Incidence and prognosis of vascular complications after transcatheter aortic valve implantation

Bibombe P. Mwipatayi, MMed, FCS, FRACS,[a,b] Alarick Picardo, MBBS,[a] Taolo Vijay Masilonyane-Jones, MBBS,[a] Robert Larbalestier, FRACS,[c] Shannon Thomas, FRACS,[d] Jennifer Turner, RN,[e] Vikram Vijayan, MRCS, FRCS,[a] and Gerald Yong, FRACP, FSCAI,[e] *Perth and Randwick, Australia*

Objective: Transcatheter aortic valve implantation (TAVI) has gained increasing global popularity as a minimally invasive option for high-risk cardiac patients. However, this operation is not without risk, particularly of significant vascular complications that increase the morbidity, mortality, and overall cost of the procedure. We aim to present our experience of TAVI-related vascular complications, including the morbidity and cost impacts of these events.

Methods: A case-series study was performed for all patients undergoing TAVI at our center. Vascular complications were defined according to the 2011 Valve Academic Research Consortium standardized end points. The data were prospectively collected from February 2009 to April 2012, and the outcomes were entered into a database and cross-checked with the hospital notes.

Results: TAVI was performed on 100 patients in our center during the study period, and the 30-day mortality was 6%. Access approaches included 81 transfemoral, 18 transapical, and one trans-subclavian access. The average patient age was 84.9 years, and 65% of the patients were male. Among the transfemoral procedures, there were 16 vascular access-related complications (VAC), including nine major and seven minor complications. The major complications included aortic dissection, iliac arterial rupture, femoral dissection, false aneurysms, and distal embolization, all of which required surgical or endovascular repair. An apical false aneurysm and an apical tear were major VAC of the transapical group, with the latter resulting in death. Patients with VAC had higher blood transfusion requirements (4.1 ± 4.5 units vs 0.9 ± 2.2 units; $P = .004$), greater length of hospital stay (16.4 ± 10.7 days vs 6.5 ± 5.1 days; $P = .001$), and increased cost (A\$93,448 ± 21,435 vs A\$69,932 ± 15,007; $P = .002$) compared with the non-VAC group. The predictors of vascular complications using multivariate analysis included European System for Cardiac Operative Risk Evaluation (odds ratio, 1.06; 95% confidence interval, 1.02-1.10; $P = .001$) and diabetes mellitus (odds ratio, 5.07; 95% confidence interval, 1.17-21.88; $P = .03$). Occurrence of major VAC did not affect in-hospital or 30-day mortality rates and was not associated with poorer survival.

Conclusions: Vascular complications affect perioperative management and outcomes following TAVI. Our findings show that these complications often require urgent surgical or endovascular repair and result in increased blood transfusions, greater length of hospital stay, and significantly increased costs. Diabetes mellitus and logistic European System for Cardiac Operative Risk Evaluation may be predictive of VAC and should be considered during TAVI patient selection. (J Vasc Surg 2013;58:1028-36.)

Aortic stenosis (AS) is one of the most common cardiac valve pathologies. The prevalence of AS increases with age and population-based studies report a prevalence between 2.8% and 4.6% for patients over 75 years old.[1] Surgical aortic valve replacement (SAVR) is the most effective

therapy for AS. However, up to two-thirds of patients with symptomatic AS are excluded from surgical intervention secondary to high perioperative risk profiles.[2]

Since the first-in-man procedure was performed in 2002,[3] transcatheter aortic valve implantation (TAVI) has been evolving. Published results now suggest mortality rates similar to SAVR at 2 years for high-risk patients.[4] In patients not suitable for SAVR, TAVI has been reported to reduce 2-year mortality and valve-related symptoms.[5] Advances in assessment, materials, technique, and aftercare have led to vast improvements in the provision of TAVI programs worldwide over the past 10 years.

Several procedure-related pitfalls have been identified. These include central and peripheral vascular complications, of which acute kidney injury, stroke, and access site complications are the most widely recognized.[6-8]

The occurrence of vascular complications after TAVI is associated with significant morbidity and mortality that increase the overall procedure cost. Precautions to avoid complications entail a thorough vascular evaluation of prospective TAVI patients. There is a high prevalence of peripheral arterial disease in the elderly patients that

constitute the majority of TAVI patients.[9-11] Vascular anatomy is pertinent in evaluating the safety of large sheath access, where current devices feature 18-26F (French size) access sheaths. The risk of access site vascular injury and distal plaque embolization must be evaluated before performing the procedure. Alternative strategies must be employed as necessary.[8,11-14]

In this study, we aim to determine the incidence, implications, and determinants of vascular complications following TAVI performed at a single center in Western Australia.

METHODS

Patient population. Transcatheter aortic valve implantation was initiated for high-risk AS patients as a state-wide service based in Royal Perth Hospital, Western Australia in 2009. Patients with symptomatic severe AS were offered TAVI if they were considered to have a high operative risk (generally defined as age ≥80 years old and/or logistic European System for Cardiac Operative Risk Evaluation [EuroSCORE] ≥20%, or the presence of other high-risk factors that are not included in the Euro SCORE).[15,16] All patients that were not candidates for opened surgical repair were considered for TAVI and included in our database. The EuroSCORE is a surgical risk scoring system developed in 1999 from a multinational European database. The model provides an estimate of a patient's anticipated 30-day mortality according to the patient demographic characteristics, cardiovascular and noncardiovascular risk factors, and procedural variables. A multidisciplinary heart team, comprised of interventional cardiologists, cardiothoracic surgeons, cardiac anesthetists, and a vascular surgeon, were involved in the selection of all patients. The leading interventional cardiologist performed all TAVI procedures (G.Y.), and any potential vascular problems were addressed or discussed with the leading vascular surgeon (B.M.). Informed consent was obtained from all patients (for the therapeutic procedure, clinical and procedural data collection). The local ethical committee approved the registry.

