The safety of deep hypothermic circulatory arrest in aortic valve replacement with unclampable aorta in non-octogenarians

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Abstract

OBJECTIVES: Aortic valve replacement (AVR) in patients with severely atherosclerotic aortas (porcelain aorta) presents a significant technical challenge. Two strategies are deep hypothermic circulatory arrest (DHCA) during conventional surgery and transcatheter aortic valve replacement (TAVR). The aim of this study was to examine the outcomes in patients who underwent DHCA for AVR with a porcelain aorta to identify whether older patients are more suitable for TAVR.

METHODS: Between October 2004 and December 2012, 122 patients underwent AVR using DHCA for atherosclerotic aorta. Patients with concomitant valve surgery were excluded. Overall, 63.9% (78/122) were of age <80 (non-octogenarian group, NOG) and 36.1% (44/122) were >80 (octogenarian group, OG). Of the total cohort, 62.3% (76/122) had concomitant coronary artery bypass graft surgery.

RESULTS: The mean age for the whole cohort was 75.7 ± 8.5 years; 70.2 ± 8.1 years for the NOG and 83.4 ± 2.6 years for the OG (P = 0.001). The OG had a higher rate of preoperative renal failure (20.5%, 9/44 vs 7.7%, 6/78, P = 0.048) and trends towards a greater history of cerebrovascular disease (9.1%, 4/44 vs 1.3%, 1/78, P = 0.056), but fewer reoperations (6.8%, 3/44 vs 19.2%, 15/78, P = 0.069). Cardiopulmonary bypass time, aortic cross-clamp time and circulatory arrest time were similar between the two groups. Postoperative complication rates were similar except for permanent stroke (OG 18.2%, 8/44 vs NOG 6.4%, 5/78, P = 0.065). The overall operative mortality rate was 8.2% (10/122); however, the OG had significantly higher operative mortality compared with the NOG (15.9%, 7/44 vs 3.8%, 3/78, P = 0.035). One- and 5-year survival rates were 88.9 and 79.3% for the NOG versus 75.0 and 65.9% for the OG (P = 0.027), respectively.

CONCLUSIONS: Postoperative neurological events and operative mortality were, respectively, 3- and 4-fold higher in octogenarians undergoing AVR using DHCA. Such patients may represent suitable candidates for TAVR if favourable outcomes are demonstrated in patients with atherosclerotic aortas. Surgical AVR remains the standard treatment option with excellent outcomes for patients <80 years old with unclampable aortas.

Keywords: Porcelain aorta • Aortic valve replacement • Deep hypothermic circulatory arrest

INTRODUCTION

Severe atherosclerotic calcification in the ascending aorta, also known as a ‘porcelain aorta’, precludes cardiac surgeons from placing an aortic cross-clamp due to the increased risk of systemic embolism and stroke [1, 2]. In coronary artery bypass grafting (CABG) or mitral valve surgery, alternative techniques such as off-pump CABG or ventricular fibrillatory arrest can be used to avoid cross-clamping the aorta. However, in the case of aortic valve replacement (AVR), an aortic cross-clamp is needed prior to aortotomy and, therefore, deep hypothermic circulatory arrest (DHCA) may be required with porcelain aortas. This adds another level of surgical complexity to an already high-risk patient with calcific degeneration. A new treatment option has emerged for high-risk patients undergoing AVR, namely transcatheter aortic valve replacement (TAVR). TAVR has been proved to be an alternative option for inoperable or extremely high-risk patients [3–5].

With more evidence accumulating, an increasing number of technically inoperable patients are treated with TAVR, and a porcelain aorta is the leading cause for technical inoperability. Recent ad hoc analysis of a randomized controlled study showed that 23% of patients undergoing TAVR were for technical reasons, and porcelain aorta was the most common reason for technical inoperability [6].

Surgical outcomes in patients with porcelain aortas undergoing AVR have been reported. The operative mortality rate is reported to be 4–14% with a 6–17% stroke risk [7–10]. Although these numbers may be high compared with standard patients undergoing AVR, we believe that not all patients should undergo TAVR. TAVR has some disadvantages which can be avoided by traditional open surgery, such as increased risk of paravalvular leak and complete heart block [3–5].

The aim of this study was to analyse the outcomes of patients undergoing AVR with DHCA for porcelain aorta, and compare the outcomes between octogenarians and non-octogenarians. We hypothesized that, with increased age, there is a higher likelihood
of requiring DHCA for patients undergoing AVR with porcelain aortas.

