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ADULT CARDIAC

# Transapical aortic valve replacement is a safe option in patients with poor left ventricular ejection fraction: results from the Italian Transcatheter Balloon-Expandable Registry (ITER)†

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## Abstract

**OBJECTIVES:** The most commonly used accesses for transcatheter aortic valve implantation (TAVI) are the transfemoral (TF-TAVI) and the transapical (TA-TAVI) ones. There are concerns about TA-TAVI use in patients with reduced left ventricular ejection fraction (LVEF). The aim of this retrospective multicentre study was to compare the outcomes of TA-TAVI and TF-TAVI in patients with poor LVEF.

**METHODS:** Patients with LVEF ≤35% were included in the analysis. Data were obtained from the Italian Transcatheter Balloon-Expandable Registry (ITER), which enrolled patients undergoing TAVI with the Sapien bioprosthesis in 33 national centres. Patients were divided into 2 groups according to the access: TA or TF. A multivariable logistic regression analysis was performed in order to evaluate whether the type of approach (TA and TF) has an impact on outcomes.

**RESULTS:** Between 2007 and 2012, 1882 patients were enrolled in the Registry. LVEF ≤35% was found in 208 (11.1%) patients. TA-TAVI and TF-TAVI were performed in 69 (33.2%) and 139 (66.8%) patients, respectively. Overall 30-day mortality was 11.6% and 7.9% in TA and TF patients, respectively ($P = 0.45$). Overall Kaplan–Meier survival was significantly higher in the TF-TAVI group (log rank: $P = 0.003$). Age [odds ratio (OR) 1.066, $P = 0.016$], creatinine (OR: 2.301, $P < 0.001$), preoperative permanent pacemaker (OR: 4.662, $P = 0.035$) and TA approach (OR: 2.577, $P = 0.006$) were identified as independent predictors of overall mortality at follow-up. However, the TA approach resulted an independent variable of mortality only 3 years after TAVI.

**CONCLUSIONS:** TAVI yields good results in patients with depressed LVEF. Age, preoperative creatinine and preoperative pacemaker are independently associated with mortality. The TA access is associated with mortality only after 3 years of follow-up, thus probably reflecting a worse general clinical status of these patients.

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Keywords: Transcatheter aortic valve implantation • Left ventricular ejection fraction • Aortic valve

## INTRODUCTION

Transcatheter aortic valve implantation (TAVI) yields excellent outcomes in high-risk and inoperable patients with severe aortic valve stenosis [1, 2], and recently, it has also been demonstrated to be non-inferior to conventional surgery in intermediate-risk patients [3-6]. TAVI may be performed through several approaches: transfemoral (TF), transapical (TA), trans-subclavian and transaortic, but TA and TF are the 2 most commonly used approaches. The great majority of TAVI procedures are now performed through a TF access, and this is for several reasons. TF-TAVI is completely percutaneous, and it may be easily performed with no general anaesthesia. Furthermore, many physicians are concerned about potential injury to the left ventricle by the apical surgical manipulation performed during TA-TAVI [7, 8]. This concern is particularly high with regard to patients with a preoperative already impaired left ventricular ejection fraction (LVEF). It has been demonstrated that LVEF changes occur in a minority of patients after TA-TAVI and that these changes do not have a significant impact on patient outcomes. It has also been shown that in patients with a severely depressed LVEF, there is a greater likelihood of function improvement after TA-TAVI [9]. Nevertheless, it is still unclear whether TA-TAVI yields worse outcomes than TF-TAVI in patients with preoperative depressed LVEF. The aim of this retrospective multicentre study was to compare the outcomes of TA-TAVI and TF-TAVI in patients with poor LVEF.

## MATERIALS AND METHODS

We analysed data from the Italian Transcatheter Balloon-Expandable Registry (ITER), which includes all TAVI patients receiving a balloon-expandable device (Sapien and Sapien XT, Edwards Lifesciences, Irvine, CA, USA; Sapien 3 was still not available during the study period) at 33 Italian centres between 2007 and 2012. The ITER is a 'real-world' and 'all-comers' registry. Consequently, patients, procedural strategies and surgical techniques were selected according to single-site policies, experiences and protocols. Data were locally recorded by each investigator, and subsequently, the coordinator centre collected all records in a single repository.

