Clinical and hemodynamic outcomes of “all-comers” undergoing transapical aortic valve implantation: Results from the Italian Registry of Trans-Apical Aortic Valve Implantation (I-TA)

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Objective: The aim of this study was to assess clinical and hemodynamic outcomes of transapical aortic valve implantation (TA-TAVI) in patients enrolled in the Italian Registry of Trans-Apical Aortic Valve Implantation (I-TA).

Methods: From April 2008 until November 2010, 504 patients from 20 Italian centers were enrolled in the I-TA registry. Mean logistic EuroSCORE and Society of Thoracic Surgeons score were $24\% \pm 16\%$ and $11\% \pm 4\%$, respectively. Mean follow-up was 9.2 ± 6.5 months (range, 1-26 months). Outcomes were analyzed according to intraoperative complications, procedural volume (high-volume centers, >20 cases; low-volume centers, < 20 cases) and learning curve (first 50% cases vs second 50% cases of each center).

Results: All-cause overall mortality was 8.3% (42 patients). Device success was 99% (500/504 patients). Intraoperative severe complications occurred in 24 (4.8%) patients. Overall 2-year survival was $71.5\% \pm 6.2\%$. At discharge, peak and mean gradients were 16.4 ± 11.2 and 8.7 ± 4.1 mm Hg, respectively, and effective orifice area was 1.67 cm^2 . These values remained stable at 3, 6, and 12 months after surgery. Independent risk factors for mortality after TA-TAVI were as follows: New York Heart Association class III and IV (odds ratio [OR], 4.43; 95% confidence intervals [CI], 1.28-15.40; $P = .02$); logistic EuroSCORE greater than 20 (OR, 1.83; 95% CI, 1.02-3.29; $P = .04$); creatinine concentration greater than $200 \mu\text{mol/L}$ (OR, 2.56; 95% CI, 1.07-6.15; $P = .03$), and intraoperative complications (OR, 5.80; 95% CI, 2.68-12.55; $P < .001$). There were no significant differences in outcomes between high- and low-volume centers and between the first and the second 50% of cases.

Conclusions: TA-TAVI represents a safe and effective alternative treatment for patients who are inoperable or at high risk for surgery. The occurrence of an intraoperative complication significantly affects survival. Procedural volume and learning curve have no impact on patient survival. (J Thorac Cardiovasc Surg 2011;142:768-75)

Although surgical aortic valve replacement (SAVR) remains the treatment of choice in patients with severe symptomatic aortic valve stenosis (SSAVS), recent data strengthen the role of transcatheter aortic valve implantation (TAVI) as an alternative treatment in high-risk or inoperable patients. It has been demonstrated that TAVI

significantly reduces the rate of death and the rate of repeat hospitalization when compared with optimal medical therapy in inoperable patients.¹ These observations are of utmost importance, particularly if we consider that about 30% of patients with SSAVS are not referred for SAVR for several reasons.² Thus far, there is a large amount of

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Abbreviations and Acronyms

CI	= confidence intervals
I-TA	= Italian Registry of Trans-Apical registry Aortic Valve Implantation
MPG	= mean transvalvular pressure gradient
NYHA	= New York Heart Association
OR	= odds ratio
PPG	= peak transvalvular pressure gradient
SAVR	= surgical aortic valve replacement
SSAVS	= severe symptomatic aortic valve stenosis
STS	= Society of Thoracic Surgeons
TAVI	= transcatheter aortic valve implantation
TA-TAVI	= transapical transcatheter aortic valve implantation
TF-TAVI	= transfemoral transcatheter aortic valve implantation

data analyzing patient outcomes after TAVI. However, the great majority of these reports include mixed transapical (TA-TAVI) and transfemoral (TF-TAVI) patient populations. The Italian Registry of Trans-Apical Aortic Valve Implantation (I-TA registry) is an independent, prospective, spontaneous multicenter registry that includes all TA-TAVI procedures performed in Italy since this procedure became available in 2008. The aim of this study was to report clinical and hemodynamic results after TA-TAVI in patients included in the I-TA registry, as well as to evaluate the impact of intraoperative complications, learning curve, and procedural volume on patient outcomes.

