

# Does adding a Root Replacement in Type A Aortic Dissection Repair Provide Better Outcomes?

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## Abstract

Background: Acute type A aortic dissection (ATAAD), is a surgical emergency often requiring intervention on the aortic root. There is much controversy regarding root management; aggressively pursuing a root replacement, versus more conservative approaches to preserve native structures. Methods: Electronic database search we performed through PubMed, Embase, SCOPUS, google scholar and Cochrane identifying studies that reported on outcomes of surgical repair of ATAAD through either root preservation or replacement. The identified articles focused on short- and long-term mortalities, and rates of re-operation on the aortic root. Results: There remains controversy on replacing or preserving aortic root in ATAAD. Current evidence supports practice of both trends following an extensive decision-making framework, with conflicting series suggesting favourable results with both procedures as the approach that best defines higher survival rates and lower perioperative complications. Yet, the decision to perform either approach remains surgeon decision and bound to the extent of the dissection and tear entries in strong correlation with status of the aortic valve and involvement of coronaries in the dissection. Conclusions: There exists much controversy regarding fate of the aortic root in ATAAD. There are conflicting studies for impact of root replacement on mortality, whilst some study's report no significant results at all. There is strong evidence regarding risk of re-operation being greater when root is not replaced. Majority of these studies are limited by the single centred, retrospective nature of these small sample sized cohorts, further hindered by potential of treatment bias.

Does adding a Root Replacement in Type A Aortic Dissection Repair Provide Better Outcomes?

*Running Head: Root Repair in Type A Dissection*

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*Conclusions:* There exists much controversy regarding fate of the aortic root in ATAAD. There are conflicting studies for impact of root replacement on mortality, whilst some study's report no significant results at all. There is strong evidence regarding risk of re-operation being greater when root is not replaced. Majority of these studies are limited by the single centred, retrospective nature of these small sample sized cohorts, further hindered by potential of treatment bias.

## Introduction

Acute type A aortic dissection (ATAAD), is a surgical emergency with the potential for catastrophic consequences because of any delays in intervention, with a lethality rate of 1-2% per hour following symptom onset<sup>1</sup>. Annual incidences reported from 2.5-6 per 100,000 patient-years<sup>2</sup>, reaching as high as 8.7 per 100,000 patient-years likely resulting from our ageing population as a leading contributor.<sup>3</sup> ATAAD, a disaster where the repair process is never clear nor obvious, with every second crucial to saving the patient's life.

In cases of ATAAD, often there is the involvement of the aortic root potentially resultant of extension of the primary tear. It is possible that root pathologies independent of the primary tear are discovered and may result in concomitant treatment. Surgical intervention on the aortic root remains controversial and debatable.<sup>4,5,6,7</sup>

Acute aortic dissection repair can necessitate a variety of operations, from simple replacement of the ascending aorta to aortic root replacement or a version of total arch replacement. There are differing opinions regarding what constitutes the "appropriate" repair of the acutely dissected aorta,<sup>4-8, 13-27</sup> a tear tailored approach is a trend that we normally follow; however, this is not generalizable across many different centers.

During the surgical repair, when it comes down to the fate of the aortic root there remains a large amount of controversy in the literature.<sup>4,5,6,7</sup> The following remains unanswered :

1. Should a surgeon perform the Bentall procedure, radically replacing the complete root with all its sinuses, or conservatively repair the primary damage and preserve the native root structures?
2. What are the implications of these decisions on mortality, and the risks of re-operation?

Another rather ambiguous matter remains which is decision-making framework on aortic root intervention. This is rather scattered with different complexities seen in ATAAD, hence, no quantitative assessment exists.

The implementation of optimum treatment strategies from the initial diagnosis to complete repair can improve the prognostic outcome, from the mortality of 90% without intervention to upwards of a 70% chance of survival.<sup>8</sup> Henceforth, thoughtful decision making process, operative planning, meticulous surgical technique, and intrinsic understanding of hypothermic circulatory arrest and central nervous system preservation are all sought for optimum outcomes.

