David versus Bentall – a comparison of early and late results after aortic valve-sparing reimplantation and aortic root replacement

Dissertation
zur Erlangung des akademischen Grades
Dr. med.
an der Medizinischen Fakultät
der Universität Leipzig

eingereicht von Lukas Helmut Michael Schamberger
geboren am 16. April 1993 in Münster
angepfertigt an der Universitätsklinik für Herzchirurgie, Herzzentrum Leipzig
betreut von Prof. Dr. Sergey Leontyev
Prof. Michael A. Borger, MD PhD

Beschluss über die Verleihung des Doktorgrades vom: 22.06.2021
Table of Contents

1. Summary ............................................................................................................. 1
2. Constitutive publications ................................................................................... 4
3. Introduction ......................................................................................................... 5
  3.1 Definition and epidemiology ................................................................................ 5
  3.2 Aetiology and risk factors .................................................................................... 5
  3.3 Symptoms and complications ............................................................................. 6
  3.4 Surgical intervention ........................................................................................... 6
    3.4.1 Bentall procedure........................................................................................................ 6
    3.4.2 David procedure ......................................................................................................... 7
4. Premise of the study and publications presented ........................................... 8
  4.1 State of research................................................................................................. 8
  4.2 Objectives ........................................................................................................... 8
  4.3 Patient selection.................................................................................................. 9
  4.4 Follow-up .......................................................................................................... 11
  4.5 Statistical analysis............................................................................................. 11
5. Publication A ..................................................................................................... 13
6. Publication B ..................................................................................................... 21
7. Discussion ......................................................................................................... 29
  7.1 Findings and results.......................................................................................... 29
7.2 Findings in the context of current research ....................................................... 30

7.3 Limitations......................................................................................................... 31

8. Conclusion ........................................................................................................ 32

9. References......................................................................................................... 33

10. Acknowledgements ........................................................................................ 38

11. Appendix.......................................................................................................... 39

11.1 Darstellung des eigenen Beitrags zu Publikation A......................................... 40

11.2 Darstellung des eigenen Beitrags zu Publikation B......................................... 41

11.3 Selbstständigkeitserklärung ............................................................................ 42

11.4 Lebenslauf ...................................................................................................... 43

11.5 Publikationsliste .............................................................................................. 44
1. Summary

Aneurysms of the aortic root and ascending aorta often require surgical correction. Currently, two common alternatives exist: The Bentall procedure has traditionally been used successfully for many decades, utilising an aortic valve prosthesis to replace the aortic valve and a conduit to replace the aneurysmic aorta. The more recent approach has been to reimplant suitable aortic valves utilising a dacron graft as well as replacing the affected aortic segment. The most widely used technique thereof is the David procedure.

The decision for either operation depends greatly on patient circumstance and preference, as well as the recommendation of the operating surgeon. This is due to the associated features and disadvantages of the procedures at hand that make the careful choice of technique vital. Previous research has shown promising results for the equivalence, if not superiority, of the David procedure in certain patient groups, as well as in comparison to the Bentall procedure overall. At the same time, there are concerns about the David approach regarding the durability, perioperative risk, and long-term outcomes, among others. Regardless, avoidance of anticoagulation postoperatively has made it an attractive choice for patients who do not want to or cannot receive anticoagulants. While the David procedure has shown these beneficial properties, it has been widely limited to cases where the aortic valve is deemed suitable. Over the last decade, several studies have assessed the usage of David procedure for cases that did not previously seem to be a fit, such as patients with bicuspid aortic valves, who are now deemed suitable.

With the David procedure becoming more widely applied and the application of the operation being extended, the question arises, whether the Bentall procedure remains the gold standard for correction of aortic root pathology.

Several studies have been conducted over the years, but because cases are comparatively few, evidence is still lacking.

For this, we conducted a study into the short and long-term outcomes of patients who underwent either Bentall or David procedures at the Leipzig Heart Centre between 2000 and 2015. Pre-operative, operative and post-operative data was gathered, and a follow-up was conducted through questionnaires, reports by physicians and telephone surveys. Statistical analysis was performed to gain data on perioperative mortality, adverse outcomes and long-term effects, such as bleeding incidents, reoperation rates and overall mortality, among others.
This resulted in two publications that form the basis of this dissertation: Publication A sought to compare the outcomes of David cases with those who received correction with the Bentall procedure, including both mechanical valve prostheses and biological replacements. Publication B compared David cases to biological Bentall replacements. This subgroup analysis was done because both procedures avoid long term-anticoagulation.

We found that both the David and Bentall operation had excellent early and long-term results, with comparable outcomes for early and late mortality among others. Furthermore, we did not see an increased risk of reoperation for the David procedure during our observational period. We recorded a higher incidence of serious bleeding events in the Bentall group (Publication A). The comparison of bioprosthetic Bentall cases to the David group showed equivalent outcomes for both procedures without significant difference in endpoints.

While patient preferences and circumstances should still be considered, our investigations showed clear advantages for the David procedure in the analysed patient group. We concluded that the David operation is the preferable operation in patients with appropriate pathoanatomy, because long-term complications associated with prosthetic heart valves remain a major concern and it has shown to mitigate said complications.
1. Summary

**Key question**

What are the short and long-term results after aortic valve-sparing re-implantation (David) vs aortic root replacement (Bentall) operation?

**Key findings**

30-day mortality, long-term mortality and reoperation rates are similar for the two procedures. Age, smoking and previous cardiac surgery are independent predictors of long-term mortality. The Bentall operation is associated with an increased risk of serious bleeding.

**Conclusion**

The David operation results in lower risk of bleeding compared to the Bentall operation without increased risk of reoperation. The David operation may be considered the gold standard for patients with aortic root aneurysms and pliable valve cusp morphology.

*Figure 1 – Summary abstract*
2. Constitutive publications

The following publications form the basis of this dissertation:

---


*p. 13-20*

---


*p. 21-28*

* Authors have contributed equally.
3. Introduction

3.1 Definition and epidemiology

Aneurysms of the ascending aorta constitute a circumscribed entity of disease, which is defined as a dilation of the vessel between aortic valve and brachiocephalic artery by more than 50% its size\(^1,2\). For the purpose of treatment and etiological grouping, thoracic aortic aneurysms and more specifically the proximal aortic type are usually regarded separately from other forms of aneurysmal disease. Although there is conclusive evidence that abdominal and thoracic aneurysms occur concurrently in certain patients\(^3\). The incidence of thoracic aortic aneurysms has been reported to be as wide as 7.1 to 16.3 per 100.000 per year with increasing prevalence, and men being significantly more affected\(^4,5\). Total deaths due to any aortic aneurysms amounted to over 150.000 worldwide in 2013\(^6\). Of all thoracic aortic aneurysms, the majority are aneurysms of the ascending aorta\(^1,7\). Although incidence and mortality of ascending aortic aneurysms are comparatively lower, they still contribute to significant burden of disease in specific patient groups\(^1,8\).

3.2 Aetiology and risk factors

Generally, ascending aortic aneurysms develop due to a multitude of factors: Soft tissue degeneration, medial degeneration and loss of smooth muscle cells in the vascular structure develop through wall stress, inflammatory and genetic conditions\(^9\). Some authors have argued that, even in cases with seemingly different aetiology, thoracic aortic aneurysms - ascending aortic aneurysms in particular - can largely be explained by genetic abnormalities and should be considered a largely genetic disease\(^10,11\). Currently, the most commonly accepted risk factors for developing proximal aortic aneurysms are hereditary conditions affecting the connective tissue, such as Marfan and Loeys-Dietz syndrome, hypertension and associated causes thereof, as well as smoking and inflammatory conditions, such as vasculitis of the aorta, as is the case in Takayasu arteritis and Giant cell arteritis\(^9\). Bicuspid aortic valves, which represent the most common of congenital cardiac defects, also predispose to thoracic aortic aneurysms; 40% of all patients with bicuspid aortic valves develop concomitant thoracic aortic aneurysms\(^12,13\). Although rare, syphilitic aortic changes can sometimes be the cause of ascending aortic aneurysms\(^14\).
3.3 Symptoms and complications

Patients with proximal aortic aneurysm are usually asymptomatic and most aneurysms are found by chance or because of screening procedures in selected patient populations, unless the aneurysm causes distinct symptoms through associated valve pathology, dissection or rupture\textsuperscript{10}. The latter occur frequently and regularly in untreated patients and are the major reason why surgical intervention needs to be considered for all symptomatic patients and aneurysms of a certain size\textsuperscript{15}. The risk of rupture or dissection is mainly driven by two main factors, namely aetiology of the aneurysm, i.e. whether there is genetic cause, and diameter of the aneurysm. It is well documented that familial thoracic aortic aneurysms grow faster than other aneurysms and are predisposed to rupture\textsuperscript{9}.

3.4 Surgical intervention

The pharmacological treatment of aneurysmal disease of the thoracic aorta, while still widely applied, is of controversial benefit. Some studies have shown a small, but significant protective effect of beta-blockers and other anti-hypertensive medications, while others have proposed that their use does not pose significant advantages over non-treatment and some have raised concerns about their harmfulness\textsuperscript{9,10}. Eventually, surgical correction of the aneurysm is required. Guidelines currently suggest that symptomatic aneurysms of the ascending aorta of all sizes, and asymptomatic aneurysms of the ascending aorta should be surgically corrected when the diameter of the aneurysm is 55mm or larger in the general population, and 50mm or larger for patients with Marfan syndrome (including those with marfanoid symptoms or habitus), or patients with bicuspid aortic valves and certain risk factors, such as severe hypertension or growth rates of >3mm/year\textsuperscript{15–18}. Stricter rules for earlier intervention still apply for patients with connective tissue disease and in special circumstances, such as desired pregnancy\textsuperscript{15,19}. Furthermore, lower thresholds can apply in specialized centres for certain patients\textsuperscript{15,20}.