For this analysis, we included only patients with preoperative LVEF ≤35% who had undergone TA-TAVI or TF-TAVI. Patients were divided into 2 groups according to the access: TA-TAVI or TF-TAVI. Preoperative clinical characteristics were defined according to EuroSCORE definitions [10] and postoperative outcomes were defined according to the updated Valve Academic Research Consortium (VARC)-2 definitions [11]. The echocardiographic measurements were performed according to the current recommendations of the European and American Societies of Echocardiography. In particular, LVEF was calculated using the Simpson biplane method, and aortic regurgitation was classified as absent/trivial (0), mild (1+), moderate (2+) and severe (3+). Local ethics committee approved data collection, and patient consent for the procedure, as well as for data collection, was always obtained. Patients underwent clinical and echocardiographic follow-up at each study site before the operation and at discharge. Follow-up examinations were performed in a time interval of 3-6 months and 1 year after TAVI and on a yearly basis thereafter, according to each centre policy, and then sent to the coordinator centre. All the other details of the ITER have been described elsewhere [12].

### Statistical analysis

Continuous variables are presented as mean (standard deviation) or median (interquartile range), and categorical variables are shown with frequency and proportion. Comparison between groups (TA versus TF) was made using the Wilcoxon-Mann-Whitney test for continuous variables and the $\chi^2$ or the Fisher's exact test for categorical variables as appropriate. Kaplan-Meier method was used to estimate overall survival considering the time of surgery as the time origin. Survival curves were compared using the log-rank test. Because initial data exploration revealed that the proportional hazards assumption of the Cox model was invalid, to assess whether the type of access was a risk factor for clinical outcome, a multivariable logistic regression analysis was performed. Variables, other than age and gender, were included in the multivariable analysis if found to be statistically significant at the univariable analysis with a $P < 0.2$ or if judged to be clinically relevant in the 2 types of access. Odds ratios with 95% confidence intervals were calculated. To evaluate LVEF trend over time, an analysis of repeated measures was performed using mixed-model approach.

All statistical tests were 2-sided. $P$-values of ≤0.05 were considered statistically significant and were conducted using the SAS software package, version 9.3 for Windows (SAS Institute, Cary, NC, USA).

## RESULTS

A total of 1882 patients undergoing TAVI through TF and TA access were enrolled in the ITER during the study period. LVEF ≤35% was found in 208 (11.1%) patients who represented the population of our study. TA-TAVI and TF-TAVI were performed in 69 (33.2%) and 139 (66.8%) patients, respectively. Preoperative patients' characteristics are summarized in Table 1. Mean age was 80.6 ± 6.8 years, and it was not significantly different between the groups. Logistic EuroSCORE was higher in TA patients (36.4 ± 17.5% vs 29.8 ± 17.8%, $P = 0.004$). TA-TAVI patients were more likely to have peripheral vascular disease (59.4% vs 23.7%, $P < 0.001$), to have undergone a previous cardiac operation (36.2% vs 18.7%, $P = 0.006$) and to have a history of coronary artery disease (63.8% vs 42.5%, $P = 0.004$). The other preoperative variables were similar between groups. Table 2 presents baseline echocardiographic data. Mean preoperative LVEF was 29.9% in both groups ($P = 0.82$). Transaortic gradients were significantly higher in the TF-TAVI group (peak gradient: 70.8 mmHg vs 62.1 mmHg, $P = 0.005$; mean gradient: 43.9 mmHg vs 37.8 mmHg, $P = 0.005$). Table 3 presents operative data and complications in all patients and in the 2 groups. There are no significant differences in terms of major intraoperative complications. Table 4 sets out the postoperative results (according to VARC-2

