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## Aorta: Research

# The Aortic Root in Acute Type A Dissection: Repair or Replace?



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## ABSTRACT

**BACKGROUND** The effect of an “aggressive” approach on the aortic root in acute type A aortic dissection (ATAAD) remains insufficiently explored.

**METHODS** Retrospective analysis was conducted between 1992 and 2020 of a single-center, prospective cohort of consecutive patients aged  $\geq 18$  years diagnosed with ATAAD. Patients were divided into 2 groups: aortic root replacement (ARR; prosthetic or valve-sparing root replacement,  $n = 141$ ) and conservative root approach (CRA; root sparing of partially dissected root,  $n = 90$ ; and supracoronary ascending replacement in nondissected root,  $n = 68$ ). Inverse probability weighting was used to compare patients with different preoperative characteristics. Mean follow-up was 5.1 (0–21) years in ARR and 7.1 (0–25) years in CRA.

**RESULTS** The frequency of ARR increased over the years, with 19% and 78% of patients undergoing ARR in the earliest and most recent periods, respectively. Early mortality decreased over the years, despite a more aggressive approach, and remained lower in ARR. CRA was associated with a higher hazard of late mortality (hazard ratio, 1.38; 95% CI, 1.12–1.68;  $P = .001$ ) and reintervention (hazard ratio, 2.08; 95% CI, 1.44–3.56;  $P = .001$ ). After CRA, new-onset aortic valve insufficiency was a common cause of reintervention.

**CONCLUSIONS** Over the years, there was a gradual increase in the root replacement approach in ATAAD. Root replacement was associated with better long-term survival and fewer reinterventions compared with the conservative approach, whereas the in-hospital mortality decreased during these years. Hence, aggressive root replacement is safe and may be applied in ATAAD with good long-term clinical results, without increased hospital mortality.

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Acute type A aortic dissection (ATAAD) is a life-threatening condition requiring immediate surgical intervention to avoid lethal complications, including cardiac tamponade, rupture of the aorta, end-organ malperfusion, and acute heart failure due to coronary artery involvement or acute-onset aortic valve regurgitation.<sup>1,2</sup> Without surgical intervention, the early mortality rate (within 48 hours) is approximately 50%.<sup>3,4</sup> Improvements in diagnostic and therapeutic procedures have allowed the early mortality rate to decline to 10% to 15%.<sup>5,6</sup>

Historically, the cornerstone of surgical treatment of ATAAD has been replacement of the ascending aorta. In its most conservative fashion, the operation is restricted

to this procedure, even when dissection of the aortic root is present. The aortic root can be preserved and usually the valve is “resuspended” while the wall of the root is glued or otherwise reinforced. Alternatively, aortic root replacement (ARR) can be performed, either with preservation of the valve (valve-sparing root replacement) or by replacement with a composite valved conduit graft. After operation for ATAAD, late reoperations on both the proximal (aortic root) and distal (aortic