TAVI procedure and postprocedural monitoring. Devices. Transfemoral TAVI was performed using either a balloon-expandable Edwards SAPIEN (Edwards Life-sciences, Irvine, Calif) or the self-expandable Medtronic CoreValve (Medtronic CV, Irvine, Calif) prosthesis. The balloon expandable valve required a 22-24F arterial sheath in the earlier phase of the program before changing to an 18-19F arterial sheath. The self-expanding valve required an 18F arterial sheath. A transapical approach (require up to 26F arterial sheath) was available with the balloon expandable valve, however, a trans-subclavian approach was only available with the self-expanding valve.

Approach selection. Once a patient had been identified as a TAVI candidate, the route of approach was determined as transfemoral, transapical, or trans-subclavian. No evidence-based guidelines are available for this decision. However, a number of criteria and parameters are reported in the literature that might favor one approach over the other.[17,18] For the transfemoral approach, a minimum iliac-femoral diameter of 6-6.5 mm was required for an 18-19F sheath, and a minimum of 7-8 mm was needed for a 22-24F sheath. Calcification, vessel tortuosity, aneurysms of the abdominal aorta, plaque, and an unfolded or tortuous aortic arch were considered when predicting the success of device passage into the valve position. The assessment of the diameter and the calcifications and tortuosity of the iliac arteries and of the aorta were evaluated with invasive aortography and multislice computed tomographic angiography. The transfemoral approach was used as the first choice unless contraindicated.

Procedure. Transfemoral TAVI was performed in the coronary catheterization laboratory under fluoroscopic guidance. The procedural steps have been well described previously.[3-5] Percutaneous vascular closure using the preclosure technique[19] was used in all cases except one. These devices included the Perclose ProGlide Suture-Mediated Closure System (Abbott Vascular, Santa Clara, Calif) or the ProStar XL Percutaneous Vascular Surgical System (Abbott Vascular). Three ProGlide devices were used for 22-24F sheath access (suture deployed at 2, 10, and 12 o'clock), and one ProStar device was used for 18-19F sheath access. An open common femoral artery exposure was performed in one patient with an aortobifemoral graft. In every case, access site hemostasis and distal limb perfusion was confirmed by angiography after completion of the procedure.

Data collection and study end points. The lead interventional cardiologist prospectively collected all data. Medical records and databases were reviewed, and the following information was gathered: baseline characteristics, periprocedural data, comorbidities, and laboratory parameters (full blood count and renal function) before and after the TAVI procedure.

The designated primary study end points were any vascular complications. These were categorized in accordance with the Valve Academic Research Consortium (VARC) guidelines, which designate vascular access-related complications (VAC) into major and minor complications. The "access site" is defined as any location (arterial or venous) traversed by a guidewire, a catheter, or a sheath (including the left ventricular apex and the aorta). The term 'access related' is defined as any adverse clinical consequence possibly associated with the access sites used during the procedure.[13] The secondary study end points included length of hospital stay, the incidence of life-threatening or major bleeding, in-hospital mortality, and cumulative mortality. Healthcare utilization was obtained in terms of the total direct and indirect costs of the index hospitalization using all the reports from the different cost centers in the hospital. Any complications associated with the left ventricle apex site during transapical TAVI were also reported as an end point.

Statistical analysis. Categorical data were expressed as the number of patients and percentage, whereas continuous variables were expressed as the mean ± standard deviation (95% confidence interval [CI]) or median with
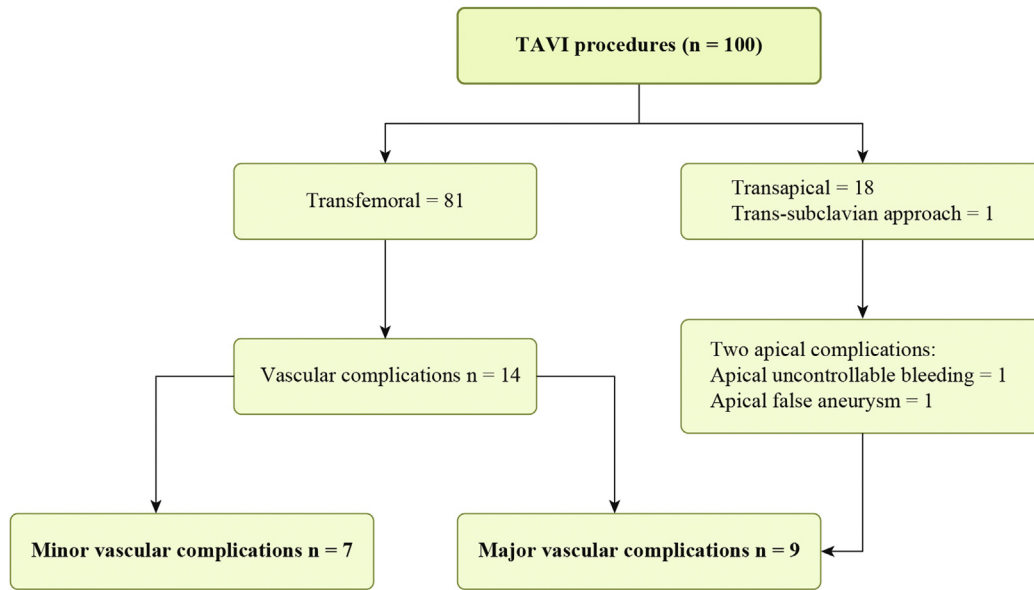
Fig 1. Perth (Western Australia) transcatheter aortic valve implantation (*TAVI*) program. Flow chart showing the patients who underwent TAVI on the basis of the Western Australian TAVI program at Royal Perth Hospital, Australia from February 2009 to July 2012.

interquartile range. Baseline, periprocedural and postprocedural characteristics, and outcome measures between patients who experienced vascular complications and those without vascular complications were compared with the use of χ^2 test, Mann-Whitney test, and *t*-test. An estimation of the cumulative mortality between the two groups of patients was performed with the Kaplan-Meier method, and events were compared by the log-rank test. A two-sided *P* value of less than .05 was considered significant.