definitions). Although device success was lower in the TF group (11.5% vs 4.4%), the difference was not statistically significant ($P = 0.09$), and it was mainly due to a higher incidence of high gradients in TF patients (7.2% vs 0%). TA patients showed a significantly higher incidence of postoperative atrial fibrillation (15.2% vs 2.2%, $P < 0.001$). Other outcomes were similar between groups. Furthermore, we did not observe significant haemodynamic differences between TA and TF patients (Table 5). In fact, postoperative transvalvular gradients, LVEF and pulmonary artery pressure were similar between groups. In particular, the incidence of postoperative aortic regurgitation was not found to be different in the 2 groups. LVEF at discharge was 36.6 ± 18.6% and 36.9 ± 9.3% in the TA and TF group, respectively ($P = 0.72$). Overall, VARC mortality was 9.1% (19 patients), and it was not different between groups: 11.6% (8 patients) and 7.9% (11 patients) in TA and TF patients, respectively ($P = 0.45$). Median follow-up was 22 months (interquartile range: 21– 75 months). At 1 year, LVEF was 43.4 ± 11.1% and 44.1 ± 11.8% in the TA and TF groups, respectively ($P = 0.66$). Figure 1 shows LVEF changes in the 2 groups. It is evident that LVEF significantly improves in the 2 groups over time ($P < 0.001$), with no differences between groups ($P = 0.90$). Overall survival according to Kaplan–Meier analysis is shown in Fig. 2. The 2 populations have similar survival up to 2 years, but then the TA curve suddenly drops. One-year overall survival according to Kaplan–Meier analysis was 71 ± 5.5% and 78.8 ± 3.5% in TA-TAVI and TF-TAVI, respectively, 2-year survival was 51.7 ± 6.4% and 64 ± 4.3% in TA-TAVI and TF-TAVI, respectively, 3-year survival was 34.6 ± 6.9% and 58.7 ± 4.7% in TA-TAVI and TF-TAVI, respectively, and 4-year survival was 22.2 ± 8.5% and 55.1 ± 5.7% in TA-TAVI and TF-TAVI, respectively. Therefore, overall survival was significantly higher in the TF-TAVI group (log rank: $P = 0.003$). The results of the multivariable logistic regression model are presented in Table 6. In this model, the preoperative variables independently associated with overall mortality at follow-up were age [odds ratio (OR): 1.066, 95% confidence interval (CI): 1.012–1.122; $P = 0.016$], creatinine (OR: 2.301, 95% CI: 1.517–3.489; $P \leq 0.001$), preoperative permanent pacemaker (OR: 4.662, 95% CI: 1.306–16.646; $P = 0.035$) and TA approach (OR: 2.577, 95%CI: 1.240–5.359; $P = 0.006$). However, the TA approach was not significantly associated with mortality at 1 year (OR: 1.31, 95% CI: 0.541–3.170), not at 2 years (OR: 1.627, 95% CI: 0.770–3.440) and also not at 3 years (OR: 2.078, 95% CI: 0.998–4.329).

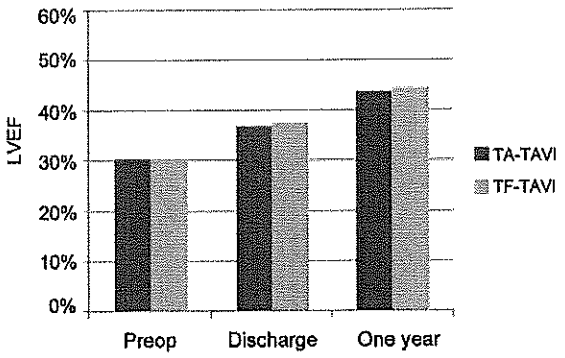


Figure 1: LVEF changes. There is a significant improvement after TAVI with no differences between TA and TF approaches. LVEF: left ventricular ejection fraction; TA: transapical; TF: transfemoral; TAVI: transcatheter aortic valve implantation.

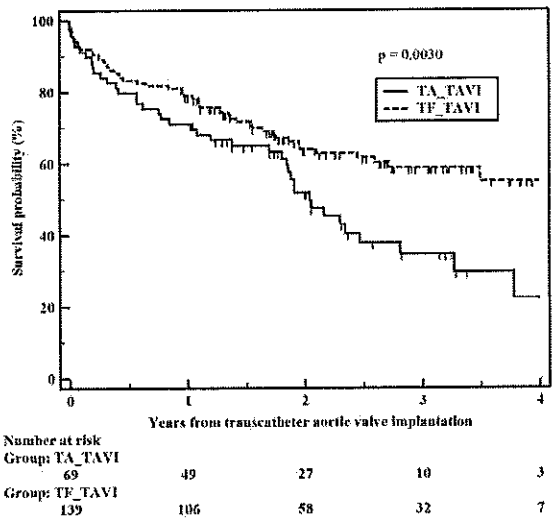


Figure 2: Kaplan–Meier analysis shows that survival after TA-TAVI and TF-TAVI in patients with poor left ventricular ejection fraction is similar during the first 2 years. Then, patients who underwent TA-TAVI have worst survival. TA: transapical; TF: transfemoral; TAVI: transcatheter aortic valve implantation.