3.4.1 Bentall procedure

The most popular and arguably most established surgical correction technique for aneurysms of the ascending aorta is the replacement of the aortic valve and affected portion of the aorta
with a conduit, namely the *Bentall procedure*. Invented by Hugh Bentall and Antony de Bono in 1968, the technique allows for the correction of aortic pathology and associated valve defects: The aortic root and valve are replaced with an aortic valve and conduit, while the coronary arteries are reattached to the conduit\textsuperscript{21}. As the approach utilises artificial valve replacement, in the case of mechanical valves an often-times lifelong treatment with anticoagulants is necessary, as is mostly with biological valves for the first three months postoperatively. Another shortfall of the technique is the durability of biological aortic valves, which makes reoperation and replacement necessary, which – especially in younger patients – limits the usefulness of biological valve replacement\textsuperscript{22}. Furthermore, the prevention of thrombosis through means of anticoagulation comes at the cost of risking bleeding incidents, such as intracranial bleeding, as well as relying on significant patient compliance.

### 3.4.2 David procedure

An alternative technique was introduced in 1992 by Tirone David, who had operated on a patient in a new fashion for the first time in 1989 by reimplanting the native aortic valve into a dacron graft\textsuperscript{23–25}. The operation became known as the aortic valve-sparing reimplantation technique or *David procedure*. By implantation of native aortic cusps, the procedure also allows for the avoidance of anticoagulation and hence the aforementioned risks. Although widely applied, certain disadvantages of the procedure exist. One of the major limitations so far has been the viability of aortic valve cusps for reimplantation, i.e. the valve must be surgically salvageable and retain its intended function once reimplanted. This has so far widely limited the procedure to cases which do not involve valve pathologies that change the morphology of the native cusps, for example degenerative aortic stenosis. Nevertheless, the David procedure is being applied successfully in more challenging scenarios, e.g. the setting of bicuspid aortic valves\textsuperscript{26}. In fact, over the last two decades, the David procedure has been postulated to be equal, if not superior to the Bentall procedure: Some authors have recommended the David operation as the new gold standard for proximal aortic arch replacement\textsuperscript{27}. 

4. Premise of the study and publications presented

4.1 State of research

Making the right recommendations and decisions in the clinical setting relies largely on the evidence provided by empirical studies, and in the circumstances of emerging surgical techniques, procedures must be tested against the current gold-standard of care. Because ascending aortic aneurysms are comparatively rare and the reporting of the disease, its treatment and outcomes is not standardised, large patient volume reports and studies are lacking. Large, multicentre studies are also limited due to the relative shortage of centres performing David operations on a large-scale basis.

In 2012, Leontyev et al. published the isolated results of 179 patients after undergoing correction of proximal aortic disease with the David procedure at the Leipzig Heart Centre. The study showed excellent results for mortality, long-term survival and reoperation rates.

Several other studies have compared Bentall and David techniques and have found heterogenous evidence: While generally the David procedure is seen as a viable alternative to the Bentall procedure, some researchers have found higher rates of reoperation among David patients during follow up, as well as no clear clinical advantage for either procedure.

Some investigations have reported notably higher rates of reoperation as well, but a clear benefit of lower rates of bleeding and thromboembolism events in David groups compared to the Bentall operation. More recent research has shown clear advantages for the David reimplantation technique, with reduced cardiac mortality and valve-related complications compared to the Bentall procedure.

4.2 Objectives

It is therefore necessary to perform large patient volume comparisons of the procedures at hand. For this purpose, we conducted a study into the differences of short and long-term outcomes regarding mortality and rate of reoperation, as well as other endpoints between David and Bentall procedures. Our publications aimed to investigate whether the aortic valve-sparing reimplantation technique (David) or the aortic root replacement operation (Bentall) showed clear advantages over the other.
To this aim, we sought to compare early, medium and long-term outcomes of the two patient groups regarding mortality, reoperation and adverse events:

To assess the early postoperative outcomes we recorded and compared, among others, mortality and stroke rate, and factors significantly associated with postoperative cerebrovascular accident (CVA) or early mortality. Furthermore, we analysed data regarding the medium- and long-term mortality at five and ten years, and also independent predictors of long-term mortality to identify risk factors that might be associated with mortality. As described above, the stability of the repair or replacement after surgery is an important factor in comparing the techniques. It is therefore paramount to record and find possible differences in reoperation rates.

We examined freedom from reoperation times for patients with and without connective tissue disease and native tricuspid versus bicuspid aortic valves. To find risk factors associated with this, we analysed for independent predictors of freedom from reoperation. We also recorded causes for reoperation and compared those for both groups. Because adverse events, such as myocardial infarction, major bleeding events, strokes and endocarditis represent important endpoints for comparison of surgical outcomes we recorded and statistically processed those outcomes for the follow-up period. Additionally, mortality rates among those requiring reoperation and freedom from mortality can be different in both groups and must be taken into account. We decided to compare this in our investigation for each respective group of patients requiring reoperation. Also, we analysed freedom from all valve-related events between groups, to assess the potential combined difference in valve-related events for both groups.

### 4.3 Patient selection

A consecutive total of 1318 patients received aortic root correction between January 2000 and December 2015 at the Leipzig Heart Centre, of which 1005 underwent a Bentall and 313 a David procedure. Patients who had presented with endocarditis had already received replacement of the aortic valve or had concurrent valve surgery other than the aortic valve were excluded. Because of the retrospective nature of the study conducted, a nearest-neighbour propensity score analysis was performed.

We initially included patients who required replacement of the ascending aorta due to aortic dissection. Several studies have shown that the David procedure can be a safe alternative to the Bentall procedure for those patients\(^ {32-34}\). Nonetheless, we decided to exclude cases of Type A aortic dissection to sharpen the focus and scope of the study.
We excluded these patients from the originally identified patients of interest, along with cases already marked for exclusion due to the aforementioned indications, and conducted a new propensity score analysis in the same fashion, which resulted in 261 David and 262 Bentall patients.

For Publication B, patients who received mechanical prostheses in the Bentall group were excluded from the matched pool, bringing the number of patients for this investigation to 261 David and 150 biological Bentall patients.

Figure 2 – Final patient selection
4.4 Follow-up

A mail survey was undertaken annually in addition to reporting from the respective treating physicians to ensure follow-up after surgery regarding mortality and complications and adverse events. To improve the currency, consistency, and completeness of the data, phone interviews with patients from both groups were conducted from May to July 2018. This included questions about vital status, date and cause of death (where applicable), questions regarding adverse events since the date of surgery, as well as reoperations and cardiac surgical interventions and the date they were performed. All answers were electronically logged in an anonymous fashion.

4.5 Statistical analysis

Studies conducted in settings that compare the outcome of procedures performed by surgeons face a common dilemma: To receive the most valid results, data needs to be obtained and analysed in a way that is designed to greatly minimise confounding variables. Usually this can be achieved by conducting prospective studies that are randomised and double-blinded. The nature of surgical procedures, however, does not make them easily accessible to these methods. First, blinding the surgeon to the procedure performed is all but impossible because of the complexity of the procedure itself, the different approaches, as well as the individual assessment of each patient prior to the operation. Secondly, patients need to be informed about the procedure conducted, not only because of the ramifications for everyday life, but also the practicability of post-operative care. While sham-interventions have been conducted in different surgical settings, the application in complex cardiac procedures seems unlikely. This makes the realisation of a randomised controlled trial to test the efficacy of surgical procedures very difficult.

To try and eliminate confounding variables, a different approach was chosen for the studies presented; by statistically reducing bias through propensity score matching.

Propensity score matching aims to create comparable groups from the patient pool. This is done by assigning each patient a propensity score, which signifies the likelihood of receiving a certain treatment by taking into account confounding variables, such as age, gender and pre-existing conditions (refer Figure 2). Then a case match is conducted to achieve comparable groups. As a method, we employed a 1:1 nearest neighbour match.

[11]
The Kaplan-Meier method was used to assess early, medium and long-term mortality, as well as freedom from reoperation. Also, a binary logistic regression analysis model was used to search for parameters linked to higher risk of postoperative CVA. To detect independent predictors of long-term mortality and freedom from reoperation, a Cox proportional hazard analysis was utilised. P-values of < 0.05 were considered statistically significant.

All data was analysed using SPSS (SPSS Statistics 25.0, IBM Corp, Armonk, NY, USA).

Further description of the statistical methods used can be found in the respective publications.
5. Publication A
Early and Late Results After David vs Bentall Procedure: A Propensity Matched Analysis

Sergey Leontyev, MD, PhD,* Lukas Schamberger, MD,* Piroze M. Davierwala, MD, Konstantin Von Aspern, MD, Christian Etz, MD, PhD, Sven Lehmann, MD, PhD, Martin Misfeld, MD, PhD, and Michael A. Borger, MD, PhD

Department of Cardiac Surgery, Leipzig Heart Centre, University of Leipzig, Leipzig, Germany

Background. The aim of this study was to compare the short- and long-term outcomes of patients who underwent aortic valve-sparing reimplantation (David) vs aortic root replacement (Bentall) operations in a propensity-matched analysis.

Methods. The study compared the data of propensity-matched patients who underwent David (n = 261) or Bentall (n = 262) procedures from 2000 to 2015. The mean age at surgery in the entire cohort was 53 ± 13 years, and 19.7% (n = 103) of the study patients were female. Connective tissue disease was present in 9.4% (n = 49) of patients, whereas 37.1% (n = 194) presented with a bicuspid aortic valve.

Results. The overall 30-day mortality was 1.1% (n = 6) and was not significantly different in patients with the David compared with the Bentall operation (0.4% [n = 1] vs 1.9% [n = 5]; P = .1). The 5- and 10-year survival rates were 93.7 ± 1.8% vs 93.8 ± 1.6% and 84.4 ± 4.7% vs 89.5 ± 3.2% for David vs Bentall, respectively (log-rank P = .98).

Aortic root replacement – or Bentall procedure – and aortic valve reimplantation – or David procedure – are 2 established methods for treatment of patients with aortic root disease. Whereas the modified Bentall procedure is still the procedure of choice in most centers, the David aortic valve-sparing reimplantation technique has been associated with excellent outcomes in specialized centers. Younger patients with pliable aortic cusps may particularly benefit from the David procedure because it avoids the well-documented long-term problems associated with prosthetic heart valves. Although several studies have compared the short- and long-term outcomes of the Bentall and David procedures, the number of long-term studies with substantial patient group sizes is small.3,5

Cox regression analysis identified age, smoking and previous cardiac surgery as independent predictors of long-term mortality. Freedom from reoperation did not significantly differ between patient groups (89.5 ± 3.4% vs 87.8 ± 4.1% 10 years postoperatively; log-rank P = .71). Bentall-treated patients had a higher rate of serious bleeding during follow-up (P = .025).

