Transcatheter aortic valve implantation in patients with ascending aortic dilatation: safety of the procedure and mid-term follow-up

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Abstract

OBJECTIVES: Transcatheter aortic valve implantation (TAVI) does not enable concomitant or simultaneous ascending aortic intervention. This investigation evaluates the safety of TAVI in patients with ascending aortic dilatation and demonstrates mid-term follow-up.

METHODS: From November 2007 to December 2012, among 1143 patients with severe aortic stenosis screened for TAVI, a cohort of 457 patients met the inclusion criteria. Of these, a total of 98 patients [71% males, median age 85.0 (9.0) years] were diagnosed with concomitant ascending aortic dilatation (4.0–5.0 cm). An additional 2 patients had an ascending aortic diameter of >5.0 cm. The mid-term follow-up (652.2 patient-years) was 100% complete.

RESULTS: There was no iatrogenic dissection in patients with dilatated ascending aorta. Intraoperative aortic rupture occurred in 1 patient with mildly dilated ascending aorta. One-year survival rates in patients with dilated and non-dilated ascending aorta were 65 of 75 (87%) and 201 of 242 (83%, \( P = 0.573 \)). The mean ascending aortic diameter remained stable at 4.1 (0.2) and 4.7 (0.2) cm in patients with mild and moderate dilatation, respectively, with a median follow-up of 14 months after TAVI. Two patients with an aortic diameter of over 5.0 cm survived the procedure and expired 7 and 20 months after TAVI due to tumour and heart failure, respectively.

CONCLUSIONS: Ascending aortic dilatation is diagnosed in almost one-fourth of patients treated with TAVI. Their intraprocedural risk of adverse aortic events is low. The ascending aortic dilatation does not affect mid-term survival in the TAVI population.

Keywords: Transcatheter aortic valve implantation • Ascending aortic aneurysm

INTRODUCTION

In patients with critical aortic stenosis and ascending aortic aneurysm undergoing open aortic valve replacement (AVR), the current American College of Cardiology (ACC) Foundation guidelines recommend concomitant repair when the diameter of the ascending aorta is >4.5 cm [1] to avoid the catastrophic events of acute type A aortic dissection or rupture.

Since transcatheter aortic valve implantation (TAVI) became an alternative for high-risk patients [2–4], more and more patients undergo TAVI and their ascending aorta dilatation, if present, remains untreated. However, in contrast to surgical AVR, the ascending aorta during the TAVI procedure remains untouched and inaccessible to the surgeon. Therefore, the ACC recommendations for concomitant intraoperative repair of the dilated ascending aorta cannot be applied in TAVI circumstances.

The goal of the present study was to demonstrate the incidence of aortic dilatation in patients undergoing TAVI, to evaluate the procedure’s safety in patients with ascending dilatation compared with those with ‘normal aorta’ and to demonstrate the fate of the unreplaced dilated ascending aorta after TAVI in mid-term follow-up.

MATERIALS AND METHODS

Patient population

The study population includes the prospective cohort of consecutive patients with severe aortic stenosis screened for TAVI from November 2007 to December 2012 at a single centre. All patients had an increased surgical risk profile due to their comorbidities. The indication to perform TAVI was based on a consensus by the Institutional Heart Team, comprising cardiac surgeons, cardiologists and anaesthesiologists. Among 1143 patients screened for TAVI, a group of 457 (all with tricuspid aortic valve) met the TAVI inclusion criteria. Of these, a total of 98 patients had concomitant ascending aortic dilatation (4.0–5.0 cm) and were compared with 357 patients with non-dilated aorta.
ascending aorta (<4.0 cm). Two patients with ascending aortic aneurysm (diameter >5.0 cm) were excluded from the analysis (Fig. 1).

Transcatheter aortic valve implantation procedure

TAVI was performed in a hybrid operating room by the Institutional Heart Team. All patients were under general anaesthesia and had transoesophageal echocardiography (TEE). A perfusionist with a prepared heart-lung-machine was present throughout the procedure in the operating room. Transapical or trans-femoral accesses were gained in the usual fashion [3]. Trans-femoral route as a less invasive delivery option was preferable. All patients underwent implantation of the Edwards Sapien or Sapien XT (Edwards Lifesciences, Irvine, CA, USA) as has been previously described [3].

Ascending aorta dimension

In all patients ascending aorta diameter was assessed prior to TAVI by computed tomography (CT) angiography, transthoracic echocardiography (TTE) and TEE. At the latest follow-up visit, all patients underwent TTE. The change of proximal ascending aorta diameter was calculated using the echocardiographic data and presented for patients with mild (4.0–4.4 cm) and moderate (4.5–5.0 cm) ascending aortic dilatation.