PATIENTS AND METHODS**I-TA Registry**

We analyzed data of 504 patients with SSAVS enrolled in 20 Italian cardiac surgery centers from April 2008 to September 2010. Details about the number of patients enrolled in each center and the time period are provided in [Appendix 1](#). Data were collected at each study site and then sent (anonymized) to the University of Padova for storage and analysis. The study was approved by the ethics committee and patient informed consent was always collected. We included in the analysis all patients who received a TA-TAVI since the beginning of the TAVI program of each center to obtain a “real-world,” “all-comers” experience.

Procedure

All procedures were performed with the patient under general anesthesia according to the usual technique.³ All patients received a Sapien pericardial bioprosthesis (Edwards Lifesciences, Irvine, Calif) via a transapical approach. A 23-mm valve was implanted in the presence of an aortic annulus diameter of 21 mm or less, whereas a 26-mm valve was implanted in annuli larger than 21 mm. In the case of an annulus measuring 21.5 mm, the decision on whether to implant a 23-mm or a 26-mm valve was based on the amount and distribution of calcium and on root dimensions. Valve size 29 was not yet available during the study period. Indications for TAVI were

as follows: (1) SSAVS (with or without aortic valve regurgitation) with an aortic valve area less than 0.8 cm² and mean transaortic gradient greater than 40 mm Hg, logistic EuroSCORE greater than 20%, and Society of Thoracic Surgeons (STS) score greater than 10%; (2) ascending porcelain aorta. Patients were excluded if the diameter of the aortic annulus was less than 18 mm or more than 25 mm or if their postprocedural life expectancy was less than 1 year. We did not consider specific age limits for TAVI. Each case was discussed by the local “TAVI team,” which included a cardiac surgeon, an interventional cardiologist, and an anesthesiologist. Inasmuch as the vast majority of these centers follow a “transfemoral first” policy, the transapical approach was chosen in patients with severe disease of the aortoiliac–femoral arterial vessels or in patients with small peripheral vessels. The role of the anesthesiologist was mainly related to the respiratory aspect of patients: in case of severe pulmonary insufficiency, a transfemoral procedure with the patient awake was always considered the best option. The procedures were performed by the “TAVI team” in a conventional operating room with a portable C-arm fluoroscopic system (10 centers), in a fully equipped hybrid operating room (3 centers), or in the catheterization laboratory (7 centers).

Follow-up

Patients underwent clinical and echocardiographic assessment at the study site before the operation, at hospital discharge, 3 and 6 months after TA-TAVI, and every 6 months thereafter.

Data and Definitions

Preoperative risk factors were defined according to the EuroSCORE classification (http://www.euroscore.org/euroscore_scoring.htm). Device success was defined, according to the Valve Academic Research Consortium definitions, as follows: (1) successful access, delivery, and deployment of the device and successful retrieval of the delivery system; (2) correct position of the device in the proper anatomic location; (3) intended performance of the prosthetic heart valve (aortic valve area > 1.2 cm² and mean aortic valve gradient < 20 mm Hg or peak velocity < 3 m/s, without moderate or severe prosthetic valve regurgitation); (4) only 1 valve implanted in the proper anatomic location. Thirty-day mortality was defined as “all-cause” and “cardiovascular” according to the Valve Academic Research Consortium definitions.⁴ We were not able to use the Valve Academic Research Consortium definitions for echocardiographic data inasmuch as these were published in January when all echocardiographic examinations had already been performed. Immediate postoperative aortic regurgitation was evaluated, after valve deployment and removal of the transaortic guidewire, using both transesophageal and aortic angiography. The echocardiographic measurements were performed according to the current recommendations.⁵ Peak (PPG) and mean (MPG) transvalvular pressure gradients were derived by using the modified Bernoulli equation and the effective orifice area was calculated with the continuity equation.⁶ The angiographic evaluation of aortic regurgitation was made according to the method described by Sellers and colleagues.⁷ Aortic regurgitation was classified as absent, trivial (1+/4+), mild (2+/4+), moderate (3+/4+), or severe (4+/4+)⁸ on the basis of data obtained from both the diagnostic procedures. The impact of procedural volume on patient outcomes was analyzed by comparing overall survival at follow-up between patients operated on in high-volume and low-volume centers. High- and low-volume centers were defined according to the number of *total* procedures performed: “high volume” when there were more than 20 procedures; “low volume” with fewer than 20 procedures. The impact of learning curve on patient outcomes was analyzed by comparing the overall survival of the first 50% versus the second 50% of patients for each center.

