2-20-2024

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Recommended Citation

Lo Russo, G. V., Alarouri, H. S., Al-Abcha, A., Vogl, B., Mahayni, A., Sularz, A., Hatoum, H., Collins, J., Crestanello, J. A., & Alkhouli, M. (2024). Association of Bovine Arch Anatomy With Incident Stroke After Transcatheter Aortic Valve Replacement. *Journal of the American Heart Association, 13*(4), e032963.
http://doi.org/10.1161/JAHA.123.032963
Retrieved from: https://digitalcommons.mtu.edu/michigantech-p2/556

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Journal of the American Heart Association

ORIGINAL RESEARCH

Association of Bovine Arch Anatomy With Incident Stroke After Transcatheter Aortic Valve Replacement

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BACKGROUND: Acute ischemic stroke complicates 2% to 3% of transcatheter aortic valve replacements (TAVRs). This study aimed to identify the aortic anatomic correlates in patients after TAVR stroke.

METHODS AND RESULTS: This is a single-center, retrospective study of patients who underwent TAVR at the Mayo Clinic between 2012 and 2022. The aortic arch morphology was determined via a manual review of the pre-TAVR computed tomography images. An "a priori" approach was used to select the covariates for the following: (1) the logistic regression model assessing the association between a bovine arch and periprocedural stroke (defined as stroke within 7 days after TAVR); and (2) the Cox proportional hazards regression model assessing the association between a bovine arch and long-term stroke after TAVR. A total of 2775 patients were included (59.6% men; 97.8% White race; mean±SD age, 79.3±8.4 years), of whom 495 (17.8%) had a bovine arch morphology. Fifty-seven patients (1.7%) experienced a periprocedural stroke. The incidence of acute stroke was significantly higher among patients with a bovine arch compared with those with a nonbovine arch (3.6% versus 1.7%; *P*=0.01). After adjustment, a bovine arch was independently associated with increased periprocedural strokes (adjusted odds ratio, 2.16 [95% CI, 1.22–3.83]). At a median follow-up of 2.7 years, the overall incidence of post-TAVR stroke was 6.0% and was significantly higher in patients with a bovine arch even after adjusting for potential confounders (10.5% versus 5.0%; adjusted hazard ratio, 2.11 [95% CI, 1.51–2.93]; *P*<0.001).

CONCLUSIONS: A bovine arch anatomy is associated with a significantly higher risk of periprocedural and long-term stroke after TAVR.

Key Words: aortic stenosis ■ bovine arch ■ stroke ■ transcatheter aortic valve replacement

Transcatheter aortic valve replacement (TAVR) has become the standard treatment for most patients with severe symptomatic aortic stenosis. Acute ischemic stroke complicates 1.6% to 4.3% of TAVR procedures and is associated with significant morbidity and mortality.[1] Despite temporal improvements in TAVR outcomes overall, the incidence of postprocedural stroke has only marginally declined. Hence, identifying predictors of TAVR-related stroke remains essential to devising effective preprocedural and postprocedural stroke-mitigation strategies.[2,3]

Conventional aortic arch anatomy features 3 main branches: the brachiocephalic trunk, the left common carotid artery, and the left subclavian artery. However, anatomic variants are common, observed in up to 15% to 20% of patients.[4–7] The most common variant, commonly known by the misnomer "bovine" aortic arch, denotes a common origin of the brachiocephalic trunk and the left common carotid artery. The reported

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This article was sent to Amgad Mentias, MD, Associate Editor, for review by expert referees, editorial decision, and final disposition.

For Sources of Funding and Disclosures, see page 9.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- This study provides novel evidence of the association between aortic arch anatomy and post–transcatheter aortic valve replacement stroke.
- A bovine aortic arch is associated with a 2-fold increase in periprocedural and long-term risk of stroke after the procedure.

What Are the Clinical Implications?

- Bovine aortic arch should be considered an independent risk factor for periprocedural and long-term post–transcatheter aortic valve replacement stroke.
- Further studies are needed to identify effective stroke prevention strategies for this high-risk population.

Nonstandard Abbreviations and Acronyms

CEP	cerebral embolic protection
TAVR	transcatheter aortic valve replacement

prevalence of this variant ranges from 13.6% to 20%, with a higher prevalence observed among people of African descent.[4,5] The presence of a bovine arch has been associated with a higher risk of acute stroke in the general population.[8,9] We hypothesized that a bovine arch anatomy is also associated with an increased risk of postprocedural and long-term stroke in patients undergoing TAVR. To study this potential correlation, we leveraged a large registry of consecutive patients undergoing TAVR at a tertiary center.

METHODS

Study Population

Using the Society of Thoracic Surgeons and American College of Cardiology TVT (Transcatheter Valve Therapy) registry, we conducted a single-center, retrospective study of patients who underwent TAVR at Mayo Clinic Hospital (Rochester, MN) between February 8, 2012, and June 3, 2022 (n=2815). Of those, patients with a pre-TAVR cardiac/thoracic computed tomography angiography with adequate visualization of the aortic arch (n=2775) were included in our study.

