Journal of the American College of Cardiology
© 2010 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 55, No. 11, 2010
ISSN 0735-1097/10/$36.00
doi:10.1016/j.jacc.2009.12.014

Transcatheter Aortic Valve Implantation for the Treatment of Severe Symptomatic Aortic Stenosis in Patients at Very High or Prohibitive Surgical Risk

Acute and Late Outcomes of the Multicenter Canadian Experience

Josep Rodés-Cabau, MD,* John G. Webb, MD,† Anson Cheung, MD,† Jian Ye, MD,† Eric Dumont, MD,* Christopher M. Feindel, MD,‡ Mark Osten, MD,‡ Madhu K. Natarajan, MD,§ James L. Velianou, MD,§ Giuseppe Martucci, MD,‖ Benoît DeVarennes, MD,‖ Robert Chisholm, MD,¶ Mark D. Peterson, MD,¶ Samuel V. Lichtenstein, MD,† Fabian Nietlispach, MD,† Daniel Doyle, MD,* Robert DeLarochellière, MD,* Kevin Teoh, MD,§ Victor Chu, MD,§ Adrian Dancea, MD,‖ Kevin Lachapelle, MD,‖ Asim Cheema, MD,¶ David Latter, MD,¶ Eric Horlick, MD‡

Quebec City and Montreal, Quebec; Vancouver, British Columbia; and Toronto and Hamilton, Ontario, Canada

Objectives The aim of this study was: 1) to evaluate the acute and late outcomes of a transcatheter aortic valve implantation (TAVI) program including both the transfemoral (TF) and transapical (TA) approaches; and 2) to determine the results of TAVI in patients deemed inoperable because of either porcelain aorta or frailty.

Background Very few data exist on the results of a comprehensive TAVI program including both TA and TF approaches for the treatment of severe aortic stenosis in patients at very high or prohibitive surgical risk.

Methods Consecutive patients who underwent TAVI with the Edwards valve (Edwards Lifesciences, Inc., Irvine, California) between January 2005 and June 2009 in 6 Canadian centers were included.

Results A total of 345 procedures (TF: 168, TA: 177) were performed in 339 patients. The predicted surgical mortality (Society of Thoracic Surgeons risk score) was 9.8 ± 6.4%. The procedural success rate was 93.3%, and 30-day mortality was 10.4% (TF: 9.5%, TA: 11.3%). After a median follow-up of 8 months (25th to 75th interquartile range: 3 to 14 months) the mortality rate was 22.1%. The predictors of cumulative late mortality were peri-procedural sepsis (hazard ratio [HR]: 3.49, 95% confidence interval [CI]: 1.48 to 8.28) or need for hemodynamic support (HR: 2.58, 95% CI: 1.11 to 6), pulmonary hypertension (PH) (HR: 1.88, 95% CI: 1.17 to 3), chronic kidney disease (CKD) (HR: 2.30, 95% CI: 1.38 to 3.84), and chronic obstructive pulmonary disease (COPD) (HR: 1.75, 95% CI: 1.09 to 2.83). Patients with either porcelain aorta (18%) or frailty (25%) exhibited acute outcomes similar to the rest of the study population, and porcelain aorta patients tended to have a better survival rate at 1-year follow-up.

Conclusions A TAVI program including both TF and TA approaches was associated with comparable mortality as predicted by surgical risk calculators for the treatment of patients at very high or prohibitive surgical risk, including porcelain aorta and frail patients. Baseline (PH, COPD, CKD) and peri-procedural (hemodynamic support, sepsis) factors but not the approach determined worse outcomes. (J Am Coll Cardiol 2010;55:1080–90) © 2010 by the American College of Cardiology Foundation

From the *Quebec Heart and Lung Institute, Laval University, Quebec City, Quebec, Canada; †St Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada; ‡Toronto General Hospital, University of Toronto, Toronto, Ontario, Canada; §Hamilton General Hospital, McMaster University, Hamilton, Ontario, Canada; ‖Royal Victoria Hospital, McGill University, Montreal, Quebec, Canada; and the ¶St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada. Drs. Rodés-Cabau, Webb, Cheung, Ye, Dumont, DeVarennes, and Horlick are consultants for Edwards Lifesciences, Inc. Dr. Cheung is a speaker for Edwards Lifesciences Inc. Dr. Ye has received a small amount of honoraria from Edwards Lifesciences Inc. Dr. DeVarennes is a consultant for ATS Medical.

Manuscript received October 2, 2009; revised manuscript received November 11, 2009, accepted December 17, 2009.

Transcatheter aortic valve implantation (TAVI) has emerged as an alternative to surgical aortic valve replacement (SAVR) for patients with symptomatic severe aortic stenosis considered to be at very high or prohibitive operative risk (1–6). Both the transfemoral (TF) and transapical (TA) approaches have been used for TAVI with the Edwards valve system (Edwards Lifesciences, Inc., Irvine, California) (1–5). Patients have usually been evaluated for TAVI in the setting of a program including interventional cardiology and cardiac surgery teams, with the selection of 1 approach over the other on the basis of the size and/or disease of iliofemoral arteries. However, most studies have evaluated the results of TAVI separately according to the approach (TF vs. TA) used, and very few single-center series have determined the results of a global TAVI program including both approaches for the treatment of symptomatic severe aortic stenosis (7–9).

See page 1091

The TAVI technology has been mostly applied in very old patients with a high number of comorbidities (1–9). Operative risk score calculators (i.e., logistic EuroSCORE, Parsonett score, Society of Thoracic Surgeons Predicted Risk of Mortality [STS-PROM] score) that take into consideration the most important patient comorbidities have been used to determine which patients are at very high or prohibitive surgical risk. However, many elderly patients are deemed inoperable on the basis of comorbidities not included in surgical risk calculators (10). Therefore, a high proportion of patients have been refused for SAVR and have undergone TAVI on the basis of risk factors such as porcelain aorta or frailty (1–9), neither of which is included in the surgical risk calculators. To date, the safety and efficacy of TAVI procedures have been measured by comparing the procedural and 30-day results with predicted operative mortality as calculated by surgical risk calculators, but no studies have determined the results of TAVI in patients with porcelain aorta or frailty, 2 of the most frequent comorbidities in elderly patients with severe aortic stenosis not included in the surgical risk scores. The objectives of this multicenter study were: 1) to evaluate the acute and midterm follow-up results and prognostic factors of a comprehensive TAVI program including both the TF and TA approaches for the treatment of severe aortic stenosis in patients at very high or prohibitive surgical risk; and 2) to determine the results of this TAVI program in patients deemed inoperable because of either porcelain aorta or frailty.