Statistical Analysis

Continuous data are expressed by mean $\pm$ 1 standard deviation or median as appropriate. Categorical data are summarized by reporting the percentages. Cumulative survival was estimated using the Kaplan-Meier

method. Categorical values were compared by the χ^2 test, and continuous variables were compared by the Mann-Whitney test. Survivals were compared by the log-rank test. A stepwise logistic regression analysis was used to determine the predictive factors of late mortality. Statistical analyses were performed using STATISTICA software (release 9.1; Statsoft Inc, Tulsa, Okla).

RESULTS

Patient Population

Preoperative characteristics are summarized in Table 1. Mean age was 81 ± 6 years (range, 44-95 years), and 60.7% were female. The 44-year-old patient was scheduled for TAVI for an extremely severe case of porcelain aorta derived from previous chest irradiation owing to a history of malignant lymphoma. Mean logistic EuroSCORE was $24\% \pm 16\%$ (range, 7%-87%) and mean STS score was $11\% \pm 4\%$ (range, 3%-45%). Previous percutaneous coronary intervention was performed in 114 (22.6%) patients and a previous cardiac operation was performed in 83 (16.5%). A total of 419 (83.1%) patients were in New York Heart Association (NYHA) functional class III-IV.

Early Results

Valve sizes 23 and 26 were used in 183 (36.3%) and 321 (63.7%) patients, respectively. Device success was 99% (500 patients). In 4 patients device success was not achieved for the following reasons: in 3 patients the insertion of a second valve was required because of malpositioning of the first prosthesis and in 1 patient the transapical valve embolized in the left ventricle and the patient underwent conventional SAVR. A total of 24 (4.8%) severe intraoperative complications occurred. Causes of intraoperative complications were as follows:

- Emergency cardiopulmonary bypass or extracorporeal membrane oxygenation for refractory cardiogenic shock was required in 10 (1.9%) patients
- Cardiopulmonary resuscitation for severe hemodynamic impairment after valve deployment was performed in 5 (1%) patients
- Coronary artery occlusion requiring percutaneous coronary intervention with or without coronary stenting occurred in 5 (1%) patients
- Severe intraoperative bleeding occurred in 4 (0.8%) patients

All-cause 30-day mortality was 8.3% (42 patients). Cardiovascular 30-day mortality was 6.7% (34 patients). Causes of overall 30-day mortality were as follows: cardiogenic shock/multiorgan failure in 15 patients, sepsis in 8 patients, major ventricular arrhythmia in 5 patients, mesenteric ischemia in 6 patients, stroke in 6 patients, and severe hemorrhage in 2 patients.

TABLE 1. Preoperative characteristics in 504 patients

Characteristics	No. of patients*	%
Logistic EuroSCORE (%)	26.3 ± 13.8	
STS score (%)	11 ± 4	
Age (y)	81.2 ± 6.5	
LVEF (%)	52.4 ± 13.6	
Aortic peak gradient (mm Hg)	74.7 ± 23.3	
Aortic mean gradient (mm Hg)	47.4 ± 15.4	
Aortic valve area (cm ²)	0.53 ± 0.18	
Creatinine (mg/dL)	1.3 ± 0.8	
Female sex	306	60.7
Arterial hypertension	402	79.8
Diabetes	139	27.6
NYHA class III-IV	419	83.1
COPD	173	34.3
Dialysis	24	4.8
Previous cardiac surgery	83	16.5
Severe ascending aortic calcifications	108	21.4
Mitral regurgitation (3+/4+)	41	8.1
Peripheral vascular disease	229	45.4
Neurologic dysfunction	39	7.7
Atrial fibrillation	119	23.6
Pulmonary hypertension	49	9.7
History of coronary artery disease	254	50.4
Previous PCI	111	22
Previous CABG	72	14.3
Untreated	71	14.1

STS, Society of Thoracic Surgeons; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting. *The number of patients begins with the category "female sex."

