Novel insights on outcome in horizontal aorta with self-expandable new-generation transcatheter aortic valve replacement devices

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Abstract

Background: The impact of a horizontal aorta (HA) on adverse events (AE) following transcatheter aortic valve replacement (TAVR) is dealt controversially. Using new-generation self-expandable devices, we aimed to reevaluate an appropriate threshold of the aortic root angulation (ARA) in terms of HA and its impact on outcome.

Methods: The 466 consecutive patients, who underwent transfemoral TAVR with self-expandable new-generation devices, were analyzed. Patients were classified into cases with HA (ARA ≥ 51°; n = 225; 48%) and without HA (ARA <51°; n = 241; 52%). Primary endpoints were device success and 30-day mortality. Secondary endpoints were specific AE according to VARC-2 definitions.

Results: Contrast use (107.6 ± 50.1 vs. 94.1 ± 46.1 ml; p = .033) and radiation dose (3,176 [1,928–5,596] vs. 2,651 [1,643–4,394] Gy cm²; p = .016) were higher in HA. Primary device success was comparable (97.1 vs. 97.8%; p = .773). A 30-day mortality (3.3 vs. 0.4%; p = .038, plogrank = 0.025), stroke (7.1 vs. 2.7%; p = .033), and major vascular complications (MVASC) (6.6 vs. 2.7%; p = .050) were more frequent in HA. Pronounced calcification of the noncoronary cusp and left ventricular outflow tract, the condition of HA, as well as repositioning maneuvers were independent predictors for overall specific AE.

Conclusion: An HA above 51° is associated with an increased rate of stroke, MVASC, and 30-day mortality. Valve size and asymmetric calcification affect the incidence of repositioning maneuvers and subsequent VARC-2 AE, indicating that an HA—together with specific anatomic features—remains a crucial factor for TAVR-related outcome with self-expandable new-generation devices.

Abbreviations: AS, aortic stenosis; AR, aortic regurgitation; ARA, aortic root angulation; AU, Agatston units; HA, horizontal aorta; LCC, left coronary cusp; LVOT, left ventricular outflow tract; NCC, noncoronary cusp; MSCT, multislice computer tomography; RCC, right coronary cusp.

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1 | INTRODUCTION

Several improvements in transcatheter aortic valve replacement (TAVR) catapulted this treatment to the first-line strategy in symptomatic severe aortic stenosis (AS) at high, moderate, and even at low risk.\(^1,2\) In the past, a horizontal aorta (HA) was demonstrated to pose challenges during valve delivery of self-expandable TAVR prostheses with inherent adverse events (AE).\(^3-5\) Hitherto, HA was defined by an aortic root angulation (ARA) above 48° between the horizontal plane and the plane of the aortic annulus in coronal projection.\(^6\) Nevertheless, the threshold was adjusted in old-generation devices, and current studies on old and new-generation devices yielded controversial results questioning the impact of HA on procedural success and outcome.\(^6-9\) Therefore, we aimed to: (a) redefine the HA threshold using new-generation self-expandable devices, (b) evaluate the concomitant impact on the procedural success and 30-day outcome in a large cohort, and (c) clarify independent factors for specific AE including calcification distribution that have not been yet considered in detail.

2 | METHODS

2.1 | Study population

We retrospectively enrolled 466 consecutive patients with severe symptomatic AS, who underwent transfemoral TAVR at our heart center with self-expandable devices (Corevalve Evolut R and Pro; Medtronic, Minneapolis, MN) between December 2014 and May 2019. Patients were further separated into cases with (ARA ≥ 51°; n = 225; 48.3%) and without HA (ARA <51°; n = 241; 51.2%; please see below). This threshold was used from a median calculation and further calculations mentioned also in the statistic section. All procedures were performed according to current guidelines and under local anesthesia. Patients with a bicuspid aortic valve, prior aortic valve replacement, or insufficient multislice computer tomography (MSCT) data were excluded to guarantee comparability.