Conclusions. Both the David and Bentall operations are associated with excellent early and long-term results in patients with aortic root aneurysmal disease. The David operation is associated with less bleeding than the Bentall operation, without an increased risk of reoperation. Because of avoidance of bleeding and other long-term complications associated with prosthetic heart valves, the David operation is preferable to the Bentall operation in patients with appropriate pathoanatomy.


The aim of this study was to compare retrospectively the short- and long-term outcomes of patients undergoing either a Bentall procedure or a David operation by using a propensity-matched analysis.

Patients and Methods

Between January 2000 and December 2015, a total of 1318 consecutive patients underwent aortic root surgery with a Bentall (n = 1069) or David (n = 315) technique at our center (Leipzig Heart Center, Leipzig, Germany). Patients with infective endocarditis at the time of admission, patients who had undergone a previous replacement of the aortic valve, patients who required concomitant valve surgery (eg, replacement or repair of the mitral valve),

© 2020 by The Society of Thoracic Surgeons
Published by Elsevier Inc.

Dr Leontyev discloses a financial relationship with Medtronic and Abbott (St Jude Medical); Dr Lehmann with Abbott (St Jude Medical); Dr Borger with Edwards Lifesciences, Medtronic, Abbott (St Jude Medical), and CryoLife.

0003-4975/536.00
https://doi.org/10.1016/j.athoracsur.2019.10.020

*Dr Leontyev and Schamberger contributed equally to this work.

Accepted for publication Oct 7, 2019.
and patients with acute type A aortic dissection were excluded. Subsequent patients were matched using propensity score analysis to minimize differences in baseline variables, thus resulting in a total of 261 David and 262 Bentall patients. In accordance with the guidelines of The Society of Thoracic Surgeons, early mortality was defined as all-cause mortality at 30 days.

The study was approved by the local ethics committee, and individual patient consent for this retrospective review was waived.

Follow-up was performed annually either by mail questionnaire or by contacting the respective cardiologist or general practitioner to assess mortality and complications after surgery. Additionally, we conducted a phone questionnaire from March to July 2018 to improve response rates.

Overall follow-up completeness was 88%, with no significant difference between the David and Bentall groups (David, 11%; Bentall, 14%; \( p = .24 \)). An average duration of 5.0 ± 3.6 years was recorded overall, with no differences between groups (David, 4.8 ± 3.3; Bentall, 5.2 ± 3.9; \( p = .12 \)) and ranging from 1.0 to 16.3 years.

Operative Technique

For patients undergoing a Bentall operation, the aortic valve was replaced by a mechanical or biologic valve, and the surrounding aortic wall and proximal ascending aorta were replaced in the usual fashion. Our operative technique for the David operation has been previously described in detail. Patient selection for the David or Bentall operation was mostly dependent on the evaluation of the aortic cusps as viable for a David procedure, an assessment of patients’ attributes (eg, age, comorbidities, lifestyle, family planning), and the availability of an experienced surgeon. In 1 patient, who was scheduled to undergo a David operation, the procedure was converted to a Bentall operation because of intraoperative failure of aortic cusp reimplantation with resultant aortic insufficiency.

Statistical Analysis

Data were imported to SPSS (SPSS Statistics 25.0, IBM Corp, Armonk, NY) for description and analysis. Categorical data are shown as total numbers and proportion in percentages and were compared using the \( \chi^2 \) test or the Fisher exact test as appropriate. Continuous variables are expressed as mean ± SD and were compared using the Student t test or the Wilcoxon-Mann-Whitney test as appropriate. Normal distribution of measurements was determined using the Shapiro-Wilk test.

To minimize selection bias and obtain comparable groups, we used a propensity score matching analysis and determined the likelihood that a patient would undergo either a David or a Bentall procedure. For this analysis, a 1:1 nearest neighbor propensity score matching approach was used. As matching variables, the following parameters were included: age, date of surgery, left ventricular ejection fraction, priority, body surface area, sex, smoker status, previous cerebrovascular accident (CVA), previous cardiac surgery, arterial hypertension, pulmonary hypertension, peripheral vascular disease, chronic obstructive pulmonary disease, diabetes mellitus, hyperlipidemia, coronary artery disease, and previous percutaneous coronary intervention. In outcome analysis, the Kaplan-Meier method with 95% confidence intervals (CIs) was used to determine early and long-term mortality, as well as freedom from reoperation. We used a binary logistic regression analysis model to identify factors associated with a higher risk of postoperative CVA. Furthermore, Cox proportional hazard analysis for independent predictors of long-term mortality and freedom from reoperation, presented as hazard ratios (HRs) and 95% CIs, was used. A \( p \) value of <.05 was considered statistically significant.

Results

Preoperative Characteristics

The preoperative clinical characteristics for all 523 matched patients, subdivided by surgical group, are presented in Table 1. The mean age of patients was 53 ± 13 years, and 19.7% (\( n = 103 \)) of the study patients were female. Emergency cases accounted for 1.5% (\( n = 8 \)) of patients. In the David group, we observed significantly more patients with connective tissue disease. In contrast, bicuspid valve disease was found more often in the Bentall group.

Operation Data

The total length of surgery was significantly longer for David operations (231 ± 54 minutes) compared with Bentall operations (199 ± 63 minutes), as were aortic cross-clamp time and total cardiopulmonary bypass times (all \( p < .001 \)). In 42.7% of all Bentall procedures, the aortic valve was replaced with a mechanical prosthesis, with the remainder receiving a biologic conduit (Table 2).

Early Outcomes

Overall in-hospital mortality and 30-day mortality were 1.0% (\( n = 5 \)) and 1.1% (\( n = 6 \)), respectively. There was no observable difference in early outcome between groups. The total CVA rate was 1.7% (\( n = 9 \)) and was similar in both groups (Table 3). A logistic regression analysis did not reveal any factors significantly associated with postoperative CVA or early mortality.

Medium- and Long-Term Outcomes

Estimated 5- and 10-year survival rates were 93.8 ± 1.2% and 87.2 ± 2.7% for all patients, respectively (Figure 1). There was no difference in survival between the David and Bentall operations at any time (log-rank \( p = .98 \)). Cox regression analysis identified age at surgery (HR, 1.05; 95% CI, 1.02 to 1.08; \( p < .001 \)), smoking (HR, 2.76; 95% CI, 1.38 to 5.52; \( p = .004 \)), and previous cardiac surgery (HR, 4.71; 95% CI, 1.79 to 12.96; \( p = .002 \)) as independent predictors of long-term mortality.

Freedom from reoperation at 5 and 10 years was 96.2 ± 1.0% and 88.4 ± 2.8% for all patients, respectively.
Table 1. Preoperative Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total n = 523</th>
<th>David n = 261</th>
<th>Bentall n = 262</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>53 ± 13</td>
<td>53 ± 15</td>
<td>53 ± 12</td>
<td>.96</td>
</tr>
<tr>
<td>Female</td>
<td>103 (19.7)</td>
<td>57 (21.8)</td>
<td>46 (17.6)</td>
<td>.22</td>
</tr>
<tr>
<td>COPD</td>
<td>12 (2.3)</td>
<td>7 (2.7)</td>
<td>5 (1.9)</td>
<td>.56</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>58 (11.1)</td>
<td>30 (11.5)</td>
<td>28 (10.7)</td>
<td>.77</td>
</tr>
<tr>
<td>Dialysis</td>
<td>3 (0.6)</td>
<td>2 (0.8)</td>
<td>1 (0.4)</td>
<td>.56</td>
</tr>
<tr>
<td>Diabetes</td>
<td>30 (5.7)</td>
<td>15 (5.7)</td>
<td>15 (5.7)</td>
<td>.99</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>149 (28.3)</td>
<td>67 (25.7)</td>
<td>81 (30.9)</td>
<td>.18</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>396 (75.7)</td>
<td>191 (73.2)</td>
<td>205 (78.2)</td>
<td>.18</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>339 (64.8)</td>
<td>165 (63.2)</td>
<td>174 (66.4)</td>
<td>.44</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>9 (1.7)</td>
<td>4 (1.5)</td>
<td>5 (1.9)</td>
<td>.74</td>
</tr>
<tr>
<td>Smoker</td>
<td>209 (40.0)</td>
<td>99 (37.9)</td>
<td>110 (42.0)</td>
<td>.34</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>15 (2.9)</td>
<td>7 (2.7)</td>
<td>8 (3.1)</td>
<td>.8</td>
</tr>
<tr>
<td>LVEF (%) &lt;30</td>
<td>5 (1.0)</td>
<td>2 (0.8)</td>
<td>3 (1.1)</td>
<td>.66</td>
</tr>
<tr>
<td>LVEF (%) 30-50</td>
<td>106 (20.3)</td>
<td>54 (20.7)</td>
<td>52 (19.8)</td>
<td>.81</td>
</tr>
<tr>
<td>LVEF (%) &gt;50</td>
<td>412 (78.8)</td>
<td>205 (78.5)</td>
<td>207 (79.0)</td>
<td>.90</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>16 (3.1)</td>
<td>8 (3.1)</td>
<td>8 (3.1)</td>
<td>.99</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>49 (9.4)</td>
<td>44 (16.9)</td>
<td>5 (1.9)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Marfan syndrome</td>
<td>36 (6.9)</td>
<td>31 (11.9)</td>
<td>5 (1.9)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>12 (2.3)</td>
<td>12 (4.6)</td>
<td>0 (0.0)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Loeys-Dietz syndrome</td>
<td>1 (0.2)</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
<td>.32</td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>194 (37.1)</td>
<td>41 (15.7)</td>
<td>153 (58.4)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Aortic insufficiency only</td>
<td>374 (71.5)</td>
<td>250 (95.8)</td>
<td>124 (47.3)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>First-degree</td>
<td>69 (13.2)</td>
<td>62 (23.8)</td>
<td>7 (2.7)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Second-degree</td>
<td>176 (33.7)</td>
<td>125 (47.9)</td>
<td>51 (19.5)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Third-degree</td>
<td>127 (24.3)</td>
<td>63 (24.1)</td>
<td>64 (24.4)</td>
<td>.94</td>
</tr>
<tr>
<td>Fourth-degree</td>
<td>2 (0.4)</td>
<td>0 (0.0)</td>
<td>2 (0.8)</td>
<td>.16</td>
</tr>
<tr>
<td>Aortic stenosis only</td>
<td>42 (8.0)</td>
<td>0 (0.0)</td>
<td>42 (16.0)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>First-degree</td>
<td>1 (0.2)</td>
<td>0 (0.0)</td>
<td>1 (0.4)</td>
<td>.32</td>
</tr>
<tr>
<td>Second-degree</td>
<td>10 (1.9)</td>
<td>0 (0.0)</td>
<td>10 (3.8)</td>
<td>.001*</td>
</tr>
<tr>
<td>Third-degree</td>
<td>31 (5.9)</td>
<td>0 (0.0)</td>
<td>31 (11.8)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Fourth-degree</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Combined aortic insufficiency and stenosis</td>
<td>95 (18.2)</td>
<td>0 (0.0)</td>
<td>95 (36.3)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Aortic diameters (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Root</td>
<td>44 ± 10</td>
<td>45 ± 9</td>
<td>44 ± 10</td>
<td>.12</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>50 ± 9</td>
<td>53 ± 9</td>
<td>48 ± 8</td>
<td>&lt;.001*</td>
</tr>
</tbody>
</table>

*Statistically significant for P < .05.