Methods

In 2005, the Canadian TAVI program was approved by the Department of Health and Welfare (Ottawa, Ontario, Canada) for compassionate clinical use in patients with symptomatic severe aortic stenosis considered nonoperable or very high surgical risk candidates. All consecutive patients who underwent TAVI between January 2005 and June 2009 in 6 Canadian centers with the Cribier-Edwards, Edwards-SAPIEN or SAPIEN XT valve (Edwards Lifesciences) in the setting of the Canadian compassionate clinical use program were included. All potential candidates for TAVI were evaluated by a multidisciplinary team composed of interventional cardiologists and cardiac surgeons who determined the eligibility of the patient for TAVI. Patients considered eligible for TAVI underwent a systematic workup protocol that included Doppler echocardiography, coronary angiography, aorto-iliofemoral angiography, and computed tomography. Depending on the size, disease, and degree of calcification of iliofemoral arteries the patients were selected for TF or TA approach. Starting in May 2007, all cases were presented, discussed, and finally approved for TAVI (TF or TA approach) in a weekly conference call including interventional cardiologists and cardiac surgeons of participating centers. Patients' comorbidities were defined with the STS risk score definitions. Pulmonary hypertension (PH) was defined as a pulmonary systolic pressure >60 mm Hg as estimated by Doppler echocardiography or measured by cardiac catheterization. Frailty was defined as a syndrome of decreased reserve and resistance to stressors, resulting from multiple declines across multiple physiologic systems leading to vulnerability to adverse outcomes (11). No systematic tests were performed for the evaluation of frailty, and patients were considered nonoperable because of frailty mainly on the basis of the criteria of the medical team evaluating them. Indeed, at least 2 cardiac surgeons had to agree when frailty was the main criterion determining inoperability, and the specific reasons for the decision had to be detailed during the weekly conference call. Porcelain aorta was defined as an extensive circumferential calcification of the thoracic aorta as assessed by computed tomography and/or fluoroscopy. Baseline clinical and echocardiography data were prospectively gathered in each participating center. All patients provided written informed consent for the procedures.

Procedures and 30-day outcomes. The TF and TA procedures were performed as previously described (1–5). The Edwards valve (Cribier-Edwards, Edwards-SAPIEN, SAPIEN XT) was used in all cases. The 23-mm valve was implanted if the transesophageal echocardiographic measurement of the aortic annulus was between 17 and 21 mm, and the 26-mm valve was implanted if the aortic annulus measured between 22 and 25 mm.

Abbreviations and Acronyms

CI = confidence interval
CKD = chronic kidney disease
COPD = chronic obstructive pulmonary disease
HR = hazard ratio
MI = myocardial infarction
MR = mitral regurgitation
OR = odds ratio
PH = pulmonary hypertension
SAVR = surgical aortic valve replacement
STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality
TA = transapical
TAVI = transcatheter aortic valve implantation
TF = transfemoral

Procedural success was defined as the implantation of a functioning valve within the aortic annulus, without intraprocedural mortality. Major procedural complications included valve embolization, need for a second valve, need for hemodynamic support with balloon counterpulsation or femoral-femoral extracorporeal circulation, conversion to open heart surgery, major access site complications, and life-threatening arrhythmias. Major access site complications were defined as those leading to either severe bleeding requiring blood transfusion, fatal bleeding, or need for surgical or transcatheter repair. In the TA approach, both the occurrence of myocardial tears requiring further surgical repair and accidental damage of a coronary artery during apical repair were also considered major access complications. Major post-procedural (30-day) complications included stroke, myocardial infarction, sepsis, need for hemodialysis, and need for a permanent pacemaker. Doppler-echocardiography was performed at hospital discharge in all patients who survived the procedure. Procedural and 30-day events and echocardiographic data were prospectively recorded in each of the participating centers. After the procedure patients received aspirin (80 mg/day) indefinitely and clopidogrel (75 mg/day) for 3 to 6 months.

Follow-up. Clinical follow-up was carried out in clinical visits and/or through phone contact. The timing and frequency of the clinical follow-up was determined by each participating center. Most patients were followed at 6 months to 1 year after the procedure and annually thereafter. Death and re-intervention at any time during the follow-up period were recorded.

Statistical analysis. Qualitative variables were expressed as percentages, and quantitative variables were expressed as mean (SD) or median (25th to 75th interquartile range). Comparison of numerical variables was performed with the Student *t* test or Wilcoxon rank sum test, depending on variable distribution. The chi-square test or Fischer's exact test was used to compare qualitative variables. Procedural and outcome results of TF and TA approaches are provided but not compared, due to the differences in baseline characteristics between groups. A stepwise logistic regression analysis including all variables with p value <0.2 in the univariate analysis was used to determine the predictive factors of 30-day mortality. A Cox multivariate analysis including all variables with p value <0.2 in the Cox univariate analysis was used to determine the predictive factors of cumulative late mortality. Survival rates up to 2 years were presented as Kaplan-Meier curves, and the log-rank test was used for comparison between patients with porcelain aorta and frailty and the rest of the study population. Differences were considered statistically significant at p values <0.05. The data were analyzed with SAS statistical software version 9.1.3 (SAS Institute, Inc., Cary, North Carolina).

Results

A total of 396 patients were considered potential candidates for TAVI by the multidisciplinary team of each center. Of these, 5 patients were turned down during the weekly conference call (of 291 patients presented since May 2007) and 52 patients were included in the PARTNER (Placement of AoRTic TraNscathetER Valve) trial, leading to a final study population of 339 patients who underwent TAVI under the Canadian compassionate clinical use TAVI program (Fig. 1). One-hundred sixty-seven patients (49.6%) were selected for TF approach, and 172 patients (50.7%) were selected for TA approach. Six patients who had had unsuccessful TF procedure underwent a second TA (n = 5) or TF (n = 1) procedure later on, leading to a total of 345 TAVI procedures (168 TF, 49%; 177 TA, 51%). Baseline clinical and echocardiographic characteristics of the study population are shown in Table 1.

Procedural and 30-day outcomes. Procedural and 30-day outcomes are shown in Table 2. The procedure was successful in 322 (93.3%) cases. Procedural, post-procedural, and cumulative 30-day mortality were 1.7% (n = 6), 8.7% (n = 30), and 10.4% (n = 36), respectively. Reasons for unsuccessful procedure were at least 1 of the following: balloon instability during aortic balloon valvuloplasty that precluded valve implantation attempt (n = 1, 0.3%), inability to advance the delivery catheter through iliofemoral arteries (n = 5, 1.4%), major vascular complications (n = 2, 0.6%), inability to cross the native aortic valve (n = 5, 1.4%), valve embolization with no implantation of a second valve (n = 6, 1.7%), and procedural death (n = 6, 1.7%). The reasons leading to procedural death were major vascular complications (n = 2, 0.6%), severe left ventricular dysfunction after valve implantation (n = 2, 0.6%), cardiac perforation (n = 1, 0.3%), and acute severe MR after balloon valvuloplasty (n = 1, 0.3%). Major access site complications were the most frequent procedural complication (45 cases, 13%) and occurred in TF (22 cases, 13.1%) and TA (23 cases, 13.0%) cases. Valve embolization occurred in 7 procedures (2%), and a second valve was implanted in 9 procedures (2.6%) because of valve embolization, valve malposition, and/or severe transvalvular or peri-valvular prosthetic regurgitation. A total of 14 patients (4.1%) needed hemodynamic support with aortic balloon counterpulsation (n = 3, 0.9%) or extracorporeal circulation (n = 10, 2.9%) or both (n = 1, 0.3%), due to severe maintained hypotension or hemodynamic collapse secondary to acute severe left ventricular dysfunction (n = 10, 2.9%), ventricular apical bleeding (n = 3, 0.9%), or cardiac perforation (n = 1, 0.3%).