All patients provided written informed consent for TAVR and the use of clinical, procedural, and follow-up data for research. The study procedures were in accordance with the Declaration of Helsinki, and the institutional Ethics Committee of the Heinrich-Heine University approved the study protocol (4080). The study is registered at clinical trials (NCT01805739).

2.2 | Study endpoints

The primary endpoint was defined as device success and 30-day mortality. Secondary endpoints were defined as occurrence of specific AE according to VARC-2 definitions.\(^10\)

2.3 | Statistical analysis

The collected data included patient characteristics and imaging findings. Continuous data were described by mean and SD, median or upper and lower 95% confidence interval (CI), interquartile ranges, and categorical variables by frequencies and percentages. Statistical significance was analyzed with the use of the two-sided Student’s t test for continuous variables and the Fisher’s exact test for categorical variable, as appropriate. The influence of covariates on specific AE was tested by univariate and multivariate logistic regression analysis. Covariates associated with AE in the univariate analysis (p < .1) were entered into the multivariate model and stepwise backward elimination was used. Receiver-operating-characteristic curves were described as c-indices (area-under-the-curve [AUC]) with 95% CI. The optimal cutoff values were defined by Youden’s index (YI), the point at which the value of “sensitivity + specificity − 1” was maximal. The data analysis was performed using the statistical software SPSS (version 22.0, SPSS Inc., Chicago, IL) and GraphPad Prism (version 8.0, GraphPad Software, San Diego, CA). All statistical tests were two-tailed, and a value of p < .05 was considered statistically significant.

2.4 | Three-dimensional image analysis of MSCT

MSCT images were transferred to a dedicated workstation for three-dimensional volume-rendered reconstruction (3mensio Structural Heart, Pie Medical Imaging BV, Maastricht, The Netherlands) after performance according to TAVR-related standardized recommendations for CT image acquisition.\(^11\) Dimensions were determined with the use of workstation tools. The total aortic valve calcification (AVC), detailed leaflet calcification, and calcium amount of the upper left ventricular outflow tract (LVOT) was expressed as recalculated Agatston units (AU). In general, upper and lower levels were defined according to the median and interquartile range. The ARA was defined as the angle between the horizontal plane and the plane of the aortic annulus, calculated from a coronal projection. While the previously described threshold (ARA ≥ 48°) for lower device success was established in old-generation devices, in this study, a new overall median resulting in an ARA ≥ 51° was used to define HA. The identification of an optimal cutoff value by determination of the YI failed due to seldom events concerning device success (YI = 0.24; c-index 0.56, 95% CI 0.37–0.57; p = .464) and other multifactorial influenced events. For further details, please see Figure 1. However, all determined cutoff values for ARA combined with AE varied between 49 and 57°, by majority located at 51°, strengthen the hypothesis of a critical ARA above 48° using new-generation devices.

KEYWORDS
aortic stenosis, femoral, imaging modalities
3 | RESULTS

3.1 | Baseline characteristics

In general, HA (as median and mean ARA ≥ 51) was more common in obese patients (ARA ≥ 51: BMI 27.6 ± 5.4 vs. 26.0 ± 4.6; p = .001). The logistic EuroScore I was higher (ARA ≥ 51: 27.4 ± 15.8 vs. 24.6 ± 14.8; p = .045), probably linked to a higher systolic pulmonary artery pressure (ARA ≥ 51: 34.4 ± 25.7 vs. 29.5 ± 23.8 mmHg; p = .033). All others clinical and functional characteristics did not significantly differ in patients with and without HA. Mean ARA was higher in HA patients, accompanied by a larger aortic root anatomy. Further baseline information is displayed in Supplementary files Table S1.

