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ABSTRACT

Transfemoral approach stands as the reference access-route for transcatheter aortic valve implantation (TAVI). Nonetheless, alternatives approaches are still needed in a significant proportion of patients. This study aimed at comparing outcomes between transthoracic-approach (transapical or transaortic) and transarterial-approach (transcarotid or sub-clavian) TAVI. Data from 191 consecutive patients who underwent surgical-approach TAVI from May 2009 to September 2017 were analyzed. Patients were allocated in two groups according to the approach. The primary endpoint was the 30-day composite of death of any cause, need for open surgery, tamponade, stroke, major or life-threatening

bleeding, stage 2 or 3 acute kidney injury, coronary obstruction, or major vascular complications. During the study period, 104 patients underwent transthoracic TAVI (transapical: 60.6%, transaortic: 39.4%) whereas 87 patients underwent transarterial TAVI (sub-clavian: 83.9%, transcarotid: 16.1%). Logistic EuroSCORE I tended to be higher among transthoracic-TAVI recipients. In-hospital and 30-day composite endpoint rates were 25.0% and 11.5% (p = 0.025), and 26.0% and 14.9% (p=0.075) for the transthoracic and transarterial cohorts, respectively. Propensity score-adjusted logistic regression demonstrated no significant detrimental association between the 30-day composite endpoint and transthoracic access (OR: 2.12 95% CI: 0.70-6.42; p=0.18). Transarterial TAVI was associated with a shorter length of stay (median: 6 vs. 7 days, p<0.001). TAVI approach was not an independent predictor of mid-term mortality. In conclusion, non-transfemoral transarterial-approach TAVI is safe, feasible, and associated with comparable rates of major perioperative complications, and mid-term mortality compared with transthoracic-approach TAVI.

KEYWORDS: Aortic stenosis, Transcatheter aortic valve implantation, Surgical approaches

Since the publication of the randomized Placement of Aortic Transcatheter Valves (PARTNER) trials[1–3], transcatheter aortic valve implantation (TAVI) is recognized as an efficient therapy for treatment of severe aortic stenosis in inoperable, high and intermediate-risk patients. Transfemoral approach, as the less invasive and safest access, stands as the reference access route for TAVI. Although non-transfemoral approaches are decreasing with the miniaturization of delivery systems, in a recent national registry 17.2% of patients were still treated by non-transfemoral accesses[4]. Alternative approaches requiring a surgical contribution include transaortic, transapical, sub-clavian, and, lately, transcarotid access. Transapical access is well-described[5] and provides acceptable results. The transaortic approach requires to expose the ascending aorta using a mini-sternotomy or a right thoracotomy, and is associated with similar outcomes as transapical access[6,7]. Considering their invasiveness, the use of these transthoracic approaches is decreasing. Sub-clavian access is a safe method, showing comparable results to transfemoral approach[8], however with the same limitations regarding vessel anatomy, and being unsuited for patients with thoracic artery grafts. Transcarotid access tends to represent a growing proportion of alternative accesses, despite

ongoing questions regarding the risk of stroke[9,10]. Given the paucity of direct comparisons of alternative accesses in the current literature, the aim of this study was to compare short and mid-term outcomes between patients undergoing transthoracic (transapical or transaortic) TAVI and transarterial (transcarotid or sub-clavian) TAVI.

METHODS

All patients who underwent a non-transfemoral approach TAVI at our institution (Rennes University Hospital, Rennes, France) from May 2009 to September 2017 were included. Details regarding the pre-procedural evaluation and follow-up modalities were previously published[11]. Details regarding the access selection process by the Heart Team are provided in the **supplementary appendix**. All patients gave written informed consent for the procedures and anonymous collection of their data, which were prospectively gathered in an electronic database. The institutional review board waived specific consent for this study due to its retrospective and observational nature.

Chronic lung disease was defined as a restrictive lung disease or a chronic obstructive pulmonary disease. Cerebrovascular disease was defined as a previous carotid surgery or a stenosis ≥ 50% of carotid or vertebral arteries. Peripheral artery disease included artery stenosis ≥ 50%, claudication and previous vascular surgery. Surgical risk was estimated with the logistic EuroScore I, the logistic EuroScore II and the Society of Thoracic Surgeons Predicted Risk Of Mortality score. Valve Academic Research Consortium 2 (VARC-2) standards were used to define hostile chest, severe liver disease and all study endpoints[12].