A total of 30 patients (8.7%) died within the 30 days after TAVI. The causes of death for these patients were: multiorgan failure (n = 6, 1.7%), major bleeding (n = 5, 1.4%), pneumonia/septicemia (n = 4, 1.2%), stroke (n = 2, 0.6%), ventricular arrhythmia (n = 2, 0.6%), congestive heart failure (n = 2, 0.6%), cardiogenic shock (n = 1,

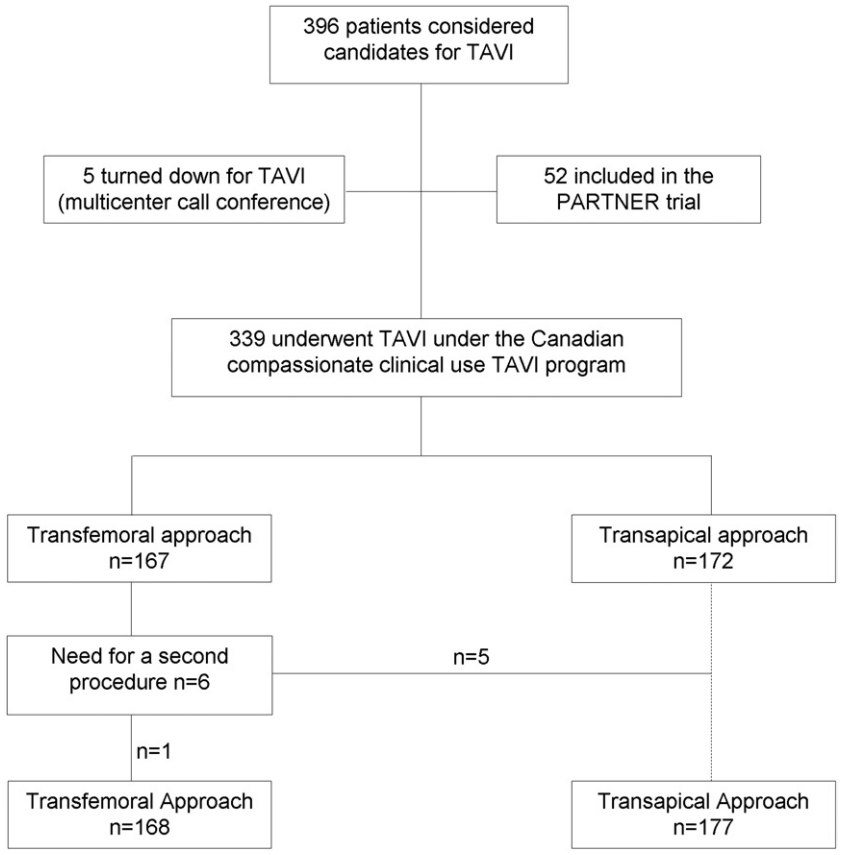

Figure 1 **Canadian Transcatheter Aortic Valve Implantation Program**

Flow chart showing the patients who underwent transcatheter aortic valve implantation (TAVI) on the basis of the Canadian compassionate clinical use program. PARTNER = Placement of AoRTic TraNscathetER Valve trial.

0.3%), sudden unexplained death (n = 2, 0.6%), myocardial infarction (n = 1, 0.3%), late (48 h) ventricular embolization of the valve leading to cardiogenic shock (n = 1, 0.3%), pulmonary embolism (n = 1, 0.3%), peripheral embolism (n = 1, 0.3%), aortic rupture (n = 1, 0.3%), and severe mitral regurgitation (MR) likely secondary to mitral leaflet perforation (n = 1, 0.3%). The clinical and procedural characteristics of the patients who died within 30 days after TAVI compared with those who survived are shown in Table 3. The predictive factors of cumulative 30-day mortality identified by multivariate analysis were PH (odds ratio [OR]: 2.09, 95% confidence interval [CI]: 1.02 to 4.43, p = 0.048), severe MR (OR: 3.01, 95% CI: 1.09 to 8.24, p = 0.033), and the need for peri-procedural hemodynamic support (OR: 6.84, 95% CI: 2.04 to 22.93, p = 0.002).

Mean aortic gradient and aortic valve area decreased and increased, respectively, from 46 ± 17 mm Hg and 0.63 ± 0.17 cm^2 at baseline to 10 ± 4 mm Hg and 1.55 ± 0.41 cm^2 at discharge ($p < 0.0001$ for both). Most patients (84%) had some degree of residual aortic regurgitation at hospital discharge (trivial or mild: 78%; moderate: 5%; severe: 1%).

Porcelain aorta and frail patients. Porcelain aorta was present in 61 patients (18%). Baseline and procedural characteristics of patients with porcelain aorta are shown in Table 4. Patients with porcelain aorta were younger; were more frequently female; exhibited a lower STS-PROM score and creatinine values; and had a lower prevalence of cerebrovascular disease, PH, and severe MR. Approximately one-half of the patients with porcelain aorta underwent TAVI by TF approach. The procedure was successful in 98.4% of the patients, but valve malposition requiring the implantation of a second valve tended to be more frequent in these patients. The stroke and 30-day mortality rate were 1.6% and 11.5%, respectively, with no differences compared with patients without porcelain aorta. Frailty was a comorbidity in 85 patients (25%). Baseline and procedural characteristics of frail patients are shown in Table 4. Frail patients were older and more frequently women, exhibited a lower weight and body mass index, and were associated with a higher STS-PROM score and a lower rate of prior CABG. Procedural and 30-day mortality rates (2.4% and 8.2%, respectively) were similar to that of the rest of the study population, but frail patients more frequently devel-

Table 1 Baseline Characteristics of the Study Population (n = 339)

Variables	All Patients (n = 339)	Transfemoral (n = 162)	Transapical (n = 177)	p Value
Age (yrs)	81 ± 8	83 ± 8	80 ± 8	0.009
Male sex	152 (44.8)	91 (56.1)	61 (34.5)	<0.0001
BMI (kg/m^2)	26 ± 5	26 ± 5	26 ± 5	0.934
Diabetes	79 (23.3)	37 (22.8)	42 (23.7)	0.898
Dyslipidemia	241 (71.1)	104 (64.2)	137 (77.4)	0.020
Hypertension	252 (74.3)	102 (62.9)	150 (84.7)	<0.0001
Current smokers	20 (5.9)	8 (4.9)	12 (6.8)	0.645
NYHA functional class				
I–II	29 (8.6)	11 (6.8)	18 (10.2)	0.332
III–IV	308 (90.9)	150 (92.6)	158 (89.3)	
Chronic atrial fibrillation/flutter	115 (33.9)	66 (40.7)	49 (27.7)	0.012
Coronary artery disease	234 (69.0)	110 (67.9)	124 (70.1)	0.723
Previous myocardial infarction	173 (51.0)	82 (50.6)	91 (51.4)	0.913
Previous PCI	99 (29.2)	47 (29.0)	52 (29.4)	1.00
Prior coronary artery bypass grafting	116 (34.2)	49 (30.2)	67 (37.9)	0.169
Cerebrovascular disease	77 (22.7)	27 (16.7)	50 (28.2)	0.013
Peripheral vascular disease	120 (35.4)	31 (19.1)	89 (50.3)	<0.0001
COPD	100 (29.5)	45 (27.8)	55 (31.1)	0.551
Creatinine (μmol/l)	119 ± 83	124 ± 85	113 ± 81	0.232
eGFR <60 ml/min	191 (56.3)	86 (53.1)	104 (58.8)	0.325
Dialysis	10 (2.9)	7 (4.3)	3 (1.7)	0.203
STS-PROM score (%)	9.8 ± 6.4	9.0 ± 5.8	10.5 ± 6.9	0.034
Porcelain aorta	61 (17.9)	28 (17.3)	33 (18.6)	0.779
Frailty	85 (25.1)	42 (25.9)	43 (24.3)	0.802
Pulmonary hypertension	84 (25.0)	35 (21.6)	49 (27.7)	0.256
Severe mitral regurgitation	27 (8.0)	18 (11.1)	9 (5.1)	0.045
Mean aortic gradient (mm Hg)	46 ± 17	48 ± 18	44 ± 17	0.079
Aortic valve area (cm^2)	0.63 ± 0.17	0.63 ± 0.16	0.63 ± 0.18	0.928
LVEF (%)	55 ± 14	55 ± 14	56 ± 14	0.721
LVEF <40%	54 (15.9)	26 (16.1)	28 (15.8)	1.00

Values are expressed as n (%) or mean ± SD.