3.2 | General procedurals in HA

Procedural details and clinical outcomes are displayed in Table 1. Four hundred and sixty-six patients were treated with transfemoral TAVR using by majority the self-expandable Corevalve Evolut R (n = 430; 92.3%) or Corevalve Evolut Pro (n = 36; 7.7%). Contrast use (ARA ≥ 51: 107.6 ± 50.1 vs. 94.1 ± 46.1; p = .033) and radiation dose (ARA ≥ 51: 3.176 [1.928–5.596] vs. 2.651 [1.643–4.394] Gyxcm²; p = .016) was elevated in HA. Predilatation and postdilatation maneuvers were similar between both groups, only repeated repositioning maneuvers were more frequently used in HA (ARA ≥ 51: 5.8 vs. 0.9%; p = .004).

3.3 | Primary outcome in HA

Primary device success was comparable in both cohorts and high as well between 97 and 98%. Intraprocedural complications were also similar in HA and none-HA. Interestingly, 30-day mortality was elevated in the HA cohort (ARA ≥ 51: 3.3 vs. 0.4%; p = .038, Plogrank = .025). The mean ARA in all deceased patients was high with an average of 54.3. With only nine deceased patients, no multivariate analysis concerning an ARA ≥ 51 (and other covariates) as independent predictors for mortality can be offered. The logistic EuroScore I was higher in deceased patients (31.0 ± 16.0 vs. 26.0 ± 14.4; p = .304) compared to the overall cohort but did not reach significance due to case numbers.

3.4 | Secondary outcome in HA

Besides 30-day mortality, several outcomes were attenuated by horizontal anatomy: Stroke (ARA ≥ 51: 7.1 vs. 2.7%; p = .033) and major vascular complications (MVASC) (ARA ≥ 51: 6.6 vs. 2.7%;
TABLE 1  Procedural and postprocedural outcome

| Procedural data                      | Overall (n = 466; 100%) | ARA < 51° (=none-HA) (n = 225; 48.3%) | ARA ≥ 51° (=HA) (n = 241; 51.2%) | p-Value |
|--------------------------------------|-------------------------|--------------------------------------|----------------------------------|---------|
| Valve sizes                          |                         |                                      |                                  |         |
| 23 mm                                | 7 (1.5)                 | 7 (3.1)                              | 0 (0.0)                          | .006*   |
| 26 mm                                | 152 (32.6)              | 85 (37.8)                            | 67 (27.8)                        | .023*   |
| 29 mm                                | 200 (42.9)              | 90 (40.0)                            | 110 (45.6)                       | .225    |
| 34 mm                                | 107 (23.0)              | 43 (19.1)                            | 64 (26.6)                        | .020*   |
| CoreValve Evolut R/CoreValve EvolutPRO | 430/36 (92.3/7.7)       | 200/25 (88.9/11.1)                   | 230/11 (95.4/4.6)                | .061    |
| Contrast, ml                         | 101.1 ± 48.6            | 94.1 ± 46.1                          | 107.6 ± 50.1                     | .003*   |
| Fluoroscopy time, min                | 18.2 (13.9–23.8)        | 18.0 (13.4–23.0)                     | 18.5 (14.7–24.2)                 | .303    |
| Dose area product, Gy × cm²          | 2,912 (1,791–4,811)     | 2,651 (1,643–4,394)                  | 3,176 (1,928–5,596)              | .016*   |
| Predilatation                        | 215 (46.2)              | 102 (55.3)                           | 113 (46.9)                       | .508    |
| Postdilatation                       | 54 (11.6)               | 23 (10.2)                            | 31 (12.9)                        | .388    |
| Resheath/recapture of valve          | 53 (11.4)               | 22 (9.8)                             | 31 (12.9)                        | .310    |
| Repeated resheath/recapture          | 16 (3.4)                | 2 (0.9)                              | 14 (5.8)                         | .004*   |
| Intraprocedural complications        |                         |                                      |                                  |         |
| Immediate stroke                     | 1 (0.2)                 | 1 (0.4)                              | 0 (0.0)                          | .483    |
| Aortic dissection                    | 0 (0.0)                 | 0 (0.0)                              | 0 (0.0)                          | 1.00    |
| Annulus rupture                      | 0 (0.0)                 | 0 (0.0)                              | 0 (0.0)                          | 1.00    |
| Coronary obstruction                 | 1 (0.2)                 | 0 (0.0)                              | 1 (0.4)                          | 1.00    |
| Peripheral vascular complications    | 39 (8.4)                | 15 (6.7)                             | 24 (10.0)                        | .242    |
| Valve embolization                   | 10 (2.1)                | 4 (1.8)                              | 6 (2.5)                          | .753    |
| Conversion to surgery                | 0 (0.0)                 | 0 (0.0)                              | 0 (0.0)                          | 1.00    |
| Need of second valve                 | 9 (1.9)                 | 3 (1.3)                              | 6 (2.5)                          | .506    |
| Tamponade                            | 0 (0.0)                 | 0 (0.0)                              | 0 (0.0)                          | 1.00    |
| AR > mild                            | 7 (1.7)                 | 1 (0.4)                              | 6 (2.5)                          | .287    |
| CPR                                  | 3 (0.6)                 | 1 (0.4)                              | 2 (0.8)                          | 1.00    |
| Procedural death                     | 2 (0.4)                 | 1 (0.4)                              | 1 (0.4)                          | 1.00    |
| Disturbances of heart rhythm         | 26 (5.6)                | 10 (4.4)                             | 16 (6.6)                         | .321    |
| Primary device success               | 454 (97.4)              | 220 (97.8)                           | 234 (97.1)                       | .773    |
| ARI                                  | 23.9 ± 7.9              | 23.0 ± 7.8                           | 24.7 ± 7.9                       | .026*   |

