greater by transoesophageal echocardiogram (TOE), (internal diameter) or 4.4 to 4.6 cm or greater by computed tomographic (CT) imaging and/or magnetic resonance imaging (external diameter) (COR: IIa, LOE:C).

Patel *et al.* reporting the John Hopkins Institution's experience in VSRR in children, slightly differentiated form the above guidelines (26). Thus, an elective ARR is recommended in patients with MFS, non-specific connective tissue disorder or non-connective tissue disorders, when the aortic root diameter is >5.0 cm or the rate of aortic root growth is >1.0 cm, or there is progressively worsening AI. Given the greater risk of aortic catastrophe in adults with Loeys-Dietz syndrome, it is recommended an earlier ARR when aortic root diameter is >4.0 cm or expands >0.5 cm/year. For children (<18 years) with severe craniofacial features (Loeys-Dietz type I) surgery is advised at an aortic root Z-score >3.0 or aortic root expanding >0.5 cm/year, while for children with mild craniofacial features (Loeys-Dietz II), surgical intervention is recommended at an aortic root Z-score >4.0 or an aortic root that expands >0.5 cm/year (*Table 2*).

Types of VSRR operations

The Bentall procedure was first described 5 decades ago and yet, remained the standard approach in patients who has coexistence of connective tissue disorders and aortic root aneurysms. Techniques to preserve the native valve during an ARR are more recent and can be categorized broadly to remodelling or reimplantation. In the early

Table 2 Current guidelines for root replacement in patients with Loeys-Dietz syndrome at John Hopkin Institution

Pathology	Z-Score	Rate of growth (cm/year)
Loeys-Dietz I (<18 years)	>3.0	>0.5
Loeys-Dietz II (<18 years)	>4.0	>0.5

iterations of these procedures, the remodelling operation (which is also described as David II or Yacoub procedure) involves replacement of the sinuses with a three-tongued Dacron graft; the graft edges are then sewn to the annulus and a small remnant of the aortic sinus. The remodelling procedure originally was designed to faithfully reproduce the shape of the sinuses, however it failed to stabilize the annulus and in some patients led to "splaying of the graft tongues" over time and subsequent loss of central leaflet coaptation and development of AI (5,28). On the contrary, the reimplantation procedure (also known as the David I) uses a Dacron cylinder to completely enclose the aortic root complex; the graft sits around the valve rather than atop it; and as such, stabilizes the annulus and has a lower rate of late AI (5).

Recently, there have been development of various custom-design prostheses that can be used to combine the neo-aortic sinuses of the remodelling procedure to provide proper annular stabilization of the reimplantation technique, aiming to give a more reliable and satisfactory long-term valve competencies. Working on this direction, De Paulis (1,29) has developed the Valsalva graft which is a commercially available gelatin-impregnated aortic root prosthesis which is currently welcoming an increasing use in valve-sparing surgery. This prosthesis has three major three components: a collar with horizontally orientated crimps or pleats, a skirt with vertically orientated pleats that make the sinus segment more compliant, and a long tubular segment with horizontal pleats. Its dimensions permit a faithful anatomic creation of the aortic root, and laboratory evidence supports the contention that it facilitates valve opening and closure, thereby minimizing leaflet stress and strain. As such it combines "the best of both worlds" of reimplantation and remodelling principles yet is readily available and can be implanted with a reproducible and straightforward technique. The Valsalva graft sizes range from 24 to 34 mm, a range that meets the requirements of nearly all patients who are suitable candidates for valve-sparing procedures. *Table 3* is summary of different types of VSRR procedures.