BMI = body mass index; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS-PROM = Society of Thoracic Surgeons Predicted Risk Of Mortality.

oped acute renal failure requiring hemodialysis in the post-operative period.

Late outcomes. Clinical follow-up was available in all patients at a median of 8 months (25th to 75th interquartile range: 3 to 14 months) after TAVI. A total of 39 patients (11.5%) died during the follow-up period, at a median of 162 days (25th to 75th interquartile range: 72 to 390 days) after the TAVI procedure. Of these, 26 patients (7.7%) died of noncardiac causes (respiratory = 13, hemorrhagic or ischemic stroke = 3, renal failure = 3, cancer = 2, cachexy = 2, amyotrophic lateral sclerosis = 1, pancreatitis = 1, subdural hematoma = 1). The baseline and procedural characteristics of the patients who died during the follow-up period compared with those who survived are shown in Table 5. The predictors of cumulative late mortality were post-procedural sepsis (hazard ratio [HR]: 3.49, 95% CI: 1.48 to 8.28), need for peri-procedural hemodynamic support (HR: 2.58, 95% CI: 1.11 to 6), PH (HR: 1.88, 95% CI: 1.17 to 3), chronic kidney disease [CKD] (HR: 2.30, 95% CI: 1.38 to 3.84), and chronic obstructive pulmonary disease [COPD] (HR: 1.75, 95% CI: 1.09 to 2.83). Figure 2 shows the Kaplan-Meier survival curves for the entire study population and for the TF and TA groups. Survival rates at 1- and 2-year follow-up were, respectively, 76% (95% CI: 71% to 82%) and 64% (95% CI: 56% to 74%) for the entire study population; 75% (95% CI: 68% to 82%) and 65% (95% CI: 53% to 75%) for the TF group; and 78% (95% CI: 71% to 85%) and 64% (95% Cl: 52% to 80%) for the TA group. The percentage of patients free of death, MI, or stroke at 1- and 2- year follow-up were, respectively, 72% (95% CI: 67% to 78%) and 60% (95% CI: 53% to 71%) for the entire study population; 73% (95% CI: 65% to 81%) and 63% (95% CI: 52% to 75%) for the TF group, and 72% (95% CI: 65% to 81%) and 59% (95% CI: 47% to 75%) for the TA group. Figure 3 shows the Kaplan-Meier survival curves for patients with porcelain aorta or frailty as comorbidities. Patients with porcelain aorta tended to have a better survival rate at 1-year follow-up (86%, 95% CI: 77% to 95% vs. 74%,

Table 2 Procedural and 30-Day Outcomes

Variables	All Procedures (n = 345)	Transfemoral (n = 168)	Transapical (n = 177)
Procedural variables			
Successful procedure	322 (93.3)	152 (90.5)	170 (96.1)
Procedural death	6 (1.7)	3 (1.8)	3 (1.7)
Valve embolization	7 (2.0)	5 (3.0)	2 (1.1)
Need for a second valve	9 (2.6)	4 (2.4)	5 (2.8)
Conversion to open heart surgery	6 (1.7)	2 (1.2)	4 (2.3)
Need for hemodynamic support	14 (4.1)	7 (4.2)	7 (3.9)
Major access site complications	45 (13.0)	22 (13.1)	23 (13.0)
Stroke	2 (0.6)	1 (0.6)	1 (0.6)
Coronary obstruction	3 (0.9)	1 (0.6)	2 (1.1)
Life-threatening arrhythmias	28 (8.1)	12 (7.1)	16 (9.0)
30-day outcomes			
Myocardial infarction	4 (1.2)	1 (0.6)	3 (1.7)
Stroke	8 (2.3)	5 (3.0)	3 (1.7)
Sepsis	10 (2.9)	5 (3.0)	5 (2.8)
Need for hemodialysis	9 (2.6)	3 (1.8)	6 (3.4)
Need for permanent pacemaker	17 (4.9)	6 (3.6)	11 (6.2)
30-day mortality	36 (10.4)	16 (9.5)	20 (11.3)

Values are expressed as n (%).

95% CI: 68% to 80%, p = 0.14). There were no cases of structural valve dysfunction at follow-up, and only 1 patient required SAVR at 8-month follow-up due to endocarditis.

Discussion

This multicenter study including a large series of patients diagnosed with severe symptomatic aortic stenosis deemed inoperable or at very high surgical risk showed that a global TAVI program including both TF and TA approaches was associated with a 30-day mortality of 10.4% and a cumulative mortality rate of 22.1% after a mean follow-up of nearly 1 year. The characteristics of the population and the size of the catheters determined the greater use of the TA approach, which was undertaken in more than one-half of the patients. The presence of severe PH and severe MR but not the STS-PROM score were predictive factors of 30-day mortality. The procedural variable associated with 30-day mortality was any complication leading to the need for hemodynamic support. Predictive factors of cumulative late mortality were peri-procedural need for hemodynamic support, post-procedural sepsis, PH, COPD, and CKD. The TAVI approach (TF vs. TA) had no prognostic value in acute and late outcomes. Patients diagnosed with porcelain aorta or frailty had similar 30-day and late results compared with the rest of the study population. Porcelain aorta patients were associated with a relatively low risk of peri-procedural stroke (1.6%), although with a wide CI, and those who survived the procedure also tended to have a lower risk of death at 1-year follow-up.

TAVI global program including TF and TA approaches. The retrograde TF approach has become the approach of choice for TAVI. The TA approach appeared as a complementary option for those who were noncandidates for the TF

Table 3 Clinical and Peri-Procedural Characteristics of the Patients, According to the Occurrence of 30-Day Mortality