Postprocedural outcome

| CPR                                  | 10 (2.1)                | 2 (0.9)                              | 8 (3.3)                          | .108    |
| 30-day mortality                     | 9 (2.0)                 | 1 (0.4)                              | 8 (3.3)                          | .038*   |
| Bleeding complications               |                         |                                      |                                  |         |
| Disabling                            | 5 (1.1)                 | 0 (0.0)                              | 5 (2.1)                          | .062    |
| Major                               | 24 (5.2)                | 10 (4.4)                             | 14 (5.8)                         | .537    |
| MVASC                                | 22 (4.7)                | 6 (2.7)                              | 16 (6.6)                         | .050    |
| Stroke                               | 23 (4.9)                | 6 (2.7)                              | 17 (7.1)                         | .033*   |
| Sepsis                               | 4 (0.9)                 | 1 (0.4)                              | 3 (1.2)                          | .624    |
| AKI I–III                            | 61 (10.3)               | 19 (8.4)                             | 33 (13.8)                        | .279    |
| New RRT                              | 10 (2.1)                | 2 (0.9)                              | 8 (3.3)                          | .108    |
| New PPI                              | 74 (15.9)               | 32 (14.3)                            | 42 (17.4)                        | .377    |
| In-hospital stay, days               | 10.0 (7.0–15.3)         | 9.0 (7.0–14.0)                       | 11.0 (8.0–18.0)                  | <.0001* |
| ICU stay, days                       | 2.0 (1.0–4.0)           | 2.0 (1.0–3.0)                        | 2.0 (1.0–4.0)                    | .006*   |
were more frequent in HA, accompanied by prolonged in-hospital and intensive care unit (ICU) stay. Intraprocedurally, immediate overall "peripheral vascular complications" were higher (ARA ≥ 51°: 10.0 vs. 6.7%; p = .050), while only two-thirds of them were reported as "MVASC" according to VARC-2 criteria and therefore lower. Concordantly, immediate intraprocedural stroke was lower than in the hospital course due to periprocedural and late neurological events. All other outcomes were similar. To evaluate the impact on frequently described and immediate analyzed AE in the context of HA, multivariate analysis was established on a cohort of 119 patients with any of the following specific AE: absence of device success, stroke, need for permanent pacemaker implantation (PPI), and MVASC. Establishment of a composite endpoint for multivariate analysis failed due to combined event numbers (at least two combined endpoints, n = 11). Overall specific AE occurred more often in HA, even when including balanced events like absence of device success or PPI (ARA ≥ 51°: 30.7 vs. 20.0%; p = .011).