## DISCUSSION

The main findings of this study are that (i) TAVI is a safe option in patients with poor preoperative LVEF and (ii) in this particular subset of patients, the TA access is significantly associated with mortality only 3 years after TAVI, thus probably reflecting a worse clinical preoperative status of these patients. Poor LVEF is considered an important risk factor for mortality following conventional surgical aortic valve replacement (AVR). Similarly, poor LVEF has been identified as a risk factor for poor outcomes also after TAVI [13, 14]. Interestingly, TAVI yields outcomes similar to or even better than those of surgical AVR in this high-risk group of patients. In a propensity-matched study using data from the Italian OBSERVANT registry, Onorati *et al.* [15] showed that, in patients with severe left ventricular systolic dysfunction, both TAVI and AVR are valid treatment options, with comparable hospital mortality and periprocedural morbidity. Furthermore, it has also been shown that, in patients with poor preoperative LVEF, those undergoing TAVI have better LVEF recovery when compared with AVR patients [16]. Overall, VARC mortality in our study cohort was 9.1%. A similar finding was reported by Fraccaro *et al.* [17] who found a mortality rate of 10% in TAVI patients with LVEF ≤35% and a 3% mortality in those with preserved left systolic function ($P = 0.010$). Although it is commonly assumed that the surgical manipulation of the left ventricular apex worsens the functioning of an already suffering left ventricular myocardium, the data do not support this belief. We did not observe any significant difference between TA-TAVI and TF-TAVI regarding VARC mortality, and all other major postoperative complications like myocardial infarction, stroke, bleeding and acute kidney injury. Furthermore, LVEF significantly improved after TAVI (Fig. 1), doing so from 30% preoperatively to 43% postoperatively, and we could not determine any difference in the improvement rate between patients undergoing TA-TAVI or TF-TAVI. In a previous study, we demonstrated that in TA-TAVI patients, the likelihood of LVEF improvement was higher in those