The following variables were included in the model for the prediction of vascular complications: sheath size, diabetes mellitus, coronary artery disease, cerebrovascular disease, chronic obstructive pulmonary disease, hypertension, dyslipidemia, baseline estimated glomerular filtration rate, logistic regression model of EuroSCORE (logistic EuroSCORE), body mass index, and hemoglobin. Univariate logistic regression analyses were applied to identify factors associated with overall vascular complications. A multivariate stepwise logistic regression analysis that included variables with *P* value <.1 in the univariate analysis was used to determine the independent predictors of overall vascular complications. The derived CI was subsequently adjusted with a bootstrapping procedure to overcome the potential model over-fitting caused by the small number of patients and outcome event. A receiver operating characteristic curve was generated with all statistically significant variables, and the area under the curve did provide a measure of discrimination according to Hosmer and Lemershow classification. A negative binomial regression model was used for modelling over dispersed count outcome variables. Analyses were conducted using PASW 18 (SPSS, Chicago, Ill) and STATA v. 12 (Stata Corp, College Station, Tex).

RESULTS

In this study, 100 patients underwent TAVI at Royal Perth Hospital between February 2009 and July 2012. A transfemoral approach was used in 81 patients and a transapical approach was used in 18 patients. One patient had a trans-subclavian approach (Fig 1). The procedure was successful in 98% of patients, and the 30-day mortality rate was 6%. Two patients died within 24 hours of the TAVI procedure. The first patient had a low valve position during the procedure associated with severe paravalvular aortic regurgitation requiring a "valve-in-valve" bailout. This resulted in an apical tear that could not be repaired and resulted in death. The second patient developed severe aortic regurgitation after balloon aortic valve replacement resulting in severe compromise needing cardiopulmonary resuscitation prior to successful implantation of the transcatheter heart valve. The resuscitation led to rib fracture and liver laceration, which resulted in death.

Baseline and periprocedural characteristics. The baseline patient characteristics and periprocedural characteristics are summarized in Table I. The significant risk factors identified in the patients who had VAC were coronary artery disease, previous myocardial infarction and/or percutaneous coronary intervention, diabetes mellitus, dyslipidemia, hypertension, and logistic EuroSCORE. Sheath size, valve size, porcelain aorta, and vascular approach were not significantly different between patients with or without VAC.

Primary outcome. VAC occurred in 16% of patients (n = 16). These complications included common femoral artery dissection (3), apical complications (2), access site bleeding (1), false aneurysms (5), an iliac artery rupture

Table I. Baseline characteristics of the patients and periprocedural characteristics

Variables	All patients (n = 100)	Patients without VAC (n = 84)	Patients with VAC (n = 16)	P value
Age, years	84.9 ± 6	84. 8 ± 6.3	85.1 ± .4.5	.85
Male sex, %	65	56 (66.7)	9 (56.2)	.43
BMI, kg/m²	26 (IQR: 23.2-28.8)	26 (IQR: 23.3-28.8)	25 (IQR: 24-26.4)	.57
Chronic kidney disease (eGFR < 60 mL/min per 1.73 m²), %	38	32 (38.1)	6 (37.5)	.96
Coronary artery disease, %	67	65 (77.4)	2	**.009**
Previous myocardial infarction, %	33	32	1	.03
PCI, %	40	39 (46.4)	1 (6.2)	**.001**
CABG, %	30	29 (34.5)	1 (6.2)	.05
Cerebrovascular disease, %	29	27 (42.1)	2 (12.5)	.12
Diabetes mellitus, %	36	21 (25)	11 (68.7)	**.002**
Hypertension, %	57	56	1	**.001**
Dyslipidemia, %	53	52	1	**.003**
Chronic obstructive pulmonary disease, %	20	18 (21.4)	2 (12.5)	.09
Severe chronic obstructive pulmonary disease, %	6	5 (5.9)	1 (6.2)	.96
Logistic EuroSCORE[a]	17.9 (IQR: 9-23.8)	12.8 (IQR: 9-21.45)	23.6 (IQR: 18.7-42.45)	.03
STS[b]	5.35 (IQR: 3.8-6.9)	5.63 (IQR: 3.6-7.1)	5.59 (IQR: 4-5.9)	.49
Baseline laboratory parameters				
Hemoglobin, g/L	120.2 ± 15.4	120.8 ± 15.9	118.3 ± 16.9	.55
Serum creatinine, mmol/L	101.5 ± 28.7	103.2 ± 30.1	99.2 ± 28.9	.59
eGFR (mL/min per 1.73 m²)	64.9 ± 19.5	64.7 ± 19.9	66.9 ± 22.8	.96
Cardiac status				
Mean LVEF, %	52.3 ± 11.1 (27-79)	51.9 ± 11.2 (27-79)	54.2 ± 10.8 (30-72)	.48
NYHA class ≥ III, %	93	77 (91.7)	16 (100)	.59
Porcelain aorta, %	6	5 (5.9)	1 (6.2)	.35
Periprocedural variables				
Transfemoral approach, %	81	67 (79.8)	14 (87.5)	.68
Sheath size	20.6 ± 3.2	20.6 ± 3.3	20.3 ± 3.3	.91
Valve size	25.9 ± 2.2	25.9 ± 2.3	26.4 ± 2.1	.44

BMI, Body mass index; *CABG*, coronary artery bypass graft; *eGFR*, estimated glomerular filtration rate; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *IQR*, interquartile range; *LVEF*, left ventricular ejection fraction; *NA*, not applicable; *NYHA*, New York Heart Association; *PCI*, percutaneous coronary intervention; *SD*, standard deviation; *STS*, Society of Thoracic Surgeons; *TAVI*, transcatheter aortic valve implantation; *VAC*, vascular access-related complications.