The potential identification of an optimal valve-size-dependent cutoff value for specific AE by the determination of the YI failed in most of the valve sizes except from the 26 mm device (YI = 0.33; ARA > 52°; c-index 0.62, 95% CI 0.52–0.73; p = .038). For further details, please see Supplemental Figure S1. The distribution of specific AE was similar between the several valve sizes and device types. Please see Figure 2a.

Linear parameters were further categorized into lower and upper median thresholds for binary multivariate analysis. Unadjusted univariate analysis depicted several confounders, summarized in Table 2. 

### Table 1 (Continued)

| Overall (n = 466; 100%) | ARA < 51° (=none-HA)(n = 225; 48.3%) | ARA ≥ 51° (=HA)(n = 241; 51.2%) | p-Value |
|-------------------------|--------------------------------------|----------------------------------|---------|
| Specific AE (absence of device success, stroke, PPI, major vasc. complications) | 119 (25.5) | 45 (20.0) | 74 (30.0) | .011* |
| Composite endpoints (at least 2 from above) | 11 (2.4) | 5 (2.2) | 7 (4.2) | .547 |

Note: Values are mean ± SD, median ± interquartile range, or n (%).

Abbreviations: AE, adverse events; AKI, acute kidney injury; AR, aortic regurgitation; ARA, aortic root angulation; ARI, aortic regurgitation index; CPR, cardiopulmonary resuscitation; HA, horizontal aorta; ICU, intensive care unit; MVASC, major vascular complications; PPI, permanent pacemaker therapy; RRT, renal replacement therapy.

![Figure 2](https://image.wileyonlinelibrary.com/doi/figure/10.1002/hep.30788/fig-2)
A table with data from a scientific paper is shown. The table is titled "Univariate and multivariate regression analysis of specific AE and combined ROC" and contains data on various factors associated with adverse events (AE) and their statistical significance. The table includes columns for univariate analysis, multivariate analysis, and combined ROC analysis, with OR (95% CI) and p-values for different factors such as aortic root angulation (ARA), aortic valve calcification (AVC), noncoronary cusp (NCC), and more.

The text surrounding the table mentions that multivariate regression analysis depicted pronounced calcification of the noncoronary cusp (NCC; OR 1.72 [1.07–2.07], p = .014*), and resheath/recapture maneuvers (OR 2.14 [1.13–4.07], p = .019*) as independent predictors for overall specific AE (please see also Figure 2b). C-statistic revealed a mediocre association of the combined aforementioned parameters with specific AE (Figure 2c; Table 2: AUC = 0.63; 95% CI = 0.57–0.69; p < .0001).

The need of postprocedural PPI was significantly enhanced in HA using a 34 mm device size (Figure 3b; 34 mm: ARA ≥ 51°: 35.7 vs. 21.9%; p = .009). However, the large system failed to be a dependent or independent predictor for PPI, whereas a valve size of 26 mm was highly preventive for PPI need. Other risk factors showed no association.

Distribution of MVASC was similar between the several valve sizes (Figure 3c). MVASC were independently linked to female sex, a pronounced AVC ≥ 1,462 AU, and an ARA ≥ 51°. C-statistic revealed a mediocre association of the aforementioned parameters with MVASC (AUC = 0.71; 95% CI = 0.59–0.83; p = .001). Subanalysis of failing device success was not established due to small sample size (12 events) but is somehow reflected by overall specific AE analysis. Comparison of such rare events like absence of device success and composite endpoints revealed a threefold enhanced risk for the several events.