The primary endpoint was the 30-day rate of major perioperative complications defined as the composite of death of any cause, need for open surgery, tamponade, stroke, major or life-threatening bleeding, stage 2 or 3 acute kidney injury, coronary obstruction, or major vascular complications. Secondary endpoints were in-hospital and 30-day rates of the components of the primary endpoint and survival at follow-up.

Patients were included, according to the access site used, in the transthoracic (transapical or transaortic access) or transarterial (sub-clavian or transcarotid access) groups. Continuous variable are

presented as mean ± standard deviation or median (interquartile range) depending on their distribution, which was assessed using the Kolmogorov-Smirnov test, and were compared using t tests or the Mann-Whitney U test as appropriate. Categorical variables are summarized as numbers (percentages), and were compared using chi-square tests or the Fisher exact test. Survival rates were summarized using Kaplan-Meier estimates, and log-rank tests were used to compare groups. To evaluate the impact of access-site on the rate of the primary endpoint while adjusting for baseline differences between groups, propensity score-adjusted multivariable logistic regression was performed. Results are expressed as adjusted odds ratio (OR) with its 95% confidence interval (CI). The propensity score was calculated as the probability of undergoing transthoracic access using a non-parsimonious logistic regression model. Details regarding variables included in the propensity score can be found in the **supplementary appendix**. The propensity score model had adequate calibration (Hosmer-Lemeshow goodness-of-fit p=0.46) and discrimination (c-statistic=0.93, 95% CI: 0.89-0.97). Predictors of all-cause mortality were analyzed using univariable and multivariable proportional hazard models (cumulative outcomes). The proportional hazard assumption was tested by plotting log-minus-log survival. Variables with p-values <0.1 in univariable analysis and the access-route were included in the multivariable analysis. Statistical analysis was performed with the use of Statistical Package for Social Sciences version 22 (SPSS, Chicago, IL, USA). All tests were 2-sided at the 0.05 significance level.

RESULTS

During the study period, 191 patients (female sex: 39%) had a non-transfemoral approach TAVI, among which 87 patients (mean-age: 79.3±6.7 years) underwent a transarterial approach and 104 patients (mean-age: 78.0±9.9 years) a transthoracic approach. Sub-clavian access was performed in 73 patients (38.2%), transcarotid in 14 patients (7.3%), transaortic in 41 patients (21.5%), and transapical in 63 patients (33.0%). **Supplemental Figures 1 and 2** show the annual number of each alternative access, and the annual proportion of all TAVI represented by each of these accesses. Baseline characteristics of the study population according to the approach are summarized in **Table 1.** Coronary artery disease was significantly more frequent in the transthoracic group than in the

transarterial group (68.3% vs. 48.4%; p=0.008). Patients of the transthoracic group harbored a higher burden of cerebrovascular disease (18.4% vs. 3.4%; p=0.001) and hostile chest (5.8% vs. 0.0%; p=0.03). Prevalence of peripheral artery disease was similar in both groups. Mean Logistic EuroScore I tended to be higher in patients treated with the transthoracic approach (14.9% vs. 12.0%; p=0.053). Echocardiographic parameters were similar between groups.

Procedural characteristics are described in **Table 2**. General anaesthesia was used in all transthoracic procedures, and in 90.8% of the transarterial ones (p = 0.002). Balloon-expendable valves were much more frequently implanted in the transthoracic group (96.2% vs. 26.4%; p<0.001). Device success was achieved in 95.2% of transthoracic TAVI recipients compared with 85.1% of their transarterial counterparts (p=0.024). Major intra-procedural complications were comparable between groups (Table 2).