Study End Points

We stratified the study's patients into 2 groups according to the presence or absence of a bovine arch morphology (defined as a common origin of the brachiocephalic trunk and the left common carotid artery). The primary end point was the association between a bovine arch anatomy and periprocedural stroke (defined as an acute stroke occurring within 7 days after the procedure).[10] The secondary end point was the association between a bovine arch anatomy and long-term stroke after TAVR. This study was approved by the Mayo Clinic Institutional Review Board, and a requirement for patient consent was waived as it was determined to be a minimal-risk, observational research study. This study complies with the Strengthening the Reporting of Observational Studies in Epidemiology guideline (see Strengthening the Reporting of Observational Studies in Epidemiology checklist in the Supplemental Material).[11] Data used in this study are available upon reasonable request submitted to the corresponding author.

Stroke and Aortic Arch Morphology Assessment

A manual review of the medical records was conducted by 2 independent reviewers (G.V.L. and H.S.A.) to: (1) identify patients who had adequate preprocedural thoracic computed tomography angiography performed; (2) assess and classify the aortic arch configuration; and (3) determine the timing, type, anatomic location, severity, and clinical outcomes of stroke. For stroke assessment, ischemic stroke was defined as an acute onset of focal neurologic signs or symptoms conforming to a focal or multifocal vascular territory within the brain, spinal cord, or retina (Neurologic Academic Research Consortium [NeuroARC] type 1A or 1aH) and fulfilling 1 of the following criteria: (1) signs or symptoms lasting ≥24 hours or until death, with pathologic or neuroimaging evidence of central nervous system infarction, or absence of other apparent causes; or (2) signs lasting <24 hours, with pathologic or neuroimaging confirmation of central nervous system infarction in the corresponding vascular territory. Hemorrhagic stroke was defined as an acute onset of neurologic signs or symptoms, resulting from intracranial bleeding, specifically intracerebral or subarachnoid hemorrhage, not caused by trauma (NeuroARC type 1b or 1c). A stroke that did not meet either of these definitions was classified as a "stroke not otherwise specified"; specifically, this was defined as an acute onset of neurologic signs or symptoms persisting ≥24 hours or until death but without sufficient neuroimaging or pathologic evidence to be classified (NeuroARC type 1d).[7] We categorized the anatomic location of stroke using neuroimaging as hemispheric, cerebellar, or brainstem. To assess the severity of stroke, we used the National Institutes of Health Stroke Scale scoring system, with a National Institutes of Health Stroke Scale score of 1

Table 1. Comparison of Baseline Characteristics Between Patients With a Nonbovine Arch Versus a Bovine Arch

Characteristic	Nonbovine arch (n=2280)	Bovine arch (n=495)	*P* value
Age, y	81 (74.0–85.0)	81 (75.0–86.0)	0.40
LVEF, %	60 (51.0–65.0)	62 (54.0–66.0)	0.02*
LVEF ≥50%	1778 (78.0)	411 (83.0)	0.01*
LVEF 40%–49%	225 (9.9)	37 (7.5)	0.99
LVEF 30%–39%	159 (7.0)	29 (5.9)	0.37
LVEF <30%	118 (5.1)	18 (3.6)	0.10
GFR, mL/min per 1.73 m^2	44 (34.1–64.3)	44 (35.5–54.9)	0.57
BSA, m^2	1.95 (1.8–2.1)	1.94 (1.8–2.3)	0.20
Aortic valve area, cm^2	0.87 (0.7–0.9)	0.84 (0.7–0.9)	0.24
Aortic valve mean gradient, mm Hg	42 (35.0–49.0)	42 (36.0–49.0)	0.94
Aortic valve peak gradient, mm Hg	67 (58.0–77.0)	67 (58.0–81.0)	0.07
Aortic valve peak velocity, m/s	4.1 (3.8–4.4)	4.2 (3.8–4.5)	0.05*
STS score, %	4.3 (2.6–7.2)	4.1 (2.4–6.85)	0.14
KCCQ-12 score	52.6 (34.4–73.4)	56.3 (38.5–78.1)	0.04
White race	2227 (97.6)	486 (98.1)	0.51
Female sex	900 (39.4)	221 (44.6)	0.03*
Hypertension	2026 (88.8)	448 (90.5)	0.20
Diabetes	786 (34.5)	188 (37.9)	0.13
Smoking	70 (3.10)	13 (2.62)	0.61
NYHA class III-IV	1496 (65.6)	331 (66.8)	0.52
Carotid artery stenosis	316 (13.8)	82 (16.5)	0.11
Peripheral artery disease	1147 (50.3)	247 (49.9)	0.91
Prior stroke or TIA	344 (15.1)	78 (15.7)	0.68
Prior myocardial infarction	510 (22.4)	105 (21.2)	0.60
Atrial fibrillation/flutter			0.62
Nonparoxysmal	488 (21.4)	94 (18.9)	
Paroxysmal	397 (17.4)	104 (21.1)	
Porcelain aorta	94 (4.12)	21 (4.24)	0.89
Prior CABG	473 (20.7)	108 (21.8)	0.56
Prior mitral valve procedure	12 (0.52)	6 (1.21)	0.08
Prior aortic valve procedure	295 (12.9)	52 (10.5)	0.15
Severe chronic lung disease	216 (9.50)	48 (9.70)	0.97
Heart failure	602 (26.4)	115 (23.2)	0.81
Bicuspid aortic valve	70 (3.07)	13 (2.6)	0.61
Moderate-severe aortic valve calcification	603 (26.4)	110 (22.2)	0.17