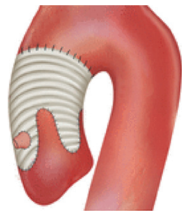
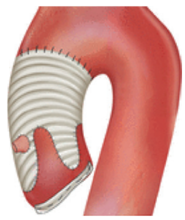
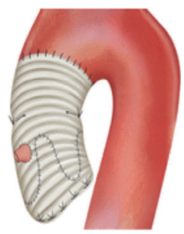
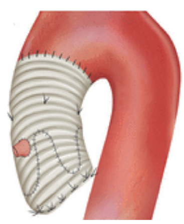
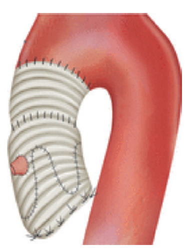
Reimplantation *vs.* remodelling

VSRR operations have been at the forefront of modern surgical practice for a number of decades and can be generally classified as either 'remodelling' procedures pioneered by Yacoub in 1979 or 'reimplantation' procedures by David in 1988 (4,32). Yacoub's remodelling technique is implemented to replace all three aortic sinuses using a triple-tongued shaped graft, there by recreating the normal configuration of the sinuses and tubular junction whilst excluding the aortic ventricular junction (33). However, remodelling is historically associated with a potential lack of sufficient annular stabilization and therefore the long-term stability of the procedure has been the subject of some debate (34). David's reimplantation technique is characterized whereby the whole AV is both preserved and the securely sewn inside a Dacron tube graft (4). The aim of root reimplantation is to correct annular ectasia and the dilation of the STJ. This is achieved by anchoring the aortic graft proximally at the aortic ventricular junction beneath the leaflets with the commissures sewn inside the graft (35). The main problem generally associated with reimplantation is the fact that the sinuses of Valsalva, important for regulating leaflet dynamics, are eradicated thereby altering the normal dynamic motion of the aortic annulus (36,37). Remodelling is associated with a shorter procedural time in comparison of reimplantation. The fundamental underlying concept of both of these procedures is to remove any pathologic root dilation to restore AV function.

After many years of development and research both of these procedure types have significantly improved to the extent that it is possible to complete neo-sinuses reconstruction and annular stabilization in reimplantation and remodelling operations respectively offering long-term durability by combining optimum root geometry and cusp dynamics (38-40).

A recent systematic review and meta-analysis by Tian *et al.* comparing outcomes between remodelling and reimplantation procedures for valve sparing surgeries in aortic root aneurysm patients (41). Thirteen different centres with a combined total of 1,338 patients who underwent either Yacoub [606] or David [732] procedures were included. The results from this analysis demonstrated comparable outcomes for both of the techniques, with early mortality ranged 0–6.9% and 0–6% for Yacoub and David groups respectively (41). However, there is higher rate of AI reported utilizing the Yacoub technique (41). The study reported favourable outcomes in utilizing David technique

Table 3 Different types of VSRR procedures

VSRR operation name	Type of VSRR	Diagram	Brief summary
David I	Reimplantation		David I is the original reimplantation procedure, which uses a 26- to 30-mm cylindrical tube graft (4)
David II/Yacoub	Remodelling		David II replaces the sinuses with a three-tongued Dacron graft; the graft edges are sewn to the annulus and a small sinus remnant (5)
David III	Remodelling		David III incorporates a strip of polytetrafluoroethylene that is felt externally across the base of the non-coronary sinus from trigone to trigone of the mitral valve in order to minimise subsequent annular dilatation (30)
David IV	Reimplantation		David IV is a reimplantation technique using a 4-mm larger graft size with graft plication at the sinotubular junction above the tops of the commissures (30)
David V	Reimplantation		David V uses an even larger graft size (6–8 mm bigger than that predicted by the Feindel-David formula), which is “necked down” at both the bottom and the top ends to create graft pseudosinuses (30)
David V (Stanford modification)	Reimplantation		The Stanford modification is a simplified David V procedure using 2 separate grafts ❖ A large graft used proximally for the pseudosinuses. this is “necked down” on the back table with 2 to 3 5-0 AT-1 Tevdek (Teleflex Medical, Research Triangle Park, NC) plication sutures in all 3 commissures to fix the annulus at a present diameter before tying the bottom row of sutures ❖ The bottom suture line consists of 10 to 12 horizontal mattress sutures, which are tied loosely because the diameter of the proximal end of the graft has already been made smaller (31)

in patients as Marfan's, presentation with type A dissection and excessive dilatation of the annulus which subsequently impairs the aortic root integrity (41). It also stressed that careful selection of patients for each technique is key for success in VSRR operations (41).

