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Outcomes of transfemoral transcatheter aortic valve implantation at hospitals with and without on-site cardiac surgery department: insights from the prospective German aortic valve replacement quality assurance registry (AQUA) in 17 919 patients

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Aims Performing transcatheter aortic valve implantation (TAVI) at hospitals with only cardiology department but no cardiac surgery (CS) on-site is at great odds with current Guidelines.

Methods and results We analysed data from the official, prospective German Quality Assurance Registry on Aortic Valve Replacement to compare characteristics and in-hospital outcomes of patients undergoing transfemoral TAVI at hospitals with ($n = 75$) and without CS departments ($n = 22$). An interdisciplinary Heart Team was established at all centres (internal staff physicians at hospitals with on-site CS; in-house cardiologists and visiting cardiac surgical teams from collaborating hospitals at non-CS hospitals). In 2013 and 2014, 17 919 patients (81.2 $\pm$ 6.1 years, 55% females, German aortic valve (GAV) score 2.0 5.6 $\pm$ 5.8%, logistic EuroSCORE I 21.1 $\pm$ 15.4%) underwent transfemoral TAVI in Germany: 1332 (7.4%) at hospitals without on-site CS department. Patients in non-CS hospitals were older (82.1 $\pm$ 5.8 vs. 81.1 $\pm$ 6.1 years, $P < 0.001$), with more frequent co-morbidities. Predicted mortality risks per GAV-score 2.0 (6.1 + 5.5 vs. 5.5 $\pm$ 5.9%, $P < 0.001$) and logEuroSCORE I (23.2 $\pm$ 15.8 vs. 21.0 $\pm$ 15.4%, $P < 0.001$) were higher in patients at non-CS sites. Complications, including strokes (2.6 vs. 2.3%, $P = 0.452$) and in-hospital mortality (3.8 vs. 4.2%, $P = 0.396$), were similar in both groups. Matched-pair analysis of 555 patients in each group with identical GAV-score confirmed similar rates of intraprocedural complications (9.2 vs. 10.3%, $P = 0.543$), strokes (3.2% for both groups, $P = 1.00$), and in-hospital mortality (1.8 vs. 2.9%, $P = 0.234$).

Conclusion Although patients undergoing TAVI at hospitals without on-site CS department were older and at higher predicted perioperative death risk, major complications, and in-hospital mortality were not statistically different, suggesting the feasibility and safety of Heart Team-based TAVI at non-CS sites. These findings need confirmation in future randomized study.

Keywords Aortic stenosis • TAVI • TAVR • Complications • Conversion • Surgery

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Introduction

The 2012 Valvular Heart Disease Guidelines of the European Society of Cardiology (ESC) mandate that transcatheter aortic valve implantation (TAVI) should be restricted to hospitals with both cardiology and cardiac surgery (CS) departments on-site.[1] The permanent accessibility of both specialities in the same institution is considered optimal for ensuring appropriate patient selection by the Heart Team as well as prompt management of potential severe complications during TAVI, ultimately requiring emergency cardiac surgery (ECS).[1] The lack of endorsement for TAVI at non-CS hospitals by practice guidelines stems from the perception of inappropriate patient selection and poor outcomes of TAVI at such sites, even in the absence of data supporting this notion.

Contemporary data from observational and randomized clinical trials, that were not yet available at the time of development of the 2012 Valvular Heart Disease Guidelines, have demonstrated the continuous evolution of TAVI to become an effective and safe treatment modality.[2,3] The risk of severe intraprocedural complications and procedural mortality has been constantly declining.[4] Rapid technological advances, better patient selection as well as growing operators' experience have been major contributors to improved procedural safety.[5] Thus, the need for ECS for complications during TAVI is currently low and ~1%.[6,7]

In Germany, numbers of TAVI procedures have increased 20-fold since 2008.[4] In 2014, 13 264 procedures were registered, exceeding the number of isolated surgical aortic valve replacements (sAVR) by almost 30%.[4] At some hospitals without on-site CS department, the Heart Team approach, which is a prerequisite for TAVI, has been realized by the in-house cardiologists and visiting cardiac surgical teams from external, collaborating hospitals. Preliminary data on the experience with this Heart Team approach in small numbers of patients undergoing TAVI at sites without on-site CS department have suggested favourable patient outcomes, supporting its feasibility and safety at such sites.[8,9]

We analysed the complete 2013 and 2014 datasets from the official German Quality Assurance Registry on Aortic Valve Replacement (AQUA/G-BA), which prospectively registers all TAVI and sAVR procedures performed in Germany, to compare patient characteristics, complications, and outcomes of patients undergoing TAVI between hospitals with and without on-site CS department.

Methods

We analysed the data on patients in the 2013 and 2014 German Quality Assurance Registry Aortic Valve Replacement of the Federal Joint Committee (G-BA), led by the independent Institute for Applied Quality Improvement and Research in Health Care (AQUA, Göttingen, Germany). The design of the AQUA Registry has been described in detail previously.[4,10] Most importantly, data collection is mandatory for all in-patient procedures in hospitals registered under §108 SGB V billing AVR to German statutory health insurance or private insurance companies (2013: 92 hospitals; 2014: 97 hospitals). According to §137 Social Security Code V (SGB V).[10] All events are defined in an elaborate form completion guide and self-adjudicated and self-reported by the sites.[4] All data are reported using standardized electronic data entry with no routine on-site monitoring. Data are pooled in a nationwide database and controlled for quality by a validated system. In case of inconsistencies or deviations from predefined quality benchmarks, a structured dialogue with the hospital is initiated to trigger individual institution designed quality improvement measures by standardized interviews.[4]

For the present analysis, hospitals performing TAVI were divided into those with both cardiology and CS departments on-site (2013: $n = 73$; 2014: $n = 75$) and those with cardiology, but without on-site CS department (2013: $n = 19$; 2014: $n = 22$). In hospitals without CS department, a Heart Team was constructed from in-house cardiologists and visiting cardiac surgical teams from external, collaborating hospitals. Patient-level data analyses were limited to transfemoral TAVI patients in order to avoid selection bias from including transaortic or transapical TAVI patients at CS hospitals which differed significantly from transfemoral TAVI patients with respect to risk profiles and comorbidities.[11]

In addition to the logistic (log)EuroSCORE I, the German aortic valve (GAV) score 2.0 was used as risk prediction tool for estimation of in-hospital mortality. The GAV-score has initially been calculated retrospectively based on data from patients undergoing isolated sAVR or TAVI in 2008 and has been shown to fit best to the population in Germany.[12] In 2014, the GAV-score has been adjusted resulting in an updated version 2.0.[13] Details of risk factors included in the logistic regression equation of the GAV-score are given in the Appendix.