Values are means ± SD. The significant P values are highlighted in bold.

[a]The logistic EuroSCORE that measures patient risk at the time of cardiovascular surgery is calculated with the use of a logistic-regression equation. Scores range from 0% to 100%, with higher scores indicating greater risk. A logistic EuroSCORE higher than 20% indicates very high surgical risk.

[b]The STS score measures patient risk at the time of cardiovascular surgery on a scale that ranges from 0% to 100%, with higher numbers indicating greater risk. An STS score higher than 10% indicates very high surgical risk. Chronic kidney disease = eGFR < 60 mL/min per 1.73 m².

(1), an external iliac dissection (1), a thoracic dissection (1), distal embolization (2), and a femoral AV fistula formation (1).

Major vascular complications occurred in nine patients (9%), and endovascular (primarily by stenting using either a cover stent in the common iliac arteries or self-expansible stent in the external iliac and common femoral arteries across the inguinal ligament) or open surgical repair was required in all patients (Table II). The total VAC rate was 20% in the ProStar group and 15% in ProGlide group. The choice of closure device was not predictive of developing major vascular complications (odds ratio [OR], 0.2; 95% CI, 0.14-28.41; Pearson χ^2 test, P = .60). Of the nine major vascular complications, one patient died within 30 days of the procedure. Most minor vascular complications were managed conservatively. However, a thrombin injection was administered for one patient who developed a false aneurysm.

Secondary outcome. Procedural outcomes and mortality rates are recorded in Table III. The average length of stay for all TAVI patients was 9.1 days. The length of stay was significantly higher in patients that had vascular complications (16.4 ± 10.7 days vs 6.5 ± 5.1 days; P = .001). Patients who developed vascular complications also had a longer high-dependency or coronary care stay, although this difference was not statistically significant (8.1 days vs 4.0 days; P = .08).

Patients with vascular complications had significantly more cases of major or life-threatening bleeding (50.0% vs 7%; P = .02) and subsequently received more transfused units of packed red blood cells (4.1 units vs 0.9 units; P = .004).

There was no difference in the in-hospital or 30-day mortality between patients with and without vascular complications. Kaplan-Meier curves (Fig 2, *A* and *B*) show that the survival rate was not statistically different

Table II. Vascular complications and management

	Sheath size	Access	VAC	VARC classification	Treatment	Outcome
1	24F	Preclose - ProGlide	Femoral dissection	Major	Endovascular repair	Satisfactory
2	26F	Transapical[a]	LV apical tear	Major	Surgical repair	Death
3	24F	Preclose - ProGlide	Site bleeding	Minor	Conservative	Satisfactory
4	18F	Preclose - ProStar	Femoral dissection	Minor	Conservative	Satisfactory
5	26F	Transapical[a]	LV apical pseudoaneurysm	Major	Surgical repair	Satisfactory
6	22F	Preclose - ProStar	False aneurysm	Minor	Thrombin injection	Satisfactory
7	18F	Preclose - ProStar	False aneurysm	Major	Surgical repair	Satisfactory
8	18F	Preclose - ProStar	Iliac rupture	Major	Endovascular repair	Satisfactory
9	18F	Preclose - ProStar	External iliac dissection	Minor	Conservative	Satisfactory
10	18F	Preclose - ProStar	Thoracic dissection and distal embolization	Major	Surgical repair	Satisfactory
11	18F	Preclose - ProStar	Femoral dissection	Minor	Conservative	Satisfactory
12	18F	Preclose - ProStar	Distal embolization	Major	Surgical repair	Satisfactory
13	18F	Preclose - ProStar	False aneurysm	Major	Surgical repair	Satisfactory
14	18F	Preclose - ProStar	False aneurysm	Major	Surgical repair	Satisfactory
15	18 Fr	Preclose - ProStar	False aneurysm	Minor	Conservative	Satisfactory
16	18F	Preclose - ProStar	Femoral AV fistula	Minor	Conservative	Satisfactory

AV, Arteriovenous; *LV,* left ventricle; *VAC,* vascular access-related complications; *VARC,* Valve Academic Research Consortium.
All cases with VAC.
[a]Anterolateral minithoracotomy approach.