Patient follow-up

Our follow-up protocol consisted of clinical examination and TTE before discharge, 30 days, 6 months and 1 year after procedure and annually thereafter. The follow-up and surveillance data were obtained by contacting the general practitioners, the patients or their family members. The median follow-up was 14 months (interquartile range, 14 months; 652.2 patient-years) and was 100% complete.

Study end-points

The primary end-point was the rate of aortic dissection and/or rupture during the TAVI procedure. The secondary end-points were in-hospital mortality, 1-year survival and ascending aorta diameter change in follow-up.

Statistical analysis

Normally distributed continuous data are reported as mean (standard deviation) and non-normally distributed data as median (interquartile range). Categorical variables are reported as counts and percentages. For comparison of continuous variables, Student’s t-test was applied when normal distribution was present while the Mann–Whitney rank sum test was used when variables were not normally distributed. Comparison of categorical variables was performed using the \( \chi^2 \) test. \( P \)-values are not presented for \( n \leq 10 \) in the subgroup. The Kaplan–Meier method was used to analyse overall survival. All statistical calculations were performed using SigmaPlot 12 (Systat Software, San Jose, CA, USA).

RESULTS

Demographics and clinical presentation

The overall patient cohort was at high risk [STS score, 10 (4.7)%] with a noticeable advanced median age [85.1 (8.6) years], 86 of 455 (18%) patients were over 90 years old and 169 of 455 (37%) patients had previous cardiac surgery. Four hundred and eighteen of 455 patients (92%) were New York Heart Association (NYHA) class III or IV. The gender distribution in all TAVI patients was well balanced with 50% males. However, male sex was more common in patients with dilatated vs non-dilatated ascending aorta, 70 of

![Figure 1: Allocation of patients to groups according to ascending aortic diameter. AA: ascending aorta.](https://academic.oup.com/ejcts/article-abstract/46/2/228/359650)

![Figure 2: Distribution of ascending aortic diameter in women (red line) and men (blue line) who underwent TAVI. Grey columns represent ascending diameter in the overall TAVI population.](https://academic.oup.com/ejcts/article-abstract/46/2/228/359650)
98 (71%) vs 158 of 357 (44%, \( P < 0.001 \)). Overall, the average ascending aorta diameter was greater in men than in women [3.7 (0.7) vs 3.4 (0.6) cm, \( P < 0.001 \), Fig. 2]. Patients with a dilated ascending aorta had a higher incidence of coronary artery disease: 53 of 98 (54%) vs 137 of 357 (38%, \( P = 0.007 \)). There were no other significant differences in clinical presentation (Table 1).

**Aortic valve stenosis characteristics**

The mean transaortic gradient was 46 (16) mmHg and aortic valve area 0.6 (0.2) cm² in all patients. The incidence of severe aortic valve insufficiency was similar in both groups; however, patients with dilated ascending aorta had a higher incidence of moderate aortic regurgitation, 24 of 98 (25%) vs 50 of 357 (14%, \( P = 0.019 \); Table 2).

**Periprocedural results**

Of the 455 patients scheduled for TAVI, 304 (67%) underwent the procedure via trans-femoral and 151 (33%) via transapical access. Trans-femoral access was more commonly performed in patients with dilated ascending aorta, 76 of 98 (78%) vs 228 of 357 (64%, \( P = 0.015 \)). Transaortic gradient after aortic valve implantation was similar in the two groups (Table 3). There was no iatrogenic aortic dissection in the entire study cohort. Intraoperative aortic valve annulus rupture with aorto-right ventricular fistula occurred in one 91-year old female patient with mildly dilated ascending aorta (4.2 cm). Due to serious comorbidities, the patient was managed conservatively and died 6 days later due to the severe right ventricular dysfunction.

**In-hospital mortality and follow-up survival**

In-hospital mortality for the study cohort was 5% (24 of 455). One-year survival rates in patients with dilated and non-dilated ascending aorta were 65 of 75 (87%) and 201 of 242 (83%, \( P = 0.573 \)). Kaplan–Meier survival analysis revealed no significant differences between the two cohorts [dilated ascending aorta: HR 4.1, 95% confidence interval (CI) 3.7–4.5 years, non-dilated ascending aorta: HR 4.1, 95% CI 3.7–4.4 years; log-rank test \( P = 0.498 \), Fig. 3].

**Fate of the mildly and moderately dilated ascending aorta**

The mean proximal ascending aortic diameter assessed with TTE remained stable at 4.1 (0.2) and 4.7 (0.2) cm in patients with mild (4.0–4.4 cm) and moderate (4.5–5.0 cm) aortic dilatation, respectively, at the median follow-up of 14 months after TAVI. We did not observe an ascending diameter increase of >0.5 cm/year nor an ascending diameter of >5.5 cm in any patients.