Statistical analysis was performed using IBM SPSS for Windows Version 22.0. Because the unadjusted cohorts differed in some variables, the results have been validated by case–control analysis comparing two matched samples (patients of hospitals with CS and without CS) with identical GAV 2.0 scores. In order to maximize the number of cases in the CS cohort to be used for the case–control group and the number of pairs with different GAV-scores, a 1:1 matching was performed. To avoid any influences of risk differences in the matched groups, only pairs with identical GAV-score 2.0 were allowed. For 555 patients of the non-CS group, one control patient undergoing TAVI in hospitals with on-site CS with identical risk score was identified. Continuous variables are presented as mean $\pm$ standard deviation and compared using the Student's *t*-test including Levene's test for both the unmatched and matched cohorts. Categorical variables are given as frequencies in percent and compared using Pearson's χ^2 test eventually with Yates correction as appropriate, also for both the unmatched and matched cohorts. For continuous variables odds ratios (95% confidence interval) and for categorical variables standardized mean differences (95% confidence interval) were calculated. A *P*-value of <0.05 was considered statistically significant.

Results

Between January 1, 2013 and December 31, 2014, a total of 17 919 patients (mean age: 81.2 $\pm$ 6.1 years; 55% females; logistic EuroSCORE: 21.1 $\pm$ 15.4%; GAV-score 2.0: 5.6 $\pm$ 5.8%) underwent TF-TAVI in Germany. Of these, 1332 (7.4%) patients underwent TAVI at hospitals without on-site CS department.

The number of hospitals performing TAVI increased from 92 in 2013 to 97 in 2014. This increase was similarly distributed among non-CS hospitals (19 in 2013 to 22 in 2014) and those with CS on-site (73 in 2013 to 75 in 2014). Numbers of patients undergoing

TAVI at non-CS hospitals declined by 19% from 735 in 2013 to 597 in 2014, while that at hospitals with on-site CS increased by 41% ($n = 9702$ in 2014 vs. $n = 6885$ in 2013). The average TAVI case-load was higher in hospitals with CS (2013: 94 vs. 37; 2014: 129 vs. 22). Among hospitals without CS departments, 6 (32%) and 3 (14%) performed >50 TAVI procedures annually in 2013 and 2014, respectively. For hospitals with on-site CS, the proportion of hospitals performing >50 procedures annually was much higher and increased over time (2013: 74%; 2014: 83%, $P < 0.001$ vs. non-CS hospitals).

Patients undergoing TAVI at hospitals without CS were older (82.1 ± 5.8 vs. 81.1 ± 6.1 years, $P < 0.001$), had higher NYHA symptom class and greater prevalence of history of coronary artery disease (CAD), peripheral vascular disease (PVD), chronic obstructive pulmonary disease (COPD), and neurologic events (*Table 1*). This resulted in overall higher predicted risks of operative mortality, according to both the GAV-score 2.0 (6.1 + 5.5 vs. 5.5 ± 5.9%, $P < 0.001$) and the logistic EuroSCORE I (23.2 ± 15.8 vs. 21.0 ± 15.4%, $P < 0.001$). Significantly fewer low-risk (logEuroSCORE <10%) and more high-risk patients (logEuroSCORE >30%) underwent TAVI at non-CS hospitals ($P < 0.001$, *Table 1*). Patients at non-CS hospitals had greater prevalence of permanent pacemaker implanted before index procedure than patients in hospitals with CS on-site (*Table 1*).

In both groups, there was a similar pattern of reasons for selecting TAVI over conventional sAVR, with patient age, frailty, and perceived high surgical risk being the three most common reasons (*Table 2*).

In the majority of patients (83.8%), TAVI was performed as an elective procedure. Procedural characteristics at hospitals without and with on-site CS are shown in *Table 3*. Procedure times as defined as time from vessel puncture to access site closure were longer in hospitals without on-site CS department (110.3 ± 48.2 vs. 79.3 ± 44.8 min, $P < 0.001$), while fluoroscopy times were similar in the two groups. The rates of severe intraprocedural