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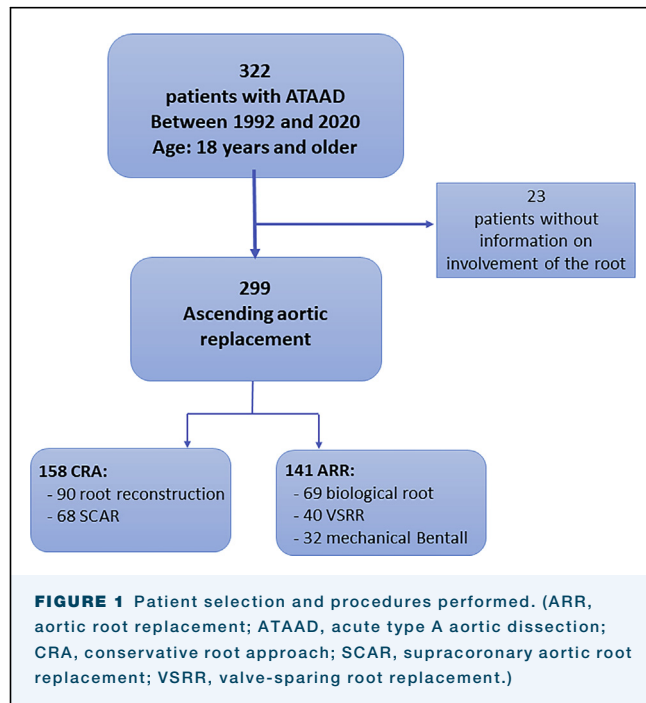
arch) parts of the aorta are frequent. Preservation of the dissected root presents a risk factor for reoperation as the reconstructed aortic root is prone to dilation or repeated dissection, often combined with detrimental effects on aortic valve function. On the other hand, a more aggressive approach to the aortic root, with a low threshold for ARR, might lower the risk of late reoperation. However, this will result in a more complex index operation. Nevertheless, the net effect of an aggressive approach to the aortic root in ATAAD on early and late outcomes remains insufficiently explored. Our aim was to study the effect of an aggressive ARR approach on early and late mortality and reoperation rates compared with the conservative root approach (CRA) in patients undergoing operation for ATAAD.

## PATIENTS AND METHODS

**PATIENTS.** Between January 1992 and January 2020, a consecutive 322 patients aged 18 years and older underwent surgical treatment for ATAAD at Leiden University Medical Center. Preoperative computed tomography (CT) scans, echocardiography images, and surgical reports were reviewed for detailed information on the extent of the dissection and surgical technique used. We excluded 23 (7.1%) patients in whom details on the involvement of the aortic root in the dissection process were missing.

Based on the extent of aortic root involvement in the dissection process and the type of treatment received, the patients were divided into the following study groups (Figure 1): patients undergoing ARR, with or without valve replacement ( $n = 141$  [47%]); and patients undergoing CRA ( $n = 158$  [53%]). Subsequently, CRA consisted of 2 groups. In patients in whom the aortic root was at least partially involved, it was subsequently “reconstructed” (ie, gluing of the dissected layers of the aortic root or resuspension of the aortic valve in case of partial involvement of the aortic root with or without use of felt for reinforcement [ $n = 90$ ]). In patients in whom the aortic root was neither dissected nor dilated and echocardiography revealed intact aortic valve function, aortic root reconstruction or replacement was deemed unnecessary at the time of intervention; these patients underwent a supracoronary ascending aorta replacement ( $n = 68$ ).

Additional comparison between ARR and CRA was done to compare the 2 groups in which at least partial involvement of the aortic root was observed. To investigate the potential influence of different and probably improved general perioperative care during the years, an additional subgroup analysis was performed for early mortality in patients operated on in 3 different eras: between 1992 and 1999; between 2000 and 2012; and after 2012.



**FOLLOW-UP.** For hospital survivors, clinical follow-up was applied by structural outpatient clinical visits at 6 months and 1 year postoperatively and thereafter biannually. In addition, CT scan follow-up was obtained at hospital discharge, 6 months, 1 year postoperatively, and thereafter biennially by means of serial standardized CT scans. If significant abnormalities were detected, additional imaging and clinical visits were scheduled. Median follow-up duration was 5.1 (0-21) years and 7.1 (0-25) years in the in ARR and CRR groups, respectively.

**STUDY END POINTS.** Primary study end points were a composite end point of death and reintervention (to account for the competing risk of death with potential reintervention) and separately the overall survival and freedom from aortic valve reintervention or reintervention on the proximal aorta (eg, due to progressive aortic root dilation or pseudoaneurysm formation). The secondary study end point was early mortality (defined as mortality within 30 days after operation or during the index hospitalization). Follow-up was 100% completed for mortality (patients were reached by outpatient clinic or telephone calls) and 89% for CT scan follow-up (ie, 11% of the patients did not appear for all structural postoperative CT scans). This study was approved by the institutional review boards of the participating centers, and informed consent was waived (G19.113).

