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ORIGINAL RESEARCH

Intermediate-Term Risk of Stroke Following Cardiac Procedures in a Nationally Representative Data Set

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Background**—**Studies on stroke risk following cardiac procedures addressed only perioperative and long-term risk following limited higher-risk procedures, were poorly generalizable, and often failed to stratify by stroke type. We calculated stroke risk in the intermediate risk period following cardiac procedures compared with common noncardiac surgeries and medical admissions.

Methods and Results**—**The Nationwide Readmissions Database contains readmission data for 49% of US admissions in 2013. We compared age-adjusted stroke readmission rates up to 90 days postdischarge. We used Cox regression to calculate hazard ratios, up to 1 year, of stroke risk comparing transcatheter aortic valve replacement versus surgical aortic valve replacement and coronary artery bypass graft versus percutaneous coronary intervention. Procedures and diagnoses were identified by International Classification of Disease, Ninth Revision, Clinical Modification codes. After cardiac procedures, 90-day ischemic stroke readmission rate was highest after transcatheter aortic valve replacement (2.05%); 90-day hemorrhagic stroke rate was highest after left ventricular assist device placement (0.09%). The hazard ratio for ischemic stroke after transcatheter aortic valve replacement, compared with surgical aortic valve replacement, in fully adjusted Cox models was 1.86 (95% confidence interval, 1.12–3.08; P=0.016) and 6.17 (95% confidence interval, 1.97–19.33; P=0.0018) for hemorrhagic stroke. There was no difference between coronary artery bypass graft and percutaneous coronary intervention.

Conclusions**—**We demonstrated elevated readmission rates for ischemic and hemorrhagic stroke in the intermediate 30-, 60-, and 90-day risk periods following common cardiac procedures. Furthermore, we found an elevated risk of stroke after transcatheter aortic valve replacement compared with surgical aortic valve replacement up to 1 year. **(*J Am Heart Assoc*. 2017;6:e006900. DOI: 10.1161/JAHA.117.006900.)**

Key Words: cardiac surgery • epidemiology • stroke

Cardiac surgery has life-saving potential for many patients, but is also associated with significant morbidity and mortality, including the complication of stroke. Existing literature on stroke risk following cardiac procedures focuses on the perioperative and long-term risk periods following cardiac surgery and known high-risk procedures, including left ventricular assist device (LVAD) placement, aortic valve replacement, coronary artery bypass graft (CABG), and percutaneous coronary intervention (PCI).[1–7] Most studies involve single centers or device registries, with small sample sizes and variable results.[8–10] Also, most studies have not stratified by stroke type or contextualized results by comparing with other procedures and medical admissions. Furthermore, there are a paucity of data related to stroke risk in the intermediate risk period after discharge from the procedure and up to 1 year of follow-up. Recently, this risk period has been highlighted by the Centers for Medicare & Medicaid Services, with penalties for readmissions within 30 days. There may also be implications for treatments to reduce stroke risk that are targeted only to an intermediate risk period.[11]

We used a nationally representative database to calculate risk of stroke in the intermediate risk period following common cardiac procedures. We hypothesized that there was an elevated risk of ischemic and hemorrhagic stroke in this period following cardiac procedures compared with common noncardiac surgeries and medical admissions. We also focused on 2 salient comparisons: (1) transcatheter aortic valve replacement (TAVR) versus surgical aortic valve replacement (SAVR) and (2) CABG versus PCI, procedures for similar underlying conditions with different degrees of invasiveness. The overall goal was to provide nationally

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Clinical Perspective

What Is New?

- Compared with noncardiac surgeries, cardiac surgeries are associated with higher rates of ischemic and hemorrhagic stroke.
- The highest rates of stroke were observed after transcatheter aortic valve replacement.
- In adjusted models, there were no differences in stroke rates comparing coronary artery bypass surgery and percutaneous coronary intervention.

What Are the Clinical Implications?

- Individuals who undergo the high-risk surgeries identified here should be closely followed for risk of stroke, and further research is needed that recognizes these high rates of stroke, in order to develop strategies to make cardiac interventions even safer from the perspective of stroke risk.

representative risk data that could help guide risk-benefit decisions and improve care in the vulnerable, but understudied, intermediate risk period.