In-hospital and 30-day outcomes of the 2 groups are depicted in **Table 3. Supplemental Tables 1 and 2** present a comparison of subclavian vs. transcarotid approaches, and transaortic vs. transapical approaches, respectively. In univariate analysis, the in-hospital composite endpoint rate was significantly higher in the transthoracic access cohort (25.0% vs. 11.5%; p=0.025), yet this difference did not persist at 30-day (26.0 vs. 14.9%, p=0.075). Propensity score-adjusted logistic regression confirmed the absence of a significant association between the 30-day composite endpoint and transthoracic access (OR: 2.12, 95% CI: 0.70-6.42; p=0.18). Albeit numerically higher in the transthoracic cohort, there was no significant difference between groups for in-hospital (4.6% vs. 7.7%; p=0.55) and 30-days (4.6% vs. 8.7%; p=0.39) mortality. Also numerically higher in the transthoracic group, incidences of most major periprocedural complications were statistically comparable between groups. One contralateral transient ischemic attack occurred 24h post-procedure in a patient who underwent left transcarotid TAVI under general anesthesia without balloon predilation. New-onset atrial fibrillation and acute kidney injury stage 2 or 3 were more prevalent in the transthoracic cohort. In the transthoracic access group, consistently with the lower use of self-expendable valves, TAVI resulted in a lower rate of permanent pacemaker implantation than in the transarterial cohort. Length of hospitalization was higher (7.0 days vs. 6.0 days; p<0.001) and patients

were less often discharged at home (42.0% vs. 68.7%; p=0.002) in the transthoracic cohort. Echocardiographic findings at discharge are presented in **Table 3**.

Median follow-up was 395 days (interquartile range [IQR]: 320-974) and was significantly longer in the transthoracic cohort (676 days, IQR: 367-1182, vs. 367 days, IQR: 204-427; p<0.001). The 1-year Kaplan-Meier survival curves are shown in **Figure 1**. At 1 year, overall survival was similar in both groups (89.6%; 95% CI: 80.1-94.7 and 84.5%; 95% CI: 75.9-90.2 with the transarterial and transthoracic approach, respectively; p=0.30). **Figure 2** summarizes the multivariable predictors of all-cause mortality at follow-up. Atrial fibrillation (HR: 2.52; 95% CI: 1.33-4.78; p=0.005), STS-PROM score (HR: 1.18; 95% CI: 1.01-1.39; p=0.04) and periprocedural stroke (HR: 5.85; 95% CI: 1.51-22.63; p=0.011) were found as independent predictors of overall mortality. Transthoracic access-route was not independently associated with mortality at follow-up (HR: 1.16; 95% CI: 0.55-2.45; p=0.70)

DISCUSSION

The main findings of this study are the following: despite a numerically lower incidence among transarterial TAVI patients, transthoracic approaches were not significantly associated with an increased rate of 30-days major perioperative adverse events or decreased mid-term survival (**Figure 3**). However, a shorter length of stay and a higher likelihood of being discharge at home were observed among transarterial TAVI recipients.

At the inception of the TAVI era, when a transfemoral approach was not feasible, a "transapical-first" policy was usually applied. Currently, strategies tend to evolve, with a priority for less invasive approaches. In a recent analysis of temporal trends in French registries[4], transapical TAVI drastically decreased over time (from 27.9% in 2010 to 4.7% in 2015 among patients receiving a balloon-expandable valve). This evolution can be explained by an increase of transfemoral TAVI (73.4% vs. 82.8%) and the expansion of alternative access-sites of more recent emergence such as the direct aortic, and, particularly, transcarotid routes (5.5% and 3.4% of 12804 patients included in the FRANCE TAVI registry, respectively). Comparable findings were previously reported in the UK

registry[13]. However, the transcarotid approach being the latest implemented in routine practice, the above-mentioned trend will likely accentuate regarding this specific access.