Table 1 Patient demographics

	Patients undergoing TF-TAVI in hospitals without CS ($n = 1332$)	Patients undergoing TF-TAVI in hospitals with CS ($n = 16\,587$)	*P*-value
Age	82.1 ± 5.8 (55–97)	81.1 ± 6.1 (33–100)	<0.001
Age ≤75 years	172 (12.9%)	2529 (15.2%)	0.022
Females (%)	722 (54.2%)	9125 (55.0%)	0.568
NYHA ≥III	1204 (90.4%)	14 079 (84.9%)	<0.001
Acute decompensated heart failure (<48 h)	54 (4.1%)	518 (3.1%)	0.062
Pulmonary hypertension	633 (47,5%)	7591(45,8%)	0.001
Systolic PA pressure >55 mmHg	257 (19.3%)	2204 (13.3%)	<0.001
Atrial fibrillation	392 (29.4%)	4925 (29.7%)	0.840
Presence of permanent pacemaker	177 (13.3%)	1868 (11.3%)	0.025
Presence of implanted cardioverter defibrillator	22 (1.7%)	282 (1.7%)	0.896
ASA ≥3	1242 (93.2%)	15 221 (91.8%)	<0.001
Left ventricular ejection fraction ≤30%	148 (11.1%)	1687 (10.2%)	0.183
CAD	804 (60.4%)	8995 (54.2%)	<0.001
Left main coronary artery involvement	67 (5.0%)	639 (3.9%)	0.034
Previous myocardial infarction	183(13.7%)	2206 (13.3%)	0.650
Previous PCI	457 (34.3%)	4856 (29.3%)	<0.001
Previous open heart surgery	238 (17.9%)	2893 (17.4%)	0.693
Insulin-dependent diabetes mellitus	178 (13.4%)	2355 (14.2%)	0.400
PVD	248 (18.6%)	2504 (15.1%)	0.012
COPD with medication	222 (16.7%)	2104 (12.7%)	0.001
Previous neurologic event	186 (14.0%)	1954 (11.8%)	0.019
Chronic haemodialysis	36 (2.7%)	515 (3.1%)	0.413
LogEuroSCORE (%)	23.2 ± 15.8 (3.1–88.8)	21.0 ± 15.4 (1.5–98.3)	<0.001
LogEuroSCORE <10%	213 (16.1%)	3945 (24.1%)	<0.001
LogEuroSCORE 10–20%	520 (39.2%)	6036 (36.9%)	
LogEuroSCORE 20–30%	259 (19.5%)	2969 (18.2%)	
LogEuroSCORE >30%	333 (25.1%)	3407 (20.8%)	
GAV-Score 2.0 (%)	6.1 ± 5.5 (0.8–57)	5.5 ± 5.9 (0.6–99.9)	<0.001

ASA, American Society of Anesthesiologists; COPD, chronic obstructive lung disease; CS, cardiac surgery; NYHA, New York Heart Association; PA, pulmonary artery; PCI, percutaneous coronary intervention; TAVI, transcatheter aortic valve implantation; TF, transfemoral.

Table 2 Reasons for selecting transfemoral-transcatheter aortic valve implantation over surgical aortic valve replacement

	Patients undergoing TF-TAVI in hospitals without CS (n = 1332)	Patients undergoing TF-TAVI in hospitals with CS (n = 16 587)	P-value
Patient age	1043 (78.3%)	11 230 (67.7%)	<0.001
Frailty	640 (48.0%)	7228 (43.6%)	0.002
High surgical risk	604 (45.3%)	8608 (51.9%)	<0.001
Patient wish	388 (29.1%)	4308 (26.0%)	0.01
Prognosis limiting comorbidity	60 (4.5%)	1622 (9.8%)	<0.001
Porcelain aorta	26 (2.0%)	823 (5.0%)	<0.001
Malignancy	28 (2.1%)	340 (2.0%)	0.896
Other	391 (29.4%)	2525 (15.2%)	<0.001

Table 3 Procedural data

	Patients undergoing TF-TAVI in hospitals without CS (n = 1332)	Patients undergoing TF-TAVI in hospitals with CS (n = 16 587)	P-value	Odds ratio for categorical var. or stand. mean difference for continuous var.	95% CI
Elective procedure	1109 (83.3%)	13 907 (83.8%)	0.578	0.958	0.825–1.113
Procedure time (min)	110.3 ± 48.2	79.3 ± 44.8	<0.001	0.688	0.632–0.744
Fluoroscopy time (min)	18.9 ± 11.7	19.9 ± 33.1	0.273	−0.031	−0.087–0.025
Intraprocedural complications	112 (8.4%)	1817 (11.0%)	0.004	0.746	0.611–0.911
Device malpositioning	19 (1.4%)	276 (1.7%)	0.512	0.855	0.535–1.366
Device embolization	6 (0.5%)	51 (0.3%)	0.373	1.467	0.629–3.425
Coronary occlusion	4 (0.3%)	62 (0.4%)	0.671	0.806	0.293–2.218
Aortic dissection	2 (0.2%)	38 (0.2%)	0.557	0.655	0.158–2.718
Annular rupture	9 (0.7%)	55 (0.3%)	0.043/0.074**	2.045	1.008–4.147
Pericardial tamponade	6 (0.5%)	171 (1.0%)	0.039	0.434	0.192–0.982
Acute cardiac decompensation	7 (0.5%)	118 (0.7%)	0.433	0.737	0.343–1.584
Cerebral embolism	2 (0.2%)	30 (0.2%)	0.799/0.933**	0.830	0.198–3.477
Aortic regurgitation ≥2	28 (2.1%)	171 (1.0%)	<0.001	2.061	1.377–3.086
Rhythm disturbances	25 (1.9%)	489 (2.9%)	0.024	0.630	0.496–0.945
Vascular injury	33 (2.5%)	739 (4.5%)	<0.001	0.545	0.383–0.776
Composite of intraprocedural complications likely to benefit from ECS	46 (3.4%)	653 (3.9%)	0.421	0.873	0.644–1.183
Conversion to open heart surgery	4 (0.3%)	115 (0.7%)	0.088	0.431	0.159–1.171

Composite of periprocedural complications likely to benefit from ECS, device malpositioning; device embolization, annular rupture, aortic dissection, coronary obstruction, and/or pericardial tamponade.
**P-value with Yates correction, because at least 20% of expected frequencies are <5!

complications were lower in the non-CS cohort. Particularly dreadful TAVI-specific complications such as annular rupture, aortic dissection, coronary obstruction, and device embolization were overall rare (<1%) and similar in both groups (*Table 3*). Conversion to sternotomy was less common at non-CS sites (0.3 vs. 0.7%, P = 0.088). Rates of post-implantation paravalvular aortic regurgitation ≥grade 2 were higher in patients undergoing TAVI in non-CS hospitals (2.1 vs. 1.0%, $P < 0.001$).