Variables	30-Day Mortality: Yes (n = 36)	30-Day Mortality: No (n = 303)	p Value
Baseline			
Age (yrs)	81 ± 9	81 ± 8	0.836
Male sex	17 (47.2)	135 (44.6)	0.721
BMI (kg/m^2)	25 ± 4	26 ± 5	0.399
Diabetes	6 (16.7)	73 (24.1)	0.407
Dyslipidemia	21 (58.3)	220 (72.7)	0.109
Hypertension	26 (72.2)	226 (74.6)	1.00
Current smokers	2 (5.6)	18 (5.9)	1.00
Chronic atrial fibrillation/flutter	13 (36.1)	102 (33.7)	0.709
Coronary artery disease	25 (69.4)	209 (69.0)	0.849
Previous myocardial infarction	23 (63.9)	150 (49.5)	0.077
Previous PCI	10 (27.8)	89 (29.4)	1.00
Prior coronary artery bypass grafting	10 (27.8)	106 (34.9)	0.460
Cerebrovascular disease	11 (30.6)	66 (21.8)	0.206
Peripheral vascular disease	13 (36.1)	107 (35.3)	0.854
COPD	12 (33.3)	88 (29.1)	0.559
Creatinine (μmol/l)	136 ± 89	117 ± 82	0.201
eGFR <60 ml/min	27 (75.0)	163 (53.8)	0.020
Dialysis	1 (2.8)	9 (2.9)	1.00
STS score (%)	10.3 ± 6.3	9.8 ± 6.5	0.609
Porcelain aorta	7 (19.4)	54 (17.8)	0.819
Frailty	7 (19.4)	78 (25.7)	0.542
Pulmonary hypertension	14 (38.9)	70 (23.1)	0.039
Severe mitral regurgitation	6 (16.7)	21 (7.0)	0.049
LVEF (%)	55 ± 15	55 ± 14	0.866
LVEF <40%	7 (19.4)	47 (15.5)	0.629
Procedural and 30-day outcome variables			
Approach			
Transfemoral	16 (44.4)	146 (48.2)	0.726
Transapical	20 (55.6)	157 (51.8)	
Unsuccessful procedure*	2 (6.7)	10 (3.3)	0.295
Valve embolization	2 (5.6)	5 (1.6)	0.164
Need for a second valve	2 (5.6)	7 (2.3)	0.246
Conversion to open heart surgery	3 (8.3)	3 (0.9)	0.018
Need for hemodynamic support	5 (13.9)	9 (2.9)	0.010
Major access site complications	9 (25.0)	36 (11.9)	0.038
Life-threatening arrhythmias	5 (13.9)	23 (7.6)	0.199
Myocardial infarction	2 (5.6)	2 (0.7)	0.057
Stroke	2 (5.6)	6 (1.9)	0.204
Sepsis	3 (8.3)	7 (2.3)	0.078
Need for hemodialysis	1 (2.8)	8 (2.6)	1.00
Need for permanent pacemaker	1 (2.8)	16 (5.3)	1.00

Values are expressed as n (%) or mean ± SD. *Excluding procedural death.
Abbreviations as in Table 1.

Table 4 Baseline Characteristics, 30-Day, and Late Outcomes, According to the Presence of Porcelain Aorta or Frailty

Variables	Porcelain Aorta			Frailty		
	No (n = 278)	Yes (n = 61)	p Value	No (n = 254)	Yes (n = 85)	p Value
Age (yrs)	82 ± 8	78 ± 8	0.001	81 ± 7	83 ± 7	0.008
Male sex	137 (49.3)	15 (24.6)	<0.0001	125 (47.2)	27 (31.8)	0.005
BMI (kg/m^2)	26 ± 5	26 ± 5	0.927	26 ± 5	25 ± 5	0.023
Weight (kg)	69.3 ± 15.2	66.8 ± 15.9	0.254	70.4 ± 15.4	64.1 ± 14.3	0.0009
Height (cm)	164.2 ± 10.8	161.4 ± 8.3	0.029	164.5 ± 10.6	161.3 ± 9.7	0.014
Diabetes	68 (24.5)	11 (18.0)	0.319	58 (23.0)	21 (26.6)	0.768
Dyslipidemia	189 (68.0)	52 (85.3)	0.012	186 (73.2)	55 (65.5)	0.121
Hypertension	215 (77.3)	37 (60.7)	0.009	194 (76.4)	58 (68.2)	0.114
Current smokers	16 (5.8)	4 (6.6)	0.759	17 (6.7)	3 (3.6)	0.426
Chronic atrial fibrillation/flutter	101 (36.3)	14 (22.9)	0.052	82 (32.3)	33 (38.8)	0.293
Coronary artery disease	191 (68.7)	43 (70.5)	0.879	177 (69.7)	57 (67.1)	0.588
Previous myocardial infarction	141 (50.7)	32 (52.5)	0.888	134 (52.8)	39 (45.9)	0.261
Previous PCI	83 (30.0)	16 (26.2)	0.642	73 (28.7)	26 (30.6)	0.784
Prior coronary artery bypass grafting	98 (35.3)	18 (29.5)	0.457	96 (37.8)	20 (23.5)	0.018
Cerebrovascular disease	71 (25.5)	6 (9.8)	0.007	62 (24.4)	15 (17.7)	0.232
Peripheral vascular disease	93 (33.5)	27 (44.3)	0.139	91 (35.8)	29 (34.1)	0.794
COPD	84 (30.2)	16 (26.2)	0.642	77 (30.3)	23 (27.1)	0.585
Creatinine (μmol/l)	124 ± 89	92 ± 37	<0.0001	121 ± 86	112 ± 73	0.395
eGFR <60 ml/min	161 (57.9)	29 (47.5)	0.155	149 (58.7)	41 (48.2)	0.102
Dialysis	10 (3.6)	0	0.219	7 (2.8)	3 (3.5)	0.717
STS-PROM score (%)	10.2 ± 6.6	7.9 ± 5.6	0.014	9.2 ± 5.6	11.6 ± 8.3	0.019
Pulmonary hypertension	75 (27.0)	9 (14.8)	0.049	54 (21.3)	30 (35.3)	0.014
Severe mitral regurgitation	19 (6.8)	8 (13.1)	0.121	18 (7.1)	9 (10.9)	0.349
LVEF (%)	55 ± 15	57 ± 11	0.314	55 ± 15	57 ± 13	0.150
LVEF <40%	48 (17.3)	6 (9.8)	0.179	44 (17.3)	10 (11.8)	0.304
Procedural and 30-day outcomes						
Approach						
Transfemoral	134 (48.2)	28 (45.9)	0.779	120 (47.2)	42 (49.4)	0.802
Transapical	144 (51.8)	33 (54.1)		134 (52.8)	43 (50.6)	
Successful procedure	261 (93.9)	60 (98.4)	0.215	240 (94.5)	81 (95.3)	1.00
Procedural death	6 (2.2)	0	0.596	4 (1.6)	2 (2.4)	0.643
Valve embolization	6 (2.2)	1 (1.6)	1.00	6 (2.4)	1 (1.2)	0.684
Need for a second valve	5 (1.8)	4 (6.6)	0.059	8 (3.2)	1 (1.2)	0.459
Conversion to open heart surgery	4 (1.4)	2 (3.2)	0.295	5 (1.9)	1 (1.2)	1.00
Need for hemodynamic support	11 (3.9)	3 (4.9)	0.723	9 (3.5)	5 (5.9)	0.352
Major access site complications	35 (12.6)	10 (16.4)	0.410	33 (12.9)	12 (14.1)	0.854
Life-threatening arrhythmias	22 (7.9)	6 (9.8)	0.610	19 (7.5)	9 (10.6)	0.368
Myocardial infarction	4 (1.4)	0	1.00	2 (0.8)	2 (2.4)	0.262
Stroke	7 (2.5)	1 (1.6)	1.00	5 (1.9)	3 (3.5)	0.419
Sepsis	9 (3.2)	1 (1.6)	1.00	6 (2.4)	4 (4.7)	0.276
Need for hemodialysis	9 (3.2)	0	0.372	3 (1.2)	6 (7.1)	0.009
Permanent pacemaker	12 (4.3)	5 (8.2)	0.204	10 (3.9)	7 (8.2)	0.148
30-day mortality	29 (10.4)	7 (11.5)	0.819	29 (11.4)	7 (8.2)	0.542
Late outcomes						
Follow-up length (months)	9.8 ± 8.3	10.7 ± 7.7	0.477	10.7 ± 8.3	8.0 ± 7.7	0.014
Cumulative mortality	65 (23.4)	10 (16.4)	0.307	56 (22.1)	19 (22.4)	1.00

Values are expressed as n (%) or mean ± SD.
Abbreviations as in Table 1.