Transapical and transaortic TAVI are associated with similar rates of complications and comparable outcomes[6,7]. Our results regarding the in-hospital and 30-days morbidity and mortality of transthoracic TAVI are consistent with these recent studies. On the contrary to transthoracic TAVI, some groups reported favourable outcomes, sometimes comparable with the transfemoral approach, with the use of transcarotid and subclavian TAVI[8,14,15]. Therefore, these alternative transarterial accesses could conceivably be superior to transthoracic ones, and should represent the first option when transfemoral TAVI cannot be performed. However, the paucity of direct comparisons between non-transfemoral approaches supporting this assumption is highlighted by the observation that transthoracic access still represents the majority of alternative access TAVI in some regions, such as the US[16]. The present study adds to a small number of publications, which investigated the potential benefits of practicing a transarterial instead of a transthoracic approach[9,17,18,19]. As in the present study, a 3 Italian centers retrospective study also reported a non-significant trend to increased peri-procedural events, which did not impact mid-term survival, with the use of transapical versus subclavian TAVI[18]. Within the larger UK registry, Fröhlich et al demonstrated a significantly higher 2-year mortality following transapical or transaortic access than after transfemoral or subclavian TAVI[17]. Recently, using propensity score-matching, Chamandi et al published the largest comparative analysis specifically involving alternative access[19]. Ninety-four transcarotid TAVI recipients were matched with 163 transthoracic TAVI patients. Transcarotid access was associated with reduced 30-days rates of new-onset atrial fibrillation, major or life-threatening bleeding, stage 2 or 3 acute kidney injury, and a shorter length of stay. Mortality, stroke and device success were comparable between groups while early safety favored transcarotid access. The present study reports largely consistent findings.

Stroke was numerically higher in the transthoracic cohort, without significant difference between groups (3.8% vs. 1.1%; p = 0.38), which may be related to the small sample size. Beyond their heavier atherosclerotic burden, new-onset atrial fibrillation, a condition considerably more prevalent after transthoracic TAVR and associated with a higher risk of 30-days cerebrovascular events[20], may significantly contribute to an increased risk among recipients of this approach. This

finding may be of paramount importance, as consistently with our results, periprocedural stroke was an independent predictor of mortality in previous studies[21]. Moreover, although local anesthesia was not consistently associated with better outcomes[22], a higher rate of periprocedural stroke has been suggested with general anesthesia following transcarotid TAVI[23]. Only 50% of transcarotid approach patients were treated under local anesthesia with sedation in the present study. Whether a broader use of local anesthesia and sedation with growing experience with this approach improves neurological outcomes should be the focus of future studies.

On the contrary, permanent pacemaker implantation was more frequent in the transarterial-access cohort. As reported in previous studies[24], this finding is related to the higher implantation rate of self-expandable valves in the transarterial group. With the expansion of TAVI to lower-surgical risk and younger patients, this result raises the major issue of potentially negative effects of long-term pacing, even if the impact of permanent pacemaker implantation after TAVI remains debated[24,25]. However, during the early experience of TAVI, subclavian approach was almost exclusively performed with self-expandable valve. Yet, with growing experience, balloon-expandable valves are increasingly implanted through this access, which should mitigate its detrimental association with post-procedural pacemaker implantation.

Several limitations need to be acknowledged. First, there were significant differences in baseline characteristics between the two groups, which we attempted to adjust for by propensity score-adjustment. Nonetheless, no statistical method can provide the degree of bias reduction obtained with randomization. Therefore, residual confounding, related to the higher burden of comorbidities observed in the transthoracic group, cannot be ruled out. Second, this is a retrospective analysis, based on a single center population with a limited number of patients in both cohorts, which implies a significant risk of type II error. Furthermore, because of the relatively recent development of this strategy in our center, the transcarotid approach was less represented than the subclavian access-route in the transarterial cohort. Considering the well-known learning-curve effect with other approaches [26,27], we can hypothesized that our lower experience regarding transcarotid procedures in comparison with others approaches potentially influenced our results. Conversely, transcarotid TAVI was likely

performed using more advanced valve technologies among patients with a lower surgical risk, which may have balanced our limited experience.

CONCLUSION

Non-transfemoral transarterial-approach TAVI is safe, feasible, and associated with comparable rates of major perioperative complications, and mid-term mortality compared with transthoracic-approach TAVI. Nonetheless, transarterial access may be associated with lower rates of new-onset atrial fibrillation, acute kidney injury, and shorter hospitalization.