Table III. Procedural and 30-day outcomes

Variables	Whole cohort (n = 100)	Patients with no VAC (n = 84)	Patients with VAC (n = 16)	P value
Procedural variables				
Procedure duration, minutes (range)	106.2 ± 43.4 (77.5-117.0)	103.4 ± 46.7 (51.0-281.0)	115.1 ± 31.6 (82.0-180.0)	.32
Screening time, minutes (range)	26.1 ± 12.5 (17.5-29.6)	25.4 ± 14.1 (8.2-72.0)	27.8 ± 6.5 (14.3-39.3)	.26
Volume contrast, mL (range)	221.8 ± 124.6 (122.2-291.2)	223.1 ± 129.7 (80.0-648.0)	218.1 ± 112.3 (100.0-443.0)	.23
Bleeding event and transfusion				
30-days life-threatening/ major bleeding[a]	14	6 (7%)	8 (50%)	.02
Number of units of packed cells transfused	1.8 ± 3.3 (0.0-15)	0.9 ± 2.2 (0-12)	4.1 ± 4.5 (0-15)	.004
30-day minor/major stroke[a]				
Minor stroke	1 (1%)	1 (0.1%)	0	NA
Major stroke	0	0	0	NA
Cardiac/renal complications[a]				
AKI[d]	18	15 (17.8%)	3 (18.7%)	.92
Periprocedural myocardial infarction[e]	6	5 (5.9%)	1 (6.2%)	.88
Length of hospital stay				
LOS,[b] days	9.1 ± 8.1 (1-30)	6.5 ± 5.1 (1-23)	16.4 ± 10.7 (1-30)	.001
HDU/ICU, days	5.1 ± 3.9 (32-24)	4 ± 1.7 (2-9)	8.1 ± 6.3 (3-24)	.08
Mortality[a]				
30-day mortality	6 (5%)	5 (5.9%)	1 (6.3%)	.96[c]
Cumulative mortality	17 (17%)	15 (17.8%)	2 (12.5%)	.53[c]

AKI, Acute kidney injury; *HDU,* high-dependency unit; *ICU,* intensive care unit; *LOS,* length of stay; *NA,* not applicable; *RIFLE,* Risk, Injury, Failure, Loss, and End-stage Kidney; *SD,* standard deviation; *VAC,* vascular access-related complications.
[a]Values are expressed as n (%), otherwise the value are expressed as mean ± SD.
[b]Total length of hospital stay including rehabilitation and ICU/HDU care periods.
[c]Log-rank test.
[d]AKI was defined as change in serum creatinine (up to 72 hours) compared with baseline. AKI was classified in three stages according to the modified RIFLE classification. Only patients who develop stage 2 and 3 AKI were included in the analysis (Supplementary Table II, online only).
[e]Clinical and/or biochemical evidence of myocardial infarction occurring ≤72 hours after the index procedure was defined as periprocedural myocardial infarction. Acute ischemic events occurring after 72 hours are considered spontaneous myocardial infarction.

(82.1% in the group of patients with no vascular complications vs 87.5% in the VAC group; *P* = .53) at 46 months follow-up. A subsequent survival analysis between the major and minor complication groups was not statistically significant (88.9% for the major VAC group vs 85.7% for the minor VAC group; *P* = .81).
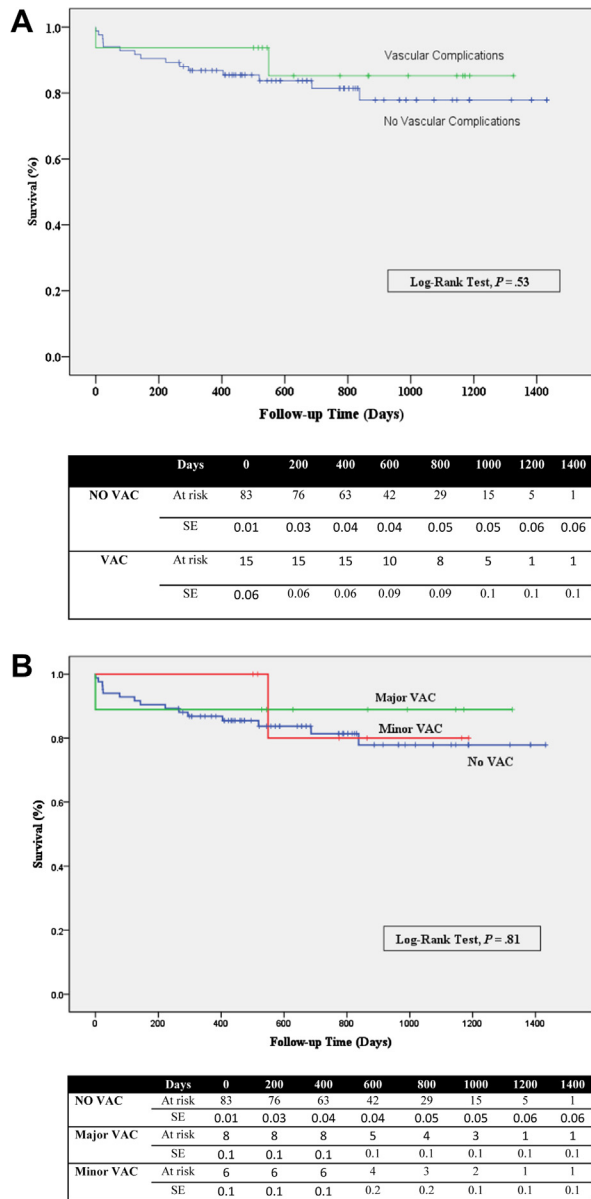
Fig 2. A, Kaplan-Meier curves of survival at 1400 days follow-up for the entire population for patients who underwent transcatheter aortic valve implantation (TAVI) with vascular complications and no vascular complications. The overall survival rate of all patients was 83%, with 82.1% for the no vascular access-related complication (VAC) group and 87.5% for the VAC group at 46 months follow-up. **B,** Kaplan-Meier curves of survival at 1400 days follow-up for the patients who underwent TAVI with major VAC, minor VAC, and no VAC. The overall survival rate of all patients was 83%, with 82.1% for the no VAC group, 88.9% for the major VAC group, and 85.7% for the minor VAC group at 46 months follow-up. *SE,* Standard error.

Table IV reports the cost breakdown for patients with and without vascular complications during TAVI. Vascular complications resulted in a statistically significant cost increase (*P* < .05) attributable to high-dependency/coronary care bed costs, medical personnel, pharmacy services, allied health service costs, laboratory and radiology costs, and the costs of ward consumables and sundries. The total gross additional mean cost incurred with a vascular complication was A\$23,526, which equated to a 33.6% mean cost increase per VAC case (*P* = .002).