### **To respect or replace?**

Following the timely diagnosis of ATAAD, the guidelines for when to perform the more extensive approach of a root replacement are reported by Lars Svensson et al.<sup>9</sup> When the primary or secondary tear extends into or originates at the site of the coronary sinuses of the aortic root, a radical root replacement is indicated. Furthermore, the dilation of the aortic root beyond 45mm below the level of sinotubular junction is indicative of the need to replace the root.<sup>9</sup>

As further reported in the guidelines it is imperative to assess the root independently and be able to verify its prospects for the preservation of the native valve structures, the integrity of the coronary ostia, and the requirement to perform the root replacement.<sup>9</sup> Svensson et al. further state that factors that affect the decision making and management of the valves in the cases of isolated aortic stenosis or aortic regurgitation, are relevantly applicable in setting of ATAAD repair. Another key indicator for pursuing a root replacement is the presence of a connective tissue disorder, such as Marfan syndrome.<sup>9,10</sup>

### **Bentall vs VSRR**

It has been a few decades since the original inception of the Bentall method<sup>11</sup>, undergoing many revolutions in surgical techniques and approaches<sup>12</sup>; however, this procedure still presents with disadvantages and issues of potential complications.<sup>13</sup> Furthermore, under certain indications the Bentall is not always the optimum interventional approach for a root replacement, in some such cases a valve-sparing root replacement (VSRR) can be considered.<sup>14</sup> Following the use of a mechanical conduit for root replacement, there is the need of lifelong anticoagulation medication; With the use of a biological conduit there is the higher risk of re-operation, an even greater negative impact on younger patients.<sup>13, 14</sup> The VSRR procedure allows the native aortic valve to be preserved, avoiding some of the cons of a complete root replacement, allowing more favorable haemodynamic outcomes.<sup>14</sup> In the recent meta-analysis of 9 studies comprising 706 patients treated for ATAAD, VSRR was systematically reviewed as an option for intervention.<sup>15</sup> Junlin Wu et al. were able to conclude that the use of VSRR in ATAAD provided highly favorable outcomes in the early and late period in comparison to the patients undergoing Bentall procedure. It should be noted that the authors had clearly stated that these amazing results for VSRR, are only achieved by the carefully considered patient selection process for the procedure.<sup>15</sup>

### **The conflict of early outcomes**

The Bentall procedure is considered a “gold standard” technique for aortic root replacement.<sup>16</sup> Over the decades the procedure itself has greatly evolved with many modifications to the original technique.<sup>11</sup> For the repair of ATAAD the Bentall procedure can be performed for a radical root replacement, or a conservative approach can be considered using a supra-commissural graft repair. By repairing the primary tear without pursuing the extensive approach, it allows the preservation of the native valvular structures. Across the literature, in-hospital and 30-day mortality are the main early outcome recorded across various studies, with a broad range of results for the comparison between the conservative repairs of the root, versus a more aggressive root replacement approach.<sup>4, 7, 17</sup>

In a retrospective study, 226 patients underwent repair for ATAAD at a single center between 1990 and 2010 (mean follow up of 9.1 years), undergoing either the Bentall method or a supra-commissural graft repair.<sup>7</sup> The authors reported in-hospital mortality of 34% for the graft repair group, which was significantly higher ( $p=0.03$ ) than the 20% in-hospital mortality using the Bentall and VSRR David procedures. Hysi I and colleagues concluded using their results that a more extensive approach allowed more favorable early outcomes.<sup>7</sup>

When critically analyzing this study by Hysi I and colleagues<sup>7</sup> it is vital to recognise, as the authors reported, that patients undergoing the more radical root replacement were much younger ( $p=0.00001$ ). Older age was reported as a significant independent factor for early mortality. Furthermore, the authors stated that the majority of the root replacements were performed more recently in the study period. When considering how strategies of surgery have evolved over the years alongside the significant effects on pre-operative characteristics, there is the strong risk of arising bias in the conclusion that are drawn.<sup>7</sup>

A fellow retrospective study published by Geirsson A and colleagues, who similarly compared the early outcomes of ATAAD repair in 221 patients also at a single center.<sup>17</sup> During the study period of 1993 to 2004 (mean follow up of 3.31 years; 99.1% complete), the center had developed an algorithmic approach for treatment. Patients always underwent aortic valve (AV) resuspension whenever feasible, only undergoing a composite root replacement when the indications were met making the initially desired valve resuspension no longer feasible. The authors reported contrasting results to those reported by Hysi I and colleagues.<sup>7</sup> The in-hospital mortality of 8.1% for AV resuspension was far lower ( $p=0.004$ ) than the 23.1% recorded for composite root replacement. The reasons for this however, although not completely clear, may possibly be attributed towards the primary indicators for root replacement which included fewer co-morbidities and a more severe primary dissection.<sup>17</sup>

Both above discussed studies have similar indications and frequencies of presented pre-operative characteristics for pursuing the extensive root replacement procedure: the presence of a connective tissue disorder such as Marfan syndrome, aortic insufficiency  $> 2$ , as well as a more proximal extension of the intimal tear towards the sinus.<sup>7, 17</sup> Geirsson and colleagues further reported that annuloaortic ectasia, bicuspid aortic valve, and aortic stenosis, were also significant pre-operative indicators sought for a root replacement. These and other aspects of the algorithm in the study by Geirsson A and colleagues allows us to infer that the higher early mortality for root replacement, maybe due to the more severe pre-operative patient characteristics and indicators which had resulted in the initially preferred AV suspension procedure to no longer be feasible.