All data are shown as n (%), unless otherwise specified.

Bentall, aortic root replacement; Bentall procedure; COPD, chronic obstructive pulmonary disease; David, David aortic valve-sparing reimplantation; LVEF, left ventricular ejection fraction.

(Figure 2), and was not significantly different between groups (log-rank P = .71). Additionally, there was no significant difference in freedom from reoperation for patients with and without connective tissue disease (log-rank P = .36) or patients with tricuspid vs bicuspid aortic valves (log-rank P = .53). The only independent predictor of freedom from reoperation was diabetes (HR, 3.62; 95% CI, 1.07 to 12.26; P = .04).

The most common indications for reoperation, which occurred in 5.0% (n = 26) of all patients, were endocarditis (David, n = 4; and Bentall, n = 6; P = .53) and aortic insufficiency (David, n = 7; and Bentall, n = 3, P = .2). The remaining patients required reoperation for aortic stenosis (David, n = 2; and Bentall, n = 4; P = .41). No significant difference in reoperation rates was observed between the David and Bentall groups. Overall mortality for those patients requiring reoperation for valve-related events (n = 26) was 15.4% (n = 4). Freedom from mortality at 5 and 10 years among those patients requiring reoperation for valve-related events was similar to that in patients who did not (log-rank P = .27). No difference in freedom from mortality was reported for David vs Bentall patients who required reoperation (log-rank P = .34).
Table 2. Operation Data

<table>
<thead>
<tr>
<th>Operation Feature</th>
<th>Total n = 523</th>
<th>David n = 261</th>
<th>Bentall n = 262</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of surgery (min)</td>
<td>215 ± 61</td>
<td>231 ± 54</td>
<td>199 ± 63</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Cross-clamp time (min)</td>
<td>101 ± 34</td>
<td>114 ± 30</td>
<td>87 ± 32</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Total cardiopulmonary bypass time (min)</td>
<td>128 ± 45</td>
<td>142 ± 42</td>
<td>114 ± 43</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Minimum body temperature (Celsius)</td>
<td>32.1 ± 4.6</td>
<td>30.9 ± 4.9</td>
<td>33.2 ± 4.0</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Prosthesis type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical</td>
<td>112 (21.4)</td>
<td>0 (0.0)</td>
<td>112 (42.7)</td>
<td></td>
</tr>
<tr>
<td>Biologic</td>
<td>150 (28.7)</td>
<td>0 (0.0)</td>
<td>150 (57.5)</td>
<td></td>
</tr>
<tr>
<td>Prosthesis model type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATS Aortic Model 500FA Open Pivot Standard</td>
<td>6 (1.1)</td>
<td>0 (0.0)</td>
<td>6 (2.3)</td>
<td></td>
</tr>
<tr>
<td>ATS Aortic Valved Graft Model 502AG</td>
<td>88 (16.8)</td>
<td>0 (0.0)</td>
<td>88 (33.6)</td>
<td></td>
</tr>
<tr>
<td>SJM Aortic Valved Graft Model CAVGJ 514</td>
<td>18 (3.4)</td>
<td>0 (0.0)</td>
<td>18 (6.9)</td>
<td></td>
</tr>
<tr>
<td>Carpentier-Edwards BioPhysio 3100 TFX</td>
<td>1 (0.2)</td>
<td>0 (0.0)</td>
<td>1 (0.4)</td>
<td></td>
</tr>
<tr>
<td>Carpentier-Edwards Perimount Magna Ease Aortic 3300TFX</td>
<td>8 (1.5)</td>
<td>0 (0.0)</td>
<td>8 (3.1)</td>
<td></td>
</tr>
<tr>
<td>Carpentier-Edwards Perimount Magna Ease Aortic 3500TFX</td>
<td>1 (0.2)</td>
<td>0 (0.0)</td>
<td>1 (0.4)</td>
<td></td>
</tr>
<tr>
<td>Carpentier-Edwards Perimount-Aortic Model 2900</td>
<td>64 (12.2)</td>
<td>0 (0.0)</td>
<td>64 (24.4)</td>
<td></td>
</tr>
<tr>
<td>Medtronic Freemstyle-Aortic Root Model 990</td>
<td>55 (10.5)</td>
<td>0 (0.0)</td>
<td>55 (21.0)</td>
<td></td>
</tr>
<tr>
<td>Medtronic Mosaic-Aortic Model 305</td>
<td>1 (0.2)</td>
<td>0 (0.0)</td>
<td>1 (0.4)</td>
<td></td>
</tr>
<tr>
<td>SJM Toronto Root</td>
<td>5 (1.0)</td>
<td>0 (0.0)</td>
<td>5 (1.9)</td>
<td></td>
</tr>
<tr>
<td>SJM Trifecta Valve</td>
<td>2 (0.4)</td>
<td>0 (0.0)</td>
<td>2 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Vascutek BioValsalva Conduit</td>
<td>13 (2.5)</td>
<td>0 (0.0)</td>
<td>13 (5.0)</td>
<td></td>
</tr>
<tr>
<td>Concomitant surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>36 (6.9)</td>
<td>18 (6.9)</td>
<td>18 (6.9)</td>
<td>.99</td>
</tr>
<tr>
<td>Total aortic arch replacement</td>
<td>16 (3.1)</td>
<td>16 (6.1)</td>
<td>0 (0.0)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Correction of CHD</td>
<td>14 (2.7)</td>
<td>7 (2.7)</td>
<td>7 (2.7)</td>
<td>.99</td>
</tr>
</tbody>
</table>

*Statistically significant for $P < .05$.

All data are shown as n (%), unless otherwise specified.

Bentall, aortic root replacement, Bentall procedure; CABG, coronary artery bypass grafting; CHD, congenital heart defect; David, David aortic valve-sparing reimplantation.

Regarding events during follow-up, we found a significantly higher rate of bleeding requiring hospitalization in Bentall-treated-patients: 1.9% (n = 5) reported such events, whereas none in the David group did (P = .025). No difference was reported for CVA (David, n = 4; Bentall, n = 8; P = .25), myocardial infarction (David, n = 0; Bentall, n = 1; P = .32), or endocarditis (David, n = 4; Bentall, n = 7; P = .36).

There was no difference in freedom from all valve-related events between groups after 5 and 10 years (David, 97.9 ± 1.2% and 93.3 ± 2.9%; Bentall, 96.1 ± 1.5% and 84.7 ± 3.8%, respectively; log rank P = .15).

Comment

Our propensity-matched analysis indicates that early and long-term results of both David and Bentall techniques are excellent, and that both operations provide a safe and reliable surgical option for patients with aortic root disease. Our findings concur with those demonstrated in several other studies from large-volume aortic centers.5.4 4

Some studies have raised concerns regarding the higher reoperation rate and lower durability of the David operation.2 5 We did not identify such trends in our study and instead observed very low perioperative mortality and follow-up reoperation rates, regardless of whether patients received the David or Bentall operation. Indeed, some investigators have found a lower rate of reoperation for David surgery when compared with biologic valve root replacement.3 10

We failed to find a clear advantage for either procedure with respect to other long-term complications such as stroke or endocarditis. Some investigators have reported more endocarditis in Bentall-treated patients,5 11 but we were unable to demonstrate such a finding. It is possible that our study was underpowered to detect such a difference, with inadequate length of follow-up. Regardless, our study clearly demonstrates that the long-term outcomes of both the David and Bentall operations are very good.