Predictors of vascular complications. Using logistic univariate regression analysis, VAC was associated with coronary artery disease (OR, 0.04; 95% CI, 0.01- 0.20; *P* = .009), previous myocardial infarction (OR, 0.11; 95% CI, 0.01-0.86; *P* = .03), and previous percutaneous coronary intervention (OR, 0.36; 95% CI, 0.21-0.64; *P* = .001). Additionally, a history of cardiac surgery (OR, 0.12; 95% CI, 0.01-1.01; *P* = .05), diabetes mellitus (OR, 6.6; 95% CI, 2.05-21.19; *P* = .002), logistic Euro-SCORE (OR, 1.07; 95% CI, 1.03-1.11; *P* = .03), hypertension (OR, 0.03; 95% CI, 0.004-0.265; *P* = .001), and dyslipidemia (OR, 0.04; 95% CI, 0.01-0.32; *P* = .003) were associated with VAC. The only independent risk factors identified to predict vascular complications using a multivariate stepwise logistic regression analysis (Table V; Fig 3) were diabetes mellitus (OR, 5.07; 95% CI, 1.17-21.88; *P* = .03) and logistic EuroSCORE (OR, 1.06; 95% CI, 1.02-1.10; *P* = .001). The occurrence of vascular complication rate was not statistically related to the sheath size used, ranging from 18F to 24F sheath for transfemoral approach and up to 26F for transapical route (mean size of sheath used between no VAC patients of 20.6F ± 3.3 vs VAC patients of 20.3F ± 3.3; *P* = .91) (Table II).

Using the negative binomial regression models with or without reporting the incidence rate ratios (IRR), the impact of vascular complications on total length of hospital stay (IRR, 2.78; 95% CI, 1.94-3.96; *P* < .05), units of blood transfusion (IRR, 4.54; 95% CI, 1.63-12.62; *P* = .004), and bleeding (OR, 6.64; 95% CI, 2.06-21.32; *P* = .001) was established.

DISCUSSION

TAVI is rapidly evolving to become the standard of care for patients with severe AS unsuitable or at severe risk for surgical AVR. Vascular complications are a cause for morbidity and mortality and, thus, remain an important determinant of TAVI outcomes. This study demonstrates that major vascular complications occur at a significant rate, often requiring surgical intervention, which leads to an overall prolonged length of hospital stay, increased blood transfusion requirements, and increased cost and resource utilization. Diabetes mellitus and a high preoperative logistic EuroSCORE (Supplementary Table I, online only) independently predict vascular complications in this cohort. From our overall learning curve of this procedure, it is crucial to interrogate the aortoiliac and femoral segments preoperatively appropriately to exclude heavily calcified, mostly circumferential calcifications associated with significant luminal reduction. Any evidence of infragenicular peripheral vascular disease should be noted and well recorded.

Table IV. Breakdown of resource usage and costs[a] (2009-2012 Australian dollar) during the procedural hospitalization according to the occurrence of vascular complications

	Cost per patient, mean ± SD		
	Patients with no VAC[b] (n = 84)	Patients with VAC (n = 16)	Mean cost difference (95% CI)
Procedures	33,454 ± 4074	34,554 ± 4362	1100 (−1201 to 4095)[f]
HDC[c]	12,200 ± 2005	19,210 ± 2418	7010 (2365-16,543)[e]
Medical personnel	3776 ± 1006	8058 ± 1677	4282 (3214-7868)[e]
Nursing staff	3744 ± 875	4775 ± 1194	1031 (867-3987)[f]
Allied health services	214 ± 91	728 ± 161	514 (−65 to 710)[e]
Laboratory services	606 ± 182	1156 ± 242	550 (58-1065)[e]
Radiology services	1284 ± 134	1893 ± 204	609 (209-1768)[e]
Pharmacy services	4798 ± 609	8070 ± 1255	3272 (1876-7899)[e]
Ward consumables and others expenses[d]	9856 ± 1863	15,004 ± 2826	5148 (1768-13,284)[e]
Total	69,932 ± 15,007	93,448 ± 21,435	23,516 (18,345-27,890)[g]

CCU, Coronary care unit; *CI,* confidence interval; *HDC,* high-dependency care; *SD,* standard deviation; *VAC,* vascular access-related complications.
[a]Adjusted costs.
[b]All vascular complications.
[c]HDC and CCU cost.
[d]Administrative, hardware depreciation, and operating theatre costs.
[e]$P < .05$.
[f]$P > .05$.
[g]P of the total cost was .002.

Table V. Multivariate stepwise logistic regression analysis of variables associated with vascular complications

Variable	Coefficient	OR (95% CI)	SE[a]	P value
Logistic EuroSCORE	3.27	1.06 (1.02-1.10)	0.02	.001
Diabetes mellitus	2.18	5.07 (1.17-21.88)	3.78	.03
Intercept	−4.67	0.02 (0.01-0.11)	0.02	<.05

CI, Confidence interval; *EuroSCORE,* European System for Cardiac Operative Risk Evaluation; *OR,* odds ratio; *SE,* standard error; *TAVI,* transcatheter aortic valve implantation.
Patients with diabetes mellitus that underwent TAVI are five times more likely to sustain vascular complication than those who do not have diabetes mellitus.
[a]The derived SE was adjusted with bootstrapping procedure.

Fig 3. Logistic model for vascular access-related complications (VAC) with receiver operating characteristic (*ROC*) curve. Using predicted probabilities for factors that predict strongly vascular complication occurrence after transcatheter aortic valve implantation (TAVI), we can draw the ROC curve. The area under the ROC curve is nearly 0.82; this is considered to have an excellent discrimination for these two factors to predict VAC after TAVI.