**Outcome of patients with ascending aortic aneurysm**

Two patients with severe aortic stenosis and ascending aortic aneurysm (diameter 5.5 and 5.7 cm, age 87 and 91 years) underwent uncomplicated TAVI. They survived the procedure and expired 7 and 20 months after TAVI due to tumour and heart failure, respectively.

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**Table 1:** Demographics, clinical presentation and cardiac risk factors in patients with dilated and non-dilated ascending aorta undergoing the TAVI procedure

<table>
<thead>
<tr>
<th>All (n = 455)</th>
<th>Dilated ascending aorta (n = 98)</th>
<th>Non-dilated ascending aorta (n = 357)</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>85.1 (8.6)</td>
<td>85.0 (9.0)</td>
<td>85.2 (8.6)</td>
</tr>
<tr>
<td>Over 90 years</td>
<td>86 (18.9)</td>
<td>18 (18.4)</td>
<td>68 (19.0)</td>
</tr>
<tr>
<td>Male gender</td>
<td>228 (50.1)</td>
<td>70 (71.4)</td>
<td>158 (44.3)</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td>Peripheral vascular disease</td>
<td>169 (37.1)</td>
<td>38 (38.8)</td>
</tr>
<tr>
<td>Carotid stenosis (&gt;60%)</td>
<td>97 (21.3)</td>
<td>14 (14.3)</td>
<td>83 (23.2)</td>
</tr>
<tr>
<td>COPD</td>
<td>167 (36.7)</td>
<td>37 (37.8)</td>
<td>130 (36.4)</td>
</tr>
<tr>
<td>Baseline creatinine level (mg/dl)</td>
<td>1.1 (0.6)</td>
<td>1.2 (0.6)</td>
<td>1.1 (0.5)</td>
</tr>
<tr>
<td>Dialysis</td>
<td>7 (1.5)</td>
<td>2 (2.0)</td>
<td>5 (1.4)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>190 (41.8)</td>
<td>53 (51.4)</td>
<td>137 (38.4)</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>169 (37.1)</td>
<td>38 (38.8)</td>
<td>131 (36.7)</td>
</tr>
</tbody>
</table>

**NYHA**

<table>
<thead>
<tr>
<th>All (n = 455)</th>
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<th>Non-dilated ascending aorta (n = 357)</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>3 (0.7)</td>
<td>0</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Class II</td>
<td>29 (6.4)</td>
<td>5 (5.1)</td>
<td>24 (6.7)</td>
</tr>
<tr>
<td>Class III</td>
<td>243 (53.4)</td>
<td>51 (52.0)</td>
<td>192 (53.8)</td>
</tr>
<tr>
<td>Class IV</td>
<td>175 (38.5)</td>
<td>42 (42.9)</td>
<td>133 (37.3)</td>
</tr>
<tr>
<td>Cardiac risk factors</td>
<td>Previous smoker</td>
<td>95 (20.9)</td>
<td>20 (20.4)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>4 (0.9)</td>
<td>0</td>
<td>4 (1.1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>344 (75.6)</td>
<td>79 (80.6)</td>
<td>265 (74.2)</td>
</tr>
<tr>
<td>Diabetes melitus</td>
<td>136 (29.9)</td>
<td>28 (28.6)</td>
<td>108 (30.3)</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>295 (64.8)</td>
<td>68 (69.4)</td>
<td>227 (63.6)</td>
</tr>
<tr>
<td>STS score (%)</td>
<td>10 (4.7)</td>
<td>10 (4.8)</td>
<td>11 ± (4.5)</td>
</tr>
</tbody>
</table>

Continuous values are median (IQR); categorical values are \( n \) (%).

DISCUSSION

Despite new endovascular advances, open surgical repair still remains the gold standard in the treatment of dilated proximal aorta. A small number of case reports have described endovascular methods to treat ascending aortopathy [5–7], but no specific endovascular device is currently available for such application. In contrast to surgical AVR in patients undergoing the TAVI procedure, concomitant ascending aortic intervention is not feasible. To date, it remains unknown whether endovascular manipulation in the vulnerable dilatated proximal aorta is safe and what the fate of the untreated dilatated ascending aorta is in patients who undergo TAVI.