In-hospital mortality was not different in hospitals without and with on-site CS department (3.8 vs. 4.2%, $P = 0.396$, *Table 4*). There were no differences with respect to neurologic events (2.6 vs. 2.3%, $P = 0.452$), myocardial infarction, or vascular complications during the in-hospital period (*Table 4*). The rate of new permanent pacemaker implantation was higher in hospitals without on-site CS (19.8 vs. 15.8%, $P < 0.001$). Of note, less patients undergoing TAVI at non-CS hospitals were transferred to other hospitals rather

Table 4 Postprocedural outcomes

	Patients undergoing TF-TAVI in hospitals without CS (n = 1332)	Patients undergoing TF-TAVI in hospitals with CS (n = 16 587)	P-value	Odds ratio for categorical var. or stand. mean difference for continuous var.	95% CI
In-hospital death	50 (3.8%)	703 (4.2%)	0.396	0.881	0.658–1.181
In-hospital death for the composite of intraprocedural complications likely to benefit from ECS	17/46 (37.0%)	220/653 (33.7%)	0.771	1.154	0.621–2.145
Cerebrovascular event	35 (2.6%)	378 (2.3%)	0.452	1.157	0.815–1.644
Delirium requiring treatment	47 (3.5%)	635 (3.8%)	0.582	0.919	0.680–1.242
Myocardial infarction	3 (0.2%)	60 (0.4%)	0.418	0.622	0.195–1.985
Low cardiac output	33 (2.5%)	431 (2.6%)	0.789	0.952	0.665–1.363
Resuscitation	39 (2.9%)	493 (3.0%)	0.927	0.985	0.707–1.371
Vascular complications	134 (10.1%)	1479 (8.9%)	0.161	1.217	1.010–1.466
Need for transient dialysis	15 (1.1%)	373 (2.2%)	0.007	0.500	0.295–0.832
Atrial fibrillation at discharge	315 (23.6%)	3811 (23.0%)	0.700	1.038	0.910–1.184
New pacemaker/ICD implantation	264 (19.8%)	2620 (15.8%)	<0.001	1.318	1.144–1.517
Days in hospital after TF-TAVI	11.0 ± 7.5 (0–93)	10.4 ± 7.5 (0–162)	0.005	0.080	0.024–0.136
Transfer to another hospital	142 (10.7%)	2501 (15.1%)	<0.001	0.672	0.562–0.804
Discharge to rehabilitation unit	186 (14.0%)	3074 (18.5%)	<0.001	0.714	0.608–0.837
Discharge to nursing facility	12 (0.9%)	77(0.5%)	0.029	1.949	1.058–3.591

Composite of periprocedural complications likely to benefit from ECS, device malpositioning, device embolization, annular rupture, aortic dissection, coronary obstruction, and/or pericardial tamponade.

than discharged home when compared with CS hospitals with on-site CS (10.7 vs. 15.1%, $P < 0.001$).

Intraprocedural complications likely to benefit from ECS (composite of device malposition, embolization, annular rupture, aortic dissection, coronary obstruction, and/or pericardial tamponade) occurred in 46 (3.4%) patients undergoing TAVI at non-CS hospitals and in 653 (3.9%) patients at hospitals with on-site ($P = 0.421$). Among these patients, conversion to ECS at non-CS hospitals was also similar in the two groups (non-CS 13.0 vs. CS 16.5%, $P = 0.679$). Patients with annular rupture were less often treated with ECS (1/9 at non-CS hospitals vs. 22/55 at hospitals with on-site CS, $P = 0.193$). In-hospital mortality of patients with complications likely to benefit from ECS was similar at non-CS and CS hospitals (37.0 vs. 33.7%, $P = 0.771$). In-hospital mortality of patients requiring ECS for intraprocedural complications was 50% in non-CS hospitals and 62.5% in hospitals with on-site CS ($P = 0.694$). Outcomes of annular rupture were dismal at both non-CS and on-site CS hospitals (in-hospital mortality: 55.6 and 74.5%, respectively). The proportion of patients discharged to other hospitals or rehabilitation units rather than home was similar in non-CS and CS hospitals (23.9 vs. 29.9%, $P = 0.415$).

Patient characteristics of matched-pair analysis (555 patients with identical GAV-score 2.0 in each group) are shown in *Table 5*, and procedural complications and outcomes are shown in *Table 6*. Of note, intraprocedural complications (9.2 vs. 10.3%, $P = 0.543$) as well as postprocedural complications including strokes (3.2% for both groups, $P = 1.00$) were similar to matched patients treated at hospitals without and with on-site CS with the exception of higher post-implantation aortic regurgitation ≥grade 2 in the non-CS group. Most notably, in-hospital death was similar in the matched cohort in the two groups without and with on-site CS (1.8 vs. 2.9%, $P = 0.234$) (*Table 7*).

Discussion

The absence of on-site CS department is considered an absolute contraindication for TAVI by the 2012 Valvular Heart Disease ESC Guidelines.[1] Based on more contemporary evidence of improved procedural safety, the German Cardiac Society updated an earlier position paper on transfemoral TAVI in 2014.[14] This supported hospitals without on-site CS department to perform TAVI if they had a contractually documented cooperation with an external CS department and a joint interdisciplinary decision-making for patient selection was ensured.[14] Nonetheless, the Federal Joint Committee as the supreme decision-making body of the joint self-government of physicians, dentists, hospitals, and health insurance funds in Germany considered the expert consensus recommendation of the 2012 ESC Guidelines the best available evidence and recently concluded that the presence of both cardiology and CS departments in the hospital is a prerequisite to perform TAVI, precluding performance of TAVI at non-CS hospitals.[15] However, for non-CS hospitals that already performed TAVI, a transition phase of 1 year was granted to establish the standards of on-site CS.[15]