**Table 1:** Preoperative clinical variables

| | All ($n = 208$) | TA-TAVI ($n = 69$) | TF-TAVI ($n = 139$) | *P*-value |
|---|---|---|---|---|
| Age, years [mean (SD)] | 80.6 (6.8) | 79.6 (7.4) | 81.1 (6.5) | 0.16 |
| Gender (female), *n* (%) | 88 (42.3) | 24 (34.8) | 64 (46.0) | 0.12 |
| Body mass index, mean (SD) | 24.9 (3.9) | 25.1 (3.9) | 24.9 (3.9) | 0.96 |
| Hypertension, *n* (%) | 170 (81.7) | 59 (85.5) | 111 (79.9) | 0.32 |
| Diabetes mellitus, *n* (%) | 81 (38.9) | 28 (40.6) | 53 (38.1) | 0.73 |
| Insulin-dependent diabetes mellitus, *n* (%) | 39 (18.8) | 17 (24.6) | 22 (15.8) | 0.13 |
| Creatinine, mg/dl [mean (SD)] | 1.6 (1.2) | 1.5 (0.8) | 1.6 (1.3) | 0.42 |
| Glomerular filtration rate, ml/min/1.73 $m^2$ [mean (SD)] | 39.0 (18.3) | 39.0 (16.9) | 38.9 (19.1) | 0.91 |
| Haemoglobin, g/dl [mean (SD)] | 12.0 (1.6) | 12.0 (1.8) | 12.0 (1.6) | 0.97 |
| Logistic EuroSCORE, % [mean (SD)] | 32.0 (17.9) | 36.4 (17.5) | 29.8 (17.8) | **0.004** |
| Logistic EuroSCORE II, % [mean (SD)] | 12.3 (12.3) | 11.5 (8.0) | 12.7 (14.5) | 0.24 |
| STS mortality score, % [mean (SD)] | 12.7 (10.6) | 12.5 (8.8) | 12.8 (11.6) | 0.30 |
| Peripheral vascular disease, *n* (%) | 74 (35.6) | 41 (59.4) | 33 (23.7) | **<0.001** |
| COPD, *n* (%) | 51 (24.5) | 13 (18.8) | 38 (27.3) | 0.18 |
| Neurological dysfunction, *n* (%) | 15 (7.2) | 4 (5.8) | 11 (7.9) | 0.78 |
| Critical preoperative state, *n*(%) | 20 (9.6) | 8 (11.6) | 12 (8.6) | 0.5 |
| Previous cardiac surgery, *n* (%) | 51 (24.5) | 25 (36.2) | 26 (18.7) | **0.006** |
| sPAP ≥60 mmHg, *n* (%) | 45 (21.6) | 16 (23.2) | 29 (20.9) | 0.70 |
| LVEF <30, *n* (%) | 133 (63.9) | 24 (34.8) | 51 (36.7) | 0.79 |
| LVEF ≥30 and ≤50, *n* (%) | 67 (32.2) | 45 (65.2) | 88 (63.3) | 0.79 |
| Creatinine >2.2 mg/dl or dialysis, *n* (%) | 34 (16.3) | 14 (20.3) | 20 (14.4) | 0.28 |
| Dialysis, *n* (%) | 15 (7.2) | 4 (5.8) | 11 (7.9) | 0.79 |
| Previous acute myocardial infarction, *n* (%) | 62 (29.8) | 29 (42.0) | 33 (23.7) | **0.007** |
| Conduction rhythm, *n* (%) | | | | 0.093 |
| Sinus rhythm | 130 (62.5) | 40 (58.0) | 90 (64.7) | |
| Atrial fibrillation | 58 (27.9) | 18 (26.1) | 40 (28.8) | |
| Pacemaker | 20 (9.6) | 11 (15.9) | 9 (6.5) | |
| Previous coronary artery disease, *n* (%) | 103 (49.5) | 44 (63.8) | 59 (42.4) | **0.004** |
| Coronary artery disease at the time of intervention, *n* (%) | 57 (27.4) | 25 (36.2) | 32 (23.0) | **0.027** |
| Porcelain aorta, *n* (%) | 16 (7.7) | 4 (5.8) | 12 (8.6) | 0.59 |
| Aortic balloon valvuloplasty, *n* (%) | 24 (11.5) | 9 (13.0) | 15 (10.8) | 0.63 |
| New York Heart Association functional class, *n* (%) | | | | 0.21 |
| I | 2 (1.0) | 0 | 2 (1.4) | |
| II | 18 (8.7) | 4 (5.8) | 14 (10.1) | |
| III | 138 (66.3) | 43 (62.3) | 95 (68.3) | |
| IV | 50 (24.0) | 22 (31.9) | 28 (20.1) | |

TA: transapical; TF: transfemoral; TAVI: transcatheter aortic valve implantation; COPD: chronic obstructive pulmonary disease; sPAP: systolic pulmonary artery pressure; LVEF: left ventricle ejection fraction.