Whilst comparing both of these single-center retrospective studies,<sup>7, 17</sup> it is important to consider the indications and methodologies put in place for the decision making process regarding the surgical approach targeting the aortic root. Geirsson A and colleagues had a standardized and structured algorithmic approach towards the surgical management of ATAAD, always performing AV resuspension wherever feasible. The surgical strategy in the study by Hysi I and colleagues, although without such an algorithmic approach, was only well guided by “perioperative findings and surgeon’s habitude”<sup>7</sup> The resultant homogenous cohort allowed by the standardised strategies reported by Geirsson A and colleagues<sup>17</sup>, allows it to be well recognized as a strength for their study. The authors had reported that their management strategies discussed in the paper were able to contribute to their improved overall entire cohort in-hospital mortality rate of 12.7%.<sup>17</sup>

The results for operative mortality reported by Peterss S and colleagues (2016)<sup>18</sup>, comparing the operative mortality between the two groups showed statistically insignificant results, however the study did show that the in-hospital stay was significantly longer by 5.1 days ( $p=0.048$ ) in the root replacement group compared to that of root sparing technique in the repair of ATAAD.

In other articles that were reviewed (refer to Table A), there were no further statistically significant differences when comparing early outcomes between whether or not a root replacement is performed in the treatment of ATAAD.

### **Replacing the root, a burden on mid to long term outcomes?**

Yang B and colleagues<sup>5</sup> reported a set of contrasting results from their single center study, compared to various other articles as seen in Table A. From a cohort of 94 patients (10 patients had no root procedure), the 4 year Kaplan-Meier survival for the small sample size of 45 patients undergoing root repair was 91%. The patients in the root replacement group underwent either the Bentall ( $n=24$ ), or the VSRR David procedure ( $n=15$ ). The Bentall group was independently compared with the conservative repair group, and the reported 4 year survival was significantly lower at 39% ( $p = 0.03$ ). The authors suggest that previous studies which

may have caused higher mortality in the root repair groups were caused by the use of surgical glue which was not used in this study.<sup>5</sup> Following adjustments made for; “age, sex, coronary artery disease, pre-operative severe aortic insufficiency, previous cardiac surgery, and cardiac tamponade”<sup>5</sup>, it was then stated in this study that the mortality risk was comparable ( $p=0.24$ ). In addition, no statistically significant difference was reported between root repair and VSRR David procedure ( $p=0.25$ ).<sup>5</sup> The retrospective nature and short follow up period (mean of 22 months), as well as the fact that the study is based on a single surgeons experience, adds significant limitations to the conclusions being drawn.

The study published by Hysi I and colleagues (2015)<sup>7</sup> have reported outcomes showing improved long term survival for complete aortic root replacement, contrasting the results to Yang B and colleagues.<sup>5</sup> This study had a far longer mean follow up period of 9.1 years (109.2 months), compared to the study by Yang B and colleagues discussed above which had a mean follow up time of 22 months only. In addition to this, Hysi I and colleagues reported their long term survival outcomes at 5, 10 and 15 years showing continuously at multiple time points that the group of 82 patients that underwent the Bentall ( $n=77$ ) or Tirone David ( $n=5$ ) procedure, showed far favourable results ( $p=0.03$ )<sup>7</sup> compared to the group that underwent supracommissural repair. This is in contrast to the aforementioned study, where the authors had only reported outcomes for a single point in their follow up time for a 4 years survival result.<sup>5</sup> However it is again important to appreciate that as the aortic root replacement group was reported to be more recent in the study<sup>7</sup> compared to conservative repairs, the study does acknowledge this may have been a source of bias as a consequence of surgical strategy evolution.

Similarly to the discussed short term outcomes, various different studies<sup>4, 19, 20</sup> have reported no statistically significant long term results when comparing these mentioned approaches for aortic root management. It is important to appreciate, however, the very significant indications and requirements for a radical root replacement method to be implemented at all. Patients that underwent a more extensive approach of root replacement were generally younger, and with fewer co-morbidities, as well as more likely to have had a more extensive dissection. The presentation of poor morphology and physiology of the root, as well as the presence of connective tissue diseases, were strong indicators for root replacement across the studies in this review. Furthermore, the highly limiting retrospective and single-center characteristics are vital for consideration when reviewing the data of articles in Table A.