Table 5 Case–control analysis: patient characteristics

	Patients undergoing TF-TAVI in hospitals without CS ($n = 555$)	Patients undergoing TF-TAVI in hospitals with CS ($n = 555$)	*P*-value
Age	83.0 ± 4.4 (66–95)	83.0 ± 4.4 (66–95)	1.00
Females (%)	338 (60.9%)	338 (60.9%)	1.00
NYHA ≥III	479 (86.3%)	437 (78.7%)	<0.001
Previous myocardial infarction	34 (6.1%)	38 (6.8%)	0.626
Pulmonary hypertension	234 (42.2%)	234 (42.2%)	1.00
Systolic PA pressure >55 mmHg	80 (14.4%)	50 (9.0%)	0.005
Atrial fibrillation	140 (25.2%)	132 (23.8%)	0.577
Presence of permanent pacemaker	48 (8.6%)	49 (8.8%)	0.915
Presence of implanted cardioverter defibrillator	5 (0.9%)	5 (0.9%)	1.00
ASA ≥3	490 (88.3%)	499 (89.9%)	0.386
Left ventricular ejection fraction ≤30%	9 (1.6%)	9 (1.6%)	1.00
CAD	261 (47.0%)	261 (47.0%)	1.00
Left main coronary artery involvement	5 (0.9%)	5 (0.9%)	1.00
Previous PCI	136 (24.5%)	131 (23.6%)	0.726
Previous open heart surgery	45 (8.1%)	45 (8.1%)	1.00
Insulin-dependent diabetes mellitus	22 (4.0%%)	21 (3.8%)	0.877
PVD	61 (11.0%)	54 (9.7%)	0.337
COPD with medication	86 (15.5%)	51 (9.2%)	0.001
Previous neurologic event	68 (12.3%)	60 (10.8%)	0.452
Chronic haemodialysis	2 (0.4%)	3 (0.5%)	0.654/1.00**
LogEuroSCORE (%)	16.4 ± 9.0 (3.5–56.4)	16.0 ± 9.1 (3.3–56.2)	0.462
GAV-score 2.0 (%)	3.7 ± 1.4 (1.3–12.9)	3.7 ± 1.4 (1.3–12.9)	1.00

Table 6 Case–control analysis: procedural data

	Patients undergoing TF-TAVI in hospitals without CS ($n = 555$)	Patients undergoing TF-TAVI in hospitals with CS ($n = 555$)	*P*-value	Odds ratio for categorical var. or stand. mean difference for continuous var.	95% CI
Elective procedure	502 (90.5%)	497 (89.5%)	0.617	1.1053	0.7465–1.637
Procedure time (min)	108.8 ± 48.1	74.2 ± 42.2	<0.001	0.765	0.643–0.887
Fluoroscopy time (min)	19.5 ± 13.4	21.5 ± 42.7	0.293	−0.063	−0.181–0.055
Intraprocedural complications	51 (9.2%)	57 (10.3%)	0.543	0.884	0.594–1.316
Device malpositioning	9 (1.6%)	8 (1.4%)	0.806	1.127	0.432–2.943
Device embolization	2 (0.4%)	2 (0.4%)	1.00/0.616**	1.00	0.140–7.125
Coronary occlusion	2 (0.4%)	4 (0.7%)	0.387/0.649**	0.498	0.091–2.731
Aortic dissection	1 (0.2%)	2 (0.4%)	0.563	0.499	0.045–5.520
Annular rupture	4 (0.7%)	4 (0.7%)	1.00/0.723	1.00	0.249–4.019
Pericardial tamponade	4 (0.7%)	7 (1.3%)	0.363	0.568	0.165–1.9525
Acute cardiac decompensation	4 (0.7%)	2 (0.4%)	0.413/0.682**	2.007	0.366–11.004
Cerebral embolism	1 (0.2%)	1 (0.2%)	1.00/0.479**	1.00	0.062–16.028
Aortic regurgitation ≥ 2	15 (2.7%)	6 (1.1%)	0.047	2.542	0.979–6.600
Rhythm disturbances	8 (1.4%)	12 (2.2%)	0.367	0.662	0.268–1.632
Vascular injury	14 (2.5%)	22 (4.0%)	0.175	0.639	0.323–1.262
Conversion to open heart surgery	2 (0.4%)	5 (0.9%)	0.255/0.448**	0.398	0.077–2.059

Table 7 Case–control analysis: postprocedural outcomes

	Patients undergoing TF-TAVI in hospitals without CS (n = 555)	Patients undergoing TF-TAVI in hospitals with CS (n = 555)	P-value	Odds ratio for categorical var. or stand. mean difference for continuous var.	95% CI
In-hospital death	10 (1.8%)	16 (2.9%)	0.234	0.618	0.278–1.374
Cerebrovascular event	18 (3.2%)	18 (3.2%)	1.00	1.00	0.515–1.943
Delirium requiring treatment	18 (3.2%)	15 (2.7%)	0.596	1.207	0.601–2.419
Myocardial infarction	1 (0.2%)	1 (0.2%)	1.00	1.00	0.062–16.028
Low cardiac output	6 (1.1%)	11 (2.0%)	0.222	0.541	0.198–1.472
Resuscitation	10 (1.8%)	18 (3.2%)	0.126	0.547	0.250–1.197
Vascular complications	39 (7.0%)	46 (8.3%)	0.429	0.835	0.536–1.300
Need for transient dialysis	3 (0.5%)	8 (1.4%)	0.130	0.372	0.098–1.408
Atrial fibrillation at discharge	111 (20.0%)	125 (22.5%)	0.304	0.860	0.645–1.147
New pacemaker/ICD implantation	114 (20.5%)	105 (18.9%)	0.497	1.108	0.824–1.489
Days in hospital after TF-TAVI	10.4 ± 7.1 (0–93)	9.8 ± 6.4 (0–56)	0.139	0.088	−0.029–0.207
Transfer to another hospital	43 (7.7%)	86 (15.5%)	<0.001	0.458	0.311–0.674
Discharge to nursing facility	5 (0.9%)	2 (0.4%)	0.255/0.448**	2.514	0.486–13.011

**P-value with Yates correction, because at least 20% of expected frequencies are, 5!

Our analysis of the official, prospective German AQUA registry comprised >1000 patients who underwent TAVI at hospitals without on-site CS department. Although patients at non-CS sites were older and at higher predicted risk of operative mortality, rates of complications (with the exception of moderate-to-severe aortic regurgitation), and in-hospital mortality were in fact not different from patients undergoing TAVI in hospitals with on-site CS department. These findings were confirmed in a matched-pair analysis of 555 patients with identical GAV-score 2.0 in each group, demonstrating that complications and in-hospital mortality were not statistically significantly different.