**STATISTICAL ANALYSIS.** Categorical data are presented as counts with proportions. Continuous data are presented as means (standard deviation or range) when normally

distributed or medians (interquartile range) when not normally distributed. For categorical data, the  $\chi^2$  test or the Fisher exact test was used for comparison between groups. For continuous data, an unpaired *t*-test or Mann-Whitney *U* test, depending on distribution, was used. Univariable logistic regression analysis was performed to study potential variables affecting early mortality. Candidate variables with a *P* value of  $< .10$  or clinically relevant were tested in a multivariable model. [Supplemental Table 1](#) displays the details.

Inverse probability weighting (IPW) was applied to balance the differences in preoperative characteristics between the ARR and CRA groups. Variables used for propensity score calculation are displayed in [Supplemental Table 2](#). IPW was used to estimate the average treatment effect.<sup>3,4</sup> Standardized mean differences were calculated to determine covariate balance before and after IPW, with a cutoff value  $< 0.2$  accepted as nonsignificant difference. A graphic view of weights between root reconstruction and root replacement after IPW is displayed in the [Supplemental Figure](#). Survival and freedom from valve reintervention were analyzed with the adjusted Kaplan-Meier estimator with inverse probability of treatment weighting, and adjusted Cox regression was used for the analysis of association of variables with outcome (*P* value of  $< .1$  or clinically relevant).<sup>5,6</sup> The proportional hazard assumption was met by visual inspection (log-log curves). All tests were performed 2 sided, and a *P* value of  $< .05$  was considered statistically significant. To avoid informative censoring, survival and freedom from reintervention were presented with the cumulative incidence function from a competing risk analysis (using the R “*cmprsk*” package). For the statistical analysis, R (version 4.2.0; R Foundation for Statistical Computing) and GraphPad Prism (version 9.3.1 for Windows; GraphPad Software) were used.

**SURGICAL STRATEGY.** Between 1992 and 2020, the surgical strategy for treating ATAAD evolved. In the early study period, our strategy was based on replacement of the ascending aorta and reconstruction of the aortic root, if necessary, by resuspension of the valve or gluing the root, with or without felt (conservative approach). When conservation of the root was not deemed feasible, the root including the valve was usually replaced by a mechanical valved conduit (Bentall procedure). In most cases, the aortic arch was not replaced. From 2006 onward, a more aggressive approach to the aortic root was gradually incorporated. When the dissection extended to the aortic root or significant dilation of the aortic root was present at the time of operation ( $>40$  mm in diameter in most cases), ARR was performed. Biologic valved conduits were favored, and in selected patients, valve-sparing ARR was performed (the reimplantation

technique, except for 1 patient who underwent a hemi-Yacoub procedure).

In addition to the changes in the approach to the aortic root, a more aggressive approach was gradually applied on the distal aorta, with a growing number of patients undergoing hemiarch replacement and, in selected patients, total arch replacement with or without frozen elephant trunk. In addition, various cannulation techniques were used, with changes during the course of the study. Before 2006, femoral artery cannulation was the “gold standard.” From 2006 onward, subclavian artery cannulation became the preferred strategy. In case of aortic arch operation, deep hypothermia was standard and almost always combined with bilateral antegrade cerebral perfusion.

## RESULTS

[Table 1](#) shows the preoperative characteristics of the patients both at baseline and after IPW analysis.

**EARLY OUTCOMES.** Early mortality was 14.9% and 22.6% in ARR and CRA, respectively (*P* = .005). The time-related differences in early mortality rates and type of proximal aortic procedures performed are shown in [Figure 2](#). Early mortality decreased over the years from 34% in the 1992-1999 period to 9% in the 2013-2020 period. The major reason of mortality was multiorgan/heart failure (38% in ARR and 48% in CRA), followed by neurologic events (22% in ARR and 28% in CRA) and progression of dissection in 6% of CRA. The rest was identified as other/unknown. Of note, an increasing number of patients underwent ARR during the course of the study, with most patients undergoing biologic or valve-sparing root replacement in the most recent period. Additional analysis of the 3 operation periods to adjust for era of operation showed the study period 1992-1999 to be associated with higher probability of early mortality. However, this was observed in both ARR (odds ratio [OR], 3.83; 95% CI, 1.91-3.57; *P* = .007) and CRA (OR, 6.77; 95% CI, 1.92-23.91; *P* = .003).