Values are median (interquartile range) or number (percentage). BSA indicates body surface area; CABG, coronary artery bypass grafting; GFR, glomerular filtration rate; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons; and TIA, transient ischemic attack.

*The *P* value reached statistical significance ($P \leq 0.05$).

to 5 indicating a mild stroke; a score of 6 to 14 indicating a moderate stroke; and a score of ≥15 indicating a severe stroke.[1,12]

Statistical Analysis

Normality was assessed using the Shapiro-Wilk or Kolmogorov-Smirnov test, as appropriate. Continuous variables were reported as mean±SD or median and interquartile range (IQR) for skewed distributions. Categorical variables were reported as frequencies with percentages. Comparisons were made between the 2 groups using Student's *t* test or the Mann-Whitney *U* test for continuous variables and the Pearson χ^2 or Fisher exact test for categorical variables, as appropriate. To assess the association between a bovine aortic arch and periprocedural stroke, we developed an "a priori" multivariable logistic regression model that incorporated covariates known to be predictors of post-TAVR stroke, as previously described in the literature, along with other covariates that may be associated with periprocedural stroke in theory. Covariates included in the model were: prior aortic valve procedure; body surface area; hypertension; glomerular filtration rate; age; peripheral artery disease; prior stroke or transient ischemic attack; carotid artery stenosis; urgent or emergent procedure; transapical access; access site other than transapical or transfemoral; and porcelain aorta.[12] The goodness of fit of the logistic regression model was verified using the Hosmer-Lemeshow test; the computed *P* value was >0.05, indicating a "good fit." The odds ratios (ORs) were reported with their corresponding 95% CIs. For the time-to-event analysis, the follow-up time was computed from the date of the procedure to the date of the last known follow-up, death, or event (ie, stroke). The probability of stroke, stratified on the basis of the aortic arch anatomy, was graphically displayed using the Kaplan-Meier method and was compared using the log-rank test. To estimate the overall long-term hazard ratio (HR) for stroke associated with a bovine arch, an a priori multivariable Cox proportional hazards regression analysis was used, incorporating the same variables included in the multivariable logistic regression model. Estimated HRs were reported with their corresponding 95% CIs. To assess for heterogeneity in the association between a bovine arch and long-term stroke after TAVR, subgroup analyses of the Cox proportional hazards regression model were performed for the following: valve-in-valve procedure (yes versus no); porcelain aorta (yes versus no); valve sheath access site (transfemoral versus alternative); diabetes (yes versus no); carotid artery stenosis (yes versus no); sex (male versus female); glomerular filtration rate (≥60 versus <60 mL/min per 1.73 m^2); left ventricular ejection fraction (≥30% versus <30%); age (≥75 versus <75 years); and atrial fibrillation/flutter

Table 2. Comparison of Periprocedural and Postprocedural Characteristics Between Patients With a Nonbovine Arch Versus a Bovine Arch

Characteristic	Nonbovine arch (n=2280)	Bovine arch (n=495)	*P* value
Urgent or emergent procedure	280 (12.3)	53 (10.7)	0.35
Shock or inotrope use	18 (0.8)	2 (0.4)	0.36
Transfemoral access	2064 (90.5)	451 (91.1)	0.81
Transapical access	162 (7.1)	36 (7.2)	0.91
Access site other than transapical or transfemoral	54 (2.4)	8 (1.6)	0.30
General anesthesia	689 (30.2)	138 (27.7)	0.30
Balloon-expandable valve	1977 (86.7)	434 (87.6)	0.27
Successful implant	2221 (97.4)	480 (96.9)	0.48
Device migration or embolization	7 (0.3)	2 (0.4)	0.71
Contrast volume, mL	48 (35.0–60.0)	50 (36.5–56.5)	0.05*
Fluoroscopy time, min	12.1 (9.0–17.0)	12.3 (9.0–18.0)	0.17
Pacemaker implant	393 (17.2)	91 (18.4)	0.18
Major vascular complications	13 (0.6)	0	0.12
Minor vascular complications	47 (2.1)	16 (3.22)	0.14
Aortic annular rupture	4 (0.2)	1 (0.2)	0.88
Aortic dissection	11 (0.5)	1 (0.2)	0.40
Cardiac arrest	37 (1.6)	9 (1.8)	0.71
Cardiac perforation	33 (1.5)	9 (1.8)	0.51
Conversion to open heart surgery	19 (0.8)	2 (0.4)	0.32
New-onset atrial fibrillation	69 (3.0)	11 (2.2)	0.38
Periprocedural and postprocedural MI	6 (0.3)	1 (0.2)	0.81
Periprocedural and postprocedural PCI	10 (0.4)	2 (0.4)	0.94
Antithrombotic therapy at discharge	n=2219	n=490	
SAPT	95 (4.3)	12 (2.4)	0.06
DAPT	285 (12.8)	68 (13.9)	0.51
Anticoagulation	111 (5.0)	26 (5.3)	0.76
SAPT+anticoagulation	1511 (68.1)	337 (68.8)	0.65
DAPT+anticoagulation	217 (9.8)	47 (9.6)	0.93