Given the other known risks associated with mechanical or biologic aortic valve replacement, such as thromboembolism, anticoagulation-related bleeding, and structural valve deterioration, one could consider the David operation the preferable option in patients with aortic root aneurysmal disease and suitable anatomy. Indeed, we observed a higher rate of serious bleeding requiring hospitalization in the Bentall group (1.9% vs
Table 3. Early Postoperative Outcomes for David vs Bentall Operations

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Total n = 532</th>
<th>David n = 261</th>
<th>Bentall n = 262</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory failure</td>
<td>37 (7.1)</td>
<td>20 (7.7)</td>
<td>17 (6.5)</td>
<td>.5</td>
</tr>
<tr>
<td>Low cardiac output</td>
<td>5 (1.0)</td>
<td>0 (0.0)</td>
<td>5 (1.9)</td>
<td>.025*</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>New pacemaker</td>
<td>18 (3.4)</td>
<td>6 (2.3)</td>
<td>12 (4.6)</td>
<td>.15</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>9 (1.7)</td>
<td>6 (2.3)</td>
<td>3 (1.1)</td>
<td>.31</td>
</tr>
<tr>
<td>Deep sternal wound infection</td>
<td>1 (0.2)</td>
<td>0 (0.0)</td>
<td>1 (0.4)</td>
<td>.32</td>
</tr>
<tr>
<td>Sepsis</td>
<td>5 (1.0)</td>
<td>3 (1.1)</td>
<td>2 (0.8)</td>
<td>.65</td>
</tr>
<tr>
<td>Dialysis</td>
<td>8 (1.5)</td>
<td>3 (1.2)</td>
<td>5 (1.9)</td>
<td>.48</td>
</tr>
<tr>
<td>Reoperation for bleeding</td>
<td>32 (6.1)</td>
<td>18 (6.9)</td>
<td>14 (5.5)</td>
<td>.46</td>
</tr>
<tr>
<td>Redo surgery</td>
<td>7 (1.3)</td>
<td>3 (1.1)</td>
<td>4 (1.5)</td>
<td>.71</td>
</tr>
<tr>
<td>Aortic insufficiency</td>
<td>77 (14.9)</td>
<td>63 (24.1)</td>
<td>14 (5.4)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>First-degree</td>
<td>76 (14.7)</td>
<td>62 (23.8)</td>
<td>14 (5.4)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Second-degree</td>
<td>1 (0.2)</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
<td>.32</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Aortic diameters (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Root</td>
<td>29 ± 3</td>
<td>30 ± 3</td>
<td>28 ± 3</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>30 ± 10</td>
<td>31 ± 3</td>
<td>29 ± 3</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>56 ± 10</td>
<td>57 ± 8</td>
<td>54 ± 12</td>
<td>.001*</td>
</tr>
<tr>
<td>&lt;30%</td>
<td>5 (1.0)</td>
<td>0 (0.0)</td>
<td>5 (1.9)</td>
<td>.02*</td>
</tr>
<tr>
<td>30-50%</td>
<td>147 (28.3)</td>
<td>64 (24.5)</td>
<td>83 (32.0)</td>
<td>.06</td>
</tr>
<tr>
<td>&gt;50%</td>
<td>373 (71.8)</td>
<td>197 (75.5)</td>
<td>176 (67.7)</td>
<td>.049*</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>6 (1.1)</td>
<td>1 (0.4)</td>
<td>5 (1.9)</td>
<td>.1</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>5 (1.0)</td>
<td>1 (0.4)</td>
<td>4 (1.5)</td>
<td>.18</td>
</tr>
<tr>
<td>Hospital stay length (d)</td>
<td>12 ± 7</td>
<td>12 ± 7</td>
<td>12 ± 8</td>
<td>.35</td>
</tr>
</tbody>
</table>

*Statistically significant for P < .05.  †Four patients died before postoperative echocardiographic data could be obtained.
All data are shown as n (%), unless otherwise specified.
Bentall, aortic root replacement; Bentall procedure; David, David aortic valve-sparing reimplantation.

0%; P = .025). In addition to a lower rate of bleeding, the David operation has been demonstrated to be associated with a better quality of life compared with Bentall procedures with mechanical valve replacement.13,15 One should keep in mind that the David operation is a complex surgical procedure that requires specialized surgical training and experience to be successfully performed.16 Moreover, a nuanced selection of patient pathoanatomy is necessary because reconstruction of the aortic valve may not be possible in some patients. For example, patients with nonpliable or restrictive aortic valve cusps are generally poor candidates for the David procedure. Inappropriate cusp pathoanatomy probably explains our observed increased rate of bicuspid aortic valve disease in Bentall-treated patients (Table 1), although the David operation is possible in many patients with bicuspid aortic valves.17,18 In addition, our data suggest that the David procedure requires significantly longer operating times. Therefore, patients undergoing a David operation should be assessed for whether extended myocardial-protection and cardiopulmonary bypass time can safely be tolerated.

Not surprisingly, we found that age is an independent predictor of long-term mortality. Consequently, younger patients (eg, individuals with connective tissue disease) may greatly benefit from the David operation as the procedure of choice because this group of patients usually requires correction of aortic root disease earlier in life, and reduction of risks over the course of a lifetime is thus a key concern. In addition to the reduced risk of long-term bleeding incidents mentioned earlier, other studies have also suggested excellent outcomes for the David operation in patients with Marfan syndrome or bicuspid aortic valves.19,20

It has been previously stated that key limitations for the David operation are the availability of surgical expertise and centers with a high volume of procedures, as well as precise and reliable identification of suitable aortic valve disorders.10 These factors limit the use of the David procedure as the operation of choice in emergencies and in areas without access to specialized medical centers. To solve this problem and make the David operation more widely available, an increase in trained surgeons and appropriate medical facilities would be necessary. Given that emergency indications for aortic root replacement, such as acute type A aortic dissection, are rare, having hospitals reach a necessary number of procedures each year in line with recommended guidelines may be problematic, and the Bentall operation would therefore remain the operation of choice for these patients. For patients who present for elective surgery, however, the standardization and implementation of the procedure
into surgical training curricula should be a priority, as well as a continued effort to ensure benchmarked reporting of results and possible centralization of resources.

Several studies have found that the David operation may be equal, if not superior, to the Bentall operation in patients with aortic root disease. Patients with hereditary connective tissue disorders such as Marfan syndrome may particularly benefit from the David operation because of their young age of presentation. Esaki and colleagues demonstrated that young patients who undergo David treatment showed improved midterm...
survival when compared with patients undergoing mechanical Bentall procedures. In 1 of the largest series to date, the long-term follow-up of patients who underwent David-procedures, Ouozunian and associates demonstrated statistically significant improved survival and decreased major adverse valve-related rates in David-treated patients when compared with propensity-matched mechanical and biologic Bentall-treated patients. In addition, these investigators demonstrated decreased cardiac morbidity and severe bleeding rates in David-treated patients, without any increase in reoperations. On the basis of these observations, one can conclude that the David operation should be considered the procedure of choice for all patients with aortic root disease and appropriate aortic valve cusp pathology because of the ability to minimize long-term risks associated with prosthetic heart valves.

Study Limitations
Our study aimed to make early and long-term results between the David and Bentall procedures more comparable. For this we used propensity score-matched groups to minimize selection bias. Propensity scores are valuable tools for lowering bias, but of course they cannot eliminate selection bias. In this regard, a randomized trial would be required. However, we believe it is unlikely that such a trial will be performed any time in the near future. Furthermore, at 88% follow-up completeness, we acknowledge that this could add to skewing of outcomes.

Conclusion
Both the David and Bentall operations are associated with very good early and long-term results for correction of aortic root disease. Short- and long-term mortality, as well as freedom from reoperation, for both groups are equally good, but serious bleeding is more common in Bentall-treated patients. The David operation should therefore be seen as the gold standard for patients in need of correction of aortic root disease, provided the aortic valve cusp pathologic features are appropriate. In older patients or in patients who may not tolerate increased myocardial ischemic and cardiopulmonary bypass times, the Bentall operation is an acceptable alternative.

References
6. Publication B
David aortic valve-sparing reimplantation versus biological aortic root replacement: a retrospective analysis of 411 patients

Lukas Schamberger 1 · Sergey Leontyev 1 · Piroze Minoo Davierwala 1 · Konstantin Von Aspern 1 · Sven Lehmann 1 · Martin Misfeld 1 · Michael Andrew Borger 1

Received: 22 May 2019 / Revised: 29 August 2019 / Accepted: 1 September 2019 © Indian Association of Cardiovascular-Thoracic Surgeons 2019

Abstract

Objectives This study aimed to compare short- and long-term results for patients undergoing either aortic valve-sparing reimplantation (David) procedure (AVr-D) or biological aortic root replacement (Bentall) procedure (ARr-B-bio) for aortic root pathology.

Methods We compared outcomes for patients who underwent AVr-D (n = 261) or ARr-B-bio (n = 150) between 2000 and 2015 at our institution. The mean age of patients was 55 ± 13 years and 21.7% (n = 89) were female. ARr-B-bio patients were significantly older than AVr-D patients (58 ± 10 vs 53 ± 15 years, p < 0.001) and had a significantly lower incidence of connective tissue disorders (2.0% vs 16.9%, p < 0.001). Follow-up was complete in 88% of patients.

Results Mortality at 30 days was 1.2% (n = 5) overall, at 0.4% (n = 1) significantly lower in the AVr-D group compared with 2.7% (n = 4) in the ARr-B-bio group (p = 0.04). Postoperative low cardiac output was more common in ARr-B-bio patients (n = 4) versus AVr-D patients (n = 0; p = 0.008). The occurrence of postoperative strokes was 2.2% (n = 9) in both groups, without significant differences (p = 0.84). Five- and ten-year survival was 93.7 ± 1.8% and 84.4 ± 4.7% in patients who received AVr-D and 90.9 ± 2.6% and 84.6 ± 5.4% for ARr-B-bio patients (log-rank p = 0.37). Using Cox regression analysis, age (HR 1.06; 95% CI 1.02–1.10, p = 0.002), smoking (HR 2.74; 95% CI 1.28–5.86, p = 0.01), and emergency surgery (HR 6.58; 95% CI 1.69–25.54, p = 0.007) were found to be independent predictors of long-term mortality.

There was no difference in freedom from reoperation between AVr-D (89.4 ± 3.4% at 10 years) and ARr-B-bio (80.4 ± 7.5% at 10 years, log-rank p = 0.66) patients, nor for freedom from stroke, bleeding, myocardial infarction, or endocarditis during follow-up.

Conclusions Short-term outcomes for both AVr-D and ARr-B-bio are excellent in patients with aortic root pathology. The long-term outcomes were associated with comparable survival and freedom from reoperation. AVr-D may be preferable to ARr-B-bio in patients with suitable pathoanatomy.

Keywords Elective aortic arch surgery · Outcome · Risk factors · Long-term results

Introduction

Surgical correction of aortic root pathology consists mostly of two widely used procedures: replacement of the entire aortic root (modified Bentall procedure) or aortic valve-sparing aortic root replacement (David procedure). The choice of procedure is important since adverse events, deterioration of valves, or conduit and lifestyle adjustments may have serious consequences for patients, especially younger individuals. Since the AVr-D procedure has shown promising outcomes without the need for anticoagulation, it is often the procedure of choice for patients with suitable aortic root pathoanatomy in specialised treatment centres [1]. A widely used alternative is the aortic root replacement Bentall (ARr-B) procedure, consisting of the replacement of the aortic root and native aortic valve with either a mechanical or biological conduit. Both the David and the biological Bentall (ARr-B-bio) procedures seem to offer similar advantages regarding long-term avoidance of...
anticoagulation and may be considered in select young patients [2, 3].