Renal dysfunction, cardiac tamponade, and preoperative shock were identified as risk factors of early mortality; however, multicollinearity was observed. Cardiac tamponade was identified as the most significant risk factor of early mortality with an OR of 4.51 (*P* < .001). Interestingly, CRA was associated with higher early mortality (OR, 1.61; 95% CI, 1.10-2.36; *P* = .01). This association remained statistically significant even after adjustment for preoperative cardiac tamponade and era of index operation (OR, 1.42; 95% CI, 1.10-1.98; *P* = .03) and was higher in the subgroup of root reconstruction in which the root was involved within the CRA group (OR, 1.90; 95% CI, 1.27-2.84; *P* = .002).

**TABLE 1 Baseline Characteristics of Patients in the Raw Cohort and IPW-Adjusted Cohort**

| Variable                             | Baseline Characteristics |                  |         |       | After IPW Adjustment |                  |         |       |
|--------------------------------------|--------------------------|------------------|---------|-------|----------------------|------------------|---------|-------|
|                                      | CRA<br>(n = 158)         | ARR<br>(n = 141) | P Value | SMD   | CRA<br>(n = 158)     | ARR<br>(n = 141) | P Value | SMD   |
| Age, y                               | 61 (27-82)               | 59 (20-87)       | .29     | 0.14  | 59 (27-82)           | 58 (21-87)       | .48     | -0.11 |
| Male                                 | 86 (54.4)                | 92 (65.2)        | .06     | -0.24 | 96 (60)              | 89 (63)          | .15     | -0.11 |
| Hypertension                         | 68 (43.0)                | 43 (30.5)        | .03     | -0.27 | 99 (63)              | 92 (65)          | .22     | -0.13 |
| Hyperlipidemia                       | 5 (3.2)                  | 7 (5.3)          | .56     | 0.02  | 11 (6.9)             | 9 (6.4)          | .78     | 0.02  |
| Diabetes mellitus                    | 2 (1.3)                  | 4 (3.0)          | .58     | 0.04  | 4 (2.5)              | 4 (3.0)          | .71     | 0.05  |
| COPD                                 | 5 (3.2)                  | 9 (6.8)          | .28     | 0.08  | 10 (6.3)             | 9 (6.8)          | .59     | 0.08  |
| Vascular disease                     | 23 (14.6)                | 26 (19.5)        | .37     | 0.11  | 25 (15.8)            | 23 (16.3)        | .70     | 0.08  |
| Previous cardiac operation           | 5 (3.2)                  | 7 (5.3)          | .56     | 0.09  | 8 (5.1)              | 7 (5.3)          | .88     | -0.07 |
| eGFR, mL/min per 1.73 m <sup>2</sup> | 62 (6.1)                 | 63 (12.9)        | .03     | 0.10  | 60 (6)               | 63 (8)           | .16     | -0.11 |
| LVF                                  |                          |                  | .24     | 0.15  |                      |                  | .28     | 0.12  |
| Moderate-severe                      | 72%                      | 70%              |         |       | 72%                  | 70%              |         |       |
| AI grade >II                         | 34%                      | 42%              |         | 0.25  | 35%                  | 42%              |         | 0.16  |
| Aortic root diameter, mm             | 37 (33-42)               | 42 (39-50)       | .001    | 0.26  | 40 (33-42)           | 42 (39-49)       | .17     | 0.11  |
| Ascending aorta diameter, mm         | 41 (36-49)               | 50 (43-55)       | .09     | 0.05  | 45 (41-50)           | 48 (45-52)       | 0.11    | 0.10  |
| Clinical condition                   |                          |                  |         |       |                      |                  |         |       |
| Resuscitation                        | 7%                       | 4%               | .29     | -0.15 | 7%                   | 6%               | .42     | -0.17 |
| Tamponade                            | 28%                      | 18%              | .02     | -0.31 | 27%                  | 22%              | .06     | -0.23 |
| Shock                                | 11%                      | 12%              | .64     | 0.06  | 12%                  | 12%              | .74     | 0.08  |
| Cardiac ischemia                     | 5%                       | 6%               | .39     | 0.11  | 4%                   | 5%               | .62     | 0.12  |
| Neurologic dysfunction               | 18%                      | 20%              | .55     | 0.09  | 18%                  | 18%              | .74     | 0.10  |
| Peripheral ischemia                  | 5%                       | 11%              | .05     | 0.22  | 8%                   | 10%              | .20     | 0.25  |