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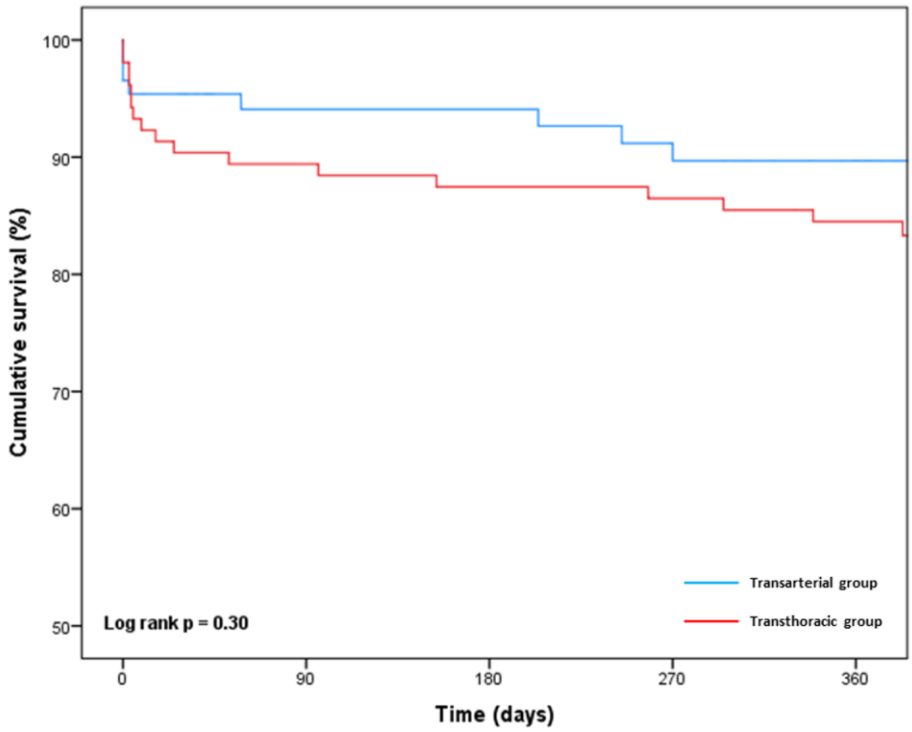


Patients at risk					
Transarterial group	87	71	68	61	52
Transthoracic group	104	93	90	89	84

Figure 1 - Rates of all-cause mortality

Kaplan-Meier curves at 1-year follow-up for overall mortality according to the access site.