Continuous venovenous hemofiltration for class F acute kidney injury (according to the Risk, Injury, Failure, Loss, End-stage kidney disease [RIFLE] classification)⁹ was required in 31 (6.1%) patients.

Trivial and mild aortic regurgitation (1-2+/4+), mainly owing to perivalvular leak at hospital discharge, was found in 138 (29.9%) and 40 (8.6%) patients, respectively. Permanent pacemaker implantation was required in 27 (5.3%) patients. Incidence of major stroke was 3% (15 patients). Incidence of periprocedural acute myocardial infarction was 1.6% (8 patients). Median intensive care unit stay was 2 days (quartiles 1-3) and mean hospital stay was 9 ± 4 days.

Follow-up

Follow-up was 100% complete. Mean follow-up was 9.2 ± 6.5 months (range, 1-26 months). One-year overall Kaplan-Meier survival was $81.4\% \pm 2.2\%$. Two-year overall Kaplan-Meier survival was $71.5\% \pm 6.2\%$ (Figure 1). Late mortality occurred in 34 patients. Cardiovascular late mortality occurred in 22 patients. Causes of late mortality were congestive heart failure in 12 patients, sepsis/

FIGURE 1. Two-year Kaplan-Meier overall survival of 504 patients after transcatheter aortic valve implantation (TAVI).

pneumonia in 8 patients, sudden death in 5 patients, cerebrovascular accident in 5 patients, cancer in 3 patients, and liver cirrhosis in 1 patient.

Kaplan-Meier overall survival of patients operated on in high- and low-volume centers at 18 months was $78.3\% \pm 9.4\%$ and $73.9\% \pm 8.1\%$, respectively ($P = .3$) (Figure 2).

Kaplan-Meier overall survival at 18 months of the first 50% and the second 50% of patients of each center was $77.2\% \pm 7.3\%$ and $81.5\% \pm 7.8\%$, respectively ($P = .9$) (Figure 3). The variable with a significant impact on overall survival at follow-up was the occurrence of an

FIGURE 2. Kaplan-Meier overall survival of patients operated on in high- and low-volume centers at 18 months. TAVI, Transcatheter aortic valve implantation.

FIGURE 3. Kaplan-Meier overall survival at 18 months of the first 50% and the second 50% of patients of each center. TAVI, Transcatheter aortic valve implantation.

intraoperative complication. Kaplan-Meier overall survival at 18 months was significantly lower in patients who had an intraoperative complication ($37.3\% \pm 4.6\%$) when compared with patients who did not have any complication ($80.7\% \pm 8.6\%$) ($P < .001$) (Figure 4). The following variables were found to be risk factors for 30-day mortality at the univariate analysis: age older than 85 years, NYHA class III-IV, logistic EuroSCORE greater than 20%, creatinine levels greater than $200 \mu\text{mol/L}$, preoperative dialysis, and intraoperative complications. Multivariate analysis identified the following as independent predictors for mortality: NYHA class III and IV (odds ratio [OR], 4.43; 95% confidence intervals [CI], 1.28-15.40; $P = .02$); logistic EuroSCORE greater than 20% (OR, 1.83; 95% CI, 1.02-3.29; $P = .04$); creatinine greater than $200 \mu\text{mol/L}$ (OR, 2.56; 95% CI, 1.07-6.15; $P = .03$), and intraoperative complications (OR, 5.80; 95% CI, 2.68-12.55; $P < .001$). There were no cases of structural valve deterioration and endocarditis of the aortic bioprosthesis during follow-up. A significant NYHA class improvement was observed at follow-up (16% of patients were in NYHA class III-IV at follow-up vs 83.1% preoperatively; $P < .001$). Hemodynamic data are shown in Table 2. At discharge, PPG and MPG were 16.4 ± 11.2 mm Hg and 8.7 ± 4.1 mm Hg, respectively. Effective orifice area was 1.67 cm^2 at discharge. A significant reduction of PPG and MPG from the preoperative to the postoperative period was found ($P < .001$); these values remained stable at 3, 6, and 12 months after surgery. Furthermore, a significant increase of aortic valve area was

FIGURE 4. Kaplan-Meier survival at 18 months of patients with and without intraoperative complications. TAVI, Transapical aortic valve implantation.

documented ($P < .001$) and no changes in the degree of aortic regurgitation were found.