The text also notes that abbreviations for AE, adverse events; ARA, aortic root angulation; AVC, aortic valve calcification; AU, Agatston units; LVOT, left ventricular outflow tract; NCC, noncoronary cusp; PPI, permanent pacemaker therapy; ROC, receiver-operating-characteristic; RRT, renal replacement therapy.

### Table 2: Univariate and multivariate regression analysis of specific AE and combined ROC

|                     | Univariate analysis | Multivariate analysis | Combined ROC (only independent predictors) |
|---------------------|---------------------|-----------------------|---------------------------------------------|
|                     | OR (95% CI)         | p -Value              | AUC 95% CI p -Value                         |
| **A) Any specific AE** |                     |                       |                                             |
| ARA ≥ 51°           | 1.61 (1.06–2.46)    | .026*                 | 0.63 0.57–0.69 <.0001*                       |
| NCC ≥ 589 AU        | 1.86 (1.21–2.84)    | .004*                 |                                             |
| LVOT calcification >36 AU | 1.69 (1.11–2.58) | .015*                 |                                             |
| LVOT diameter >23.5 mm | 1.51 (0.98–2.34)   | .064                  |                                             |
| Valve size 26 mm    | 0.59 (0.43–0.94)    | .027*                 |                                             |
| ARA (°)             | 1.77 (1.16–2.71)    | .008*                 | 1.77 (1.12–2.80) .014*                      |
| Resheath/recapture of valve | 2.11 (1.16–3.83) | .014*                 | 2.14 (1.13–4.06) .019*                      |
| **B) Stroke**       |                     |                       |                                             |
| Porcelain aorta     | 3.05 (1.07–8.68)    | .037*                 | 0.70 0.58–0.81 .002*                        |
| Previous RRT        | 4.28 (1.15–15.60)   | .031*                 |                                             |
| Severe peripheral kinking | 3.49 (1.37–8.91) | .009*                 |                                             |
| CAD                 | 0.49 (0.21–1.14)    | .099                  |                                             |
| LVOT calcification >36 AU | 3.82 (1.39–10.46) | .009*                 |                                             |
| ARA (°)             | 2.77 (1.07–7.16)    | .035*                 |                                             |
| Valve size 29 mm    | 3.22 (1.30–7.98)    | .012*                 | 3.87 (1.46–10.27) .007*                     |
| **C) PPI**          |                     |                       |                                             |
| Valve size 23 mm    | 4.09 (0.90–18.66)   | .096                  |                                             |
| Valve size 26 mm    | 0.52 (0.29–0.95)    | .032*                 |                                             |
| **D) Major VASC**   |                     |                       |                                             |
| Female sex          | 3.27 (1.09–9.833)   | .035*                 | 4.39 (1.43–13.53) .010*                     |
| AVC ≥ 1,462 AU      | 2.22 (0.89–5.55)    | .088                  | 2.87 (1.12–7.35) .028*                      |
| NCC ≥ 589 AU        | 2.22 (0.89–5.55)    | .088                  |                                             |
| LVOT calcification >36 AU | 2.79 (1.07–7.26) | .036*                 |                                             |
| ARA (°)             | 2.60 (1.00–6.76)    | .051                  | 2.66 (1.01–7.01) .047*                      |

Note: Covariates associated with AE in the univariate analysis (p < .1) were entered into the multivariate model and stepwise backward elimination was used. Only covariates with p < .1 are shown even when all covariates were tested by univariate analysis.