Major vascular complications, as defined according to VARC guidelines, have been reported for other TAVI series. These rates range from 9.5% to 51.6% with associated two- to threefold increases in 30-day mortality.[15,20]

Our study identified several important findings that warrant discussion. We have consolidated current reports of the advances in equipment and methods and demonstrate that vascular complication rates are decreasing, and TAVI can be performed with relative safety in high-risk patients. In 100 patients, we reported major and minor vascular complication rates of 9% and 7%, respectively. This finding is comparable with the recent meta-analysis of VARC clinical outcomes that consolidated 3519 patients from 16 studies and reported a pooled estimated major, minor, and total vascular complication rate of 11.9%, 9.7%, and 18.8%, respectively.[20]

Consistent with other published studies, we found that patients with VAC had a significantly higher risk of life-threatening or major bleeding within 30 days. These patients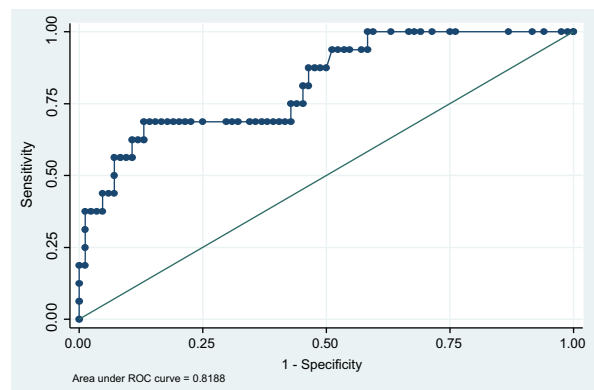 subsequently required a significantly higher number of blood transfusions. Although multiple published reports have shown an increased rate of 30-day mortality associated with major vascular complications,[20-22] we have failed to demonstrate this association. Additionally, we did not identify decreased long-term survival in patients with VAC. We did not demonstrate any difference in acute kidney injury and postprocedural myocardial infarction between the two groups (Table III; Supplementary Table II, online only).

Several reports on TAVI-associated vascular complications have been published over the past few years to investigate causes and risk factors for vascular complications. Sheath to femoral artery ratio (SFAR), early center

experience, femoral artery calcium score, sheath diameter, peripheral artery disease, and female sex have all been reported as predictors for vascular complications.[20,21] However, the only independent predictors for VAC currently identified and reported are female sex and sheath size. Genereux et al first reported female gender as a significant predictor using results from the Placement of AoRTic TraNscathetER Valve (PARTNER) trial (hazard ratio, 2.31; 95% CI, 1.08-4.98; *P* = .03).[23] These researchers initially hypothesized that the smaller femoral artery diameters in women with subsequent greater SFAR may be a contributing factor. However, after adjusting for SFAR, female sex was a strong independent predictor and suggests the possibility of an intrinsic female predisposition to periprocedural complication with TAVI. Van Mieghem et al recently also substantiated this finding by pooling the TAVI databases of five European centers and evaluating results from 986 patients who underwent transfemoral TAVI. They reported both female sex (OR, 1.63; 95% CI, 1.12-2.36) and the use of a >19F system (OR, 2.87; 95% CI, 1.68-4.91) as independent predictors for major vascular complications.[14,24]

In our study, we identified seven factors that were associated with an increased risk of vascular complications: coronary artery disease, previous percutaneous coronary infarction, previous myocardial infarction, dyslipidemia, hypertension, and the logistic EuroSCORE. Interestingly, our multivariate analysis identified two independent predictors of vascular complication: logistic EuroSCORE (OR, 1.06; 95% CI, 1.02-1.10; *P* = .001) and diabetes mellitus status (OR, 5.07; 95% CI, 1.17-21.88; *P* = .03) (Table IV). The use of logistic EuroSCORE as an independent predictor is suggestive of higher VAC risk in high-risk patients, presumably because of comorbidities. However, further research to corroborate and investigate this finding is warranted. Notably, we did not identify sex as having any influence on vascular complications.

While the risk factors we identified and those previously published are reasonably common in the TAVI patient population and therefore may be overlooked, operator knowledge of this increased risk should generate extra vigilance of the potential to cause injury, as the additional costs, morbidity, and resource usage associated with VAC is substantial.

In our study, the total mean cost was significantly higher in patients who sustained vascular complications (mean cost difference: A$23,516; *P* = .002). This additional cost was significant across nearly all sectors (Table V). Most of the additional cost differences resulted from high dependency, coronary care costs, and overall ward costs. The increased length of stay due to complications (16.4 days vs 6.5 days; *P* = .001) was certainly a major contributor to this additional ward cost and resource usage. To the best of our knowledge, this study is the first that has reported the cost and resource management associated with vascular complications. While Reinhol et al reported a 19.1% increase in costs associated with major bleeding complications following transfemoral TAVI (mean gross increase =

€6426 [≈A$8150]),[25] our cost analysis has revealed a mean 33.6% cost increase incurred from vascular complications. A comparison of our baseline costs with Reinhol's publication indicates that our baseline costs are considerably higher. However, in the PARTNER trial, Reynolds et al have reported the mean total index admission costs for TAVI via the transfemoral approach to be $73,219, which is similar to our baseline cost (A$69,932).[26,27] Nonetheless, our study emphasizes that the additional cost and resource usage associated with VAC is significant, and care should be taken to minimize this expenditure. Our cost analysis included both major and minor vascular complications collectively. Therefore, we anticipate that the cost increase from only major VAC to be even greater.