The aim of this study was to compare short- and long-term outcomes of ARr-B-bio versus AVr-D patients in a retrospective analysis.

**Patients and methods**

A total number of 1318 consecutive patients underwent surgical correction of aortic root pathology with an ARr-B (n = 1005) or AVr-D (n = 313) technique at our centre between 2000 and 2015. Patients with the previous replacement of the aortic valve, infective endocarditis at time of index operation, and concomitant valve surgery (e.g. mitral valve replacement or repair) were excluded. Propensity score matching was used to address differences in baseline variables between AVr-D and ARr-B patients, resulting in 301 AVr-D and 299 ARr-B patients. Subsequently, exclusion of mechanical ARr-B patients and patients with type A aortic dissection resulted in a total 261 AVr-D and 150 ARr-B-bio patients, which form the focus of this study.

A yearly follow-up to assess mortality and post-surgical complications was conducted. Follow-up was obtained by contacting the patient or treating physicians by mail and/or phone questionnaire. Follow-up was complete in 88% of patients after a period ranging between 1.0 and 16.1 years, and a mean of 4.9 years.

**Operative technique**

Patients undergoing ARr-B-bio received a biological conduit with the removal of the native aortic valve and the surrounding aortic wall and proximal ascending aorta [4]. A description of our operative technique for AVr-D has been previously provided [5]. The decision of whether a ARr-B-bio or AVr-D operation was performed depended on several variables including aortic cusp pathology, patient factors such as age and comorbidities, as well as lifestyle requirements and family planning, and the availability of an experienced surgeon. Due to intraoperative failure of aortic cusp reimplantation, one patient who was planned for AVr-D received ARr-B-bio instead. This patient was analysed in the AVr-D group, however, in accordance with the intention-to-treat principle.

**Definitions**

In accordance with STS guidelines, early mortality was defined as all-cause mortality at 30 days. Definitions of other outcomes have been previously described by our group [5, 6].

**Statistical analysis**

Data were imported to SPSS (SPSS Statistics 25.0; Chicago, IL, USA) for description and analysis. Categorical data are shown as total numbers and proportions in percent throughout the manuscript and were compared using the χ² test or Fisher’s exact test as appropriate. Continuous variables are expressed as mean ± standard deviation (SD) and were compared using the Student’s t test or Wilcoxon-Mann-Whitney test as appropriate. Normal distribution of measurements was determined using the Shapiro-Wilk test. Furthermore, the Cox proportional hazard analysis was performed to determine the independent predictors of long-term mortality and freedom from reoperation, presented as hazard ratios (HR) and 95% confidence intervals (CIs). A p value < 0.05 was considered statistically significant.

**Results**

**Preoperative characteristics**

A summary of the patients’ preoperative baseline characteristics is given in (Table 1). The mean age at surgery was 55 ± 13 years for the entire cohort and 21.7% (n = 89) were female. Patients in the ARr-B-bio group were significantly older than AVr-D patients and had a significantly lower incidence of connective tissue disorders. In addition, ARr-B-bio patients were more likely to have a bicuspid aortic valve and undergo emergency surgery.

**Operation data**

The total length of surgery was significantly longer in AVr-D than ARr-B-bio patients (Table 2). In addition, aortic cross-clamp times and total cardiopulmonary bypass (CPB) times were significantly longer in the AVr-D group.

**Early outcomes**

Thirty-day mortality was 1.2% (n = 5) overall, with significantly more deaths in the Bentall group (2.7%, n = 4) than David group (0.4%, n = 1; p = 0.04). The total stroke rate was 2.2% (n = 9) and similar in both groups (p = 0.84). A low cardiac output was observed in the Bentall group, significantly more than in the patients who received AVr-D (p = 0.008). Furthermore, postoperative echocardiographic data showed significantly more cases of minimal aortic insufficiency in the postoperative period within the David group (23.8%, n = 62) compared with the Bentall group (8.0%, n = 12; p < 0.001). There was no significant difference between groups for any other reported early outcomes (Table 3).
Table 1 Preoperative clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total n = 411</th>
<th>AVr-D n = 261</th>
<th>ARr-B-bio n = 150</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55 ± 13</td>
<td>53 ± 15</td>
<td>58 ± 10</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Female</td>
<td>89 (21.7)</td>
<td>57 (21.8)</td>
<td>32 (21.3)</td>
<td>0.91</td>
</tr>
<tr>
<td>COPD</td>
<td>10 (2.4)</td>
<td>7 (2.7)</td>
<td>3 (2.0)</td>
<td>0.67</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>50 (12.2)</td>
<td>30 (11.5)</td>
<td>20 (13.3)</td>
<td>0.58</td>
</tr>
<tr>
<td>Dialysis</td>
<td>3 (0.7)</td>
<td>2 (0.8)</td>
<td>1 (0.7)</td>
<td>0.91</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25 (6.1)</td>
<td>15 (5.7)</td>
<td>10 (6.7)</td>
<td>0.71</td>
</tr>
<tr>
<td>Hyperlipemia</td>
<td>122 (29.7)</td>
<td>67 (25.7)</td>
<td>55 (36.7)</td>
<td>0.019*</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>320 (77.9)</td>
<td>191 (73.2)</td>
<td>129 (86.0)</td>
<td>0.003*</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>266 (64.7)</td>
<td>165 (63.2)</td>
<td>101 (67.3)</td>
<td>0.4</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>9 (2.2)</td>
<td>4 (1.5)</td>
<td>5 (3.3)</td>
<td>0.23</td>
</tr>
<tr>
<td>Smoker</td>
<td>161 (39.2)</td>
<td>99 (37.9)</td>
<td>62 (41.3)</td>
<td>0.50</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>15 (3.6)</td>
<td>7 (2.7)</td>
<td>8 (5.3)</td>
<td>0.17</td>
</tr>
<tr>
<td>LVEF</td>
<td>58 ± 9</td>
<td>58 ± 9</td>
<td>59 ± 10</td>
<td>0.67</td>
</tr>
<tr>
<td>&lt; 30%</td>
<td>3 (0.7)</td>
<td>2 (0.8)</td>
<td>1 (0.7)</td>
<td>0.91</td>
</tr>
<tr>
<td>30-50%</td>
<td>88 (21.4)</td>
<td>54 (20.7)</td>
<td>34 (22.7)</td>
<td>0.64</td>
</tr>
<tr>
<td>&gt; 50%</td>
<td>320 (77.9)</td>
<td>205 (78.5)</td>
<td>115 (76.7)</td>
<td>0.66</td>
</tr>
<tr>
<td>Emergency surgery</td>
<td>5 (1.2)</td>
<td>0 (0.0)</td>
<td>5 (3.3)</td>
<td>0.003*</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>13 (3.2)</td>
<td>8 (3.1)</td>
<td>5 (3.3)</td>
<td>0.88</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>47 (11.4)</td>
<td>44 (16.9)</td>
<td>3 (2.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Marfan syndrome</td>
<td>34 (8.3)</td>
<td>31 (11.9)</td>
<td>3 (2.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>12 (2.9)</td>
<td>12 (4.6)</td>
<td>0 (0.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Loeys-Dietz syndrome</td>
<td>1 (0.2)</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
<td>0.45</td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>118 (28.7)</td>
<td>41 (15.7)</td>
<td>77 (51.3)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>AI only</td>
<td>310 (75.4)</td>
<td>250 (95.8)</td>
<td>60 (40.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>1°</td>
<td>67 (16.3)</td>
<td>62 (23.8)</td>
<td>5 (3.3)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>2°</td>
<td>149 (36.3)</td>
<td>125 (47.9)</td>
<td>24 (16.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>3°</td>
<td>92 (22.4)</td>
<td>63 (24.1)</td>
<td>29 (19.3)</td>
<td>0.26</td>
</tr>
<tr>
<td>4°</td>
<td>2 (0.5)</td>
<td>0 (0.0)</td>
<td>2 (3.3)</td>
<td>0.06</td>
</tr>
<tr>
<td>AS only</td>
<td>33 (8.0)</td>
<td>0 (0.0)</td>
<td>33 (22.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>1°</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0.00</td>
</tr>
<tr>
<td>2°</td>
<td>7 (1.7)</td>
<td>0 (0.0)</td>
<td>7 (4.7)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>3°</td>
<td>26 (6.3)</td>
<td>0 (0.0)</td>
<td>26 (17.3)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>4°</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0.00</td>
</tr>
<tr>
<td>Combined AI and AS</td>
<td>57 (13.9)</td>
<td>0 (0.0)</td>
<td>57 (38.0)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Aortic diameters (mm)

| Root                  | 45 ± 9         | 45 ± 9        | 44 ± 10           | 0.18    |
| Ascending aorta       | 51 ± 9         | 53 ± 9        | 47 ± 8            | <0.001* |

All data shown as number of cases, unless specified differently, (%). AVr-D David aortic valve-sparing reimplantation, ARr-B-bio biological aortic root replacement-biological Bentall procedure, COPD chronic obstructive pulmonary disease, LVEF left ventricular ejection fraction, AI aortic insufficiency, AS aortic stenosis

*Statistically significant for p < 0.05

Medium- and long-term outcomes

In terms of medium- and long-term outcomes, there was no observable advantage for AVr-D or ARr-B-bio (log-rank p = 0.37, Fig. 1) with respect to survival. Five- and ten-year survival of the entire cohort was 92.7 ± 1.5% and 84.6 ± 3.5%, respectively. Independent predictors of mortality were age at surgery (HR 1.06; 95% CI 1.02–1.10, p = 0.002), smoking (HR 2.74; 95% CI 1.28–5.86, p = 0.01), and emergency surgery (HR 6.58; 95% CI 1.69–25.54, p = 0.007).