**Table 2:** Baseline echocardiographic data

| | All ($n = 208$) | TA-TAVI ($n = 69$) | TF-TAVI ($n = 139$) | *P*-value |
|---|---|---|---|---|
| Peak aortic gradient, mmHg [mean (SD)] | 67.9 (21.1) | 62.1 (19.8) | 70.8 (21.3) | **0.005** |
| Mean aortic gradient, mmHg [mean (SD)] | 41.2 (13.6) | 37.8 (13.5) | 43.9 (13.3) | **0.005** |
| Aortic functional area index, $cm^2$/mq [mean (SD)] | 0.445 (0.15) | 0.48 (0.16) | 0.43 (0.13) | 0.067 |
| Aortic annulus, mm [mean (SD)] | 22.6 (2.2) | 23.2 (2.1) | 22.3 (2.3) | **0.014** |
| Left ventricle ejection fraction, % [mean (SD)] | 29.9 (4.5) | 29.9 (4.7) | 29.9 (4.5) | 0.82 |
| LVDV index, ml/mq [mean (SD)] | 116.8 (53.0) | 98.3 (39.5) | 131.2 (57.8) | **0.002** |
| sPAP, mmHg [mean (SD)] | 48.1 (14.4) | 48.5 (14.4) | 47.9 (14.4) | 0.77 |
| Mitral regurgitation, *n* (%) | | | | 0.16 |
| None/trace | 53 (25.5) | 14 (20.3) | 39 (28.1) | |
| Mild | 75 (36.1) | 21 (30.4) | 54 (38.9) | |
| Moderate | 67 (33.2) | 28 (40.6) | 39 (28.1) | |
| Severe | 13 (6.3) | 6 (8.7) | 7 (5.0) | |
| Aortic regurgitation, *n* (%) | | | | 0.33 |
| None/trace | 68 (32.7) | 17 (24.6) | 51 (36.7) | |
| Mild | 95 (45.7) | 36 (52.2) | 59 (42.4) | |
| Moderate | 41 (19.7) | 15 (21.7) | 26 (18.7) | |
| Severe | 4 (1.9) | 1 (1.4) | 3 (2.2) | |

sPAP: systolic pulmonary artery pressure; TA: transapical; TF: transfemoral; TAVI: transcatheter aortic valve implantation; LVEDV index: Left ventricle end-diastolic volume index.

**Table 3:** Operative data and complications

| | All ($n = 208$) | TA ($n = 69$) | TF ($n = 139$) | *P*-value |
|---|---|---|---|---|
| Planned valve-in-valve, *n* (%) | 6 (2.9) | 1 (1.4) | 5 (3.6) | 0.35 |
| Sapien XT, *n* (%) | 138 (66.3) | 33 (47.8) | 105 (75.5) | <0.001 |
| Valve size, *n* (%) | | | | <0.001 |
| 23 mm | 81 (38.9) | 15 (21.7) | 66 (47.5) | |
| 26 mm | 106 (51.0) | 38 (55.1) | 68 (48.9) | |
| 29 mm | 21 (10.1) | 16 (23.2) | 5 (3.6) | |
| Prosthesis embolization, *n* (%) | 2 (1.0) | 1 (1.4) | 1 (0.7) | >0.99 |
| Need for extracorporeal circulation, *n* (%) | 2 (1.0) | 0 | 2 (1.4) | >0.99 |
| Conversion to sternotomy, *n* (%) | 5 (2.4) | 2 (2.9) | 3 (2.2) | >0.99 |
| Apex complications, *n* (%) | | 1 (1.4) | | |
| Coronary occulsion, *n* (%) | 5 (2.4) | 1 (1.4) | 4 (2.9) | >0.99 |
| Aortic dissection, *n* (%) | 1 (0.5) | 0 | 1 (0.7) | >0.99 |
| Bailout valve-in-valve, *n* (%) | 2 (1.0) | 0 | 2 (1.4) | >0.99 |

TA: transapical; TF: transfemoral.