approach (3–5), but only a few single-center studies have evaluated its role in a global TAVI program (7–9). The present study showed that the TA approach made it possible to treat more than one-half of the potential TAVI candidates, highlighting the relevance of this approach in a TAVI program. According to our results, previous reports from single centers with the 2 approaches showed that 32% to 52% of the patients were treated by TA approach (7–9). Interestingly, we have previously shown that a global TAVI program allowed the treatment of up to 76% of the patients refused for SAVR (7). More recently, Himbert et al. (8) showed that having the TF and TA program allowed approximately one-half of the

Table 5 Clinical and Peri-Procedural Characteristics of the Patients, According to the Occurrence of Cumulative Late Mortality

Variables	Cumulative Late Mortality		p Value
	Yes (n = 75)	No (n = 264)	
Baseline			
Age (yrs)	82 ± 8	81 ± 8	0.748
Male sex	39 (52.0)	113 (42.9)	0.326
BMI (kg/m^2)	25 ± 4	26 ± 5	0.389
Diabetes	21 (28.0)	58 (22.0)	0.226
Dyslipidemia	50 (66.7)	191 (73.3)	0.256
Hypertension	59 (78.7)	193 (73.1)	0.133
Current smokers	7 (9.3)	13 (4.9)	0.301
Chronic atrial fibrillation/flutter	33 (44.0)	82 (31.1)	0.044
Coronary artery disease	52 (69.3)	182 (69.0)	0.480
Previous myocardial infarction	46 (61.3)	127 (48.1)	0.190
Previous PCI	25 (33.3)	74 (28.0)	0.384
Prior coronary artery bypass grafting	19 (25.3)	97 (36.7)	0.076
Cerebrovascular disease	22 (29.3)	55 (20.8)	0.118
Peripheral vascular disease	30 (40.0)	90 (34.1)	0.164
COPD	30 (40.0)	70 (26.5)	0.039
Creatinine (μmol/l)	135 ± 79	114 ± 84	0.103
eGFR <60 ml/min	52 (69.3)	138 (52.3)	0.004
Dialysis	3 (4.0)	7 (2.7)	0.653
STS-PROM score (%)	11.7 ± 8.1	9.3 ± 5.8	0.004
Porcelain aorta	10 (13.3)	51 (19.3)	0.198
Frailty	19 (25.3)	66 (25.0)	0.785
Pulmonary hypertension	29 (38.7)	55 (20.8)	0.002
Severe mitral regurgitation	8 (10.7)	19 (7.2)	0.447
LVEF (%)	55 ± 15	56 ± 14	0.692
LVEF <40%	14 (18.7)	40 (15.2)	0.402
Peri-procedural variables			
Approach			
Transfemoral	40 (53.3)	122 (46.2)	0.884
Transapical	35 (46.7)	142 (53.8)	
Unsuccessful procedure*	8 (10.7)	10 (3.8)	0.913
Valve embolization	2 (2.7)	5 (1.9)	0.244
Need for a second valve	2 (2.7)	7 (2.7)	0.756
Conversion to open heart surgery	3 (4.0)	3 (1.1)	0.003
Need for hemodynamic support	6 (8.0)	8 (3.0)	0.026
Major access site complications	15 (20.0)	30 (11.4)	0.035
Life-threatening arrhythmias	6 (8.0)	22 (8.3)	0.856
Myocardial infarction	2 (2.7)	2 (0.8)	0.035
Stroke	2 (2.7)	6 (2.3)	0.948
Sepsis	6 (8.0)	4 (1.5)	0.002
Need for hemodialysis	4 (5.3)	5 (1.9)	0.098
Need for permanent pacemaker	3 (4.0)	14 (5.3)	0.744

Values are expressed as n (%) or mean ± SD. *Excluding procedural death. Abbreviations as in Table 1.

patients refused for SAVR to be treated. Reducing the catheter delivery size in the near future will increase the number of TF cases, but a high proportion of patients will still exhibit inappropriate iliofemoral arteries for accommodating ≥18-F catheters.

30-day outcomes. The 30-day mortality rate of 10.4% observed in the present study was similar to the 8.6% to 11.3% mortality rate reported in previous smaller single-center studies that included both TF and TA approaches (7–9). The predictive factors of 30-day mortality included baseline characteristics such as severe PH and MR and peri-procedural variables such as the occurrence of any complication leading to the use of hemodynamic support. Malouf et al. (12) identified the presence of severe PH as an important predictive factor of 30-day mortality in patients undergoing SAVR. Our results showed that severe PH also had a prognostic value in patients undergoing TAVI. The presence of PH makes the patient both more prone to and vulnerable during any procedural situation of hemodynamic instability and could also increase the risk of post-operative complications (13). Inoperable patients with symptomatic severe AS associated with severe MR were accepted for TAVI with the objective of improving symptoms and the expectation of reducing the degree of MR by reducing pressure overload and improving left ventricular remodeling (14,15). However, patients with severe MR had 3 times greater risk of dying within the 30 days after TAVI. The presence of severe MR might increase patient's vulnerability during peri-procedural hemodynamic changes and post-procedural complications, as with severe PH. Further research is needed to optimize the acute results of TAVI in patients with severe PH and/or MR and to determine both the reversibility of these 2 conditions and the improvement of symptoms and quality of life of these patients after TAVI. The need for peri-procedural hemodynamic support increased the risk of death at 30 days approximately 7-fold. The hemodynamic instability leading to the need for hemodynamic support was mainly secondary to either severe ventricular dysfunction after valvuloplasty and/or valve implantation or life-threatening bleeding. Importantly, although the 30-day mortality rate was high in these patients, approximately two-thirds of them survived, highlighting the potential benefits of having an extracorporeal circulation machine and a surgical backup when performing these procedures. Interestingly, the STS-PROM score was unable to identify those patients who would die within the first 30 days, and this was consistent with previous TAVI studies (8,9). In fact, the vast majority of patients who underwent TAVI would not have been operated on in the past, and new predictive risk scores including specific variables for this particular subset of patients should be developed in the future.

Late outcomes. The survival rate of 76% at 1-year follow-up was consistent with the 74% to 78% reported in previous studies including TF and TA approaches (8,9). Importantly, most deaths occurring during the follow-up period were of noncardiac origin. The predictive factors of cumulative late death in the present study included peri-procedural variables such as the need for hemodynamic support and post-procedural sepsis, a cardiovascular condition such as PH, and noncardiac comorbidities such as