Values are median (interquartile range) or number (percentage). DAPT indicates dual-antiplatelet therapy; MI, myocardial infarction; PCI, percutaneous coronary intervention; and SAPT, single-antiplatelet therapy.

*The *P* value reached statistical significance ($P \le 0.05$).

(yes versus no). Sensitivity analyses were conducted for both the logistic regression and the Cox proportional hazards regression models. For the logistic regression model, we implemented "backward elimination" and "forward selection" approaches and used a conditional *P* value cutoff of ≤0.05 for variable exit from/entry into the model (a conditional *P* value cutoff of ≤0.10 was also tested but resulted in an identical model). For the Cox proportional hazards regression model, we implemented the same approaches and used 2 conditional *P* value cutoffs for variable exit from/entry into the model: ≤0.05 and ≤0.10. The assumptions of logistic regression and Cox proportional hazards regression were tested and met. To assess for multicollinearity in the logistic regression model, variance inflation factors were calculated. The variance inflation factor was <2 for all included variables indicating minimal collinearity. $P \le 0.05$ was considered to be significant for all statistical analyses. All statistical analyses were conducted using Statistics Package for the Social Sciences, version 28.0.0.0.

RESULTS

Baseline, Procedural, and Periprocedural Characteristics

We included a total of 2775 patients (59.6% men) who underwent TAVR between February 8, 2012, and June 3, 2022. The overall mean±SD age was 79.3±8.4 years, aortic valve mean±SD gradient was 42.4±13.4 mm Hg, and Society of Thoracic Surgeons risk score was 4.2%. In the overall cohort, 495 (17.8%) had a bovine aortic arch, 398 (14.3%) had carotid artery stenosis, 422 (15.2%) had a prior stroke/transient ischemic attack, and 582 (21.0%) had nonparoxysmal atrial fibrillation.