**METHODS**

**Patients**

We identified 122 consecutive patients who underwent AVR using DHCA for severely atherosclerotic aorta between October 2004 and December 2012. Patients with concomitant other valve surgery, ascending aortic replacements for aortic aneurysms or dissections were excluded. This study was approved by the institutional review board of the Brigham and Women’s Hospital (approval number 2010P000292).

**Techniques**

A porcelain aorta was detected preoperatively by plain chest X-ray or non-contrast computed tomography. This was confirmed with manual palpation and epicardial ultrasound scans, which were used in all cases. If possible, the aorta was cannulated for arterial cannulation where calcium was absent. In some cases where the aorta was fully calcified, or for reoperations, axillary or femoral arterial cannulation was used.

All patients used DHCA and were cooled to 18°C. A left ventricular vent was placed in case of ventricular fibrillation during cooling. In the presence of aortic regurgitation, cooling was performed at a slower pace to avoid ventricular fibrillation. When ventricular fibrillation occurred, retrograde cardioplegia or systemic potassium was administered to obtain diastolic arrest. Antegrade cardioplegia was infused directly into the coronary ostia following aortotomy in most cases.

In cases where the axillary artery was used for cannulation, antegrade cerebral perfusion was performed during DHCA. Retrograde cerebral perfusion was used in some cases through the superior vena cava mostly to de-air and remove debris with retrograde flow.

Cerebral monitoring was performed using a right radial arterial pressure line, electroencephalogram (EEG) and Bispectral Index (BIS, Phillips, Eindhoven, Netherland). In addition, we have used near-infrared spectroscopy cerebral monitoring since 2006. Patients were cooled to 18°C and isoelectric EEG was obtained prior to DHCA.

The following three strategies were used depending on the extent of calcification.

First, if there was extensive ascending aortic disease, the ascending aorta was replaced using a tube graft. The patient was placed in the Trendelenburg position when the systemic temperature was 18°C and the aorta was transected at the level of the sinotubular junction and just proximal to the innominate artery. Additional endarterectomy was performed depending on the extent of disease in the distal aorta. Following the distal anastomosis using a Hemashield graft (Boston Scientific, Natick, MA, USA) or Vascutek graft (Terumo, Tokyo, Japan), arterial flow was obtained through a side branch of the tube graft or directly through the replaced graft. Cardiopulmonary bypass flow was restarted and de-airing of the distal aorta and tube graft was performed. The tube graft was then clamped and systemic perfusion re instituted at full flow. AVR and the proximal anastomosis were performed during rewarming.

Second, if the disease was localized to the site of the aortic cross-clamp, an endarterectomy of the aorta was performed under DHCA. An extended aortotomy was made and the aorta inspected and carefully debridged. Cardiopulmonary bypass flow was restarted to de-air and remove debris. The aorta was clamped at the site of the endarterectomy and systemic perfusion was restarted. AVR was performed during rewarming and the aortotomy was closed.

Lastly, if the disease was isolated to the distal ascending aorta but cross-clamping deemed unsafe, the patient was placed in the Trendelenburg position at 18°C, DHCA was instituted and an aortotomy was made in the calcium-free proximal aorta. An oblique aortotomy was made towards the non-coronary sinus and AVR was performed. Careful irrigation was performed to remove all the calcium prior to closing the aortotomy. Cardiopulmonary bypass flow was started and de-airing was performed. The aortotomy was then closed and systemic perfusion restarted. Endarterectomy of the aortic edges was often needed to close the aorta.

In cases with concomitant CABG, distal anastomoses were performed during the cooling phase. Retrograde cardioplegia or systemic hyperkalaemia was used to arrest the heart earlier in these cases. The left anterior descending artery and right coronary artery targets were revascularized first. Circumflex anastomoses were performed last since lifting the heart would cause distension. If lifting caused distension, the circumflex was revascularized after the aortic procedure. In some cases, cardiopulmonary bypass flow was reduced to 0.5 l/min under deep hypothermia to minimize distension while performing the anastomoses.

**Data collection**

Patient characteristics, medications, laboratory values and inhospital outcomes of the index surgery were collected at the time of presentation and extracted from the Brigham and Women’s Cardiac Surgery database. Data were coded according to The Society of Thoracic Surgeons National Adult Cardiac Database version 2.52 definitions, unless otherwise noted.