Since the first procedure performed in 2002,[16] TAVI has grown to a well-established and safe treatment performed in clinical routine. Annual numbers of TAVI procedures show steep increases in Germany and the USA.[4,17] In 2014, 69% of all patients ≥70 years and 89% of all patients ≥80 years undergoing treatment for isolated aortic valve disease in Germany were treated with TAVI. Miniaturization of catheter devices and refinements in TAVI technology (e.g. repositionability), better patient selection and preprocedural imaging as well as growing operators' experience have reduced complications and improved clinical and haemodynamic outcomes.[5] Currently available TAVI devices have shown low 30-day mortality rates ranging between 1% and 2%.[3] Long-term results up to 5 years have demonstrated durability of TAVI valves, with survival and quality of life comparable with patients undergoing surgical AVR.[18] Centres have already begun exploring strategies to simplify the TAVI procedure. A PCI-like 'minimalist approach' of performing TAVI in the cath lab under local anaesthesia has shown favourable results compared with 'standard' TAVI procedures performed under general anaesthesia in the hybrid operating room with transoesophageal echocardiography.[19] Even same day discharges after TAVI have been reported recently.[20] Patients preferences have been weighing increasingly in favour of being treated with this minimal-invasive procedure.[4]

Appropriate patient selection by multidisciplinary consensus as well as the immediate availability of CS for the treatment of severe intraprocedural complications have been identified as the main reasons for confining TAVI to hospitals with on-site CS departments.[21,22] Our analysis showed that patients selected for TAVI by the Heart team at non-CS hospitals were indeed older and had more comorbid conditions such as history of CAD, PVD, COPD and previous neurologic events and higher predicted surgical risks. Yet, the differences in baseline comorbid conditions did not appear to result from different reasons for selecting TAVI over sAVR. Patient age, frailty, and estimated high surgical risk were the three most common reasons in both groups. Additionally, patient wish for receiving minimal-invasive treatment was considered important for decision-making in a similar proportion of patients (1/3 and 1/4, respectively). Finally, the heart team approach resulted in similar outcomes at sites with and without CS.

Proponents of confining TAVI to hospitals with CS have further argued that this setting is more safe for patients as these institutions are best equipped for treating severe periprocedural complications that may ultimately require ECS.[21] Previous reports have already demonstrated that the risk of such complications as well as the need for ECS during TAVI have declined over time.[5,23] The present analysis corroborates these reports, showing that complications such as annular rupture (0.4%), aortic injury (0.2%), and coronary obstruction (0.4%) are rare. Overall, 119 of 17 919 (0.7%) patients required conversion to sternotomy. In hospitals without CS, 4 of 1332 (0.3%) patients were converted. The higher rate for conversion (0.7 vs. 0.3%) at sites with on-site CS

may be related to a lower threshold due to the ready availability of CS back-up at such sites or may be due to the inability to treat severe complications at non-CS hospitals. The similar in-hospital death rates in hospitals with and without on-site CS both among overall patients and patients who developed major complications suggested that severe complications after TAVI were rare and associated with high risk of death whether or not emergent surgical back-up was available. However, unlike currently when only high-risk patients undergo TAVI, indications in future may be expanded to include intermediate and possibly low-risk patients with aortic stenosis. While it is expected that rates of complications requiring ECS in such lower risk cohorts are likely to be less than that among the high-risk cohort undergoing TAVI currently, the potential to salvage such patient with ECS is likely to be much greater. Thus, inference regarding the role of potential benefit of on-site surgical programme permitting immediate expedited treatment of complications in low- or intermediate-risk patients undergoing TAVI, and its impact on outcomes of TAVI at sites with and without CS in future should not be extrapolated from current data.

It has been speculated that outcomes of patients undergoing TAVI at non-CS hospitals may in fact be worse than observed since patients with severe complications are transferred to other hospitals (i.e. for surgery) and thus the mortality may not be recorded in the registry as being occurring at such sites.[24] However, the present analysis showed that such patient transfers from sites without CS were not higher than that from CS hospitals (10.7 vs. 15.1%, $P < 0.001$). Additionally, transfer rates were similar among patients with major periprocedural complications likely to potentially benefit from ECS. Taken together, these data refute the hypothesis of more referral to other hospitals after TAVI at the sites without on-site CS. In fact, these data underscores the importance of heart team approach and appropriate collaborative patient selection rather than on-site cardiology programme for performance of TAVI with reasonably good outcomes.

As previously reported,[8] institutional case-load was significantly lower in hospitals without CS. Probably as a consequence of less routine, procedure times were significantly longer in hospitals without CS. Yet, fluoroscopy times were not different, suggesting that the actual implantation of the TAVI prosthesis did not take longer, but possibly other steps of the procedure (e.g. induction of anaesthesia, preparation of room, and devices). Nonetheless, longer procedure times were not associated with increased intraprocedural complications or worse clinical outcomes.

Finally, practice guidelines recommendations for TAVI at hospitals without onsite surgery are based on consensus opinions of physicians who are largely from major tertiary centres with both cardiology and CS on site rather than actual data to support their recommendations prohibiting the performance of TAVI at non-CS sites.[1] Data from other[8,9] and the present studies support the feasibility and safety of performing TAVI at non-CS hospitals as long as the heart team approach was instrumental before and during the procedure. While these observational data should not be considered definitive, they should at the very least stimulate a randomized large trial or a large prospective study to evaluate the efficacy and safety of doing TAVI at non-CS sites with the Heart team as a prerequisite.