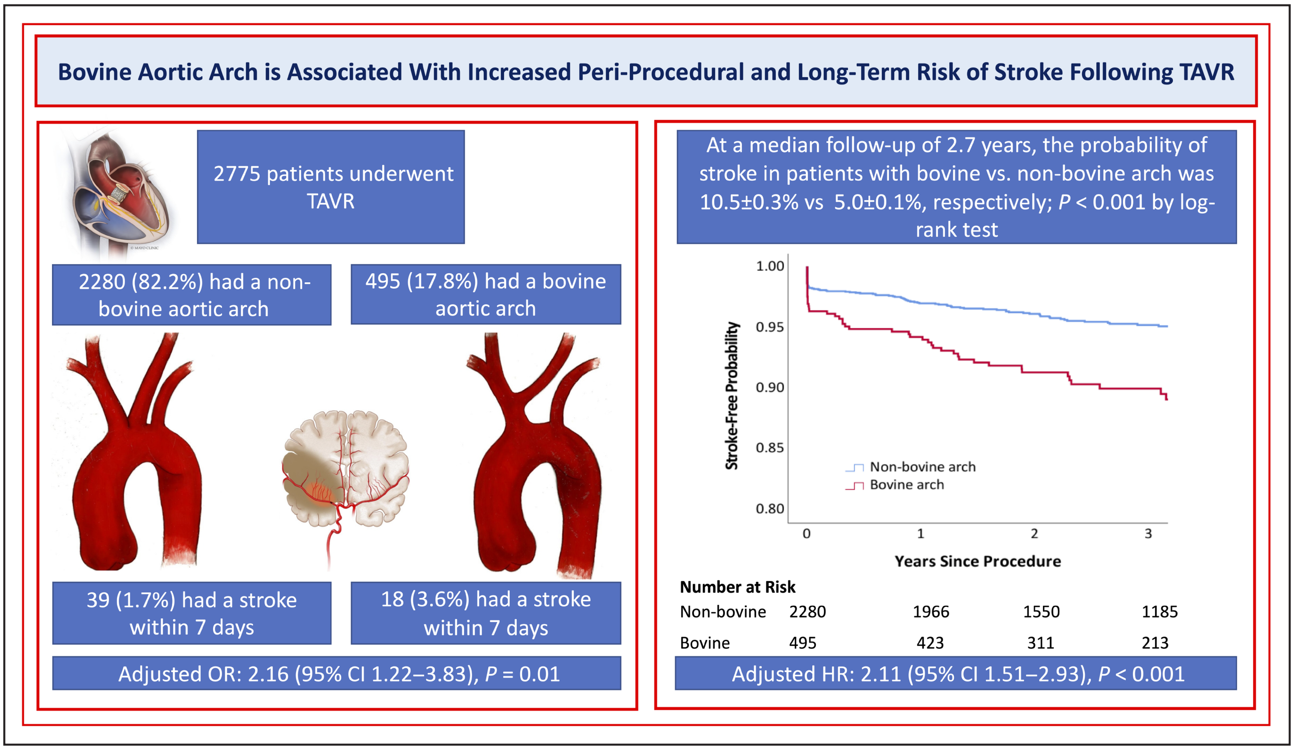

Figure. Association between bovine arch anatomy and stroke after TAVR.
A total of 2775 patients underwent TAVR. The aortic arch anatomy was assessed using pre-TAVR computed tomography images. A periprocedural stroke was defined as any stroke that occurred within 7 days after TAVR. The association between periprocedural stroke and a bovine aortic arch was evaluated using "a priori" multivariate logistic regression models. Long-term risk of stroke was estimated using an a priori Cox proportional hazards regression model and displayed using the Kaplan-Meier method. HR indicates hazard ratio; OR, odds ratio; and TAVR, transcatheter aortic valve replacement.

Baseline characteristics were comparable between the bovine arch and nonbovine arch groups, except for left ventricular ejection fraction, aortic valve peak velocity (m/s), and female sex (Table 1). Most TAVRs (2515 [90.6%]) were performed through a transfemoral access and used a balloon-expandable valve (2411 [86.9%]). Periprocedural mortality occurred in 17 patients (0.6%). Most patients were discharged on antithrombotic therapy, with the preferred regimen for most (1848 [66.6%]) being a combination of a single antiplatelet agent and an anticoagulant. Patients with a bovine arch required a marginally higher contrast volume than those with a nonbovine arch (50 [IQR, 36.5–56.5] versus 48 [IQR, 35.0–60.0] mL; *P*=0.05). No significant differences were noted between the 2 groups in terms of procedural characteristics or periprocedural complications, apart from stroke (Table 2).

Early Stroke After TAVR

Fifty-seven patients (1.7%) experienced a periprocedural stroke within 7 days of TAVR (Figure). The incidence of acute stroke was significantly higher among patients with a bovine arch (3.6% versus 1.7%; *P*=0.01), but no significant differences were noted with regard to stroke type between patients with a bovine arch and those with a nonbovine arch (Table 3). Similarly, the incidence of stroke at 30 days after TAVR was considerably higher in patients with a bovine arch (18 [3.6%] versus 41 [1.8%]; *P*=0.01). In the multivariable logistic regression model (Table 4), a bovine arch was associated with ≈2-fold increased odds of a stroke within 7 days of the procedure (OR, 2.16 [95% CI, 1.22–3.83]; *P*=0.01); this association persisted in the sensitivity analyses (Table 5). In addition, body surface area was also an independent predictor of stroke within that time period (OR [per 0.01-m^2 increase], 0.99 [95% CI, 0.97–1.00]; *P*<0.02).

Long-Term Stroke After TAVR and Its Risk Factors

Over a median follow-up time of 2.7 years (IQR, 1.6–4.3 years), a total of 167 patients (6.0%) who underwent TAVR experienced a stroke. The median follow-up time for patients in the bovine arch group was comparable to those in the nonbovine group (2.7 [IQR, 1.4–4.4] versus 2.6 [IQR, 1.5–4.2] years, respectively; *P*=0.67). Patients in the bovine group had almost a 2-fold higher incidence of stroke compared with those in the nonbovine

Table 3. Comparison of TAVR-Related Stroke Characteristics Between Patients With a Nonbovine Arch Versus a Bovine Arch