The primary outcomes of interest were operative mortality, frequency of postoperative complications and mid-term survival. Postoperative complications included cerebrovascular accident (CVA), new onset of renal failure, reoperation for bleeding, ventilation time, intensive care unit (ICU) stay and length of stay (LOS). CVAs included strokes and transient ischaemic attacks (TIAs). Mortality data were collected from hospital records, by routine patient follow-up, from our state Department of Public Health and a query of the Social Security Death Index.

**Statistical analysis**

Comparison of dichotomous variables was done with Fisher’s exact test, and are presented as percent and number of cases. Continuously distributed variables were evaluated using Student’s t-test with Levene’s test for equality of variance to assess the assumption of equal variances between populations; these data are presented as means ± standard deviations (SD). Mann-Whitney U-tests were used to evaluate non-normally distributed continuous variables, which are presented as median, and 25th and 75th percentiles. Survival was evaluated by Kaplan–Meier analyses, and group comparisons were made using a log-rank test. Statistics were performed using SPSS 13.0 (SPSS, Chicago, IL, USA), and a P-value less than 0.05 was considered statistically significant.
RESULTS

Study population

From October 2004 to December 2012, a total of 150 patients underwent AVR using DHCA for an atherosclerotic aorta. Twenty-eight patients had concomitant mitral valve and/or tricuspid valve surgery and were excluded from the study. Total of 122 comprised our study group. In this group, 63.9% (78/122) were younger than 80 years old (non-octogenarian group, NOG) and 36.1% (44/122) were ≥80 years old (octogenarian group, OG). Total follow-up time was 419 patient-years. The median follow-up was 3.3 years (percentiles 1.1, 5.6).

Patient operative characteristics are summarized in Table 2. In the whole cohort, 14.8% (18/122) of patients were reoperations from previous cardiac surgery.

When comparing the NOG and the OG, the OG had fewer patients with a history of smoking tobacco (62.8 vs 40.9%, P = 0.024) and family history of coronary artery disease (25.6 vs 9.1%, P = 0.033), but had higher incidence of preoperative renal failure (7.7 vs 20.5%, P = 0.048). The OG also exhibited a trend towards more cerebrovascular disease (1.3 vs 9.1%, P = 0.056), but fewer patients with previous cardiac surgery (19.2 vs 6.8%, P = 0.069), Preoperative conditions such as hypercholesterolaemia (87.2 vs 81.8%; P = 0.44), diabetes (29.5 vs 25.0%; P = 0.34), NYHA Class III/IV (56.6 vs 53.8%; P = 0.45) and median left ventricular ejection fraction (60 vs 60%, P = 0.92) were similar between the two groups.

Operative data

Patient operative characteristics are summarized in Table 2. In the total cohort, 73.0% (89/122) used aortic graft replacement for a porcelain aorta, 23.0% (28/122) underwent endarterectomy and 4.1% (5/122) underwent direct AVR during DHCA. Of the whole cohort, 62.3% (76/122) underwent concomitant CABG. The median time for cardiopulmonary bypass time was 214 min (percentiles: 160, 266), aortic cross-clamp time was 112 min (percentiles: 74, 153) and DHCA time was 15 min (percentiles: 9, 26). Overall, antegrade cerebral perfusion was used in 5.7% (7/122) of patients; 7.7% (6/78) in the NOG and 2.2% (1/44) in the OG, P = 0.256. Retrograde cerebral perfusion was used in 6.6% (8/122); 7.7% (6/78) in the NOG and 4.5% (2/44) in the OG, P = 0.710.

Operative morbidity and mortality

Operative morbidity and mortality are summarized in Table 3. In the total cohort, the operative mortality rate was 8.2% (10/122). The combined stroke/TIA rate was 12.3%; permanent stroke was seen in 10.7% and TIA in 1.6%. In the total cohort, 4.9% (6/122) had reoperations for bleeding and 10.7% (13/122) developed postoperative renal failure, but only one patient required haemodialysis. The median ventilation time was 11.8 h (percentiles: 6, 39), ICU stay was 89.0 h (percentiles: 48, 157) and median LOS in hospital was 9 days (percentiles: 7, 15). There was one pacemaker implantation postoperatively (0.7%).