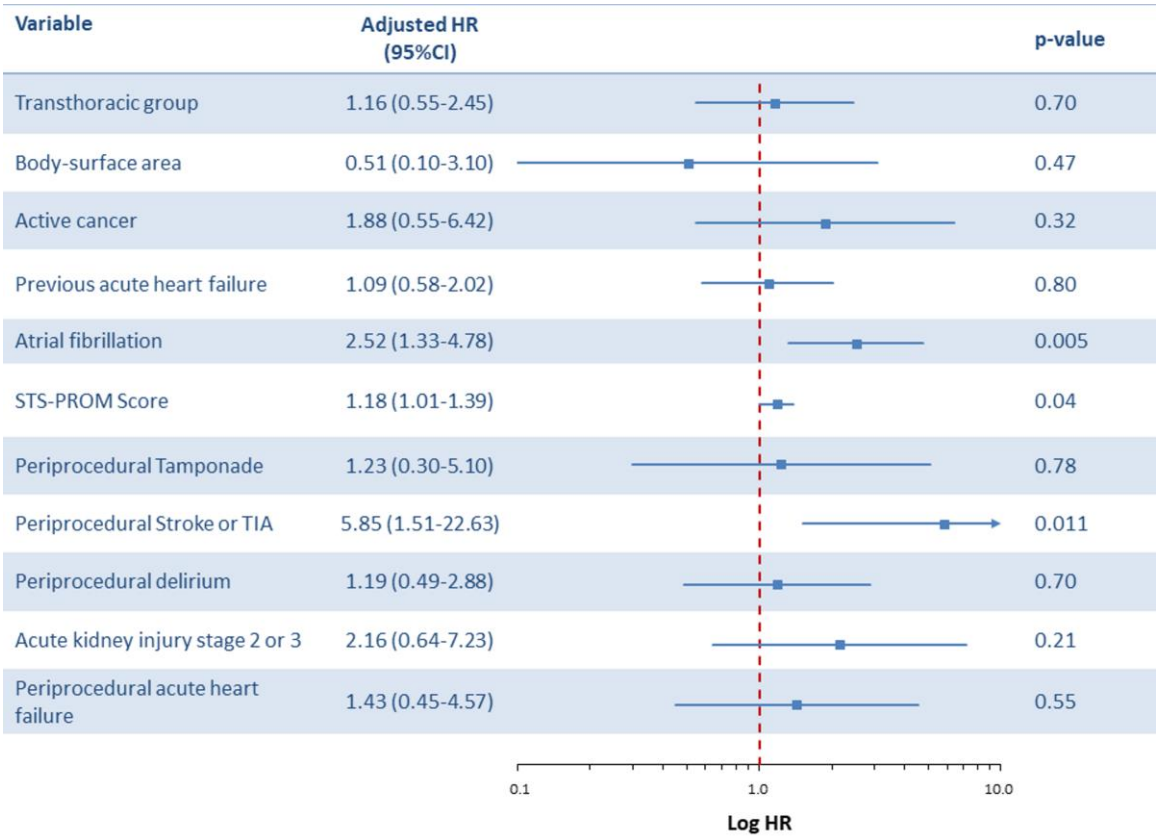
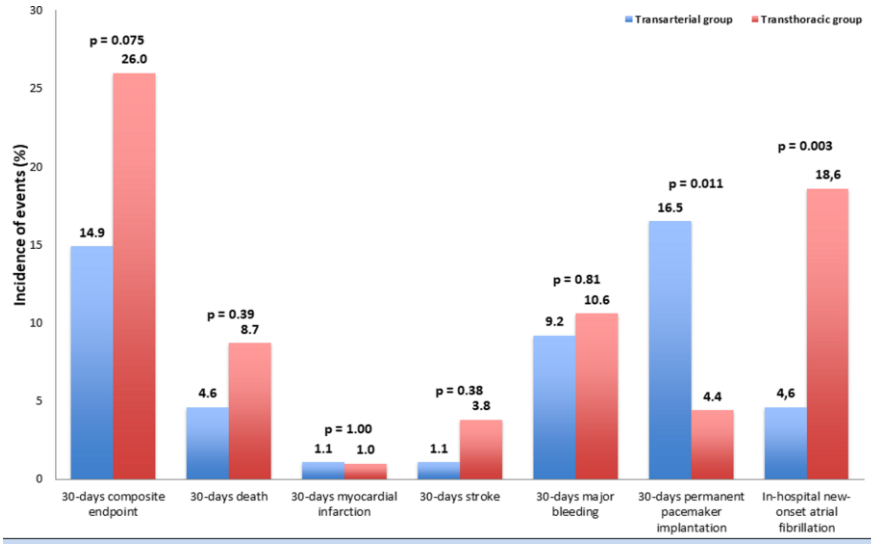


Figure 2 – Predictors of all-cause mortality at follow-up

Forest-plot showing the multivariable model for all-cause mortality, including all variables with a p-value < 0.1 in univariate analysis.

CI: confidence interval; HR: Hazard-ratio; STS-PROM: Society of thoracic surgeons predicted risk of mortality; TIA: transient ischemic attack.



Propensity score-adjusted logistic regression for the 30-day primary composite endpoint		
	Adjusted odds-ratio with 95% confidence interval	p-value
Transthoracic access	2.12 (0.70-6.42)	0.18

Figure 3 - In-hospital and 30-days outcomes according to TAVI approach

Table 1 – Baseline characteristics of the study population according to TAVI approach