Characteristic	Nonbovine arch (n=2280)	Bovine arch (n=495)	*P* value
Early stroke			
Stroke at 24 h	29 (1.3)	12 (2.4)	0.05*
Stroke at 7 d	39 (1.7)	18 (3.6)	0.01*
Stroke type			
Ischemic	38 (97.4)	18 (100)	0.49
Hemorrhagic	1 (2.6)	0	0.49
Stroke at 30 d	41 (1.8)	18 (3.6)	0.01*
Long-term stroke			
Follow-up time, y	2.59 (1.45–4.23)	2.65 (1.43–4.37)	0.67
Overall	115 (5.0)	52 (10.5)	<0.001
NIHSS class			
1–5	76 (66.1)	38 (73.1)	0.43
6–14	20 (17.4)	5 (9.6)	0.19
15–42	19 (16.5)	9 (17.3)	0.92
Stroke type			
Ischemic	107 (93.1)	51 (98.1)	0.25
Hemorrhagic	7 (6.1)	1 (1.92)	0.24
Not specified	1 (0.8)	0	0.50
Stroke location			
Right hemisphere	43 (37.4)	20 (38.4)	0.93
Left hemisphere	39 (33.9)	18 (34.6)	0.97
Bilateral hemisphere	21 (18.3)	8 (15.4)	0.63
Right cerebellum	8 (7.0)	3 (5.7)	0.76
Left cerebellum	5 (4.4)	1 (1.9)	0.43
Bilateral	8 (7.0)	4 (7.7)	0.88
Brainstem	6 (5.2)	2 (3.8)	0.68
Stroke treatment			
Conservative	108 (93.9)	46 (88.4)	0.25
Thrombolysis	4 (3.5)	3 (5.8)	0.50
Mechanical thrombectomy	3 (2.6)	3 (5.8)	0.31

Values are median (interquartile range) or number (percentage). NIHSS indicates National Institutes of Health Stroke Scale; and TAVR, transcatheter aortic valve replacement.

*The *P* value reached statistical significance ($P\leq0.05$).

group (52 [10.5%] versus 115 [5.0%]; *P*<0.001) (Figure); however, there were no significant differences between the 2 cohorts with respect to stroke type, anatomic location, or severity (as assessed by the National Institutes of Health Stroke Scale score) (Table 3). In addition, the management of stroke was comparable between the 2 cohorts.

After adjusting for relevant variables, a bovine arch was independently associated with higher long-term stroke risk after TAVR (adjusted HR, 2.11 [95% CI, 1.51–2.93]; *P*<0.001) (Table 6); sensitivity analyses conducted also showed similar results (Table 5). Other independent risk factors identified were female sex, lower body surface area, no prior coronary artery bypass grafting, and prior stroke/transient ischemic attack. This association between a bovine arch and long-term stroke risk was also consistent in subgroup analyses, with no significant interactions noted between a bovine arch and any of the subgroups with respect to long-term stroke (Table 7).

DISCUSSION

Stroke continues to complicate 2% to 3% of TAVR procedures despite the temporal improvement in transcatheter valve technologies and TAVR outcomes overall.[1,12–14] Several analyses have documented the association of post-TAVR strokes with increased morbidity, mortality, and costs at various time points.[12,15–17] In a nationwide analysis from the TVT registry, the occurrence of post-TAVR stroke was associated with a significant increase in 30-day mortality: 16.7% versus 3.7% in patients with versus without stroke, respectively (adjusted HR, 6.1 [95% CI, 5.4–6.8]; *P*<0.001).[15] The excess mortality of TAVR-associated stroke persists at 1- and 2- to 5-year follow-up. Consequently, much research has focused on discerning the risk factors associated with stroke related to TAVR. Several factors associated with an increased risk of post-TAVR

Table 4. Multivariable Logistic Regression Model of Possible Predictors of Periprocedural Stroke Within 7 Days of TAVR

Variable	Odds ratio	95% CI	*P* value
Bovine arch	2.16	1.22–3.83	0.01*
Prior aortic valve procedure	0.57	0.20–1.61	0.29
BSA, per 0.01-m^2 increase	0.99	0.97–1.00	0.02*
GFR, per 5-mL/min per 1.73 m^2 increase	0.95	0.88–1.03	0.20
Age, per 1-y increase	1.00	0.96–1.03	0.87
Peripheral artery disease	0.76	0.43–1.35	0.35
Prior stroke or TIA	1.22	0.60–2.48	0.59
Carotid artery stenosis	1.27	0.59–2.75	0.55
Urgent or emergent procedure	0.84	0.35–2.00	0.69
Transapical access	0.77	0.23–2.60	0.67
Access site other than transapical or transfemoral	1.23	0.28–5.38	0.78
Porcelain aorta	0.40	0.05–3.00	0.37
Prior CABG	0.64	0.29–1.42	0.27
Atrial fibrillation/flutter	0.92	0.53–1.60	0.76
Female	0.66	0.35–1.24	0.20
Left ventricular ejection fraction <30%	1.06	0.32–3.56	0.92

BSA indicates body surface area; CABG, coronary artery bypass grafting; GFR, glomerular filtration rate; TAVR, transcatheter aortic valve replacement; and TIA, transient ischemic attack.

*The *P* value reached statistical significance ($P\leq0.05$).

