Impact of diverse aortic pathologies on outcomes after transapical transcatheter aortic valve replacement

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Abstract
Objectives: Some patients who undergo transcatheter aortic valve replacement (TAVR) have a concomitant diverse aortic pathologies (AP). They are usually considered high-risk candidates for the procedure and require further assessment to determine the best vascular approach. The impact of these AP on TAVR is not well known as the information is scarce. We aimed to evaluate midterm clinical impact of different AP after transapical (TA)-TAVR.

Methods: Twenty patients with atherosclerotic/occluding aortic diseases (A/OAD) (porcelain aorta, Leriche Syndrome, penetrating aortic ulcer, and aortic thrombus), 24 patients with aortic morphologic diseases (AMD) (thoracic/abdominal aortic aneurysms, aortic kinking, aortic type B dissection, aortic elongation/tortuosity, and previous aortic intervention), and 11 patients with combined aortic diseases (CAD) underwent TA-TAVR treatment between January 2011 and November 2019 at our center. We conducted up to 5-years clinical follow-up.

Results: All patients were classified in the heart team as a high interventional risk. The 30-day mortality and stroke were 5% and 10% in the A/OAD, 8.3% and 0% in the AMD, and 0% and 0% in the CAD, respectively. The median time of freedom from a composite of death and cardio-cerebral adverse events was 22.1 months [95% confidence interval [CI]: 9.9–34.3] in A/OAD versus 34.3 months [95% CI: 15.6–53] in AMD versus 17 months [95% CI: 0–39.4] in CAD; p = .525. We registered neither procedural aortic injury nor aortic syndrome at follow-up. The moderate/severe paravalvular leakage rates were 5%, 0% and 0% in the A/OAD, AMD and CAD, respectively.

Conclusion: Independent of underlying AP, the TA-TAVR is a safe method and shows very promising early and midterm outcomes in patients with various AP.

Keywords
aorta no-touch, diverse aortic pathologies, TAVR
1 | INTRODUCTION

Aortic pathologies (AP) are usual finding in the elderly patients with severe aortic valve stenosis who are transcatheter aortic valve replacement (TAVR)-candidates. Generally, only few studies exist reporting on TAVR with AP. Except studies with regard to TAVR in patients with porcelain aorta and dilated aorta, there are no studies highlighting clinical outcomes of patients with various AP undergoing TAVR. As through the first preferred transcatheter route (transfemoral approach [TF]) not a whole wide spectrum of AP is feasible, we sought to evaluate early and midterm clinical outcomes after transapical (TA)-TAVR in specific groups of AP inclusive a group of patients with combined AP, where the TF approach is absolutely contraindicated.

2 | METHODS

This study was conducted to evaluate the midterm outcomes in patients with diverse AP after TA-TAVR. Between January 2011 and November 2019 a total of consecutive 1157 patients with symptomatic severe aortic stenosis underwent TAVR at our heart center (Ruhr-University Hospital Bergmannsheil, Bochum, Germany). The patients with concomitant AP were considered in the heart team as not eligible for the TF approach and underwent TA-TAVR. The study population comprised 20 patients with atherosclerotic/occluding aortic diseases (A/OAD) (porcelain aorta, Leriche Syndrome, penetrating aortic ulcer, and aortic thrombus), 24 patients with aortic morphologic diseases (AMD) (thoracic/abdominal aortic aneurysms, aortic kinking, aortic type B dissection, aortic elongation/tortuosity, and previous aortic intervention), and 11 patients with combined aortic diseases (CAD) consecutive patients receiving the TA-TAVR treatment at our center. The appropriate size of the valve and the diagnosis of the AP was determined based on computed tomographic findings. AP were defined according to the European Society of Cardiology guidelines and Valve Academic Research Consortium-2 (VARC-2) definitions. All endpoint-related outcomes were adjudicated according to the definitions provided by the VARC-2. We collected the data from hospital records, through telephone interviews with patients and referring physicians. The cause of death was obtained from the last physician involved in the patients’ treatment. The clinical follow-up was complete in 100%. The mean follow-up time was 21.3 months. The early follow-up timing was defined as the first 30 postoperative days. The midterm follow-up timing was defined as a time interval from the second postoperative month up to 5 years. The primary endpoints of the study were the 30-day and midterm mortality, the 30-day and midterm cardio-cerebral adverse events, procedural aortic injury, and 30-day and midterm aortic syndrome. The secondary endpoints were the 30-day severe/moderate paravalvular leakage (PVL) rate and the 30-day permanent pacemaker implantation (PPI) rate.