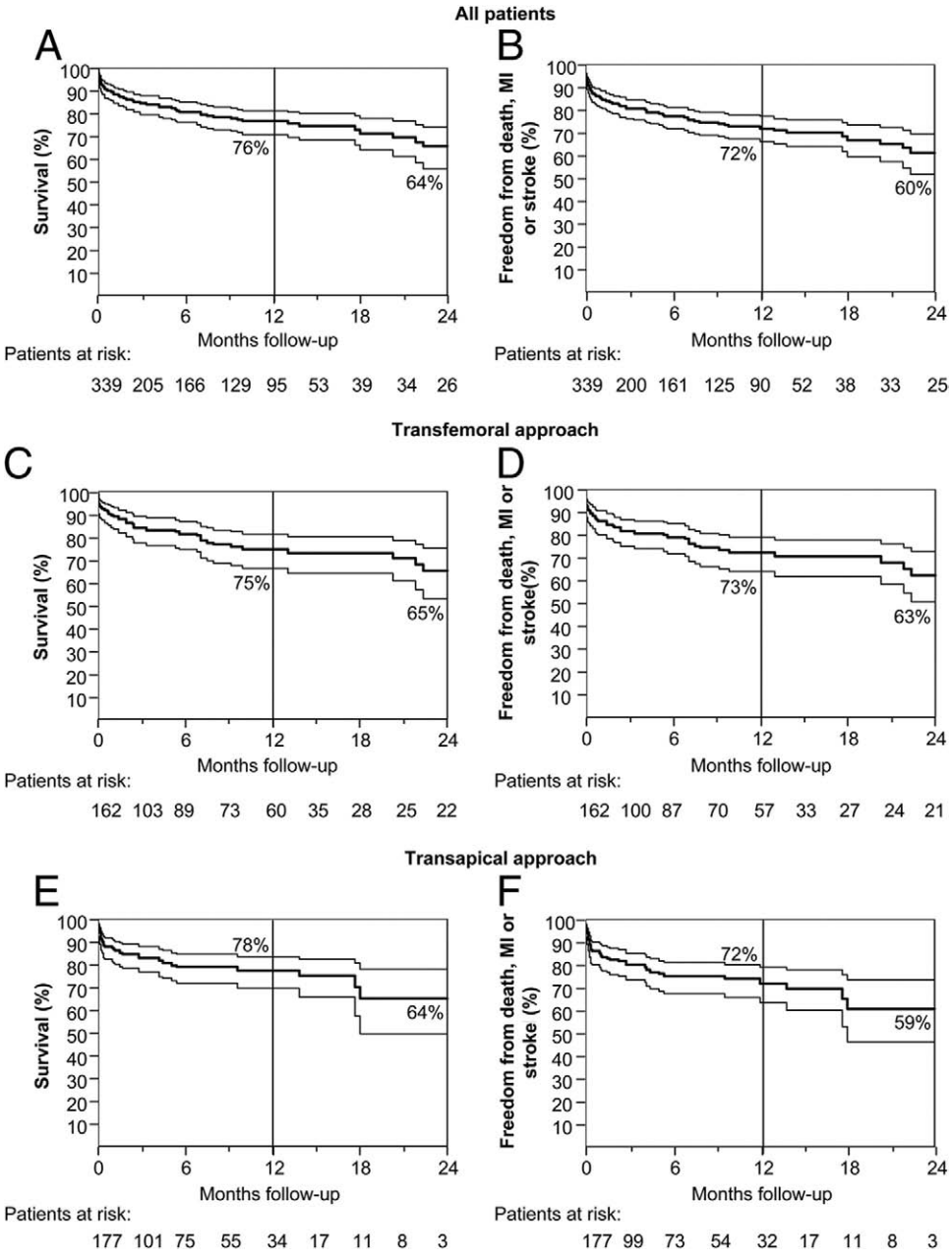

Figure 2 **24-Month Follow-Up Survival Curves**

Kaplan-Meier curves of survival and survival free of myocardial infarction (MI) and stroke at 24-month follow-up for the entire study population **(A, B)**, for patients who underwent transcatheter aortic valve implantation (TAVI) by transfemoral approach **(C, D)**, and for patients who underwent TAVI by transapical approach **(E, F)**.

COPD and CKD. Chronic obstructive pulmonary disease is a frequent morbidity in elderly patients and 1 of the leading causes of death in this population (16). Grossi et al. (17) already showed the long-term prognostic value of COPD in patients undergoing SAVR. Our findings highlight the relevance of both an accurate diagnostic and prognostic evaluation of the patients' respiratory status before performing TAVI and a close follow-up of COPD patients so that acute exacerbations can be reduced (18). Several studies have shown that CKD is an independent predictor of late mortality after SAVR in elderly patients (17,19,20), and Webb et al. (9) recently reported that this comorbidity was also a predictor of worse outcomes in patients undergoing TAVI. The mechanisms linking CKD and late mortality in our study population were probably multifactorial (21). Importantly, CKD has been associated not only with higher cardiovascular but also with higher all-cause mortality in older people (22), and this prognostic factor should probably

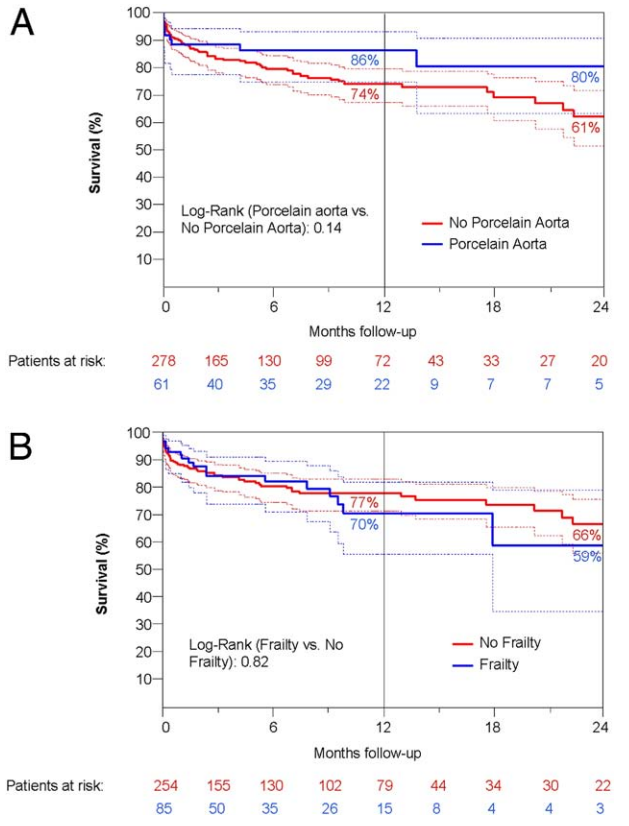

Figure 3 **24-Month Follow-Up Survival Curves in Porcelain Aorta and Frail Patients**

Kaplan-Meier curves of survival at 24-month follow-up for patients with porcelain aorta **(A)** and frailty **(B)** as comorbidities.

be taken into account when evaluating the potential benefits of the TAVI procedure at midterm follow-up, especially in very old patients with moderate to severe CKD. Finally, the TAVI approach had no prognostic value in the present study. In fact, TF and TA approaches were associated with very similar survival rates at 1-year (TF: 75%, TA: 78%) and 2-year (TF: 65%, TA: 64%) follow-up. Some previous studies suggested worse clinical outcomes associated with the TA approach, but patients undergoing TA-TAVI have been systematically associated with a higher risk profile (3–5). Himbert et al. (8) showed no prognostic value of either the TF or TA approach, consistent with our results, whereas Webb et al. (9) showed that TA approach was an independent predictor of late mortality. Future studies should further investigate the potential independent role of approach selection on TAVI outcomes.

Porcelain aorta and frailty. Surgical aortic valve replacement becomes a high-risk or even a prohibitive procedure in patients in whom the ascending aorta cannot be clamped, because of extensive calcification due to the risk of both cerebral embolism and the impossibility of safe aortic dissection and clamping (23,24). Approximately 20% (5% to 33%) of the patients undergoing TAVI are diagnosed with porcelain aorta (1–9), and the present study is the first to evaluate the procedural and late outcomes in this specific high-risk group of patients. Of high clinical relevance, the stroke rate was relatively low (1.6%), with no differences compared with the rest of the study population. However, the need for a second valve tended to be more frequent in this group of patients, probably reflecting a higher incidence of valve malposition due to either difficulty in valve positioning or valve displacement during balloon inflation in the presence of a highly calcified aorta. Although STS-PROM scores were lower, 30-day mortality remained similar to that of the rest of the study population, pointing out the high risk of this group of patients. However, those patients who survived the procedure had a relatively low late mortality, leading to a survival rate of 86% at 1-year follow-up. These results support further research into the role of TAVI for the treatment of patients with porcelain aorta.