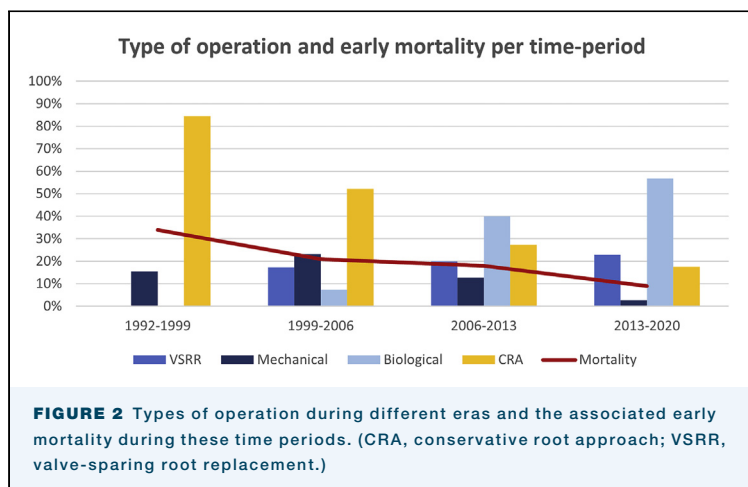
Categorical variables are presented as number (percentage). Continuous variables are presented as mean (range), mean (standard deviation), or median (interquartile range). AI, aortic insufficiency; ARR, aortic root replacement; CRA, conservative root approach; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; IPW, inverse probability weighting; LVF, left ventricular function; SMD, standardized mean difference.

Cardiopulmonary bypass and aortic cross-clamp times were longer in the ARR group (more details on operative data are presented in [Supplemental Table 3](#)). In addition to aortic root procedures, 59% of patients in the ARR group underwent hemiarch replacement compared with 40% of patients in the CRA group ( $P = .04$ ). A more extended distal aortic procedure (ie, arch or hemiarch replacement) was not associated with higher mortality (OR, 0.77; 95% CI, 0.52-1.23;  $P = .17$ ). Postoperatively, no significant differences in pericardial effusion, myocardial ischemia, and new-onset neurologic dysfunction were seen between groups ([Table 2](#)). There were no cases of postoperative spinal cord ischemia.

**CUMULATIVE INCIDENCE OF DEATH AND REOPERATION AND COMPETING RISK ANALYSIS.** Competing risk analysis predicted that after 10 years of follow-up, 32% had died without a reoperation, 14% underwent a reoperation, and 64% remained alive in the ARR group; and 52% had died without a reoperation, 23% underwent a reoperation, and 25% remained alive without reoperation in the CRA group. There were fewer events in the ARR group than in the CRA group ( $P = .02$ ). [Figure 3](#) shows details of the cumulative incidence curves.