All patients gave informed consent for data collection and the approval from Ethics Committee was obtained (Reg. No. 18-6339).

2.1 | Operative technique

Patients were carefully screened with regard not only to the native aortic valve but also individual aortic pathologies such as aortic calcification patterns, calcification burden and morphologic changes of the aorta, focusing on the pathologically changed segments of the aorta, considering the presence and position of previous surgical or endovascular implanted grafts or stents. All cases underwent TA-TAVR under general anesthesia. We modified the procedure if necessary to ensure an “aorta no-touch technique” as appropriate, depending on aortic pathology and the affected segment of the aorta. In cases with pathologies of the descending aorta, we waived insertion of a femoral artery wire and 6-French sheath. For angiographic visualization and for “landmarking” of the aortic valve, we deployed a “safety net” and a line (pigtail) through the axillary artery. In some cases with critical alteration of the aortic arch or ascending aorta, we inserted the pigtail into the left ventricle through the ventricle wall and introduced it into the ascending aorta. Before completing the valve expansion, we returned the pigtail into the left ventricle. We positioned a stiff guidewire across the aortic arch and into the descending aorta with the help of a right Judkins catheter. We did not perform balloon valvuloplasty as a mandatory step.

2.2 | Statistics

Distributions of quantitative variables are described as means (±standard deviation) and compared with the use of the Kruskal-Wallis test. Qualitative variables are summarized by count and percentage and compared with the use of the χ² test or Fisher’s exact test. The Kaplan-Meier method was used to calculate the median survival time and the group comparisons were made with the log-rank test. Data were managed with the SPSS statistical package (IBM SPSS Statistics for Windows, Version 23.0.0.2: IBM Corp.). A two-sided p value of less than .05 was considered to indicate statistical significance. No adjustment for multiple testing was performed. All the analyses were considered to be exploratory.

3 | RESULTS

3.1 | Baseline characteristics

Table 1 shows comparable preoperative data of our study cohorts. The STS-Score was high and without difference between the three study groups. The patients with A/OAD were significantly younger (72.2 ± 8.2 years). The coronary artery disease was represented with very high incidence (up to 80%), whereas...
The severe peripheral artery disease was very common disease in all the study groups with a range 50%–60%.

### 3.2 | The diversity of aortic pathologies

The A/OAD group encompasses four different AP (porcelain aorta, Leriche Syndrome, penetrating aortic ulcer, and aortic thrombus), whereas the AMD group six different AP (thoracic/abdominal aortic aneurysms, aortic kinking, aortic type B dissection, aortic elongation/tortuosity, and previous aortic intervention). Eleven patients exhibited more than one AP (CAD) (Table 2). Patients with CAD were classified in our heart team as absolute contraindicated for the TF approach. The Figure 1 shows representative bi-planar and three-dimensional reconstructed computed tomography imaging materials.

### 3.3 | Procedural characteristics

All valves were implanted successfully without procedural complications or aortic injury. There was no intraprocedural death. We were able to implant five different types of transcatheter heart valves. There were no differences in the implanted valve type in the study cohorts. Postdilation was only in the A/OAD group necessary ($p = .012$) (Table 3).

### 3.4 | Thirty-day, midterm clinical outcomes, and survival

The 30-day all-cause mortality was 5%, 8.3%, and 0% in the A/OAD, AMD, and CAD, respectively. The all-stroke rate was 10% and 0%, and 0% in the A/OAD, AMD, and CAD, respectively. We registered 5%, 0%, and 0% moderate/severe PVL and 15%, 4.7%, and 9.1% new PPI in the A/OAD, AMD, and CAD, respectively. An early or midterm aortic syndrome scenario did not occur. At midterm, we registered one patient with endocarditis in the AMD group and one patient in the A/OAD group. A valve thrombosis was not observed (Table 4).