**Table 4:** Perioperative outcomes

| | All ($n = 208$) | TA-TAVI ($n = 69$) | TF-TAVI ($n = 139$) | *P*-value |
|---|---|---|---|---|
| No device success, *n* (%) | 19 (9.1) | 3 (4.3) | 16 (11.5) | 0.091 |
| Intraoperative mortality | 4 (1.9) | 2 (2.9) | 2 (1.4) | |
| More than 1 valve implanted (TAVI or surgical) | 4 (1.9) | 1 (1.4) | 3 (2.2) | |
| Aortic regurgitation ≥moderate | 2 (1.0) | 0 | 2 (1.4) | |
| Mean aortic gradient ≥20 mmHg | 10 (4.8) | 0 | 10 (7.2) | |
| Acute myocardial infarction (≤72 h), *n* (%) | 6 (2.9) | 1 (1.4) | 5 (3.6) | 0.66 |
| Stroke, *n* (%) | | | | >0.99 |
| Disabling | 2 (1.0) | 0 | 2 (1.4) | |
| Not disabling | 3 (1.4) | 1 (1.4) | 2 (1.4) | |
| Bleeding, *n* (%) | | | | |
| Life threatening | 21 (10.0) | 10 (14.5) | 11 (7.9) | 0.42 |
| Major | 21 (10.0) | 6 (8.7) | 15 (10.8) | |
| Minor | 12 (5.8) | 5 (7.2) | 7 (5.0) | |
| Vascular complication, *n* (%) | | | | 0.24 |
| Major | 13 (6.3) | 3 (4.3) | 10 (7.2) | |
| Minor | 10 (4.8) | 1 (1.4) | 9 (6.5) | |
| Acute kidney injury (AKIN) 2–3, *n* (%) | 17 (8.2) | 7 (10.1) | 10 (7.2) | 0.51 |
| PM implantation (before discharge), *n* (%) | 10 (4.8) | 4 (5.8) | 6 (4.3) | 0.74 |
| New onset of atrial fibrillation, *n* (%) | 13 (6.3) | 10 (14.5) | 3 (2.2) | <0.001 |

TA: transapical; TF: transfemoral; TAVI: transcatheter aortic valve implantation; AKIN: acute kidney injury network; PM: pacemaker.

with LVEF ≤35% and that, even if LVEF decreased after TA-TAVI, this did not cause worse clinical outcomes [9]. Obviously, myocardial damage occurs after TA-TAVI, due to the purse-string sutures and to the perforation of the ventricular wall by the needle and by the device delivery system. This is demonstrated by a higher release of myocardial enzymes in TA patients compared with TF ones [18]. This enzyme release may be reflected by a transient segmental apical dysfunction that does not affect mortality [19]. It is likely that, even if some degree of myocardial dysfunction arises after TA-TAVI, this is far outweighed by the afterload reduction that ultimately yields beneficial final results. Furthermore, many authors have studied functional changes of left ventricular wall motion in patients undergoing TAVI through speckle-tracking echocardiography with strain assessment in order to evaluate myocardial function. The results of these studies show that global longitudinal strain improved in all TAVI patients, independently of the approach [20], and also that in TA and TF patients, the improvement of myocardial strain is similar. This suggests the conclusion that it is preprocedural strain impairment, and not the method of approach, that dictates postoperative functional recovery [21]. Our follow-up data show that late mortality is significantly higher in patients undergoing TA-TAVI. Inspection of the Kaplan–Meier curves (Fig. 2) shows that they have a parallel course for up to 2 years, but then they start to diverge. This is probably due to the worse preoperative status of TA-TAVI patients depicted by a higher rate of peripheral vascular disease, previous cardiac operations, previous acute myocardial infarction and cardiac rhythm disturbances. It is probably not due to the access itself. In fact, there is no logical reason why the apical surgical manipulation of the left ventricular apex should somehow cause decreased survival 2 years after the procedure, given that in this study early results were similar between

**Table 5:** Echocardiographic data at discharge

| | All ($n$ = 208) | TA-TAVI ($n$ = 69) | TF-TAVI ($n$ = 139) | $P$-value |
|---|---|---|---|---|
| Peak gradient (mmHg) | 18.7 ± 7.8 | 18.7 ± 6.7 | 18.6 ± 8.3 | 0.88 |
| Mean gradient (mmHg) | 10.2 ± 4.8 | 9.7 ± 3.7 | 10.5 ± 5.3 | 0.29 |
| LVEF (%) | 36.8 ± 9.1 | 36.6 ± 8.6 | 36.9 ± 9.3 | 0.72 |
| sPAP (mmHg) | 39.8 ± 11.7 | 41.1 ± 10.6 | 39.2 ± 12.2 | 0.28 |
| Mitral regurgitation, n (%) | | | | 0.85 |
| Mild | 89 (42.8) | 31 (44.9) | 57 (41) | |
| Moderate | 46 (22.1) | 17 (24.6) | 29 (20.9) | |
| Severe | 8 (3.8) | 3 (4.3) | 6 (4.3) | |
| Aortic regurgitation, n (%) | | | | 0.086 |
| Mild | 70 (33.7) | 27 (39.1) | 43 (31.1) | |
| Moderate | 9 (4.3) | 0 | 9 (6.5) | |
| Severe | 1 (0.5) | 0 | 1 (0.7) | |

TA: transapical; TF: transfemoral; TAVI: transcatheter aortic valve implantation; LVEF: left ventricular ejection fraction; sPAP: systolic pulmonary artery pressure.