In a study by Lenoir *et al.*, they compared reimplantation and remodelling with ring angioplasty over a period of more than 15 years in 142 patients with a mean follow up of 3.9 years (100% complete) (42). No in-hospital mortality was observed in either group and only 5 late deaths were recorded (ref as above). Overall 5-year survival rates were similar in for both groups (100%, P=0.98) and 5-year freedom from AV reoperation were equivalent (97%±2% in both groups, P=0.95) (42). This study concluded that mid-term outcomes following remodelling with reimplantation and extra-aortic ring annuloplasty were comparable and that implementing an extra-aortic ring annuloplasty was effective at stabilizing annular dimensions (42).

Both remodelling and reimplantation procedures can now provide good aortic root reconstruction with long term durability and have been shown to have comparable outcomes in the literature following technical advancement that has narrowed the differences between the operation types. Further research into this debate as well as additional long term follow up of current studies will provide further insight into the clinical results associated with the two surgical techniques. The ongoing evolution of remodelling and reimplantation procedures will continue to spark debate in the future decades. Several studies have reported the effectiveness of VSRR through systematic reviews and meta-analyses. One of the very early studies was by Arabkhani *et al.* (43) who aimed to look at outcomes after VSRR for aortic root aneurysms. The study included 31 articles which were analyzed, and it included 4,777 patients. Reimplantation and remodelling techniques were compared, and no difference was found between the two techniques. There was an early mortality rate of 2%, with a cumulative re-operation rate of 5%, mainly to undergo a valve replacement; severe aortic regurgitation patients pre-operatively showed a higher trend towards re-operation (43).

Following on from this, Mookhoek *et al.* (44) conducted a meta-analysis in 2016. This study was published on the premise that the Bentall procedure is considered to be the gold standard treatment in patients undergoing ARR, therefore to determine the evidence and outcomes associated with this, the study specifically examined patient characteristics and long-term outcomes given as linearized occurrence rates. This included 46 studies with a total of 7,629 patients, the reported early mortality rate was 6%; with a mean follow up of 6 years and a 2.02% late mortality rate, an aortic root re-operation rate of 0.46%, with haemorrhage rates and thromboembolic rates being reported at 0.64% and 0.77% respectively (44). The study concluded whilst aortic root re-operation rates were showing to be reducing in recent years, there were still concerns for late mortality rates along with haemorrhage and thromboembolic rates (44). Importantly, the study shows similar outcomes for patients when compared to that of Arabkhani *et al.* (43); however, re-operation rates are difficult to compare due to differences in reporting.

In 2017, a study comparing VSRR and composite ARR techniques reported on outcomes between the two different techniques (25). This study with 2,352 patients (700 VSRR and 1,652 composite) from 12 included studies showed a reduced aortic cross clamp time (mean difference 20.81; P<0.00001) and cardiopulmonary bypass time (mean difference 14.85; P<0.00001) in the composite root replacement group. Overall in hospital mortality was reported low, statistically significantly higher in hospital mortality in the composite group (OR 0.44; P=0.0002); reoperation rates were reported to be higher in the VSRR group (OR 0.68; P=0.05) (25). This is the only significant meta-analysis which compared VSRR and composite root replacement in all patients, whilst this study showed VSRR to be a viable alternative to composite root replacement, the need for longer term outcome data is a running theme in all the aforementioned meta-analyses.

On the other hand, there are two significant meta-analyses which compared VSRR with composite root replacement in MFS patients. The first study (45), published in 2014, included six randomised controlled trials with 539 patients, which found VSRR to have a lower risk of re-exploration (RR 0.48; P=0.04), thromboembolic events (RR 0.17; P=0.004) and endocarditis rates (RR 0.31; P=0.04); however, VSRR found to have an higher long-term survival rate; no statistical difference was found between the two groups for re-operation rates (RR 1.07; P=0.91). The second study (46) by Flynn *et al.* included 23 studies with 2976 patients that compared VSRR and composite root replacement. The study demonstrated VSRR to have a lower risk of thromboembolic events (OR 0.32; P=0.0008), endocarditis (OR 0.27; P=0.006) and lower haemorrhagic (OR 0.18; P=0.0003) events; again, there was no difference in re-operation rates between groups. The evidence in MFS patients' favours VSRR, which shows better outcomes for patients. There is an obvious advantage in avoiding the need for systemic anticoagulation. However, in all studies, there is still need for long-term outcome data to compare re-operation and reintervention rates and long-term mortality.