COMMENT

The I-TA registry is a prospective registry reporting the entire Italian TA-TAVI experience. The registry is spontaneous, prospective, and independent from industries. These characteristics allow an objective evaluation of “real world” outcomes without bias deriving from patient selection, thus providing a paramount picture of all TA-TAVI patients operated on during the past 3 years in Italy. Other already existing TAVI registries have different characteristics. The German and the Belgian registries^{8,10} include Edwards Sapien and Medtronic CoreValve (Medtronic, Inc, Minneapolis, Minn) and take into account transapical and transfemoral approaches; the SOURCE registry¹¹ includes only selected European centers and analyzes transapical and transfemoral Sapien valve procedures only during the first year after commercialization. The Canadian

experience¹² analyzes transapical and transfemoral procedures performed using the Edwards Sapien valve; it is very complete and exhaustive but only 6 centers are involved. The Italian CoreValve registry includes only TF-TAVI patients treated with the Medtronic CoreValve revalving system.¹³

The analysis of I-TA data showed that TA-TAVI during the first 3 years of experience in Italy was carried out with a 30-day all-cause mortality of 8.3% and with an overall 2-year survival of 71%. Variables predicting 30-day mortality after TA-TAVI were NYHA class III-IV, logistic EuroSCORE greater than 20, creatinine levels greater than 200 $\mu\text{mol/L}$, and the occurrence of intraoperative complications. Thirty-day mortality was lower than expected (predicted mortalities were 26% and 11% with logistic EuroSCORE and STS score, respectively; observed/expected [STS] mortality = 0.75) and consistent with the aforementioned registries (SOURCE, 10.3%; Germany, 8.2%; Belgium, 12%; Canada, 10.4%). Furthermore, this is a mixed population that includes inoperable patients and high-risk patients. This is an important factor if we compare I-TA 30-day mortality (8.3%) with the excellent results observed in the recently presented results of the PARTNER A trial (http://my.americanheart.org/idc/groups/ahamh-public/@wcm/@sop/@scon/documents/downloadable/ucm_425332.pdf). PARTNER A investigators reported an overall all-cause 30-day mortality, derived by an intention-to-treat analysis, of 3.4%, which is the lowest ever presented. Intention-to-treat 30-day mortality of the PARTNER A TA-TAVI subgroup was 3.8%; however, the as-treated mortality rate accounts for 8.7%, similar to I-TA and to other registries. The PARTNER trial,¹ as well as all prospective randomized studies, has strict inclusion and exclusion criteria to guarantee homogeneity among groups. However, on the other hand, these create a bias between “trial population” and “real world.” It is important to notice that all centers included in the I-TA registry have a combined transapical and transfemoral program with a “transfemoral-first” policy. This means that the vast majority of patients included in our registry had undergone a multidisciplinary selection process at the study site that was in favor of a transapical approach mainly for peripheral artery inaccessibility (stenosis or small caliber). Thus, preoperative risk profile of these patients was high not only for