Table 5. Sensitivity Analyses for the Association Between a Bovine Arch and Periprocedural and Long-Term Stroke

Conditional *P* value cutoff for exit/entry	Logistic regression models*				Cox proportional hazards regression models			
	Backward elimination models		Forward selection models		Backward elimination models		Forward selection models	
	Adjusted odds ratio (95% CI)	*P* value	Adjusted odds ratio (95% CI)	*P* value	Adjusted hazard ratio (95% CI)	*P* value	Adjusted hazard ratio (95% CI)	*P* value
0.05	2.15 (1.22–3.79)†	0.01	2.15 (1.22–3.79)†	0.01	2.08 (1.50–2.88)‡	<0.001	2.04 (1.47–2.83)§	<0.001
0.10	…	…	…	…	2.10 (1.51–2.91)‖	<0.001	2.09 (1.51–2.90)¶	<0.001

The logistic regression models and their corresponding adjusted odds ratios shown are for the association between a bovine arch and periprocedural stroke within 7 days of transcatheter aortic valve replacement; the Cox proportional hazards regression models and their corresponding hazard ratios are for the association between a bovine arch and long-term stroke after transcatheter aortic valve replacement.

*Only the results obtained from models implementing a conditional *P* value cutoff of 0.05 were reported as the results from the models implementing a conditional *P* value cutoff of 0.10 were identical.

†The model adjusted for body surface area.

‡The model adjusted for body surface area, prior stroke or transient ischemic attack, prior coronary artery bypass grafting, and sex.

§The model adjusted for prior stroke or transient ischemic attack.

‖The model adjusted for body surface area, prior stroke or transient ischemic attack, prior coronary artery bypass grafting, sex, and age.

¶The model adjusted for body surface area, prior stroke or transient ischemic attack, sex, and age.

stroke were identified, including age, sex, valve features (bicuspid or heavily calcified valves), clinical comorbidities (prior stroke, atrial fibrillation, vascular disease, and renal insufficiency), and procedural characteristics (postdilation, valve in valve). However, the impact of the anatomic features of the aorta on post-TAVR strokes has not been previously studied.

To our knowledge, this is the first study that documents an association between a bovine aortic arch anatomy and both short- and long-term risk of stroke after TAVR. In our study of nearly 3000 TAVRs, the presence of a bovine arch was associated with a 2-fold increase in periprocedural stroke. The incidence of stroke continued to be higher in the bovine arch group through midterm follow-up (≈3 years). This finding, albeit novel in the TAVR population, corroborates previous research on the association of aortic arch anatomy features with stroke in the general population. Syperek et al showed a higher prevalence of bovine arches among patients with acute ischemic strokes involving the anterior circulation versus controls (25.7% versus 17.1%; P=0.039).[9] The association between a bovine aortic arch and stroke was also documented in a study by Samadhiya et al, in which the prevalence of bovine arch configuration was 22% versus 6.0% among patients with stroke versus control patients (P=0.043).[8]

Table 6. Multivariable Cox Proportional Hazards Model for Potential Risk Factors of Long-Term Stroke After TAVR

Variable	Hazard ratio	95% CI	*P* value
Bovine arch	2.11	1.51–2.93	<0.001*
Prior aortic valve procedure	0.82	0.50–1.34	0.43
BSA, per 0.01-m^2 increase	0.99	0.99–1.00	0.02*
GFR, per 5-mL/min per 1.73 m^2 increase	1.01	0.97–1.06	0.87
Age, per 1-y increase	0.99	0.96–1.00	0.11
Peripheral artery disease	1.05	0.76–1.45	0.77
Prior stroke or TIA	1.55	1.06–2.27	0.02*
Carotid artery stenosis	1.11	0.72–1.71	0.63
Urgent or emergent procedure	1.22	0.76–1.95	0.42
Transapical access	0.66	0.34–1.28	0.22
Access site other than transapical or transfemoral	0.96	0.39–2.38	0.92
Porcelain aorta	1.19	0.60–2.38	0.62
Prior CABG	0.62	0.40–0.94	0.03*
Atrial fibrillation/flutter	0.93	0.67–1.29	0.67
Female	0.59	0.41–0.85	0.01*
Left ventricular ejection fraction <30%	1.22	0.63–2.35	0.57

BSA indicates body surface area; CABG, coronary artery bypass grafting; GFR, glomerular filtration rate; TAVR, transcatheter aortic valve replacement; and TIA, transient ischemic attack.

*The *P* value reached statistical significance (P≤0.05).