Limitations

Our analysis is the largest to date, reporting on characteristics and outcomes of >1000 patients undergoing TAVI in hospitals without on-site CS department. It is based on the complete datasets of all TAVI procedures in Germany performed in 2013 and 2014, and is therefore representative and valid and the best evidence currently available. Nevertheless, the proportion of patients undergoing TAVI at non-CS hospitals is somewhat small (only 7.4% of the overall large patient population), which was explained by reimbursement issues installed in Germany after publication of the 2012 ESC guidelines that prohibited TAVI at non-CS sites. Inherent to all non-randomized, observational registries we cannot exclude incompleteness of data, particularly as events are self-adjudicated and reported without routine on-site data verification. Nevertheless, such issues would apply for both groups (e.g. hospitals with and without on-site CS department) and are thus unlikely to affect endpoints reported in the present study. The distribution of different valve types used for TAVI could not be derived from the registry. As such, we are unable to evaluate the impact of potential differences in the use of TAVI valve types on the differences in post-implantation paravalvular leak and periprocedural pacemaker rates observed between both groups. Our analysis is limited to evaluate the association with in-hospital outcomes only and we are unable to provide insight into longer-term outcomes.

Conclusions

The present analysis of >1000 patients undergoing TAVI at hospitals without on-site CS department demonstrated that the Heart Team at non-CS sites was associated with similar patient selection. Procedural outcomes with respect to in-hospital complications and mortality were not statistically different between institutions with and without on-site CS departments. Joint decision-making and performance of TAVI in the interdisciplinary Heart Team was the key to successful TAVI. These findings should stimulate a randomized trial to confirm our results. Until then, the lack of CS department on-site should not be regarded as contraindication for TAVI.

Authors' contributions

M.B., H.E., K.B. performed statistical analysis; K.B., K.-H.K., R.H.M. handled funding and supervision; H.E., M.B. acquired the data; H.E., M.H., A.S., R.H.M. conceived and designed the research; H.E., A.S., R.H.M. drafted the manuscript; M.B., H.E., M.B., M.H., K.B., T.V., K.-H.K., R.H.M. made critical revision of the manuscript for key intellectual content.

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Appendix

Table A1 Risk factors and their relative weight in the German aortic valve-score 2.0

Risk factors in logistic regression equation	Regression coefficient	Odds ratio	95% CI [LL]	95% CI [UL]
Constant	−6.74670	–	–	–
Age (years)	0.04099	1.042	1.032	1.051
Female gender	0.14368	1.155	0.990	1.347
Body mass index <22 kg/m^2	0.20019	1.222	0.992	1.505
Body mass index >39 kg/m^2	0.02269	1.023	0.968	1.081
Heart failure of NYHA class IV	0.71739	2.049	1.707	2.460
Angina pectoris at rest or minor exertion	0.37283	1.452	1.217	1.731
Cardiogenic shock ≤48 h	0.15989	1.173	0.848	1.623
Cardiopulmonary resuscitation ≤48 h	1.36649	3.922	2.375	6.474
No pulmonary hypertension	−0.16430	0.848	0.729	0.987
Sinus rhythm	−0.24634	0.782	0.671	0.911
ASA physical status class 4	0.57306	1.774	1.493	2.107
ASA physical status class 5	1.71229	5.542	3.147	9.758
LVEF <30%	0.57500	1.777	1.461	2.162
CAD and left main stenosis	0.03854	1.039	0.975	1.108
Repeat cardiac/aortic surgery	0.09190	1.096	0.901	1.333
Infective endocarditis or septic intervention	0.83752	2.311	1.659	3.218
Diabetes mellitus, insulin-dependent or untreated	0.05848	1.060	0.865	1.299
Arterial vascular disease	0.22675	1.255	1.070	1.471
Preoperative renal replacement therapy or preoperative creatinine >2.3 mg/dL	0.85092	2.342	1.890	2.901
(Preoperative) mechanical circulatory support	0.41559	1.515	0.864	2.659

ASA, American Society of Anaesthesiologists; CAD, coronary artery disease; CI [LL], lower limit of confidence interval; CI [UL], upper limit of confidence interval; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