TABLE 2. Echocardiographic data

Valve size (no. of patients)	Preoperative*		Discharge*		3 mo*		6 mo*		12 mo*	
	23 (175)	26 (306)	23 (139)	26 (254)	23 (112)	26 (187)	23 (87)	26 (141)	23 (51)	26 (78)
PPG (mm Hg)	87 $\pm$ 25	80 $\pm$ 22	22 $\pm$ 10	23 $\pm$ 12	24 $\pm$ 10	23 $\pm$ 11	24 $\pm$ 9	22 $\pm$ 12	28 $\pm$ 8	24 $\pm$ 12
MPG (mm Hg)	53 $\pm$ 17	50 $\pm$ 14	11 $\pm$ 4	10 $\pm$ 4	11 $\pm$ 5	9 $\pm$ 3	11 $\pm$ 4	9 $\pm$ 3	14 $\pm$ 6	10 $\pm$ 5
EOA (cm ²)	0.5 $\pm$ 0.2	0.7 $\pm$ 0.3	1.7 $\pm$ 0.5	1.8 $\pm$ 0.7	1.6 $\pm$ 0.5	1.7 $\pm$ 0.7	1.5 $\pm$ 0.5	1.7 $\pm$ 0.9	1.5 $\pm$ 0.6	1.9 $\pm$ 0.8

PPG, Peak prosthesis gradient; MPG, mean prosthesis gradient; EOA, effective orifice area. *Statistically significant difference ($P < .001$) between preoperative and all the following assessments. No significant differences among postoperative examinations.

associated comorbidities but also for peripheral vascular disease. The access-related issue in TAVI literature is still unsolved. Inasmuch as all studies are based on a “transfemoral-first” policy, transapical patients have higher preoperative risk scores and worse early outcomes than transfemoral patients.^{11,12} In our registry, the incidence of severe intraoperative bleeding related to the transapical approach was only 0.8% (4 patients), which is much lower than the 16.2% of major vascular complications reported in the PARTNER B trial.¹ Unfortunately, the PARTNER A, which is the only prospective randomized trial currently available, did not have sufficient statistical power to compare TA-TAVI with either SAVR or TF-TAVI. In other words, there is no evidence that TA-TAVI should be performed as a “second-choice” treatment whenever TF-TAVI is not feasible. The cardiac surgery community should keep this issue in mind when discussing TAVI patients. Access choice should be based not only on the feasibility of a peripheral approach but above all on the specific clinical characteristics of each patient.

The impact of intraoperative complications on patient outcomes is another important issue that arises from data analysis. In our experience it was a strong determinant of 30-day mortality with negative impact on late survival: 10 (41.7%) of 24 patients with a severe intraoperative complication died at 30 days; 25% of 30-day deaths occurred in patients who had an intraoperative complication; 20-month survival of these patients was only 37%. This finding partially confirms what was already described by Rodés-Cabau and associates,¹² who indentified the need for periprocedural hemodynamic support as an independent risk factor for 30-day mortality (OR, 6.84). In view of the strong impact of intraoperative complications on patient early and late outcomes, we should direct all our efforts toward preventing and effectively managing such occurrence. Prevention can be achieved by careful patient selection, adequate procedural planning (access choice, valve sizing), and execution. The successful management of complications needs a strict safety policy whose main feature should be the multidisciplinary approach to the TAVI program. Ye and associates,¹⁴ in their series of 71 consecutive TA-TAVI patients, reported 5 early deaths in the initial 15 patients (mortality rate, 33%) of their experience. They also reported a significant improvement in terms of procedural success, malposition, and early mortality in the second half of their TF-TAVI experience.¹⁵ This is confirmed by Himbert and colleagues,¹⁶ who found early experience to be the only significant predictor of mortality. They commented that such finding emphasized the role of patient selection, equipment, and experience. In our large multicenter series of patients, we did not find learning curve or procedural volume to be significant factors affecting outcomes. This could be related to the accurate initial experience of

each center, which included center start-up phase with simulator use for each operator (physicians, technicians, and nurses), preoperative case selection and discussion with an experienced operator (proctor), equipment standardization according to manufacturer guidelines, and proctor-assisted procedures. Echocardiographic examinations found Sapien valve PPG and MMG 16.4 ± 11.2 mm Hg and 8.7 ± 4.1 mm Hg, respectively, at discharge. These values are consistent with those reported in the PARTNER trial¹ and in other reports.^{11,17,18}

This study has several limitations. The number of patients operated on in each center was not homogeneous, ranging from 5 to 88. We did not have data about comparable SAVR and TF-TAVI populations. Echocardiographic examinations were performed by different physicians using different machines.