Aortic valve reoperation was necessary in 23 patients: 8 for endocarditis, 10 for aortic insufficiency, and 5 for aortic
**Table 2**  Operation data

<table>
<thead>
<tr>
<th>Operation</th>
<th>Total (n=411)</th>
<th>AVr-D (n=261)</th>
<th>ARr-B-bio (n=150)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of surgery (min)</td>
<td>221 ± 61</td>
<td>231 ± 54</td>
<td>204 ± 67</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Aortic cross-clamp time (min)</td>
<td>105 ± 34</td>
<td>114 ± 30</td>
<td>88 ± 34</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Total cardiopulmonary bypass time (min)</td>
<td>132 ± 45</td>
<td>142 ± 42</td>
<td>116 ± 46</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Min. body temperature (Celsius)</td>
<td>31.7 ± 5.0</td>
<td>30.9 ± 4.9</td>
<td>33.1 ± 4.9</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Concomitant surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>30 (7.3)</td>
<td>18 (6.9)</td>
<td>12 (8.0)</td>
<td>0.68</td>
</tr>
<tr>
<td>Correction of CHD</td>
<td>11 (2.7)</td>
<td>7 (2.7)</td>
<td>4 (2.7)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

All data shown as number of cases, unless specified differently. (%), AVr-D David aortic valve-sparing reimplantation, ARr-B-bio biological aortic root replacement—biological Bentall procedure, CABG coronary artery bypass grafting, CHD congenital heart defect

*Statistically significant for p < 0.05

**Table 3**  Early postoperative outcomes for AVr-D vs ARr-B-bio

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Total (n=411)</th>
<th>AVr-D (n=261)</th>
<th>ARr-B-bio (n=150)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory failure</td>
<td>30 (7.3)</td>
<td>20 (7.7)</td>
<td>10 (6.7)</td>
<td>0.71</td>
</tr>
<tr>
<td>Low cardiac output</td>
<td>4 (1.0)</td>
<td>0 (0.0)</td>
<td>4 (2.7)</td>
<td>0.008*</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>New pacemaker</td>
<td>15 (3.6)</td>
<td>6 (2.3)</td>
<td>9 (6.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>9 (2.2)</td>
<td>6 (2.3)</td>
<td>3 (2.0)</td>
<td>0.84</td>
</tr>
<tr>
<td>Deep sternal wound infection</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>4 (1.0)</td>
<td>3 (1.1)</td>
<td>1 (0.7)</td>
<td>0.63</td>
</tr>
<tr>
<td>Dialysis</td>
<td>5 (1.2)</td>
<td>3 (1.2)</td>
<td>2 (1.3)</td>
<td>0.87</td>
</tr>
<tr>
<td>Reoperation for bleeding</td>
<td>25 (6.1)</td>
<td>18 (6.9)</td>
<td>7 (4.7)</td>
<td>0.36</td>
</tr>
<tr>
<td>Redo surgery</td>
<td>5 (1.2)</td>
<td>3 (1.1)</td>
<td>2 (1.3)</td>
<td>0.87</td>
</tr>
<tr>
<td>A1</td>
<td>75 (18.2)</td>
<td>63 (24.1)</td>
<td>12 (8.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>1°</td>
<td>74 (18.0)</td>
<td>62 (23.8)</td>
<td>12 (8.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>2°</td>
<td>1 (0.2)</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
<td>0.45</td>
</tr>
<tr>
<td>AS1</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Aortic diameters (mm)1</td>
<td>30 ± 3</td>
<td>31 ± 3</td>
<td>29 ± 3</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Root</td>
<td>29 ± 3</td>
<td>30 ± 3</td>
<td>28 ± 3</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>56 ± 10</td>
<td>57 ± 8</td>
<td>55 ± 12</td>
<td>0.02*</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>4 (1.0)</td>
<td>0 (0.0)</td>
<td>4 (2.7)</td>
<td>0.008*</td>
</tr>
<tr>
<td>30–50%</td>
<td>106 (25.8)</td>
<td>64 (24.5)</td>
<td>42 (28.0)</td>
<td>0.44</td>
</tr>
<tr>
<td>&gt;50%</td>
<td>300 (73.0)</td>
<td>197 (75.5)</td>
<td>103 (68.7)</td>
<td>0.13</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>5 (1.2)</td>
<td>1 (0.4)</td>
<td>4 (2.7)</td>
<td>0.04*</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>4 (1.0)</td>
<td>1 (0.4)</td>
<td>3 (2.0)</td>
<td>0.11</td>
</tr>
<tr>
<td>Hospital stay length (days)</td>
<td>11 ± 6</td>
<td>12 ± 7</td>
<td>11 ± 5</td>
<td>0.34</td>
</tr>
</tbody>
</table>

All data shown as number of cases, unless specified differently. (%), AVr-D David aortic valve-sparing reimplantation, ARr-B-bio biological aortic root replacement—biological Bentall procedure, A1 aortic insufficiency, AS aortic stenosis

*Statistically significant for p < 0.05

1 Four patients died before postoperative echocardiographic data could be obtained
stenosis, without significant difference in incidence for both groups. Freedom from reoperation at 5- and 10-years was 95.7 ± 1.3% and 85.9 ± 3.7% for all patients (Fig. 2), with no difference between groups (log-rank p = 0.66). During follow-up, 5- and 10-year freedom from reoperation was significantly lower for patients with bicuspid aortic valves compared with patients with tricuspid valves: 91.4 ± 3.3% and 79.2 ± 7.4% vs 97.3 ± 1.2% and 87.8 ± 4.3%, respectively (log-rank p = 0.048). A sub-analysis of all patients with bicuspid aortic valves did not show a significant difference in freedom from reoperation for AVr-D and ARr-B-bio (log-rank p = 0.13). There was no difference for patients with or without connective tissue disease (log-rank p = 0.58). Cox regression analysis did not reveal a significant independent predictor of freedom from reoperation.

During the follow-up period, there were no significant differences between groups with regard to freedom from stroke, bleeding, myocardial infarction, or endocarditis.

**Discussion**

Our study compared early and long-term outcomes in patients undergoing AVr-D versus ARr-B-bio surgery for aortic root pathology. Both procedures show excellent outcomes with regard to survival and reoperation rates, as well as low occurrences of strokes, bleeding events, myocardial infarction, and endocarditis during the follow-up period. Although there was no significant difference between the two procedures with regard to any of these outcomes, we recorded a significantly higher 30-day mortality for patients who received ARr-B-bio, as well as a higher incidence of low cardiac output post-surgery in the same group. While these findings are suggestive of a superior outcome for AVr-D procedures, it is likely that the significant difference in emergency procedures contributed to that result, as two of the patients with low cardiac output were treated in an emergency situation, of which one died within 30 days. A trend for higher risk of reoperation for ARr-B has previously been shared by other authors [2, 3]. It should be noted that AVr-D patients had a markedly higher incidence of connective tissue disorders in our study, which may have impacted long-term survival rates. Furthermore, deaths during follow-up in the AVr-D group included four tumour-related deaths, such as prostatic, bowel, and brain cancer, as well as one death due to epilepsy.

Since AVr-D and ARr-B-bio are often used to treat similar conditions in comparable patient populations, deciding on a treatment for individual patients can be challenging. Age, comorbidities, lifestyle, and patient preference—among others—may influence the choice of procedure performed. AVr-D avoids the known disadvantages associated with prosthetic valve replacement but is technically more difficult to perform than ARr-B-bio and associated with longer ischemic and CPB times.

Several recent studies have suggested that the AVr-D procedure can be applied to a wider range of anatomical variations, with bicuspid aortic valves showing a similar outcome to tricuspid valves [7]. In our study, we observed an increased number of reoperations for patients with bicuspid aortic valves, although the number of bicuspid patients among the AVr-D group was relatively small (n = 41) compared with patients in the ARr-B-bio group (n = 77).

It can be argued that the main advantage of AVr-D is the lifelong avoidance of anticoagulation and hence reduction of bleeding incidents, which may be particularly appealing in young patients and those with connective tissue disorders. Our study shows no clear advantage for AVr-D over ARr-B-bio with regard to bleeding incidents during the follow-up.
period. Instead, we found a significantly lower 30-day mortality for AVr-D procedures \( (p = 0.04) \), as well as a higher incidence of low cardiac output after ARr-B-bio procedures \( (p = 0.008) \) as discussed above.

One of the disadvantages of AVr-D is its complexity and difficulty to perform, reflected by prolonged operation times [8]. Long operation times may pose a problem for some patients, especially the elderly or those with left ventricular dysfunction, who cannot tolerate long ischemic times. Comparison of the left ventricular ejection fraction before and after the procedure shows that both procedures have good postoperative outcomes, but the cardiac output was slightly better in the AVr-D group. It is still advisable that those patients who are at greater risk of adverse outcome due to prolonged operation times should undergo the ARr-B-bio operation.

AVr-D requires specially trained surgeons and teams in order to be performed safely and effectively. This has long been a concern with AVr-D and the proposed solution has usually been to defer treatment to specialised centres with public reporting of outcomes [9, 10]. Indeed, consistently good outcomes for aortic root surgery can more readily be achieved in large volume centres [11], even in complex patients such as those presenting with type A aortic dissection [12]. Nonetheless, efforts should be made to make AVr-D more available and outcomes more comparable between centres [13]. To achieve this, an increase in trained surgeons and training opportunities are necessary, as well as more public reporting of outcomes in a standardised manner.

As another recent study has shown, AVr-D might also be a superior procedure to ARr-B-bio in regard to reoperation during follow-up [3]. This is contrary to previous concerns over a higher incidence of progressive aortic regurgitation after AVr-D procedures [14]. Our postoperative echocardiographic data indeed shows a higher incidence of minimal aortic insufficiency postoperatively for AVr-D compared with ARr-B-bio, but there was no significant difference shown between groups in regard to freedom from reoperation after 10 years. Although we were unable to demonstrate a lower reoperation rate in the AVr-D patients, this may have been secondary to our relatively small sample size, as well as our relatively short follow-up period over 10 years, as other studies have shown that biological replacements of the aortic valve are more likely to deteriorate after 10 years; as such, a longer follow-up period might have shown clearer differences [15, 16].

Considering our findings of similar good outcomes regarding mortality and reoperation among patients who received either AVr-D or ARr-B-bio, we recommend AVr-D for all patients requiring correction of aortic root pathology given favourable pathoanatomic conditions and preoperative patient status.