Abbreviations: AE, adverse events; ARA, aortic root angulation; AVC, aortic valve calcification; AU, Agatston units; LVOT, left ventricular outflow tract; NCC, noncoronary cusp; PPI, permanent pacemaker therapy; ROC, receiver-operating-characteristic; RRT, renal replacement therapy.
ealed no significant differences concerning device sizes or pretested overall predictors by multivariate analysis. Details are displayed in Supplemental Table S2. While several changes in the implant technique could have impacted the results of this study, we separated the whole period in two sections (a) from 2014 until 2016 and (b) 2017 until 2019. The earlier period offered well distributed specific AE between both cohorts, while the current period starting from 2017 showed more HA-related AE (Supplemental Table S3; ARA ≥ 51°: 32.1 vs. 17.2%; p = .0016). Interestingly, implantation of large devices—especially the newer 34 mm device—was simultaneously enhanced in this period with 75% of all HA-related specific AE (Supplemental Table S3; ARA ≥ 51°: 75.0 vs. 62.1%; p = .0136).

4 | DISCUSSION

To our knowledge, this is the first study addressing an adjusted threshold of ARA in new-generation devices together with an in-depth analysis of calcification distribution to clarify independent predictors of specific AE. Thus, our study revealed several novel insights on outcome in an HA:

1 30-day mortality was elevated in the HA cohort.
2 Besides 30-day mortality, several outcomes like stroke and MVASC were attenuated by a horizontal anatomy, accompanied by prolonged in-hospital and ICU stay.
3 A pronounced calcification of the NCC and LVOT, an HA by the meaning of an ARA ≥ 51°, as well as resheath/recapture maneuvers were independent predictors for overall specific AE.

A pronounced HA with an ARA > 48° was reported to attenuate acute procedural success in self-expandable but not balloon-expandable TAVR. However, the threshold was developed in old-generation devices and current studies could also demonstrate that HA seems not to affect procedural success and outcome. On the other hand, many questions are still unacknowledged, while in clinical practice HA remains still a challenge in self-expandable TAVR, often intensified by large annulus diameters, calcification burden, and extreme peripheral tortuosity. Especially larger devices are often limited in controllability, although the new-generation systems include several features to optimize device implantation in difficult and large anatomies. Among the most studies with current self-expandable prostheses, the case numbers of very large devices are limited and associations of AE depending on valve size and calcification burden are still lacking when arguing on horizontal anatomy.

4.1 | General characteristics

While the previously described threshold (ARA ≥ 48°) for lower device success was established in old-generation devices, in this study, a new overall median resulting in an ARA ≥ 51° was used to define HA. A similar threshold was also adjusted by previous studies. Contrary to other studies, the number of large prostheses—especially the 34 mm device—was comparatively high (n = 107, 23.0%) and also numerously implanted in HA (n = 64, 26.6%). Similar to numerous previous studies, contrast use and radiation dose were significantly enhanced in HA as an expression for a more technically

FIGURE 3 Distribution of several adverse events in normal (above) and horizontal aorta (below) according to device size [Color figure can be viewed at wileyonlinelibrary.com]
challenging procedure. Predilatation and postdilatation maneuvers were similar between both groups, only repeated resheath and recapture maneuvers were more frequently used in HA, closing the circle to the enhanced radiation dose and contrast use.

4.2 | Primary outcome in HA

Similar to previous studies, primary device success was not affected by HA and was favorable in both cohorts with 97–98%. Intraprocedural complications were also comparable in both cohorts. These results might probably be explained by the technical improvement of the new-generation devices. Furthermore, the Evolut Pro—based on the Evolut R model—was specifically designed to mitigate paravalvular leakage by an outer porcine pericardial wrap and was shown to offer favorable results as well. However, case numbers were limited in this study. Aortic regurgitation never exceeded a moderate degree and was generally low in both cohorts. However, even when at low rates, 30-day mortality was significantly enhanced in the HA cohort and had to be critically discussed. This phenomenon was not described before. Unfortunately, no further analyzes of dependent and independent predictors can be offered in terms of only nine deceased patients with eight cases in the HA cohort. In summary, death was multifactorial (septic, neurologic, cardiogenic, and unknown), but also linked to failing device success (n = 2) and several postprocedural complications (late coronary obstruction, stroke, PPI, and pneumonia). However, even when the number of events did not lead to statistical significance, the mean logistic EuroScore I was obviously higher in all deceased patients with an average of 31.0% as compared to the overall cohort (26.0%), the none-HA (24.6%), and the HA cohort (27.4%).