In conclusion, I-TA registry data demonstrate that in high-risk or inoperable patients with SSAVS, TA-TAVI is a safe and satisfactory therapeutic option inasmuch as it can be performed with low 30-day mortality, good 2-year survival, and with low incidence of complications related to the apical approach. Survival is not affected by either learning curve or procedural volume. NYHA class, high EuroSCORE values, high creatinine levels, and intraoperative complications were identified as independent risk factors for 30-day mortality. Longer follow-up is warranted to evaluate long-term results and to reach time points when degeneration and valve-related adverse events are more likely to occur.

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Appendix 1. Participating study sites, components of the TAVI team, start of TAVI program, and number of patients

Institution	Components of the TAVI team	Start of enrollment	Patients
Clinica Montevergine, Mercogliano	P. Rubino, L. Cota, G. Sorropago, G. Sarno, C. Moscariello, D. Catapano, V. Lucchetti, R. Mancusi, M. Agrusta	April 2008	88
Centro Cardiologico Monzino, Milan	P. Biglioli, M. Fusari, M. Agrifoglio, E. Sisillo, L. Salvi, S. Galli, G. Teruzzi	May 2008	81
San Bortolo Hospital, Vicenza	L. Salvador, P. Magagna, A. Fabbri, N. Abbiate, L. La Vecchia	October 2008	43
San Camillo Hospital, Rome	F. Musumeci, G. Luzzi, R. Violini, R. Fiorilli, P. Picozzi	June 2009	39
University of Padova	G. Gerosa, R. Bianco, A. D'Onofrio, G. Isabella, G. Tarantini, M. Napodano, C. Fraccaro, V. Gasparetto, D. Pittarello	March 2009	38
University of Turin	M. Rinaldi, M. La Torre, S. Salizzoni, I. Sheiban, M. D'Amico, C. Moretti, P. Omedè, F. Conrotto, M. Lupo	February 2009	24
Humanitas Gavazzeni Hospital, Bergamo and Rozzano	E. Vitali, P. Tartara, N. Valerio, P. Sganzerla, E. Tavasci, D. Guzzon	July 2008	22
G. Pasquinucci Heart Hospital, Massa	M. Glauber, A. Cerillo, F. Chiamonti, S. Berti, M. Mariani, P. Del Sarto	October 2008	21
University of Bologna	R. Di Bartolomeo, C. Savini, F. D. Petridis, E. Pilato, J. Pavicevic	November 2008	20
S. Raffaele Hospital, Milan	O. Alfieri, F. Maisano, M. Cioni, P. Denti, A. Zangrillo, D. Covello, A. Colombo, M. Montorfano	July 2008	18
Ospedale dell'Angelo, Venice-Mestre	E. Polesel, C. Zanchettin, A. Terrini, G. Grassi, M. Barbierato, D. Penzo	March 2009	17
University of Pavia	M. Viganò, M. Aiello, N. Vistarini, E. Bramucci, M. Ferrario, R. Veronesi, M. Maurelli	March 2009	16
Ospedale Mauriziano Umberto I, Turin	R. Casabona, S. Del Ponte, G. Punta, M. Debenedictis, I. Scrocca, C. Verdecchia, N. Lojaco	September 2009	15
S. Maria della Misericordia Hospital, Udine	U. Livi, E. Mazzaro, E. Pompei, G. Bernardi, F. Poldini	April 2009	14
S. Croce e Carle Hospital, Cuneo	C. Grossi, O. Di Gregorio, G. Steffenino, G. Baralis, A. Locatelli	June 2009	13
Clinica S. Anna, Catanzaro	M. Cassese, A. Antonazzo, G.L. Martinelli, B. Missiroli, R.M. Montesanti, A. Cuccio, P. De Fiore	February 2010	10
Ospedali Riuniti, Trieste	A. Pappalardo, E. Rauber, B. Benussi, A. Salvi, A. Percan, G. Sagrati, P. Zanei	July 2009	8
University of Parma	T. Gherli, F. Nicolini, D. Ardissino, L. Vignali, C. Grattagliano, A. Vezzani	February 2009	6
Hesperia Hospital, Modena	G. Stefanelli, D. Gabbieri, I. Ghidoni, G. Dannibale, A. Benassi, M. Meli, G. Giordano	February 2010	6
University of Verona	G. Faggian, F. Santini, F. Ribichini, G. Molinari, M. Dan	March 2010	5