Reported outcomes of VSRR in bicuspid AVs: the challenge is on

Since the very early stages of introducing VSRR into aortic surgery and the concept of preserving largest amount of native aortic tissues; the practice has shifted toward utilizing this well-established procedure in patients with bicuspid aortic valve (BAV). Bicuspid AVs affects 1–2% and such cohorts are usually young people and the root dilatation can cause aortic regurgitation (AR) at earlier stage (47) therefore, replacing the dilated root and repairing the valve has been developed as a reliable technique and its currently recommended by the recent guidelines (48).

In a very recent study by Kayatta *et al.* (49) they reported comparative 12-year outcomes in performing VSRR in patient with BAV and tricuspid AVs. They reported a higher rate of AR in BAV patients (64% *vs.* 31%, P<0.01), the mean follow-up was 39 months. The 5-year cumulative rate of grade 2+ or more of AR was higher in BAV patients but this was not significant statistically (7.7% *vs.* 2%, P=0.75) and this was not affected by the fact that BAV patients had higher rate of pre-operative grade 2+ or more of AR (P=0.62). Furthermore, there was no difference in re-operation rate and requirement for AV replacement between both cohorts (4.3% in tricuspid cohort and 7.7% in BAV, P=0.81); similarly, no significant difference reported at 5-year mortality (2% in tricuspid patients and 16% in BAV patient, P=024). Such outcomes were also reported by an earlier study from an 11-year study by Beckerman *et al.* (50). The study analyzed outcomes of 60 consecutive patients with BAV that underwent VSRR between 2005 and 2016; there was 50% rate of moderate or higher AR in BAV patients and they reported 0% rate of operative mortality, postoperative stroke or renal failure. The degree of postoperative AR was minimal, 87% of the entire cohort had AR of grade <1+. The nine-year freedom from AR grade 2+ or more was 97%. The rate of requirement of re-operations for AV intervention was only 4% at nine years. Both Kayatta *et al.* and Beckerman *et al.* recommended VSRR in patient with BAV as it gives satisfactory outcomes at mid-term and long-term.

Further studies by Bavaria *et al.* (51) and de Kerchove *et al.* (52) in their retrospective long term data; they reported excellent outcomes in patients with BAV that underwent VSRR, despite the fact that such patients with BAV had higher grade of pre-operative AR, however this didn't affect their postoperative rate of AR grade nor the requirement for further surgical interventions.

Therefore, based on the large series and the satisfactory outcomes reported at international centres, VSRR can be utilized when appropriate in patients with BAV should the surgical expertise exist in such centres.

VSRR in aortic dissection: is this a distress call?

Acute type A aortic dissection is a surgical emergency and it requires an immediate intervention to save life and protect the organs. The traditional and gold standard methods for repairing such pathology are through open repair. It involves identification of the initial entry and excision and then repair rest of the dissected tissues which can range from conservative repair of the aortic root, VSRR to total ARR, or sometimes hemi arch or even full aortic arch replacement in more extensive case (53).

The choice between different techniques of aortic root interventions is dependent on status of the AV and the severity of dissected sinus segments. Bentall procedure involves total ARR with excision of the affected sinuses, replacement of the involved AV and re-implantation of the coronary buttons. The initial results from the practice of VSRR using the remodelling technique showed high failure rate compared to ARR and therefore it was abandoned for some time (54). However, with advancement in surgical practice and inclination toward a more conservative approach and increase in learning curve, VSRR with re-implantation technique was introduced to practice and has been reported with satisfactory outcomes in the setting of ATAAD in several centres internationally (55-57). Yet, this procedure is complex and it requires advanced skills to be able to perform such procedure in a safe manner and give satisfactory outcomes; and hence patient selection should be done very carefully. Patients with extensive cardiac history, previous interventions, elderly cohort, presence of existent coronary artery disease or developed malperfusion syndrome, or those have extensive dissection involving entire root with distortion of AV are not suitable for such complex procedure (56).