	Transarterial TAVI group (n=87)	Transthoracic TAVI group (n=104)	p-value
Age (years)	79.3 ± 6.7	78.0 ± 9.9	0.60
Female sex	35 (40%)	40 (39%)	0.88
Body-mass index (kg/m²)	29.1 ± 6.7	26.4 ± 4.8	0.024
Body-surface area (m²)	1.83 ± 0.21	1.75 ± 0.20	0.025
NYHA class III or IV	40 (46%)	51 (49%)	0.77
Previous acute heart failure	31 (36%)	33 (32%)	0.65
Medical history			
Hypertension	62 (71%)	77 (74%)	0.75
Diabetes mellitus	24 (28%)	18 (17%)	0.11
Coronary artery disease*	42 (48%)	71 (68%)	0.008
Previous myocardial infarction	12 (14%)	17 (16%)	0.69
Previous coronary artery bypass grafting	15 (17%)	28 (27%)	0.12
Previous percutaneous coronary intervention	22 (25%)	31 (30%)	0.52
Previous balloon aortic valvuloplasty	8 (9%)	12 (12%)	0.64
Previous surgical aortic valve replacement	7 (8%)	5 (5%)	0.39
Other cardiac surgery	2 (2%)	3 (3%)	1.00
Atrial fibrillation	39 (45%)	34 (33%)	0.10
Previous permanent pacemaker	8 (9%)	13 (13%)	0.50
Cerebrovascular disease	3 (3%)	19 (18%)	0.001
Previous Stroke/TIA	8 (9%)	11 (11%)	0.81
Peripheral artery disease	33 (38%)	46 (44%)	0.46
Active cancer	3 (3%)	7 (7%)	0.35
Previous chest radiotherapy	5 (6%)	8 (8%)	0.78
Hostile chest	-	6 (6%)	0.03
Respiratory failure	23 (26%)	27 (26%)	1.00
Renal failure			0.64
Moderate	39 (45%)	45 (43%)	
Severe	3 (3%)	7 (7%)	
Dialysis	2 (2%)	1 (1%)	0.59
Severe liver disease	-	1 (1%)	1.00
Logistic EuroScore I	12.0 (7.0-21.0)	14.9 (9.7-23.0)	0.053
Logistic EuroScore II	3.4 (1.9-5.8)	3.4 (2.4-6.9)	0.22
STS-PROM Score	3.1 (2.2-4.8)	3.5 (2.4-4.9)	0.18
Echocardiography			
LVEF (%)	54.2 ± 12.5	54.0 ± 13.3	0.54
LVEF < 50%	25 (29%)	27 (26%)	0.75
Aortic valve area (cm²)	0.74 ± 0.16	0.75 ± 0.32	0.56
Mean aortic gradient (mmHg)	49.0 ± 15.7	47.1 ± 14.8	0.60
Mean aortic gradient <40 mmHg	20 (23%)	26 (25%)	0.87
Aortic regurgitation ≥ mild	21 (24%)	34 (33%)	0.20
Mitral regurgitation ≥ mild	23 (26%)	37 (36%)	0.21
Moderate or severe mitral stenosis	3 (3%)	3 (3%)	1.00
Systolic pulmonary artery pressure > 60 mmHg†	10/64 (16%)	17/79 (22%)	0.40

*Coronary artery disease defined as previous myocardial infarction, or previous percutaneous coronary intervention, or previous coronary artery bypass grafting, or presence of at least one lesion ≥ 50% on the preoperative coronary angiogram.

†Systolic pulmonary artery pressure was measurable by echocardiography in 145 patients.

Table 2 – Procedural characteristics of the study population according to TAVI approach.

	Transarterial TAVI group (n=87)	Transthoracic TAVI group (n=104)	p-value
Urgent procedure	3 (3%)	4 (4%)	1.00
General anesthesia	79 (91%)	104 (100%)	0.002
Approach			
Sub-clavian	73 (84%)	-	
Carotid	14 (16%)	-	
Trans-aortic	-	41 (39%)	
Transapical	-	63 (61%)	
Balloon-expandable valve	23 (26%)	100 (96%)	<0.001
Newer-generation valve*	70 (81%)	44 (42%)	<0.001
Valve type			<0.001
Edwards SAPIEN	1 (1%)	27 (26%)	
Edwards SAPIEN XT	-	30 (29%)	
Edwards SAPIEN 3	22 (25%)	43 (41%)	
Medtronic CoreValve	13 (15%)	3 (3%)	
Medtronic Evolut R	48 (55%)	1 (1%)	
Valve size (mm)			<0.001
23	15 (17%)	34 (33%)	
26	27 (31%)	50 (48%)	
29	39 (45%)	18 (17%)	
31	3 (3%)	2 (2%)	
Number of implanted valve			0.09
0	3 (3%)	-	
1	84 (97%)	103 (99%)	
2	-	1 (1%)	
Fluoroscopy time (min)	20.4 ± 7.9	13.0 ± 6.3	<0.001
Dosimetry (Gy.cm²)	82 (55-132)	82 (55-128)	0.99
Contrast volume (ml)	140 (110-199)	140 (108-177)	0.66
Device success	74 (85%)	99 (95%)	0.024
Perprocedural complications			
Perprocedural death	3 (3%)	1 (1%)	0.33
Valve embolization or ectopic deployment	1 (1%)	2 (2%)	1.00
Conversion to open surgery	2 (2%)	4 (4%)	0.69
Coronary obstruction	1 (1%)	-	0.46
Tamponade	2 (2%)	-	0.21
Annulus rupture	-	1 (1%)	1.00
Left ventricular perforation	1 (1%)	1 (1%)	1.00