**Study limitations** Our study compared early- and long-term results between AVr-D and ARr-B-bio. For this, we used a subgroup analysis of a propensity score matched comparison of AVr-D vs ARr-B, followed by exclusions of mechanical ARr-B patients. Unaccounted variables in the assignment of propensity scores and surgeon preference may have contributed to selection bias. A randomised controlled trial would alleviate most concerns regarding selection biases, but such a trial is unlikely to be performed in the near future. Also, our follow-up period may not have been long enough to show clearer advantages for either procedure.

**Conclusion**

AVr-D and ARr-B-bio are associated with very good early- and long-term results in patients with aortic root pathology. While mortality and freedom from reoperation were excellent in both groups, we therefore recommend AVr-D surgery in patients with aortic root pathology, given that aortic valve cusp pathology is suitable. ARr-B-bio remains an appropriate alternative, especially for older patients or those with comorbidities that may result in decreased ability to tolerate longer myocardial ischemic and cardiopulmonary bypass times.

**Funding** No funding

**Compliance with ethical standards** The local ethics committee approved the study and waived individual patient consent for retrospective review. This article does not contain any studies with animals performed by any of the authors.

**Conflict of interest** Lukas Schamberger declares that he has no conflict of interest.

Sergey Leontiev receives procuring honoraria fees from Medtronic, Abbott (St. Jude Medical).

Pauce M. Daviawala declares that he has no conflict of interest.

Konstantin Von Aspem declares that he has no conflict of interest.

Sven Lehmann receives honoraria fees from Abbott (St. Jude Medical).

Martin Misfeldt declares that he has no conflict of interest.

Michael Borger receives speakers' honoraria/consulting fees from Edwards Lifesciences, Medtronic, Abbott (St. Jude Medical), and CryoLife.

**References**


Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.
7. Discussion

7.1 Findings and results

Our analyses show that both the David and the Bentall procedures are safe surgical options for the correction of aortic root pathology, with generally excellent outcomes. The occurrence of adverse outcomes both during and directly after surgery, and during recovery and follow-up is very low. We could not identify differences in outcome for endocarditis, strokes, myocardial infarction or overall mortality. Reoperation rates did not vary significantly in the overall comparison of David and Bentall cases, but also no difference was found for subgroups in our second investigation of David and biological Bentall patients.

Notably, there was a higher incidence of bleeding during follow-up in the Bentall group, most likely due to the effects and risks of long-term anticoagulation on patients with mechanical prostheses in the Bentall group. This is likely the case, as our analysis in Publication B did not show significant differences in this regard, with all mechanical Bentall cases excluded.

Long-term mortality was also influenced by patient age. This supports the idea that younger patients profit more from the David procedure than the elderly: A total reduction of lifetime risk of adverse events from the effects of anticoagulation is a likely reason.

Another observation, which warrants careful consideration of patient age, is the longer operation time that we found with the David procedure. Longer operation times, as well as myocardial ischemic and cardiopulmonary bypass times might not be easily tolerated by the elderly.

Even though our investigation did not show differences in reoperation rates between David and biological Bentall cases, concerns regarding the durability of biological prostheses remain. Our study likely did not show differences because follow-up might not have been long enough: Some researchers have reported valve deterioration on mid-term follow-up, which calls for longer follow-up periods\textsuperscript{30}. 
7.2 Findings in the context of current research

Our findings are in line with several other studies that have found similar results for both techniques\textsuperscript{40,41}. Some researchers have suggested further application of valve-sparing reimplantation in Stanford type A aortic dissections\textsuperscript{42}, and several studies also suggest good outcomes in emergency settings\textsuperscript{43,44}.

Our research shows that the David procedure is safe to perform and is superior to the Bentall procedure in regard to bleeding during follow-up. This is a notion shared by other researchers in their investigations: A recent meta-analysis by Elbatarny and colleagues comparing the outcome of aortic valve-sparing against composite valve grafting techniques not only showed no difference in early complications, but also a significant long-term advantage for valve-sparing procedures in late mortality, strokes and bleeding risks\textsuperscript{45}.

The question remains whether the structural stability of bioprosthetic Bentall correction is superior, similar or inferior to the David procedure, as our research does not yield final evidence on the clear advantage of either technique after our follow-up period. Other studies have shown that the David procedure might be superior\textsuperscript{46}. More investigations in this particular field are needed.

Meanwhile, concerns regarding the higher reoperation rates of David patients compared to Bentall groups could not be corroborated in our study. Nonetheless, competence of the aortic valve post-repair remains a concern. A recent report by Berra and colleagues has described the use of a new device to intraoperatively test this\textsuperscript{47}.

In Publication A we have advocated for an extension of training and further specialisation and centralisation to provide consistently good results in using valve-sparing techniques. Recently Beckmann et al published a study detailing the effects of training and surgeon experience on the outcome after David procedures, in which they conclude that the experience of the surgeon has a significant effect on the perioperative outcome and the long-term results after surgery\textsuperscript{48}. 
7.3 Limitations

The presented publications and findings should be seen in context of their limitations.

Firstly, it might be possible that our follow-up period was too short to detect more distinct differences in the outcomes of the procedures compared. Furthermore, while our patient group is large, a larger group of patients, especially for the comparison of biological prosthesis versus reimplantation, might have been able to pick up clearer advantages for either one. Also, an investigation of bioprosthetic Bentall cases propensity matched to David cases instead of a subanalysis, could potentially better adjust for confounding variables.

Secondly, unlike randomisation, the method of propensity score matching does not eliminate or adjust for unknown confounders, but only those considered\textsuperscript{49}. This puts propensity score matching at a disadvantage compared to randomised trials. As mentioned in both publications and also remarked by other researchers, such a study is unlikely to be performed for the reasons described.
8. Conclusion

Our research shows that David and Bentall procedures are both associated with excellent outcomes, but long-term complications with the Bentall procedure pose a significant problem that can be alleviated with the David procedure. It is not just an alternative to prosthetic aortic root replacement but should be considered the gold-standard for surgery in patients with aortic root pathology, given that aortic valve cusp pathology is suitable for correction. The Bentall procedure is still an appropriate option for patients who are unlikely to tolerate longer myocardial ischemic and cardiopulmonary bypass times.

It is evident that most exceedingly superior results come predominantly from facilities with highly trained surgeons and a high patient turnover. So, it is important to emphasise that training should be extended, and treatment centralised to ensure good results. This approach could also make the procedure more available to patients considered high risk because of comorbidities or their age by keeping operation time to a minimum through surgical expertise.

The evidence to date and the research conducted into the correction of aortic root pathology point towards a wider application of aortic valve-sparing techniques in the future. Thus, it is important to ask where efforts should be focused going forward. A benchmarked standardisation of procedures and their reporting could contribute to an even clearer evidence for and against each procedure and ultimately help develop more detailed guidelines. To achieve this, multi-centre studies should be conducted over a longer time frame.

Further effort and reporting of cases and outcomes will certainly be needed in the future, not only to further scientific progress, but also to contribute to the continuous effort of finding the empirically guided, optimal solution for each patient.
9. References


36. D’Agostino RB. Propensity score methods for bias reduction in the comparison of a


10. Acknowledgements

First, I would like to thank my thesis advisor, co-author and mentor, Prof. Sergey Leontyev, who throughout the conception and execution of this thesis has been an invaluable source of knowledge and support. He was always available for questions, always ensured I had access to sources and working space and went above and beyond to make my attendance at the EACTS annual meeting possible.

I would also like to thank Prof. Michael Borger, who provided invaluable expertise and support to our publications and without whom this thesis would not have been possible.

Also, I would like to sincerely thank my co-authors who have performed surgical procedures and provided data. Especially, I would like to thank Dr. Konstantin Von Aspern for his contribution to the statistical analysis. Furthermore, I would like to extend a special thank you to all the staff at the department of cardiac surgery at the Leipzig Heart Centre who have supported me throughout my work there.

I would also like to acknowledge everyone who took part in this study and despite the stress and anguish of undergoing surgery for a serious condition agreed to help further scientific progress.

Also, I want to express my gratitude to Tim Hartung for his tips and valuable insights.

Finally, I want to thank my family and friends for their continued support and love, and especially my partner, Mikaela Lui, for her unwavering support, proofreading of this work and in general putting up with me during my studies and throughout the writing of this thesis.
11. Appendix
11.1 Darstellung des eigenen Beitrags zu Publikation A

Hiermit versichere ich, Lukas Helmut Michael Schamberger, dass ich folgenden Beitrag an der Publikation „Early and Late Results After David vs Bentall Procedure: A Propensity Matched Analysis“ erbracht habe:

- Follow-up Befragung und damit verbundene Dateneingabe
- Statistische Datenanalyse (ohne Propensity Score Matching)
- Interpretation und Aufbereitung der Ergebnisse, Erstellung des Publikationstextes, Grafiken, Tabellen
- Editing im Reviewprozess und Antworten

Leipzig, 06.06.2020

Ort, Datum

Lukas Schamberger

Unterschriften der Mitautoren:

Prof. Dr. Sergey Leontyev

Dr. Piroze Davierwala

Dr. Konstantin Von Aspern

Prof. Dr. Christian Etz

Prof. Dr. Sven Lehmann

Prof. Dr. Dr. Martin Misfeld

Prof. Michael Borger, MD PhD
11.2 Darstellung des eigenen Beitrags zu Publikation B


- Follow-up Befragung und damit verbundene Dateneingabe
- Statistische Datenanalyse (ohne Propensity Score Matching)
- Interpretation und Aufbereitung der Ergebnisse, Erstellung des Publikationstextes, Grafiken, Tabellen
- Editing im Reviewprozess und Antworten

Leipzig, 06.06.2020
Ort, Datum

Unterschriften der Mitautoren:

Prof. Dr. Sergey Leontyev

Dr. Piroze Davierwala

Dr. Konstantin Von Aspern

Prof. Dr. Christian Etz

Prof. Dr. Sven Lehmann

Prof. Dr. Dr. Martin Misfeld

Prof. Michael Borger, MD PhD
11.3 Selbstständigkeitserklärung

Erklärung über die eigenständige Abfassung der Arbeit


__________________     _______________________
Datum       Unterschrift
11.5 Publikationsliste