**OVERALL SURVIVAL.** [Figure 4](#) shows the Kaplan-Meier curves of survival in ARR and CRA. Higher overall

survival was noticed in the ARR group compared with the CRA group (hazard ratio [HR], 1.38; 95% CI, 1.12-1.68;  $P = .001$ ). The magnitude of the difference was even greater in comparing the ARR group with the subgroup of root reconstruction, in which the root was involved, within the CRA group (HR, 1.43; 95% CI, 1.14-1.80;  $P = .001$ ). Of note, dissociating survival curves were more evident during the first year after the index operation, after which parallel survival curves were



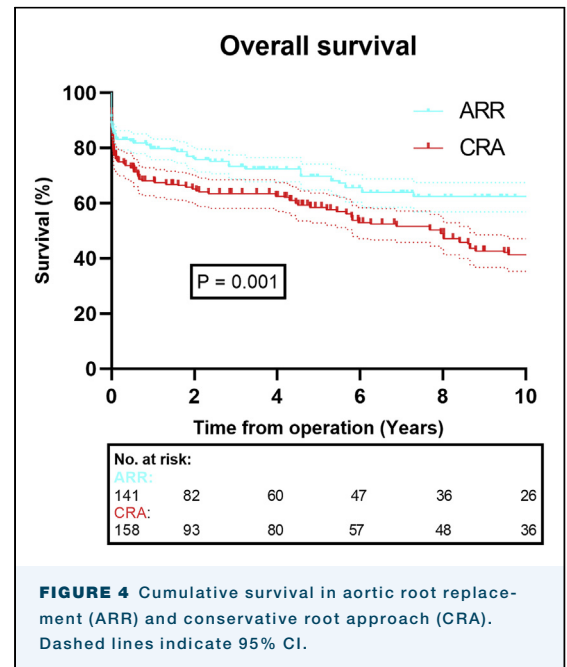
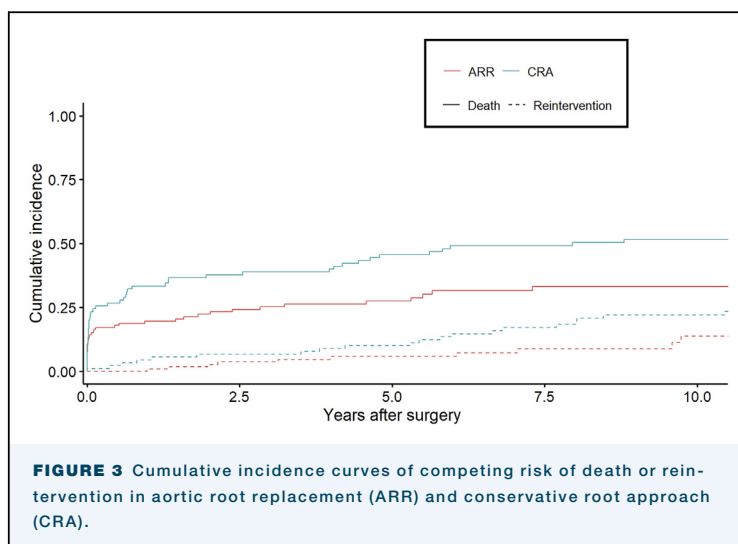
**TABLE 2 Early Complications**

|                                         | CRA<br>(n = 158) | ARR<br>(n = 141) | P value |
|-----------------------------------------|------------------|------------------|---------|
| Early mortality                         | 35 (22)          | 21 (15)          | .01     |
| Pericardial effusion                    | 32 (20)          | 34 (24)          | .42     |
| Myocardial ischemia                     | 10 (6)           | 6 (4)            | .62     |
| New neurologic dysfunction <sup>a</sup> | 19 (12)          | 14 (10)          | .70     |

<sup>a</sup>Including cerebrovascular accident and peripheral neurologic dysfunction. Values are reported as number (percentage). ARR, aortic root replacement; CRA, conservative root approach.

seen. Multivariable Cox regression analysis adjusted for age, sex, diabetes mellitus, and era of operation showed still poorer survival in CRA (HR, 1.32; 95% CI, 1.05-1.66;  $P = .02$ ).