* Edwards SAPIEN 3 or Medtronic Evolut R

Table 3 – Outcomes of the study population according to TAVI approach

	Transarterial TAVI group (n=87)	Transthoracic TAVI group (n=104)	p-value
Cumulative in-hospital outcomes			
In-hospital composite endpoint	10 (12%)	26 (25%)	0.025
In-hospital death	4 (5%)	8 (8%)	0.55
Coronary obstruction	1 (1%)	-	0.46
Tamponade	2 (2%)	4 (4%)	0.69
Myocardial infarction	-	1 (1%)	1.00
Acute heart failure	3 (3%)	10 (10%)	0.15
Stroke / Transient ischemic attack	1 (1%)	4 (4%)	0.38
Stroke	-	4 (4%)	
Transient ischemic attack	1 (1%)	-	
Major or life-threatening bleeding			
BARC 5	-	-	-
BARC 3 – total	5 (6%)	10 (10%)	0.42
BARC 3a	2 (2%)	5 (5%)	0.46
BARC 3b	3 (3%)	5 (5%)	0.73
BARC 3c	-	-	-
Minor bleeding – BARC definition	1 (1%)	5 (5%)	0.22
Vascular complications			
Major	-	-	-
Minor	2 (2%)	1 (1%)	0.59
Acute kidney injury stage 2 or 3	-	8 (8%)	0.008
Septic shock	1 (1%)	2 (2%)	1.00
Pneumopathy	2 (2%)	8 (8%)	0.11
Need for reintubation	1 (1%)	5 (5%)	0.22
Delirium	3 (3%)	10 (10%)	0.15
New-onset atrial fibrillation	4 (5%)	19 (19%)	0.003
Permanent pacemaker implantation*	13/79 (17%)	4/91 (4%)	0.011
Discharged at home	58/83 (69%)	43/93 (42%)	0.002
Length of hospitalization, days†	6.0 (4.0-7.0)	7.0 (6.0-9.0)	<0.001
Echocardiographic findings at discharge			
Left ventricular ejection fraction (%)	55.8 ± 13.2	54.9 ± 12.0	0.39
Aortic valve area (cm^2)	1.95 ± 0.54	1.78 ± 0.46	0.016
Patient-prosthesis mismatch	*n=82*	*n=95*	0.67
Moderate	9 (11%)	15 (16%)	
Severe	5 (6%)	5 (5%)	
Mean aortic gradient (mmHg)	11.4 ± 7.1	11.4 ± 5.3	0.55
Paravalvular leak	*n=83*	*n=98*	0.39
None/trace	58 (70%)	74 (76%)	
Mild	21 (25%)	23 (24%)	
Moderate	3 (4%)	1 (1%)	
Severe	1 (1%)	-	
Cumulative 30-day outcomes			
30-day composite endpoint	13 (15%)	27 (26%)	0.075
30-day death	4 (5%)	9 (9%)	0.39
Stroke	1 (1%)	4 (4%)	0.38
Myocardial infarction	1 (1%)	1 (1%)	1.00
Rehospitaliazation for heart failure	7 (11%)	7 (9%)	0.78
Major or life-threatening bleeding			
BARC 5	-	-	-

BARC 3 – total	8 (9%)	11 (11%)	0.81
BARC 3a	3 (3%)	5 (5%)	0.73
BARC 3b	5 (6%)	6 (6%)	1.00
BARC 3c	-	-	-
Major vascular complications	1 (1%)	-	0.46
Permanent pacemaker implantation*	13/79 (17%)	4/91 (4%)	0.011

*Among patients without prior permanent pacemaker.

† Among patients discharged alive from the hospital.

Composite endpoint : in-hospital occurrence of any of the following : death, need for open surgery, tamponade, stroke, major/life-threatening bleeding, stage 2 or 3 acute kidney injury, coronary obstruction, major vascular complications.