Operative mortality was significantly higher in the OG (3.9 vs 15.9%; P = 0.035) as well as combined stroke/TIA rate (6.4 vs 22.7%, P = 0.019) and permanent stroke rate (6.4 vs 18.2%, P = 0.065). Reoperation for bleeding (6.4 vs 2.3%; P = 0.42) and postoperative renal failure (11.5 vs 9.1%; P = 0.77) were similar between the two groups, as were time on the ventilator, total ICU stay and postoperative LOS. None of the patients experienced complete heart block or pacemaker postoperatively.

We examined the cause of death for operative mortality to identify the contributing factors. The cause of death was stroke in 4/10 patients, cardiac in 3/10 and other in 3/10. In the OG, the cause of death was stroke in 4/7 and cardiac in 2/7. In the NOG, there was a cardiac death in 1/3 patients, but no deaths were associated with stroke.

Survival analysis

Overall, 31 deaths occurred during the study observation period. Fig. 1 shows the Kaplan–Meier analysis of survival through 5 years.

<table>
<thead>
<tr>
<th>Table 1: Preoperative patient characteristics</th>
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<tr>
<td>Total cohort (n = 122)</td>
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<tr>
<td>------------------------</td>
</tr>
<tr>
<td>Age (years) Mean/SD</td>
</tr>
<tr>
<td>Women %/n</td>
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<tr>
<td>Smoker %/n</td>
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<tr>
<td>FHCAD %/n</td>
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<td>Diabetes %/n</td>
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<td>Hypercholesterolaemia %/n</td>
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<tr>
<td>Renal failure %/n</td>
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<tr>
<td>Preop creatinine Mean/SD</td>
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<tr>
<td>History of CVA %/n</td>
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<tr>
<td>NYHA Class III/IV %/n</td>
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<tr>
<td>Ejection fraction %/n</td>
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<td>Previous cardiac surgery %/n</td>
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FHCAD: family history of coronary artery disease; CVA: cerebrovascular accident; NYHA: New York Heart Association; SD: standard deviation; quartiles: interquartile range.
The estimated 1-year survival rate was 88.9% [95% confidence interval (CI) 81.6–96.1] for the NOG vs 75.0% (95% CI 61.6–88.4%) for the OG patients; the 5-year survival rate was estimated at 79.3% (95% CI 69.0–89.7%) and 65.9% (95% CI 50.6–81.2%) for the NOG versus the OG, respectively (P = 0.027).

**DISCUSSION**

The estimated 1-year survival rate was 88.9% [95% confidence interval (CI) 81.6–96.1] for the NOG vs 75.0% (95% CI 61.6–88.4%) for the OG patients; the 5-year survival rate was estimated at 79.3% (95% CI 69.0–89.7%) and 65.9% (95% CI 50.6–81.2%) for the NOG versus the OG, respectively (P = 0.027).

Multiple reports have been published in the literature, but the incidence of stroke and operative mortality is high compared with standard AVR without severe ascending aortic calcifications [7–10]. Gillinov et al. reported their experience in 62 patients with porcelain aortas undergoing AVR: 39% had AVR under DHCA, 26% had endarterectomy followed by aortic cross-clamp and 19% had aortic replacement. The overall hospital mortality rate was 14% with a 10% stroke rate [7]. We reported our experience from 1998 to 2004 in 70 patients: 63% underwent graft replacement, 18.5% underwent endarterectomy and 18.5% underwent direct AVR with an overall mortality rate of 4% and a stroke rate of 11% [8]. Zingone et al. reported their experience in 64 patients who underwent aortic replacement due to a porcelain aorta in which 49 was during AVR. Their operative mortality rate was 10.9% with a stroke rate of 6.3% [10].

Recently, a new alternative was introduced to the treatment of aortic stenosis. TAVR is gaining popularity in otherwise inoperable patients or extremely high-risk patients given the results of the multicentre prospective randomized controlled study (PARTNER trial) [3, 4]. Recently, a subgroup analysis of the PARTNER trial of
... porcelains, previous radiation to the chest and coronary grafts crossing the midline. Of these, porcelains aorta was the most common reason (42%). Interestingly, this group of technically inoperable patients had superior outcomes compared with the clinically inoperable group, which consisted of patients with multiple comorbidities or frailty. Although the specific numbers in the porcelains aorta group was not reported, the overall 30-day mortality rate was 4.7% and the stroke rate was 3.6% for the technically inoperable group. The mean Society of Thoracic Surgeon score for technically inoperable patients was 5.4 compared with 12.0 in the clinically inoperable group. It is worth emphasizing that many cardic surgeons and cardiologists consider that porcelains aorta is an inoperable condition even in moderate-risk patients.