Leshnower *et al.* (56) reported their experience of 43 patients that presented with ATAAD and underwent VSRR; the intervention involved either hemi-arch replacement (n=35) or total arch replacement (n=8). The operative mortality was 4.7% and at nine years there was no requirement for further surgical intervention (100% freedom from re-operation) and 94% of them had AR grade 1 or less. Urbanski *et al.* (57) reported favourable outcomes in their cohorts of 54 patients that underwent VSRR in the setting of ATAAD. The mean follow-up period was 5.2± 3.5 years for all patients (range, 0–12 years). They reported a mortality of only 1.9%, stroke rate of 3.7% and 0% valve related death at mid and long-term. Furthermore, the rate of re-operation on proximal aorta or valve was 0% at the follow up period. In a larger study by Beckmann *et al.* (55) of 109 patients that underwent VSRR for ATAAD between 1993–2015; the mean follow-up was 8.3±5.7 years. They reported a 96% freedom from having AR grade >1+ , operative mortality rate of 11% while the survival rate after discharge at 5 and 10 years was 90% and 78%, respectively. Additionally, the freedom from valve-related reoperation at 1, 5 and 10 years was reported as 96%, 88% and 85%, respectively and only 13 patients underwent re-operation related to the valve at some stage during the follow up period.

Finally, in a recent study by Tanaka *et al.* (58) of 24 patients that underwent VSRR for ATAAD using reimplantation techniques, they reported zero operative death and excellent survival outcomes at 5 and 10 years (100% at both time scales). AV reoperation was 17% and 31% at 5 and 10 years respectively. Additionally, freedom from moderate or higher AR grade was 82% and 65% at 5 and 10 years respectively.

Regardless of the great evidences above, the data reported are from single centres, retrospectively collected and of small case series than a large cohort that can impact the international practice (59-61). Therefore, patient selection for VSRR in the setting of ATAAD should be done very carefully and preferably through a multispecialty team meeting taking patient-factor related, extent of tissue damage and surgeon experience into account.

Valve sparing root repair: abort mission

The key issue following VSRR operations is the occurrence of AI. AI can be presented either as an early intraoperative finding (residual AI) or late AI (progressive AI). Technical failures if the main cause of early failure following VSRR operations which is coming from lacking the recognition of cusp prolapse. It is important that the cusps should coapt properly for at least 2 mm in the central part and just above the level of the nadir of the aortic annulus. Presence of residual AI with grades 1+ or less is acceptable, however grade 2+ or higher can contribute to significant re-intervention at later stage, especially if it is caused by leaflet prolapse (5). If AI is recognized early, re-establishment of aortic cross clamping is necessary to fix the incompletely repaired valve. However, if the valve is not beyond repair then replacement is performed and a prosthesis to be sewn within the Valsalva graft to minimize extra cross clamp times. Alternatively, a full ARR with a composite graft, homograft, or porcine bioprosthetic root can be performed.

The main cause of late failure and therefore progressive AI is degeneration of the involved aortic cusps, however this yet to be confirmed through published literature. Furthermore, presence of a rigid root has been reported to be a contributing factor in accelerating the degenerative changes in the already affected aortic cusps. Interestingly, David *et al.* suggested that development of late AI is inversely proportional to age, as elastic cusps have greater adaptability in young patients than sclerotic valves which are seen in elderly patients (62). The indications for surgical intervention in the case of late failure are the same with the isolated AVR (63). Treatment options are either the redo surgery in which the graft is opened, the valve is excised ad a new valve is sewn or implantation of new valve through the transcatheter approach (TAVI).