**Table 6:** Multivariable logistic regression analysis

| Variables | OR | 95% CI | $P$-value |
|---|---|---|---|
| Permanent pacemaker (vs sinus rhythm) | 4.662 | 1.306–16.646 | 0.035 |
| Access (TA vs TF) | 2.577 | 1.240–5.359 | 0.006 |
| Creatinine (by increase of 1 mg/dl) | 2.301 | 1.517–3.489 | <0.001 |
| Age | 1.066 | 1.012–1.122 | 0.016 |
| Gender (male vs female) | 0.995 | 0.494–2.002 | 0.262 |
| Peripheral vascular disease | 1.232 | 0.600–2.532 | 0.476 |
| Critical preoperative state | 1.824 | 0.609–5.460 | 0.885 |
| sPAP (>55 mmHg) | 0.518 | 0.205–1.308 | 0.463 |
| Atrial fibrillation (vs sinus rhythm) | 1.493 | 0.711–3.132 | 0.241 |
| Previous coronary artery disease | 1.488 | 0.670–3.304 | 0.358 |
| NYHA III (vs NYHA ≤II) | 3.173 | 0.832–12.108 | 0.097 |
| NYHA IV (vs NYHA ≤II) | 3.320 | 0.775–14.228 | 0.156 |
| Insulin-dependent diabetes mellitus | 1.138 | 0.481–2.695 | 0.276 |

TA: transapical; TF: transfemoral; sPAP: systolic pulmonary artery pressure; NYHA: New York Heart Association; OR: odds ratio; CI: confidence interval.

TA and TF. Because the TF approach is less invasive and can be performed without general anaesthesia, it was generally considered the first choice for TAVI at the great majority of the centres enrolled on the ITER. Therefore, only patients deemed unsuitable for TF-TAVI were scheduled for the TA access. This policy selected TA-TAVI patients with more preoperative comorbidities and thus explained their worse late outcomes compared with those of patients undergoing TF-TAVI. This was also confirmed by the finding that, in this particular cohort of patients with depressed preoperative LVEF, TAVI access was identified as an independent predictor of mortality only after 3 years of follow-up. The other independent predictors of mortality were age, preoperative creatinine, New York Heart Association Class IV and a preoperative pacemaker. Preoperative kidney failure and New York Heart Association Class IV are well-known risk factors for mortality after TAVI [12, 22], and this study shows that their impact is significant also in patients with poor LVEF. The presence of a preoperative pacemaker in this low LVEF group is an indicator of further severity of myocardial disease predictive of adverse outcomes [23]. It has also been shown by Buellesfeld *et al.* [24] that patients with previous permanent pacemaker implantation before TAVI have a higher risk profile, with notable differences in various baseline characteristics compared with patients without a history of permanent pacemaker implantation.

## Limitations

The limitations of the present study are those that commonly concern multicentre retrospective studies. In particular, the limitations of the ITER have already been described in a previous article [12]. With regard to this specific study, we state that we did not have data on dobutamine stress echo for the identification of contractile reserve for risk stratification prior to the procedure, and there was no echo core-lab. However, it has been demonstrated that, although the absence of contractile reserve is an important predictor of an adverse outcome, it should not preclude consideration of an interventional procedure in such patients [25].

## CONCLUSIONS

The results of the present study show that TAVI yields good results in patients with depressed LVEF and also that LVEF improves over time in both groups independently of the access. Preoperative creatinine, preoperative pacemaker, New York Heart Association ClassIV, and TA approach were independently associated with mortality at follow-up. However, TA approach resulted independently associated with mortality only after 3 years of follow-up, thus probably reflecting a worse general clinical status of these patients. Hence, the presence of poor LVEF *per se* should not contraindicate TA access in patients scheduled for TAVI.

**Conflict of interest:** A. D'Onofrio, M. Aiello, M. Cassese are proctor for Edwards Lifesciences.

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