This study is the first evaluation of TAVI procedure results and safety in patients with ascending aortic dilatation. The following points of this investigation will be discussed:

1. Ascending aortic dilatation is diagnosed in almost one-fourth of patients treated with TAVI.
2. Patients with dilated ascending aorta undergoing the TAVI procedure are at low risk of intraprocedural adverse aortic events.
3. Both in-hospital mortality and mid-term survival after TAVI are not affected by the presence of ascending aortic dilatation.

Ascending aortic dilatation is a common aortopathy with an incidence rate between 20 and 25% among patients with aortic...
steno	[8-10]. The results of this study reveal that there is a similar incidence (22%) of ascending aortic dilatation in TAVI patients. The presented TAVI cohort is on average 20 years older and has multiple comorbidities compared with open AVR patients [11]; thus, a 22% incidence rate of ascending dilatation appears to be relative low. It may result from the fact that some of the patients with aortic valve stenosis (AS) could have been operated on at an earlier age due to concomitant ascending aortic aneur
ysm when their risk spectrum allowed open surgery. Additionally, some older patients might die due to aortic dissection or rupture. Its incidence remains unknown since there are no autopsy reports on sudden death reasons in older patients.

An increasing number of clinical and basic science studies focus on the ascending aortic remodelling in the settings of AS. Recently, histological analysis demonstrated a poorer cohesion of the aortic wall in patients with a post-stenotic dilated ascending aortopathy (4.0–4.9 cm) than in those with normal aorta [9]. Furthermore, in the same study [9], there was no difference between the aortic wall cohesion in dilated aortas and aortic aneurysms (>4.9 cm). The authors postulated that patients with aortic dilatation and aneurysm have a comparable risk of aortic dissection. Another group demonstrated biomolecular changes in the ascending aorta in patients with AS at the time of AVR surgery [12]. Smooth muscle cell apoptosis correlated with aortic dimensions, and there was reduced fibrillar collagen in the setting of aortic dilatation. These findings confirm the structural changes in post-stenotic dilated aortas and add support to follow the guidelines [1] and replace the ascending aorta when its diameter is >4.5 cm in patients undergoing open AVR surgery. However, in the current era of aortic surgery with very low operative mortality and great spectrum of non-invasive diagnostic tools, the recommendation for concomitant ascending replacement remains under on-going debate. For instance, recently published clinical reports from high-volume centres reported a very low risk of late aortic events (< 2%) in long-term observational studies of patients after AVR surgery with unreplaced ascending aortic dilatation [13, 14], so that those authors suggested rather a conservative treatment strategy of the ascending aorta at the time of AVR surgery. To date, there are no published results on untreated dilated ascending aorta in patients who underwent TAVI.

The results of our study demonstrate a very low (1%) risk of intraprocedural adverse aortic events in spite of the presence of dilated ascending aorta. During the last three decades, improvement in endovascular guidewire techniques has significantly decreased dramatic complications associated with endovascular procedures even in a vulnerable dilated proximal aorta. In this study, we have demonstrated that improved endovascular manipulations permit a safe TAVI procedure via trans-femoral and trans-apical access not only in the settings of mildly and moderately dilated aorta, but also in 2 patients with aortic aneurysm with a diameter of 5.5 cm and greater. Furthermore, in patients with ascending dilation unsuitable for supra-annularly positioned self-expandable aortic valve prostheses such as the Medtronic CoreValve device, which is anatomically dependent on the ascending aortic dimension because it extends to the ascending aorta to provide coaxial alignment, intraannular implantation of balloon-expandable Edwards Sapien prosthesis can be safely performed. Several studies have evaluated the natural history of ascending aortic dilatation after open AVR surgery. Progressive dilatation of the ascending aorta has been reported in patients with bicuspid aortic valve [15]. However, in the same study, open AVR prevented further aortic dilatation in patients with tricuspid aortic valve. Other investigators demonstrated an increase in diameter of >0.3 cm in only 27 of 185 (15%) patients (follow-up 30 ± 23 months) with no patients who dilated beyond 5.5 cm [16]. Although the TAVI patient population is a highly selected group with limited comparison with the open AVR population, our findings showed no increase in the diameter of proximal ascending aorta measured by TTE after the TAVI procedure at a median follow-up of 14 months. One and a half years after the TAVI procedure, survival curves diverge showing superior survival among patients with dilated ascending aorta. However, due to small number of patients with dilated ascending aorta, this difference did not reach statistical significance.

This study is limited by several factors. Statistical analysis of risk factors for adverse aortic events could not be performed due to low number of these incidents. The cut-off values of mild (4.0–4.4 cm) and moderate aortic dilatation (4.5–5.0 cm) are arbitrary values. Furthermore, the change in ascending aortic diameter in follow-up must be interpreted with caution, since this analysis was performed according to TTE results, which enable assessment of only the very proximal part of the ascending aorta. Last, we were not able to define the reason for follow-up mortality in the majority of patients, since none of them underwent autopsy and the interview with family members or general practitioners gave us only a plausible cause of death in several cases. Therefore, our study provides information on procedural safety, but is less powerful regarding the long-term outcome in patients with dilated ascending aorta.