The bleeding is the second risk that needs to be ruled out once the cross clamp has been removed during a VSRR operation. It is reported that bleeding rate is much less observed using the reimplantation than using the remodelling VSRR technique, although the earlier remains challenging technique to accomplish such. Bleedings could occur at any site that involves anastomosis or reimplantation; however, pledgetted sutures can help in controlling these sites which are accessible. When bleeding is not possible to control, then VSRR could be converted to Bentall procedure which could help in reducing such lethal complication.

Early and late outcomes of VSRR operations

Cameron *et al.* (64) reported their clinical outcomes with aortic root repair in 372 patients who suffered MFS; among the cohort a total 269 patient underwent Bentall composite graft, while 85 patients underwent VSRR, 16 treated with ARR using homografts, and only 2 patients had ARR with porcine xenografts. Of the 85 patients who had VSRR, 40 had a David II remodelling operation and 44 patients underwent David I reimplantation procedure using the De

Paulis Dacron graft. What is important to note that the first 24 years of their study involved performing Bentall in 85% of the patients while this rate has decreased to 39% in the last 8 years of their practice. They reported zero operative mortality among the elective cohort (n=327); however, 2 deaths has been reported among the non-elective cohort (n=45). Actuarial survival was 91.9%, 85.5%, 81.0% and 75.6% at 5, 10, 15, and 20 years, respectively. They reported a total of 74 late deaths (including n=70 in Bentall, n=2 in homografts, and n=2 VSRR cohorts). Dissection or rupture of the residual aorta was reported as the main causative factor of death (10 out of 74), while significant cardiac arrhythmia reported as second main cause (9 out of 74). Of the 2 late deaths on patients with VSRR, both had undergoing David II remodelling procedure, while no late death reported among the 44 who underwent David I reimplantation. Grade 3 to 4+ AI was reported in 7 out of 40 patients that underwent David II procedure; among them only 5 required late AVR. On the contrary, none of the remaining cohort of VSRR (n=44 patients) that underwent David I reimplantation developed late grade 3 to 4+ AI and this was confirmed on echocardiographic finding at one year follow up. Finally, the most common late complications were: thromboembolism (19 patients), endocarditis (18 patients) and coronary anastomotic dehiscence (2 patients).

In a similar study by Price *et al.* (65), they reported outcomes from 165 patients with MFS who had either VSRR (n=98) or Bentall procedure (n=67). Although they reported zero in-hospital mortality, the survival rate at 10 years was higher in VSRR (96.3%±2.7% *vs.* 90.5%±4.1%). In the Bentall group there were 7 haemorrhagic events and 8 thromboembolic complications, while in the VSRR group, there were none haemorrhagic events but rather 4 events of thromboembolism. At ten years, the freedom from aortic endocarditis rate was 91.7%±5.0% in Bentall patients and 98.9%±1.0% in VSRR patients. Ten-year freedom reoperation was 92.0%±3.9% in the Bentall group and 92.9%±3.5% in the VSRR group. There was higher rate of reoperation in the remodelling technique than reimplantation form of the VSRR (n=3 *vs.* n=1, P>0.05 respectively). Similarly, grade >1+ of AI was reported to be higher in remodelling technique than in reimplantation patients.

In 2013, David (62) reported the outcomes of 364 patients who had VSRR. He published that there were 5 early deaths (reimplantation, n=4 and remodelling, n=1) while there were 32 late reported deaths (reimplantation, n=18 and remodelling, n=14). They reported a cumulative survival rate of 88.5%, 75.6% and 69.3% at 10, 15 and 20 years respectively. Additional 5 years of age was predictive of mortality. Infective endocarditis developed in only three patients while 14 patients suffered thromboembolic events. Seven patients underwent further operations on the repaired AV (reimplantation, n=3 and remodelling, n=4). Higher rate of AI was reported in the remodelling cohort of VSRR, mainly at 15 and 20 years of follow up (100%, 98.3%, 92.9%, 89.4%, 89.4% vs 100%, 98%, 93.2%, 70.7%, 63.6% in 1, 5, 10, 15, 20 years respectively). Other factors that contributed to higher rate of moderate to severe AI were incremental age of 5 years, presence of bicuspid AV at time of repair and hypertension.