Older age and frailty have been among the main reasons for considering a high (up to 33%) proportion of elderly patients diagnosed with severe symptomatic aortic stenosis as inoperable (10). Approximately one-half of the frail patients also had other comorbidities leading to a high STS-PROM score, but those patients with a lower STS-PROM score refused for SAVR because of frailty exhibited similar 30-day mortality rates as those of the rest of the study population, suggesting that frailty remains per se an important risk factor in patients undergoing TAVI. Further research will be of major importance in improving identification and management of frail patients undergoing TAVI as well as in determining the benefits of TAVI in this particular subset of patients.

Study limitations. Although the data were prospectively collected in each of the participating centers, there was no pre-specified case report form designated for the purpose of this study. However, the fact that the cases were presented with a similar presentation format in a weekly conference call ensured data uniformity and partially compensated for this limitation. The diagnosis of porcelain aorta and frailty was subjective and based on the judgment of the physician in charge of each patient. This was partially compensated, because patients were evaluated by at least 2 cardiac surgeons agreeing on the diagnosis and were presented in a weekly conference call in which investigators of other centers also had to agree on the diagnosis. However, further research is needed to provide an objective and reproducible evaluation of these 2 important criteria for inoperability.

Conclusions

The results of this large multicenter series of consecutive patients with severe aortic stenosis at very high or prohibitive surgical risk showed that a TAVI program including both TF and TA approaches was associated with comparable mortality as predicted by surgical risk calculators despite a very high-risk patient profile. Cardiac comorbidities (se-

vere PH, MR), procedural factors (need for hemodynamic support, sepsis), and noncardiac comorbidities (COPD, CKD) determined worse outcomes. Finally, the results of the study suggest that TAVI might be a good alternative for the treatment of patients with porcelain aorta and/or frailty, the 2 most common comorbidities not included in surgical risk score calculators that determined patient's inoperability. The prospective multicenter PARTNER trial, which is a randomized trial and has both arms comparing TAVI with surgical therapy and medical therapy, will further determine the safety and efficacy of TAVI for the treatment of the challenging group of patients with symptomatic severe aortic stenosis at very high or prohibitive surgical risk.

Acknowledgments

The authors thank Mélanie Côté, MSc, from the Quebec Heart and Lung Institute, for his great work on database management and technical support, and Serge Simard, MSc, for statistical analysis.

Reprint requests and correspondence: Dr. Josep Rodés-Cabau, Quebec Heart and Lung Institute, Laval University, 2725 Chemin Ste-Foy, G1V 4G5 Quebec City, Canada. E-mail: josep.rodes@criucpq.ulaval.ca.

REFERENCES

1. Cribier A, Eltchaninoff H, Tron C, et al. Treatment of calcific aortic stenosis with the percutaneous heart valve. Mid-term follow-up from the initial feasibility studies: the French experience. J Am Coll Cardiol 2006;47:1214–23.
2. Webb JG, Pasupati S, Humphries K, et al. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. Circulation 2007;116:755–63.
3. Ye J, Cheung A, Lichtenstein SV, et al. Transapical transcatheter aortic valve implantation: 1-year outcome in 26 patients. J Thorac Cardiovasc Surg 2009;137:167–73.
4. Walther T, Simon P, Dewey T, et al. Transapical minimally invasive aortic valve implantation. Multicenter experience. Circulation 2007; 116:I240–5.
5. Svensson LG, Dewey T, Kapadia S, et al. United States feasibility study of transcatheter insertion of a stented aortic valve by the left ventricular apex. Ann Thorac Surg 2008;86:46–55.
6. Grube E, Schuler G, Buellesfeld L, et al. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding corevalve prosthesis. J Am Coll Cardiol 2007;50:69–76.
7. Rodés-Cabau J, Dumont E, DelaRochellière R, et al. Feasibility and initial results of percutaneous aortic valve implantation including selection of the transfemoral or transapical approach in patients with severe aortic stenosis. Am J Cardiol 2008;102:1240–6.
8. Himbert D, Descoutures F, Al-Attar N, et al. Results of transfemoral or transapical aortic valve implantation following a uniform assessment in high-risk patients with aortic stenosis. J Am Coll Cardiol 2009;54: 303–11.
9. Webb JG, Altwegg L, Boone R, et al. Transcatheter aortic valve implantation. Impact on clinical and valve-related outcomes. Circulation 2009;119:3009–16.
10. Iung B, Cachier A, Baron G, et al. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? Eur Heart J 2005;26:2714–20.
11. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:146–56.
12. Malouf JF, Enriquez-Sarano M, Pellikka PA, et al. Severe pulmonary hypertension in patients with severe aortic valve stenosis: clinical profile and prognostic implications. J Am Coll Cardiol 2002;40:789–95.
13. Vanky FB, Hakanson E, Tamas E, Svedjeholm. Risk factors for postoperative heart failure in patients operated on for aortic stenosis. Ann Thorac Surg 2006;81:1297–304.
14. Harris KM, Malenka DJ, Haney MF, Hettleman B, Plehn JF, Griffin BP. Improvement in mitral regurgitation after aortic valve replacement. Am J Cardiol 1997;80:741–5.
15. Caballero-Borrego J, Gomez-Doblas JJ, Cabrera-Bueno F, et al. Incidence, associated factors and evolution of non-severe functional mitral regurgitation in patients with severe aortic stenosis undergoing aortic valve replacement. Eur J CardioThorac Surg 2008;34:62–6.
16. Mannino DM, Homa KM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance—United States, 1971–2000. MMWR Surveill Summ 2002;51:1–16.
17. Grossi EA, Schwartz CF, Yu PJ, et al. High-risk aortic valve replacement: are the outcomes as bad as predicted? Ann Thorac Surg 2008;85:102–7.
18. Connors AF, Dawson NV, Thomas C, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. Am J Respir Crit Care Med 1996;154:959–67.
19. Thourani VH, Myung R, Kilgo P, et al. Long-term outcomes after isolated aortic valve replacement in octogenarians: a modern perspective. Ann Thorac Surg 2008;86:1458–65.
20. Bossone E, Benedetto G, Frigiola A, et al. Valve surgery in octogenarians: in-hospital and long-term outcomes. Can J Cardiol 2007;23: 223–7.
21. Tonelli M, Wiebe N, Culleton B, et al. Chronic kidney disease and mortality risk: a systematic review. J Am Soc Nephrol 2006;17:2034–47.
22. Roderick PJ, Atkins RJ, Smeeth L, et al. CKD and mortality risk in older people: a community-based population study in the United Kingdom. Am J Kidney Dis 2009;53:950–60.
23. Coselli JS, Crawford ES. Aortic valve replacement in the patient with extensive calcification of the ascending aorta (the porcelain aorta). J Thorac Cardiovasc Surg 1986;91:184–7.
24. Wolman RL, Nussmeier NA, Aggarwal A, et al. Cerebral injury after cardiac surgery: identification of a group at extraordinary risk. Stroke 1999;30:514–22.

Key Words: transapical ■ transcatheter aortic valve implantation ■ transfemoral ■ valves.