4.3 | Secondary outcome in HA

Besides 30-day mortality, stroke, and MVASC were frequently observed in an ARA ≥ 51, accompanied by prolonged in-hospital and ICU stay. Enhanced 30-day mortality was a result of septic conditions, stroke, coronary obstruction, MVASC, and unknown reasons. Interestingly, HA was a dependent factor for overall specific AE and concerning the subcohorts of stroke and MVASC. Furthermore, HA was identified as an independent predictor for overall specific AE together with a pronounced calcification of the NCC and LVOT and resheath/recapture maneuvers. This is a novel aspect, while current studies did not identify HA as an independent risk factor. In this study, a pronounced NCC calcification >589 AU and not the total AVC was an independent predictor for AE. Di Stefano et al. included calcification burden of the aortic valve only in a semiquantitative manner and found no significant association to specific AE. In clinical practice, asymmetrical leaflet calcification and calcification of the LVOT is often experienced as a challenge during valve delivery, facilitating valve dislodgement or dislocation. Furthermore, calcification distribution has an impact on conduction disturbances, paravalvular leakage, and worst-case complications like annular ruptures, and was described several times before. The ability to resheath or recapture the device before delivery to optimize the implantation depth and accompanying functionality may be of particular advantage in HA but may also enhance vascular shear stress and embolization in specific anatomical conditions.

HA was also a dependent risk factor for stroke, while previous renal replacement therapy, severe peripheral kinking, and a 29 mm device size were identified as independent risk factors for cerebral events, supposing that the combination of anatomy-related shear forces and calcification may enhance the stroke risk especially using larger devices. In this context, it has to be pronounced that no cerebral protection device was used in any patient during the procedure. However, current studies point to multifactorial aspects in the context of stroke, and research focuses further on this topic, while TAVR towards younger and lower-risk populations will force us to discover potential risk factors for early and late stroke events.

The need for postprocedural PPI was significantly enhanced in HA using a 34 mm device size. A higher incidence of PPI was already described in the large new-generation TAVR device, and is also frequently experienced in dependency from calcification burden and implantation depth. However, the large system failed to be a dependent or independent predictor for PPI, whereas a valve size of 26 mm was highly preventive for PPI need. According to this, period-dependent observation in this study revealed that the majority of HA-related AE was linked to the current implantation era (from 2017 to 2019) using more larger devices and including the introduced 34 mm device.

It seems likely, that different device sizes may have their own critical cutoff value concerning specific AE in HA, supposing higher ARA-thresholds in smaller and lower ARA-thresholds in larger devices. Unfortunately, the potential identification of an optimal valve-size dependent cutoff value for specific AE by the determination of the YI failed except from the 26 mm device, where the critical cutoff for HA was established with an ARA above 52.

5 | CONCLUSION

Data from this analysis indicate that TAVR in an HA with self-expandable new-generation devices is feasible. An HA above 51 is associated with an increased rate of stroke, MVASC, and 30-day mortality. Valve size and asymmetric calcification affect the incidence of repositioning maneuvers and subsequent VARC-2 AE, indicating that an HA—together with specific anatomic features—remains a crucial factor for outcome after TAVR with self-expandable new-generation devices.

6 | LIMITATIONS

This study is a single-center, retrospective analysis with associated prevalent limitations, but we were able to identify two similarly sized groups using an ARA <51, even if establishment through the calculation of the YI failed. However, with only nine deceased patients,
we were not able to clarify if HA also account as independent predictor for mortality. Larger studies have to further clarify if the optimal cutoff value for HA in new-generation devices is really size dependent.

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CONFLICT OF INTERESTS
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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section at the end of this article.