In a recent systematic review and meta-analysis, Flynn *et al.* (46) reported the outcomes in MFS patients who underwent ARR. This study included 2,976 patients who were treated either with Bentall (n=1,624) or VSRR (n=1,352). They reported a significant reduction in the late mortality rate for patients having VSRR. The cumulative survival rate was 97.6%, 95.9%, 95.1%, 92.4% and 84.5% at 1, 2, 3, 5 and 10 years respectively. Additionally, VSRR was associated with lower rate of thromboembolism, late haemorrhagic complications and development of endocarditis. Nevertheless, no significant reintervention rate difference was reported between the two groups.

In 2004, Karck and colleagues (66) reported results of 119 MFS that underwent either composite graft replacement or VSRR using the reimplantation technique over a period of 23 years. Although the survival rate was higher in VSRR at 5 years, this didn't reach statistical significance (96% *vs.* 89%, P>0.05 respectively). However, there was higher rate of freedom from reoperation in the composite graft, yet this didn't reach any statistical significance (92% *vs.* 84%, P>0.05). There was higher rate of reoperation in the composite cohort (n=6 *vs.* n=4) and this was mainly related to issues with composite grafts and cusp prolapses from insufficiency primary repair. It is crucial to note that there was higher rate of thromboembolism in composite graft cohort (23% *vs.* 2% respectively). A key limitation and potential bias in the study is the big difference in the follow-up period (9.5 years for Bentall *vs.* 2.5 years for reimplantation VSRR patients) which can have direct effect on the reported outcomes.

Klotz *et al.* (67) evaluated a cohort of 315 patients that underwent VSRR (n=101 remodelling, n=214 reimplantation). There was no difference in the overall survival between both cohorts (P=0.33). The key factors that contributed to late death were age, higher NYHA grade and presence of diabetes. They reported higher rate of reoperation rate in remodelling cohort (11.7% *vs.* 5.8%) at 10 years. Kerendi *et al.* (68), analyzed the early outcomes in 110 patients that underwent ARR (n=73, Bentall *vs.* n=37, reimplantation VSRR). They reported no significant differences in pre and intraoperative parameters except that VSRR patients had longer cross-clamp times. Bentall cohort had higher mortality rates (8.2% *vs.* 5.4%); however, this was not significant statistically (P>0.05). Stroke rate, renal or respiratory failure rates were not difference in both cohorts. All the surviving patients in the VSRR (n=35) had no significant AI prior to discharge and freedom from AV replacement at a mean follow-up of 8.8 months was reported as 94.3%.

The early and mid-term outcomes of VSRR have been very encouraging. One should note that surgeon experience level and methods of patient selection are two important factors for further improvement of the outcomes. The life-long success of such procedures is not known, however, a lasting operation for 10 or 15 years in an older child or adolescent is considered as a success especially when avoiding anticoagulation (5). *Table 4* is summary of key studies in literature reporting on VSRR outcomes.

Conclusions

VSRR can certainly be a technically complex and challenging operation and it should probably be limited to experienced surgeons or centres with high volume with a team able to manage consequential problems. Although there are number of limitations, VSRR operations have undergone significant modifications over the last few years, rendering it reproducible with generalizable outcomes.

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Footnote

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Table 4 Key summary of VSRR studies and outcomes