### **The aggressive approach and Freedom from re-operation?**

The advocating of an aggressive intervention to replace the entire root is yet to receive a wide consensus.<sup>4,5,6,7</sup> Surgically replacing the entire root reduces the risk of subsequent dilation of the aorta, future occurrences of aortic insufficiency, and the possibilities of repeat dissections. These potential benefits would be expected to increase the chances of freedom from re-operation, and improving outcomes for long term survival.<sup>4</sup>

A retrospective study of 316 patients undergoing repair for ATAAD, had a small sample size of 40 patients undergoing a complete root replacement. With a mean average follow up of 26 months (94.6% complete), Nishida H et al<sup>20</sup> reported that these patients had a 100% freedom from re-operation at 5 years. This was a significantly more favorable outcome ( $p=0.029$ ) than the patients not having their aortic root replaced, who only had a 68.7% freedom from re-operation. The aortic root events that led to the need for re-intervention, included 25 aortic dilations, 3 cases of aortic insufficiency, and 1 pseudoaneurysm<sup>20</sup>; These are long term physiological complications which a root replacement can help avoid.<sup>4</sup>

A much larger study by Di Eusano et al.<sup>4</sup> comprising of 1,995 patients, reported that there was no statistically significant difference ( $p=0.770$ ) in the rates of freedom from re-operation at 3 years between the patients undergoing Bentall and VSRR methods of repair, compared to those undergoing the conservative repair procedure. However despite the large sample size, with a follow up that was only 54% complete, and results recorded at only 3 years, it is difficult to be able to use these results alone to conclude that there would be no significant differences in the long term for rates of re-operation.<sup>4</sup>

Another study in the literature which although reported statistically insignificant results, had in fact shown a clear trend of their crude results towards more favourable outcomes for root replacement in regards to

freedom from re-operation.<sup>22</sup> The 9 year freedom from re-operation was reported by Ergin M and colleagues<sup>22</sup> as 87.5% for the root replacement group, compared to 63.0% for the group without root being replaced.<sup>9</sup>

Hysi I and colleagues reported outcomes for results up to 15 years following the primary surgery and published their results with a much longer average follow up period. The authors were able to show that adding a root replacement in the treatment for ATAAD provides significantly better ( $p=0.02$ ) outcomes for freedom from re-intervention.<sup>7</sup> There were 93.4% of patients with root replaced that were free from re-operation at 15 years, compared to only 78% for those that underwent a supracommissural repair alone. This was another study where the reasons for re-operations would have had a far lower risk of occurrence had a root replacement been performed in those patients.<sup>4,7,20</sup>

Chiu P and colleagues<sup>6</sup>, had included 293 patients in their retrospective study comparing root replacement( $n=81$ ) to limited root repair( $n=212$ ), for treatment of TAAAD. The article reported an overall rate of re-operations to be 11.8% for the root repair group, compared to 0% for the root replacement group ( $p=0.001$ ). This is of course again highly limited by the short median follow up time of 2.1 years, and the results being from a single tertiary center alone.

A short follow up period which is also not well completed, adds significant limitations to the literature discussing the fate of the aortic root.<sup>4-24</sup> Given that much of the literature is already weakened by their retrospective studies based on a single center,<sup>4-26</sup> such further limitations have strong impacts on the already hindered reliability, bias, and reduced statistical power from the small sample sizes.

The study published by Castrovinci S and colleagues<sup>27</sup> comparing 199 patients that underwent Bentall ( $n=108$ ) or David ( $n=11$ ) procedures for root replacement, with those that had a conservative root repair. The study reported results for freedom from re-operation until 7 years period with a 100% follow up rate, the results for root replacement group was 96% freedom at 7 years, compared to only 80% for the conservative repair ( $p=0.02$ ). However following adjustments for propensity score matching using a considerable number of covariates, the rate of freedom from re-operation for root replacement group and without root replacement at 7 years was; 98% and 86% respectively, however now with a log-ranked  $p$  value of 0.06.<sup>27</sup>

## Conclusion

Single centre reporting with limited, non-focused indications and appropriate decision-making process for replacing the root instead of a conservative approach is an elusive target. Retrospective study design, lack of randomisation, and relatively small sample sizes, especially in patients undergoing root replacement and extent of root intervention in ATAAD repair remains controversial. Risks of re-operation contains less conflict, there being much evidence suggesting freedom from re-operation is improved with a more extensive approach. However, patients undergoing root replacement were much younger with less severe co-morbidities, potentially allowing more favourable outcomes.

## Human Studies:

No ethical approval required as no patient identifiable information involved.

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