The current study has several limitations. Although this registry had limited and strict inclusion/exclusion criteria, all patients included were initially suitable for endovascular repair of severe AS. This patient selection may have led to a selection bias of some patients who may have been suitable for open cardiac surgery. Moreover, the current data analyses are retrospective, despite being derived from prospectively collected data.

CONCLUSIONS

Vascular complications affect perioperative management and outcomes in TAVI. Vascular complications may require surgical repair and lead to prolonged hospital stay, increased overall cost, and greater resource utilization. Specific parameters, including type II diabetes status and logistic EuroSCORE, may be predictive of which patients will develop complications. These parameters should be used to guide patient selection for this procedure.

AUTHOR CONTRIBUTIONS

Conception and design: BM, RL, GY
Analysis and interpretation: BM, AP, TMJ, GY
Data collection: BM, JT, GY
Writing the article: BM, AP, TMJ, ST, VV
Critical revision of the article: BM, AP, TMJ, ST, JT, VV, GY
Final approval of the article: BM, AP, GY
Statistical analysis: BM, GY
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Supplementary Table I (online only). Risk factors, definitions, and weights in standard (score) and logistic (ß coefficient) EuroSCORE Model (www.euroscore.org)

Risk factors	Definition	Score	ß coefficient
Patient-related factors			
Age	Per 5 years or part thereof over 60 years for standard EuroSCORE and continuous for logistic EuroSCORE	1	0.0666354
Sex	Female	1	0.3304052
Chronic obstructive pulmonary disease	Long-term use of bronchodilators or steroids for lung disease	1	0.4931341
Extracardiac arteriopathy	Any one or more of the following: claudication, carotid occlusion or >50% stenosis, previous or planned intervention on the abdominal aorta, limb arteries or carotids	2	0.6558917
Neurological dysfunction disease	Disease severely affecting ambulation or day-to-day functioning	2	0.841626
Previous cardiac surgery	Requiring opening of the pericardium	3	1.002625
Serum creatinine	>200 m micromol/L preoperatively	2	0.6521653
Active endocarditis	Patient still under antibiotic treatment for endocarditis at the time of surgery	3	1.101265
Critical preoperative state	Any one or more of the following: VT or VF or aborted sudden death, preoperative cardiac massage, preoperative ventilation before arrival in the anesthetic room, preoperative inotropic support, intra-aortic balloon counter-pulsation or preoperative ARF (anuria or oliguria <10 mL/h)	3	0.9058132
Cardiac-related factors			
Unstable angina	Rest angina requiring i.v. nitrates until arrival in the anesthetic room	2	0.5677075
Left ventricular dysfunction	Moderate or LVEF ≈ 30%-50%	1	0.4191643
Left ventricular dysfunction	Poor or LVEF <30 %	3	1.094443
Recent myocardial infarction	(<90 days)	2	0.5460218
Pulmonary hypertension	Systolic pulmonary pressure >60 mm Hg	2	0.7676924
Operation-related factors			
Emergent operation	Carried out on referral before the beginning of the next working day	2	0.7127953
Other than isolated CABG	Major cardiac procedure other than or in addition to CABG	2	0.5420364
Surgery on thoracic aorta	For disorder of ascending arch or descending aorta	3	1.159787
Postinfarct septal rupture	Postinfarct septal rupture	4	1.462009
Constant ß₀	Only for logistic EuroSCORE	—	−4.789594

ARF, Acute renal failure; *CABG,* coronary artery bypass graft; *EuroSCORE,* European System for Cardiac Operative Risk Evaluation; *LVEF,* left ventricular ejection; *VF,* ventricular fibrillation; *VT,* ventricular tachycardia.

The EuroSCORE has been developed for the prediction of in-hospital mortality after adult cardiac surgery. The standard EuroSCORE system consists of three risk groups: low risk (0-2) with an expected mortality under 2%; medium risk (3-5) with an expected mortality under 5%; and high risk (≥6) with an expected mortality greater than 10%, but logistic EuroSCORE system tends to be more accurate in high-risk patients. The logistic EuroSCORE uses the same risk factors as the additive EuroSCORE to produce preoperative mortality risk via a logistic regression calculation and can be achieved with the following formula:

$$\text{Predicted mortality} = e^{(\beta_0 + \check{a}bi\ Xi)}/1 + e^{(\beta_0 + \check{a}bi\ Xi)}$$

Where

e is the natural logarithm = 2.718281828…

β_0 is the constant of the logistic regression equation = −4.789594.

β_i is the coefficient of the variable X_i in the logistic regression equation provided in the table below.

X_i = 1 if a categorical risk factor is present and 0 if it is absent.

Supplementary Table II (online only). Acute kidney injury (modified RIFLE classification)

Stage 1	Increase in serum creatinine to 150%-200% (1.5-2.0 × increase compared with baseline) or increase of ≥0.3 mg/dL (≥26.4 mmol/L)
Stage 2	Increase in serum creatinine to 200%-300% (2.0-3.0 × increase compared with baseline) or increase between >0.3 mg/dL (>26.4 mmol/L) and <4.0 mg/dL (<354 mmol/L)
Stage 3[a]	Increase in serum creatinine to ≥300% (>3 × increase compared with baseline) or serum creatinine of ≥4.0 mg/dL (≥354 mmol/L) with an acute increase of at least 0.5 mg/dL (44 mmol/L)

AKI, Acute kidney injury; *RIFLE,* Risk, Injury, Failure, Loss, and End-stage Kidney.

AKI was classified in three stages according to the modified RIFLE classification. Of clinical significance only stage 2 and 3 of AKI should be recorded to assess patient renal.

[a]Patients receiving renal replacement therapy are considered to meet stage 3 criteria irrespective of other criteria.