Author	Year	Patient No.			Early outcomes	Late outcomes					Survival (years)		
		Total	Bentall	VSRR		Late deaths	Freedom from reoperation	AI	TE (n)	Endocarditis (n)	5	10	15
Bassano *et al.* (69)	2001	69	37	32	Operative mortality was 5% (RR) and 0% (VSRR)	n/a	90% in VSRR	n/a	n/a	n/a	88% *vs.* 82%, P=0.58	n/a	n/a
Zehr *et al.* (70)	2004	203	149	54	30-day mortality 4% (Bentall), 3.7% (VSRR)	35 late deaths	96% (Bentall), 63% (VSRR)	n/a	No significant difference at 5 years	2 at 15 years	n/a	n/a	n/a
Karck *et al.* (66)	2004	119	74	45	Postoperatively 6.8% mortality in Bentall	6 (Bentall), 7 (VSRR)	92% (Bentall), 84% (VSRR)	n/a	27 (Bentall), 1 (VSRR)	n/a	89% (Bentall), 96% (VSRR)	n/a	n/a
Khaladj *et al.* (71)	2009	95	73	22	Hospital mortality was 12.6%; 15.7% Bentall, 0% VSRR	22 late deaths.	96.2% in both cohorts	n/a	n/a	3 (Bentall)	n/a	n/a	n/a
Cameron *et al.* (64)	2009	372	269	85	No deaths peri-operatively or in hospital in elective repair	74	n/a	n/a	19	18	91.9%	85.5%	81.0%
Kerendi *et al.* (68)	2010	110	73	37	Cross clamp time was longer in VSRR. No other operative differences	n/a	94.3% in VSRR group	n/a	n/a	n/a	n/a	n/a	n/a
Dias *et al.* (72)	2010	164	125	39	In-hospital mortality was 4.9%	9 deaths in both cohorts	98% in both cohorts	n/a	Higher in Bentall than VSRR P=0.0012	71.2% (Bentall), 93.5% (VSRR)	No sig differences P=0.1	n/a	n/a
Franke *et al.* (73)	2010	143	67	76	6.3% inpatient deaths	10.8% (VSRR) and 28.3% (Bentall)	n/a	n/a	n/a	n/a	85.3% (VSRR), 81.1% (Bentall)	n/a	n/a
David *et al.* (62)	2013	374	–	374	1.3% mortality rates within 90 days	32 late deaths	97.1%, 94.2% and 94.2% at 10, 15 and 20 years	Age was independent factor for AI	14	n/a	n/a	88.5%	75.6%
Skripochnik *et al.* (74)	2013	70	45	25	No perioperative difference	1-year survival: 92% (VSRR), 78% (Bentall)	100% (VSRR) at 20 months.	5.5% mild-mod (VSRR)	n/a	n/a	n/a	n/a	n/a

Table 4 (*continued*)

Table 4 *(continued)*

Author	Year	Patient No.			Early outcomes	Late outcomes					Survival (years)		
		Total	Bentall	VSRR		Late deaths	Freedom from reoperation	AI	TE (n)	Endocarditis (n)	5	10	15
Kallenbach *et al.* (75)	2013	548	452	113	Overall 4.8%; 4.9% (RR) to 1% (VSRR) (P=0.16)	55 deaths during follow-up	96.4% (Bentall), 99% (VSRR)	n/a	n/a	n/a	91%	78%	69%
Badiu *et al.* (76)	2014	370	192	178	3 operative deaths	33 deaths during follow-up	12 reoperations: 8 (VSRR), 4 (Bentall)	n/a	24	n/a	95% (VSRR), 79.3% (Bentall)	n/a	n/a
Lamana Fde *et al.* (77)	2015	324	263	61	In-hospital mortality: Bentall (6.7%) and VSRR (4.9%)	Mortality higher in Bentall (P=0.001)	14 (Bentall); 1 (VSRR)	0% (Bentall); 15.4% (VSRR)	n/a	n/a	n/a	n/a	n/a
Price *et al.* (65)	2016	165	67	98; 69 (RI), 29 (RM)	Comparison of Bentall and VSRR in Marfan syndrome. No in-hospital mortality observed	–	No difference	n/a	8 (Bentall), 4 (VSRR)	8.3% (Bentall), 1.1% (VSRR)	n/a	90.5% (Bentall) *vs.* 96.3% (VSRR)	n/a
Klotz *et al.* (67)	2018	315	0	214 (RI), 101 (RM)	n/a	No significant difference in survival between groups (P=0.11)	Reoperation at 5 years: 5.8% RI, 11.7% RM (P=0.13)	n/a	n/a	n/a	n/a	n/a	n/a

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