Figure 2 shows the Kaplan–Meier survival curves of all three groups of patients. The log-rank test showed no significant differences in median survival time (months) between three study groups; 29 (95% confidence interval [CI]: 17.4–40.5) in A/OAD versus 34.3 (95% CI: 15.4–53.2) in AMD versus 17 months (95% CI: 0–39.4) in CAD; $p = .910$. The median time of freedom from a composite of death and cardio-cerebral adverse events was 22.1 months (95% CI: 9.9–34.3) in A/OAD versus 34.3 months (95% CI: 15.6–53) in AMD versus 17 months (95% CI: 0–39.4) in CAD; $p = .525$ (Figure 3).

### 4 | DISCUSSION

The key findings of the study are: (1) AP seems to be attribute of high-risk patients and not only a mark of usual TAVR patients; (2) The TA-TAVR as an “aorta no touch”-technique has been

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**TABLE 1** Baseline characteristics

|          | CAD | AMD | A/OAD |
|----------|-----|-----|-------|
| N        | 11  | 24  | 20    |
| n (%)    |     |     |       |
| Age, years | 81 ± 7.7 | 82.5 ± 6.3 | 72.2 ± 8.2 |
| Male sex | 7 (63.6) | 19 (79.2) | 13 (65) |
| STS-Score (%) | 7.1 ± 3.7 | 6.6 ± 3.1 | 6.3 ± 4 |
| Hypertension | 8 (72.7) | 20 (83.3) | 20 (100) |
| Diabetes mellitus | 3 (27.3) | 11 (45.8) | 3 (15) |
| Coronary artery disease | 9 (81.8) | 16 (66.7) | 16 (80) |
| PTCA/PCI | 4 (36.4) | 10 (41.7) | 7 (35) |
| LVEF (%) | 50.4 ± 9.8 | 48.2 ± 11.4 | 54.2 ± 12.1 |
| Peripheral artery disease | 6 (54.5) | 12 (50) | 12 (60) |
| Previous stroke | 3 (27.3) | 4 (16.7) | 5 (25) |
| COPD | 3 (27.3) | 5 (20.8) | 10 (50) |
| Atrial fibrillation | 4 (36.4) | 12 (50) | 8 (40) |
| Mitral regurgitation ≥ 2 | 3 (27.3) | 5 (20.8) | 6 (30) |
| Creatinine mg/dL | 1.4 ± 0.7 | 1.3 ± 0.5 | 1.4 ± 0.7 |

**TABLE 2** Eleven patients with combined aortic diseases

| Combined aortic diseases (CAD) | 11 patients |
|--------------------------------|-------------|
| Patient No.1 | Descending aneurysm + Kinking + Aortic thrombus |
| Patient No.2 | Porcelain aorta + Descending aneurysm |
| Patient No.3 | Descending aneurysm + Tortuosity |
| Patient No.4 | Ascending aneurysm + Aortic thrombus |
| Patient No.5 | Aortic ulcer + Ascending aneurysm + Descending aneurysm |
| Patient No.6 | Previous aortic intervention + Type B aortic dissection |
| Patient No.7 | Previous aortic intervention + Descending aneurysm + Aortic thrombus |
| Patient No.8 | Previous aortic intervention + Descending aneurysm |
| Patient No.9 | Ascending aneurysm + Descending aneurysm + Kinking |
| Patient No.10 | Porcelain aorta + Previous aortic intervention |
| Patient No.11 | Porcelain aorta + Ascending aneurysm + Kinking |
shown as a safe method in patients with diverse AP, without aortic injury and aortic syndrome on follow-up; and (3) the diversity of aortic pathologies has no impact on survival probability and freedom from a composite of death and cardio-cerebral adverse events after TAVR for aortic stenosis.