**REINTERVENTION ON THE PROXIMAL AORTA.** Figure 5 shows the freedom from reintervention on the proximal aorta or aortic valve. Freedom from reintervention was significantly higher in the ARR group (HR, 2.08; 95% CI, 1.44-3.56;  $P = .001$ ) and even higher compared with the root reconstruction subgroup within the CRA group (HR, 2.36; 95% CI, 1.58-3.64;  $P < .001$ ). In addition, a smaller ascending aorta diameter was associated with a lower risk of subsequent proximal aortic reintervention in CRA (HR, 0.95; 95% CI, 0.92-0.98;  $P = .001$ ). No other preoperative variable (including preoperative aortic valve insufficiency and type of prosthesis) was associated with reintervention. Multivariable Cox regression analysis adjusted for maximum diameter of aorta, connective tissue disease, and era of operation showed higher hazard of reintervention in root reconstruction within the CRA group (HR, 2.02; 95% CI, 1.38-2.96;  $P = .001$ ).



Significant differences in the indication for reoperation on the proximal aorta were seen between groups (details in Supplemental Table 4). In the ARR group, aortic valve insufficiency was the most common indication for reintervention (43% of the reinterventions), followed by pseudoaneurysm formation (29%). In the CRA group, aortic valve insufficiency was the predominant indication for reintervention (75% of the reinterventions), followed by pseudoaneurysm formation (19%). Recurrent dissection of the aortic root was the indication for reintervention in the remaining patient.

## COMMENT

The results of our study demonstrate a progressive improvement of outcomes of acute operations for ATAAD during the course of the last 3 decades, despite the structural implementation of an aggressive replacement approach to the dissected aortic root. Moreover, ARR can be performed safely and seems effective at lowering the risk of late reintervention on the proximal aorta. Hence, when the aortic root is partially dissected or pathologically dilated, ARR should be considered in patients who can tolerate the longer operation and cross-clamp times.

**SURVIVAL AND TREATMENT IN DIFFERENT ERAS.** During the course of the last decades, the extent of surgical treatment of the dissected aortic root has changed. Several centers have advocated an aggressive approach

to the aortic root,<sup>7,8</sup> and a similar approach was applied in our center in the last 2 decades. This is reflected in our experience by a significant shift toward ARR, with most patients undergoing composite valved graft and valve-sparing root replacement procedures in the contemporary setting.

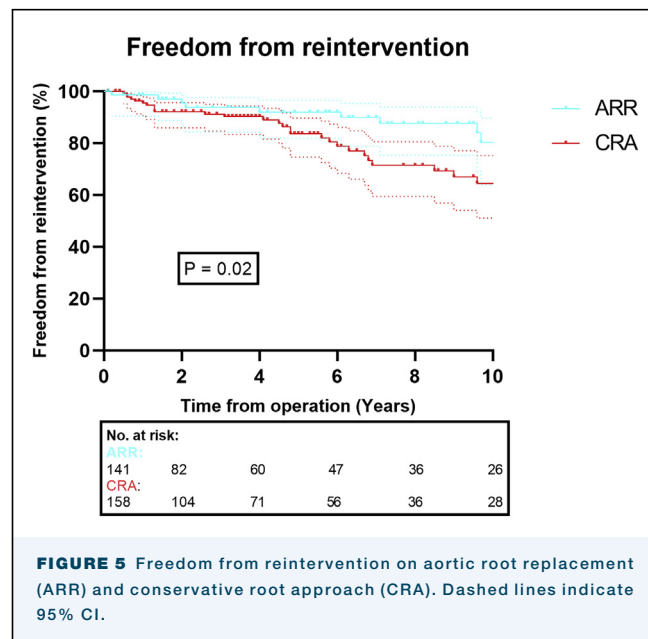
Despite the implemented extension in surgical strategy, inevitably resulting in longer operation time and procedure complexity, we observed no detrimental effect on the rate of postoperative complications. Our findings are comparable to those of earlier reports and support the safety of a more extensive surgical strategy in ATAAD.<sup>9,10</sup> Early mortality in our study was comparable to data from the International Registry of Acute Aortic Dissection database, reporting early mortality rates of 16% to 27%.<sup>11</sup>

A decline in early mortality was observed despite a gradual implementation of more extensive surgery not only on the proximal aorta but also on the distal aorta. A likely explanation for our observation is a probable improvement in perioperative management over the years. This includes general patient care, from the emergency department to the intensive care unit, with earlier diagnosis and better hemodynamic monitoring and treatment of patients in general. The additional analysis of the era of operation confirms this suggestion, whereas during the last decade, there was an improved perioperative survival. Nevertheless, the higher risk of early mortality in the CRA group could partially be explained by a higher number of patients in the CRA groups in the early era.