References

1. Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology, European Association for Cardio-Thoracic Surgery, Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Baron-Esquivias G, Baumgartner H, Borger MA, Carrel TP, De Bonis M, Evangelista A, Falk V, Iung B, Lancellotti P, Pierard L, Price S, Schafers HJ, Schuler G, Stepinska J, Swedberg K, Takkenberg J, Von Oppell UO, Windecker S, Zamorano JL, Zembala M. Guidelines on the management of valvular heart disease (version 2012). *Eur Heart J* 2012;**33**:2451–2496.
2. Reardon MJ, Adams DH, Kleiman NS, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Lee JS, Hermiller JB Jr, Chetcuti S, Heiser J, Merhi W, Zorn GL III, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Maini B, Mumtaz M, Conte JV, Resar JR, Aharonian V, Pfeffer T, Oh JK, Qiao H, Popma JJ. 2-year outcomes in patients undergoing surgical or self-expanding transcatheter aortic valve replacement. *J Am Coll Cardiol* 2015;**66**:113–121.
3. Husser O, Pellegrini C, Kessler T, Burgdorf C, Thaller H, Mayr NP, Ott I, Kasel AM, Schunkert H, Kastrati A, Hengstenberg C. Outcomes after transcatheter aortic valve replacement using a novel balloon-expandable transcatheter heart valve: a single-center experience. *JACC Cardiovasc Interv* 2015;**8**:1809–1816.
4. Eggebrecht H, Mehta RH. Transcatheter aortic valve implantation (TAVI) in Germany 2008–2014: on its way to standard therapy for aortic valve stenosis in the elderly? *EuroIntervention* 2016;**11**:1029–1033.
5. Beohar N, Kirtane AJ, Blackstone E, Waksman R, Holmes D, Minha S, Alli O, Suri RM, Svensson LG, Leon M, Kodali S. Trends in complications and outcomes of patients undergoing transfemoral transcatheter aortic valve replacement: experience from the PARTNER Continued Access Registry. *JACC Cardiovasc Interv* 2016;**9**:355–363.
6. Mack MJ, Brennan JM, Brindis R, Carroll J, Edwards F, Grover F, Shahian D, Tuzcu EM, Peterson ED, Rumsfeld JS, Hewitt K, Shewan C, Michaels J, Christensen B, Christian A, O'Brien S, Holmes D, Registry SAT. Outcomes following transcatheter aortic valve replacement in the United States. *JAMA* 2013;**310**:2069–2077.
7. Walther T, Hamm CW, Schuler G, Berkowitsch A, Kotting J, Mangner N, Mudra H, Beckmann A, Cremer J, Welz A, Lange R, Kuck KH, Mohr FW, Mollmann H, Board GE. Perioperative results and complications in 15,964 transcatheter aortic valve replacements: prospective data from the GARY Registry. *J Am Coll Cardiol* 2015;**65**:2173–2180.
8. Eggebrecht H, Mehta RH, Haude M, Sack S, Mudra H, Hein R, Brachmann J, Gerckens U, Kuck KH, Zahn R, Sechtem U, Richardt G, Schneider S, Senges J. Transcatheter aortic valve implantation (TAVI) by centres with and without an on-site cardiac surgery programme: preliminary experience from the German TAVI registry. *EuroIntervention* 2014;**105**:602–608.
9. Gafoor S, Sirotina M, Doss M, Franke J, Piayda K, Lam S, Bertog S, Vaskelyte L, Hofmann I, Sievert H. Safety of transcatheter aortic valve implantation in a hospital with visiting on-site cardiac surgery. *J Interv Cardiol* 2015;**28**:76–81.
10. Bestehorn K, Bestehorn M, Fleck E. Influence of different approaches of aortic valve replacement on the incidence of post-operative delirium in intermediate risk patients – a matched pair analysis. *Curr Med Res Opin* 2015;**31**:2157–2163.
11. Mollmann H, Bestehorn K, Bestehorn M, Papoutsis K, Fleck E, Ertl G, Kuck KH, Hamm C. In-hospital outcome of transcatheter vs. surgical aortic valve replacement in patients with aortic valve stenosis: complete dataset of patients treated in 2013 in Germany. *Clin Res Cardiol* 2016; doi: 10.1007/s00392-016-0962-4.
12. Kotting J, Schiller W, Beckmann A, Schafer E, Dobler K, Hamm C, Veit C, Welz A. German Aortic Valve Score: a new scoring system for prediction of mortality related to aortic valve procedures in adults. *Eur J Cardiothorac Surg* 2013;**43**:971–977.
13. AQUA Institute. Qualitätsindikatoren. Indikatorenbeschreibung 2014. 2014 https://sqg.aqua-institut.de/ergebnisse/leistungsbereiche/aortenklappenchirurgie-kathetergestuetzt.html (30 April 2016).

14. Kuck KH, Hamm C. Executive summary of the position paper of the German Cardiac Society on quality criteria for the implementation of transcatheter aortic valve implantation (TAVI). *Eur Heart J* 2015;**36**:328–330.
15. Federal Joint Committee. Guidelines for minimally-invasive heart valve interventions. 2015 https://www.g-ba.de/informationen/richtlinien/84/-tab/beschluesse/details/2165/listContext/beschluesse.
16. Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F, Derumeaux G, Anselme F, Laborde F, Leon MB. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. *Circulation* 2002;**106**:3006–3008.
17. Holmes DR Jr, Brennan JM, Rumsfeld JS, Dai D, O'Brien SM, Vemulapalli S, Edwards FH, Carroll J, Shahian D, Grover F, Tuzcu EM, Peterson ED, Brindis RG, Mack MJ, Registry SAT. Clinical outcomes at 1 year following transcatheter aortic valve replacement. *JAMA* 2015;**313**:1019–1028.
18. Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, Webb JG, Douglas PS, Anderson WN, Blackstone EH, Kodali SK, Makkar RR, Fontana GP, Kapadia S, Bavaria J, Hahn RT, Thourani VH, Babaliaros V, Pichard A, Herrmann HC, Brown DL, Williams M, Akin J, Davidson MJ, Svensson LG, PARTNER 1 Trial Investigators. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet* 2015;**385**:2477–2484.
19. Babaliaros V, Devireddy C, Lerakis S, Leonardi R, Iturra SA, Mavromatis K, Leshnower BG, Guyton RA, Kanitkar M, Keegan P, Simone A, Stewart JP, Ghasemzadeh N, Block P, Thourani VH. Comparison of transfemoral transcatheter aortic valve replacement performed in the catheterization laboratory (minimalist approach) versus hybrid operating room (standard approach): outcomes and cost analysis. *JACC Cardiovasc Interv* 2014;**7**:898–904.
20. Genereux P, Demers P, Poulin F. Same day discharge after transcatheter aortic valve replacement: are we there yet? *Catheter Cardiovasc Interv* 2016; **87**:980–982.
21. Vahanian A, Alfieri O. TAVI: the importance of the 'heart team' and medico-surgical centres. *Eur Heart J* 2012 http://eurheartj.oxfordjournals.org/content/33/19/2451.explore-tavi-the-importance-of-the-heart-team-and-medico-surgical-centres.
22. Mylotte D, Head SJ, Kappetein AP, Piazza N. TAVI at institutions without cardiovascular surgery departments: why? *EuroIntervention* 2014;**10**:539–541.
23. Eggebrecht H, Schmermund A, Kahlert P, Erbel R, Voigtlander T, Mehta RH. Emergent cardiac surgery during transcatheter aortic valve implantation (TAVI): a weighted meta-analysis of 9,251 patients from 46 studies. *EuroIntervention* 2013;**8**:1072–1080.
24. Doebler K. Re: 'Transcatheter aortic valve implantation (TAVI) in Germany 2008–2014: on its way to standard therapy for aortic valve stenosis in the elderly?' by Holger Eggebrecht *et al*. *EuroIntervention* 2016;**11**:1083–1085.