It is well known that parallel to the aging process of the population, the AP become frequently, so these are attendant characteristics of TAVR candidates. Interestingly, despite the high frequency of AP and the extensive research in the recent years, there are very poorly investigations which focus TAVR procedures in patients with AP. Historically, these patients have been considered as a high interventional risk, so for instance they failed under exclusion criteria in very relevant, landmark trials. The intraprocedural aortic injury are fatal complications. The most affected patients are they with attendant AP. The case reports in the literature reporting aortic injury during TAVR were significant for the presence of severe calcified aortic segments or kinked aorta and were performed through the TF approach. In all cases the outcome was fatal. All these facts illustrate that AP power and remain to be high interventional risk factor and indicate to consider an alternative "aorta-no-invasive" approach. The TA-TAVR have been shown in our study as a safe method without aortic injury. This have to be addressed mainly to the "aorta no-touch technique." We were able to show that TA-TAVR
can be performed in patients with AP with very promising early outcomes. However, the novelty insight is that no aortic syndrome occurred on follow-up after correction of the aortic valve stenosis. Furthermore, we found comparable survival probability in our cohorts independently from aortic pathology. It may indicate that there are no specific AP who would not benefit from TA-TAVR procedure or are more prone to TA-TAVR treatment. In the present time—because of numerous technological advances and design factors in compatibility with matured interventional skills and experience gained in the "TF field”—speculation is increasingly arising to forecast that up to 95% or higher portion of patients will be eligible for the TF approach. But is there any limit? TF-TAVR in some pathologies such as chronic Type B-Dissection or aortic thrombus is absolutely contraindicated. Remarkable is the feasibility of the TA-TAVR in patients with combined aortic diseases. In this group every patient exhibited at least two aortic pathologies. These patients were classified by the heart team as to be absolutely contraindicated for the TF approach. Is the TA-TAVR a singular option for treatment of such patients? Here we described the outcomes of the TA-TAVR of a very specific TAVR population since the early TAVR era using second-generation valves, namely Jena Valve or SAPIEN XT, as well. We achieved very promising results. In contrast, the most recent studies of other nontransfemoral approaches in usual TAVR populations using the most recently developed valves with very fine delivery systems, such as SAPIEN 3 and SAPIEN 3 Ultra, have shown mortality rates ranging between 4.3\% and 5.2\%, and stroke rates between 4.2\% and 7.4\%. Even though our cohort does not necessarily reflect the broader population of patients who cannot undergo other non-TF approaches, the interventional risk with other nontransfemoral approaches in patients with diverse AP remains high, as recent studies have reported considerably high rates of vascular injuries (between 4.8\% and 6.9\%). Lastly, the invasiveness of a procedure depends not only on whether it has been performed percutaneously. The TA approach represents an aorta no-touch technique and hence should be considered as the most minimally invasive technique for TAVR in patients with diverse AP for as long as evidence on other approaches is lacking.

After definitive establishment of the TF approach as the first line transcatheter approach (European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS) guidelines 2017 for the aortic valve treatment\textsuperscript{(13)}, the research on TA approach has been almost locked down. The most of the previous studies on TA approach report not necessarily of specific TAVR population like our study (aortic pathologies), but rather of "usual TAVR population."
FIGURE 2 Kaplan–Meier survival function curves for the three study groups. AMD, aortic morphologic diseases; A/OAD, atherosclerotic/occluding aortic diseases; CAD, combined aortic diseases.

FIGURE 3 Kaplan–Meier curves: Freedom from death, cardiac and cerebrovascular adverse events for the three study groups. AMD, aortic morphologic diseases; A/OAD, atherosclerotic/occluding aortic diseases; CAD, combined aortic diseases.
The new message of our study is that the TA approach still remains valuable method for patients where the utility of the first preferred TF approach is highly questionable or contraindicated.

5 | CONCLUSION

Independent of the extent and the types of AP in the TAVR population, we saw a safe methodology and very promising and reproducible clinical outcomes for a long period of time utilizing TA-TAVR in a high interventional and surgical risk patient collective.

6 | LIMITATION

This study is a retrospective and nonrandomized single-center study with limited number of patients.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Dritan Useini contributed to the conception, design, data collection, acquisition, analysis, interpretation of data, drafting, and revising of the work. Blerta Beluli contributed to the conception, design, and revising of the work. Hildegard Christ contributed to the statistics, analysis, and interpretation of data and revision. Justus Strauch contributed substantially to the design and intellectual revision of the work. All authors approve this final version for publication and agree to be accountable for all aspects of this study.

INSTITUTIONAL REVIEW BOARD APPROVAL

All patients provided informed consent for data collection, and approval for the study was obtained from the Ethics Committee of the Medical Faculty of the RUHR University, Bochum, Germany; Date: 19.10.2018; Reg. No. 18-6339.

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