CONCLUSIONS

In current high-risk AS patients classified for the TAVI procedure who have accompanying ascending aortic dilatation (4.0–5.0 cm), TAVI can be performed safely with a very low intraprocedural risk of adverse aortic events. The concomitant ascending aortic dilatation does not affect the mid-term survival in the TAVI population. However, caution should be advised when in the future, one extrapolates these results to younger patients or patients with aortic valve insufficiency, bicuspid aortic valve or other risk factors for poorer quality of the ascending aorta.

Conflict of interest: Howard C. Herrmann is consultant of Edwards Lifesciences.

REFERENCES


APPENDIX. CONFERENCE DISCUSSION

Dr G. Weiss (Vienna, Austria): Your results support the treatment philosophy of leaving the dilated aorta untouched in elderly patients with severe comorbidities and elevated STS scores undergoing TAVI procedures. I have two questions relating to your study protocol and one more question regarding your personal perspective on future patients undergoing TAVI procedures with concomitant aortic dilatation.

The first question addresses the access. In your study, the transfemoral access for TAVI was more common in patients with a dilated ascending aorta. Which criteria were relevant in choosing a transfemoral approach instead of a transapical approach, and did the diameter of the ascending aorta influence your decision for the access? The second question addresses the mortality. Do you have any information regarding aortic-related death rate during hospital stay and follow-up? And the last question. Considering that TAVI procedures will probably gain more importance in the future, and that the techniques will not only be reserved for elderly patients who are unfit for conventional surgery but may also be applicable in younger patients, based on your investigation, do you think that it is justified to extrapolate your results to the younger patient population and leave a dilated aorta untreated? What is your opinion?

Dr Rylski: The diameter of the ascending aorta did not influence our decision on the access for the TAVI procedure. The one factor that influenced the access was calcification of the femoral or iliac arteries. Concerning the second question, the in-hospital mortality rate was low. The reason for death after discharge remains unknown. We tried to figure out the reason for the later mortality; we contacted the families, but in most cases we were not able to say whether the patient died due to dissection. Regarding your last question, I think our results should not be extrapolated to the younger population of patients. Nowadays TAVI is an option only for those who are medically treated and are not candidates for the open procedure. We are now working on a new device which would enable both a transcatheter aortic valve implantation and ascending aortic repair, but this device is not yet available. I do not think that TAVI in a young patient with an ascending aortic aneurysm is a good idea. The follow-up was too short to draw the conclusion that there is no growth of the ascending aorta after TAVI.

Dr P. Deleuze (Le Plessis Robinson, France): In your daily experience do you favour a certain type of TAVI device in case of aortic dilatation?

Dr Rylski: We use the Edwards balloon-expandable valves in all of our patients in Philadelphia. There are valves which are contraindicated in the case of an ascending aortic diameter over 4.5 cm, such as the self-expandable valves with the upper portion landing in the ascending aorta. Balloon-expandable valves can be safely implanted in patients with ascending aortic dilatation.

Dr T. Modine (Lille, France): Use of the self-expandable valve is not definitely contraindicated. It is an option to observe with caution. I have a couple of questions. I guess that this dilatation that you are talking about is post-stenotic dilatation?

Dr Rylski: Correct.

Dr Modine: So it is a completely different pathology to degenerative disease?

Dr Rylski: Yes.

Dr Modine: So why do you think aortic dilatation could be a limitation for TAVI? Does it influence the indication for TAVI or not? If it is due to aortic stenosis, but you cannot see the aortic stenosis, and the majority of your patients are between 4 and 5 cm, there is no indication for surgery in that case. So why do you think there could be an issue in patients who are candidates for TAVI?

Dr Rylski: Manipulation in the ascending aorta using catheter or wires in patients with an ascending aneurysm carries a risk of acute dissection. If we have a patient with a large ascending aorta and he or she is 80 years old but is still a good candidate for open surgery, we would think about the open surgery, because manipulating in the dilated ascending aorta may be not such a good idea in these circumstances.

Dr Modine: In such patients we had only one case where we had to consider a different access. I think we can consider the indication for wrapping. You can do a direct aortic access, reducing the risk of injury to the aorta via a mini sternotomy and covering all the aorta. Thus you can treat both problems, especially if you use the SAPIEN valve. We have done this and it may offer an alternative choice of access.