The change in the cannulation strategy, with a shift to more subclavian artery and less femoral artery cannulation and establishment of a dedicated aortic surgical team, introduced in our center around 2013, may also explain better results.<sup>12,13</sup> An upside of the implemented aggressive approach to the aortic root can also be assumed as fewer bleeding complications and improved aortic valve function are likely beneficial to the patient in the early postoperative phase.

Another interesting issue is the volume of a center and of individual surgeons and its association with the outcome. As Chikwe et al<sup>14</sup> showed in a large comparative study of the Nationwide Inpatient Sample (United States), lower institution and surgeon volume is associated with poorer outcome after ATAAD. However, as is the custom in The Netherlands (especially during the past 2 decades), there are no low-volume centers in the existing 15 cardiac surgery centers. In addition, in our center, there is a dedicated aortic team, which could have influenced the results, at least during the last decade.

Moreover, there were more patients in the CRA group who died of heart failure and neurologic events compared with the ARR group. A more conservative



approach and not replacing the partially damaged aortic root may have been the reason for more coronary and valvular complications during the postoperative period, leading to more neurologic and valve-related events, such as hemodynamically significant aortic valve insufficiency and heart failure, accounting for more than half of the early deaths in the CRA group.

**REINTERVENTIONS.** Previous studies have already shown that replacement of the aortic root in ATAAD results in a lower risk of late reoperations on the proximal aorta compared with aortic root reconstruction.<sup>15,16</sup> Important risk factors for proximal aortic reoperation are preoperative aortic valve regurgitation and significant dilation of the aortic root.<sup>17</sup>

In our study, the extent of aortic root dissection and functional aortic valve impairment were more profound in the ARR group, with extensive damage favoring root replacement even in the early study periods. Hence, the extent of the damage to the aorta was not homogeneous but signals more severe disease in the ARR group. The paradigm shift toward aggressive treatment (ie, replacement of the aortic root and arch) in our center has led to a decline in late reintervention rates. Considering the safety and efficacy of an aggressive approach to the aortic root in ATAAD, the net benefit seems in favor of root replacement procedures. Moreover, it is plausible to assume that a dissected aortic root is weakened and may dilate in years after the index operation, leading to valve dysfunction over the years, especially and most probably more pronounced in the dilated aorta (ie, >4 cm), younger patients, and connective tissue disease.

Although the risk of death or major complication due to reintervention has improved during the past decades, also evident in our center,<sup>18</sup>

it will remain of major impact for quality of life and clinical outcome for the patient. A future multicentric larger study of patients operated on within the last 10 to 15 years, with comparable postoperative care, could provide a clearer answer on the survival effect of an aggressive ARR approach as a first treatment strategy in ATAAD.

**LIMITATIONS.** This study concerns a single-center experience with a heterogeneous population of patients and different extents of aortic dissection. Moreover, there were some missing variables, especially in the group of patients operated on in the early period (1990s), and there are missing echocardiograms and CT images. In addition, surgical preference and technique have changed over the years. This may lead

to interpretations that are not necessarily applicable to other patient cohorts.

**CONCLUSIONS.** In patients with ATAAD, early and late mortality decreased over the years despite the structural implementation of an aggressive approach to the dissected aortic root. ARR can be performed safely and leads to a lower risk of late reintervention on the neo-aortic root. Hence, when the aortic root is partially dissected or dilated, a root replacement strategy should be considered as the first surgical therapy.

The data underlying this article will be shared on reasonable request to the corresponding author.

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#### DISCLOSURES

The authors have no conflicts of interest to disclose.

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