There have not yet been randomized controlled studies comparing surgical AVR and TAVR in the patient population, which is the focus of this study, and so direct comparisons are not possible. However, our goal was to report our outcome in the surgical treatment of AVR with porcelains aorta and identify the patients who might benefit from surgical AVR.

Our result showed an overall operative mortality rate of 8.2% and stroke/TIA rate of 12.3%. This number is within the range of previous reports. When compared with our previous report from 1998 to 2004, the current report has a slightly older age group (current 75.7 vs 74.0 years), higher reoperations (14.8 vs 5.7%) and higher use of aortic graft replacement (73 vs 63%), which may have contributed to the differences in outcomes. We have also applied epiaortic ultrasound in all cases, which allowed us to identify the true extent of aortic calcification. This enables creating a concrete surgical strategy prior to DHCA and aortotomy. As mentioned in the Methods section, we performed aortic graft replacement in the porcelains aorta group which extends both proximally and distally. If the calcification is focal, endarterectomy was performed to enable application of the aortic cross-clamp. A proximally spared porcelains aorta was treated occasionally with direct AVR under DHCA; however, we have generally moved away from this strategy given the high stroke rate seen in our previous study [8].

None of the previous reports have identified any specific risk factors for mortality and stroke. Although previous reports have shown that increased age at AVR was not associated with increased surgical risk [15–18], it appears that this is not the case in the presence of a porcelains aorta. This was confirmed in our study; octogenarians had 4-fold higher incidence of operative mortality (15.9 vs 3.9%, P = 0.035) and 3.5-fold higher incidence of neurological events (22.7 vs 3.4%, P = 0.019).

Stroke played a major role in the outcomes of elderly patients. In the OG, there were four operative mortalities out of the eight permanent strokes that occurred; hence, the mortality rate was 50% following postoperative stroke. By contrast, there were no mortalities in the NOG out of the five permanent postoperative strokes. The cause of death was neurological in 4/7 octogenarians and 0/5 non-octogenarians. Porcelain aorta is known to be a risk factor for stroke [19], but our results show its significance increases with age.

Our operative mortality rate of 3.9% and postoperative neurological event incidence rate of 3.4% in the NOG were comparable with those reported in the TAVR subgroup analysis [6]. TAVR does have disadvantages compared with surgical AVR, including paravalvular leak and complete heart block, which is known to occur more in TAVR and is associated with worse outcomes [20]. We did not have data on paravalvular leak, but our policy is not to leave the operation theatre with any paravalvular leak that is more than mild. Our postoperative pacemaker implantation rate was 0.7%, which is significantly lower than the recently published 19.8% permanent pacemaker implantation rate due to complete heart block. In selected patients with porcelains aorta, surgical AVR may provide excellent outcomes and may be considered ‘operable’.

Device development and technical maturity are likely to improve TAVR outcomes in the future. Nevertheless, surgical treatment remains a proven safe procedure in this population, and the current study suggests that selecting patients by age maximizes these benefits.

Despite the notion among physicians including cardiac surgeons that porcelains aorta is ‘inoperable’, surgical AVR using DHCA is a viable option with good outcomes, especially in non-octogenarians.

Limitations

This is a single-institution retrospective observational cohort study and is subject to all the limitations inherent in such a design. Generalizing our findings to other populations should be done with caution. Further, the current study reflects a patient series over 8 years; changes in patient complexity and evolving surgical experience and techniques may account for findings in ways that we cannot adequately quantify.

CONCLUSION

AVR using DHCA in patients with porcelains aorta can be performed with acceptable morbidity and mortality. Octogenarians were at higher risk for postoperative strokes and mortality than were younger patients, likely related to their higher postoperative neurological events. Such patients may be suitable candidates for TAVR, given the favourable outcomes in the literature. By contrast,
younger patients can undergo conventional surgery using DHCA with excellent outcomes. Surgical intervention remains the standard treatment option for younger patients undergoing AVR with porcelain aortas.

Conflict of interest: none declared.

REFERENCES