Table 7. HRs for the Association Between Bovine Arch and Long-Term Stroke After TAVR in Subgroups

Subgroup	HR	95% CI	*P* value for interaction
Valve-in-valve procedure			0.29
Yes	2.22	1.54–3.21	
No	2.15	1.52–3.04	
Porcelain aorta			0.88
Yes	4.16	0.57–30.57	
No	2.08	1.48–2.92	
Valve sheath access site			0.23
Transfemoral	2.25	1.60–3.17	
Alternative	0.94	0.23–3.80	
Diabetes			0.052
Yes	2.11	1.30–3.43	
No	2.08	1.32–3.27	
Carotid artery stenosis			0.55
Yes	1.74	0.79–3.85	
No	2.20	1.53–3.17	
Sex			0.31
Female	2.42	1.42–4.15	
Male	1.86	1.22–2.84	
GFR, mL/min per 1.73 m^2			0.24
≥60	4.56	2.01–10.35	
<60	1.86	1.28–2.70	
LVEF, %			0.59
≥30	2.16	1.54–3.02	
<30	0.81	0.05–10.98	
Age, y			0.53
≥75	1.89	1.29–2.79	
<75	2.64	1.39–5.03	
Atrial fibrillation/flutter			0.70
Yes	2.41	1.41–4.11	
No	1.95	1.28–2.98	

GFR indicates glomerular filtration rate; HR, hazard ratio; LVEF, left ventricular ejection fraction; and TAVR, transcatheter aortic valve replacement.

These studies suggested that this anatomic variant could be a possible biomarker for embolic strokes, but this hypothesis had not been tested in the context of postprocedural strokes.

Although defining the mechanism of this observation could be challenging, the following reasons for the association between bovine arch and higher incidence of stroke can be postulated. First, the common origin of the brachiocephalic trunk and the left common carotid artery leads to a single common conduit for potential passage of debris that has a much larger area compared with vessels in the normal arch morphology. Second, differences in histologic features (intimal and adventitial thicknesses) and in the prevalence of vascular risk factors (eg, diabetes) have been discerned between patients with bovine versus normal arch anatomies, suggesting a possible association between this anatomic variant and other vasculopathies.[18] Third, flow dynamic parameters, such as flow patterns, helicity, and regional shear stress, are distinctly different between patients with normal versus aberrant aortic arch morphology, suggesting a possible flow-related mechanism to the heightened stroke risk in patients with bovine arch.[19–21]

The flow dynamic mechanism has been supported with limited empiric evidence. In elevated and time-dependent Reynolds number flows, such as in the ascending aorta, the combination of geometric curvatures and bifurcations with a pulsatile flow can lead to differences in blood mixing behavior.[22] This may impact the transport of particles through the aortic arch, although such a relationship has not been firmly established yet. Moreover, the high velocity of blood exposed to the large centrifugal force of the aortic curvature can lead to the emergence of "Dean vortices," which can potentially alter the transport of calcium particles.[23] The trajectory of particles traveling across a branching conduit was previously studied in a model of compressible flow, such as airways, which showed a tendency to deposition at merging bifurcations.[24] Farghadan et al demonstrated a potential relationship between particle deposition and transport with the near wall flow characteristics, particularly wall shear stress.[25] Also, the size of particles being transported can play a role, as large particles tend to deviate from fluid path lines.[26] Although these findings may theoretically contribute to explaining our results, caution is needed because in vivo blood flow characteristics are markedly different compared with those present in simulation and in vitro models. To further clarify and verify all these potential mechanisms, additional flow dynamic studies to characterize the transport of solid particles in the blood and to evaluate relevant flow dynamic parameters are needed.

Our study's findings have relevant clinical implications. For example, although cerebral embolic protection (CEP) devices have failed to show consistent benefit in the pivotal PROTECTED TAVR trial, they remain subject to ongoing studies. In this context, technical refinement may potentially be useful in improving the success of CEP in patients with a bovine arch.[27,28] The current design of CEP devices does not take into account aortic arch anatomic features. However, the finding that up to 1 in 5 patients referred for TAVR have a bovine arch may impact the operator's decision to use CEP and the choice of the CEP device.[29–31] Voss et al showed a 10% failure rate in the implantation of the sentinel device in patients with a bovine arch. This rate was even higher (35%) in another study conducted by Tagliari et al.[32,33] In addition, the persistent long-term risk associated with bovine arch anatomy in our study raises the question of whether antithrombotic therapy after TAVR should be tailored to account for the various anatomic variants that may be associated with long-term stroke.

Our findings must be considered hypothesis-generating and interpreted in the context of our study's several limitations. First, this was a single-center, retrospective study of a predominantly White population undergoing TAVR; hence, its findings need to be confirmed by other studies before they are generalized to other populations. Second, routine neurologic evaluation was not systematically performed in all patients, which may have led to the underestimation of the true incidence of stroke. Third, our study was underpowered to assess the impact of other less common aortic arch variants on post-TAVR stroke. Finally, although we attempted to account for most known and theoretical risk factors of stroke available in the Society of Thoracic Surgeons/American College of Cardiology TVT registry, we cannot exclude the possibility of residual confounding by variables not captured by the registry.

CONCLUSIONS

A bovine aortic arch is present in 18% of patients undergoing TAVR and is associated with a 2-fold increase in periprocedural and long-term risk of stroke after the procedure. Further studies are needed to confirm these findings and identify effective stroke-prevention strategies for this high-risk population.

ARTICLE INFORMATION

Received November 15, 2023; accepted January 11, 2024.

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Sources of Funding

None.

Disclosures

None.

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