Discussion

Dr Lars G. Svensson (*Cleveland, Ohio*). Dr D'Onofrio has presented one of the largest series on the transapical approach with good results. The 8.3% hospital mortality and 3% major stroke rate for these high-risk patients, with a significant atherosclerotic load, is remarkably good. Having been involved in the original transapical approach research with Drs Mike Mack, Todd Dewey, Thomas Walther, Fred Mohr, John Webb and his team, and from the Edwards team, Mike Mussallem, Larry Woods, Jill Trekell, Jody Akins, and Mark Dehdastian starting in 2004, it is very gratifying, despite our early hiccups, to see how the technology has matured and improved.

It is incumbent on me to compare this presentation with the results from the PARTNER A study, presented at the American College of Cardiology meeting by our upcoming president, Craig Smith. In that study, with the transfemoral approach as the default approach, if access was possible, as in your Italian study, transapical patients had more cerebrovascular disease, carotid endarterectomies, previous coronary artery bypass grafting, percutaneous coronary intervention, porcelain aorta, atrial fibrillation, obviously peripheral vascular disease, and more severe aortic valve stenoses, all of which are evidence of greater atherosclerotic load and also risk for death and stroke. The mortality and stroke rates in the PARTNER A study were equivalent to the TA arm; in other words, open aortic valve replacement was equivalent to the TA-TAVI.

Given that in Italy and the United States the transfemoral approach is the default choice for patients but has not been compared with the transapical approach, what is the likelihood in Italy that you could do a prospective randomized trial comparing transfemoral versus transapical and also including the new approach, the transaortic approach? Do you have any registry data yet for Italy for the transaortic procedure even though the current device was neither designed for this nor is ideal for the transaortic approach?

Clearly we need to aim to reduce the stroke rate to the superb low risk of 1.4% noted in the open aortic valve replacement control group in the transfemoral part of the PARTNER A trial. Have you had the opportunity to try any of the new stroke filter or carotid protection devices, including using the EMBOL-X filter (Edwards Lifesciences), particularly for the transaortic procedure?

Dr D'Onofrio. Dr Svensson, thank you for your comments and for these questions.

The great majority of centers that participated in this study followed a transfemoral-first policy. This means that about 90% of these patients underwent screening for a transfemoral procedure and, since they were not considered suitable for a transfemoral approach, they went for a transapical valve implantation. Consequently these patients had a higher risk profile in terms of peripheral arterial disease, stroke, and mesenteric ischemia. Actually, we observed a low incidence of stroke and a low incidence of access-related complications, for example, major bleeding from the left ventricular apex. If we compare these results with the incidence of major vascular complications that were reported in the SOURCE and in the PARTNER trial that ranged from 10% to 15%, the result is that to date there is no strong evidence that supports the transfemoral-first policy. Unfortunately, the PARTNER trial was not powered enough to compare the transfemoral versus the transapical approach. I think that all cardiac surgeons should be well aware of this problem when discussing TAVI cases with cardiologists.

We do not have to necessarily go straight for a transfemoral approach first and then, only if the patient is not suitable, choose the transapical technique, since we do not have evidence to support this strategy. I think that we should determine the best approach for every single patient. This registry gave us the opportunity to create a good network of centers that perform transapical procedures.

The idea of a prospective randomized trial is excellent, and I hope that we will be able to do that in the near future.

Dr Svensson. Just to address that, there are plans ahead to do a European prospective randomized trial. You might want to discuss this with Thomas Walther. Obviously in some centers it will be difficult, but for those who have the option of either procedure, you might want to talk to him. I understand there are plans at Edwards to finance this. So I would encourage those centers in Italy that can to get involved with a prospective randomized trial.

Dr D'Onofrio. I will discuss this issue with my Italian colleagues. Thank you.

Regarding your questions about the EMBOL-X filters and transaortic approach, we do not have data in this registry about transaortic procedures, and we did not collect data about the use of aortic filters to prevent embolic events.