Methods

The Nationwide Readmissions Database is a national database of readmissions for all payers and the uninsured with data on more than 14 million US admissions during the year 2013. It is 1 of 7 databases in the Healthcare Cost and Utilization Project and is derived from State Inpatient Databases from 21 states, comprising data from 49.1% of all US hospitalizations, excluding rehabilitation and long-term acute-care hospitalizations. The Nationwide Readmissions Database allows analysis of readmissions with the use of an anonymized, verified linkage identifier for each individual. The Mount Sinai Institutional Review Board reviewed and approved this project, and all analyses comply with the Healthcare Cost and Utilization Project data use agreement. Because the data are made publicly available through the Healthcare Cost and Utilization Project, the data, analytical methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

We used *International Classification of Disease, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes to identify index cardiac procedures, noncardiac procedures, and common medical admissions, as well as comorbidities. Cardiac procedures included ablation, cardioversion, CABG, cardiac catheterization, implantable cardioverter defibrillator placement, left atrial appendage (LAA) closure, LVAD placement, PCI, permanent pacemaker placement, SAVR, and TAVR. For index cardiac admissions, we excluded those with more than 1 concurrent cardiac procedure. Noncardiac surgeries included appendectomy, cystectomy, cholecystectomy, hernia surgery, hip surgery, knee surgery, nephrectomy, prostatectomy, shoulder surgery, spine surgery, and thyroid surgery. For noncardiac index admissions, we excluded those with concurrent cardiac procedures. Medical admissions included chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), pneumonia, and urinary tract infection (UTI) and were defined by appropriate *ICD-9-CM* codes in the primary diagnosis position. For medical admissions, we excluded those with concurrent cardiac procedures. Comorbidities included atrial fibrillation or atrial flutter, carotid artery disease, coagulation disorders, congestive heart failure, coronary artery disease, diabetes mellitus, hypertension, hypercholesterolemia, obesity, peripheral artery disease, renal failure, smoking history, and stroke history. Characteristics of the index hospitalization were defined by Healthcare Cost and Utilization Project and included hospital bed size (small, medium, or large), teaching hospital status (metropolitan nonteaching, metropolitan teaching, and nonmetropolitan hospital), income quartile of patient's ZIP code, and National Center for Health Statistics urban-rural location classification ("central" counties of metro areas of ≥1 million population, "fringe" counties of metro areas of ≥1 million population, counties in metro areas of 250 000–999 999 population, counties in metro areas of 50 000–249 999 population, micropolitan counties [population 10 000–49 999], and not metropolitan or micropolitan counties). The All Patient Refined Diagnosis Related Groups (APR-DRGs) are designated using 3M Health Information Systems software. APR-DRGs now classify patients into 25 major diagnostic categories, and then further subdivide patients into 4 severity of illness subclasses in terms of degree of loss of function (minor, moderate, major, or extreme) and 4 risk of mortality subclasses (minor, moderate, major, or extreme). These 2 subclasses are calculated separately and may be different from one another. Analysis of the APR-DRG has demonstrated that mortality rate correlates with increasing APR-DRG risk of mortality scores,[4] and the APR-DRG has been adapted to the VA health system.[4,5]

Primary outcomes were ischemic stroke and hemorrhagic stroke. We used *ICD-9-CM* codes previously validated in the literature to identify patients with ischemic and hemorrhagic stroke. Ischemic stroke was identified by 1 of the following *ICD-9-CM* codes: 433.x1, 434.x1, and 436; and hemorrhagic stroke was identified by 1 of the following codes: 430 and 431.[12–14] Ischemic and hemorrhagic stroke, as well as medical and surgical index events, were defined using only the primary diagnosis. To ensure that the stroke was not related to another cardiac procedure performed during the stroke readmission and therefore misattributed to the index procedure, we excluded patients who underwent a cardiac procedure during the stroke readmission.

Statistical Analysis

We calculated baseline characteristics of each group (index admission for cardiac procedure, noncardiac surgery, and medical admission). For medical comorbidities and characteristics of the index hospitalization, we calculated means and SDs for continuous variables and frequencies and percentages for categorical variables.

We calculated readmission rates as the number of readmissions attributed to ischemic and hemorrhagic stroke within 30, 60, and 90 days of discharge from the index hospitalization, and reported rates as a percentage. In order to account for different age distributions within each group, we age-standardized rates to the 2010 US population. For ischemic stroke outcomes, we excluded index admissions with an ischemic stroke diagnosis, and for hemorrhagic stroke outcomes, we excluded index admissions with a hemorrhagic stroke diagnosis, because the objective was to study patients readmitted with these diagnoses. To calculate 30-day readmission rates, we excluded index hospitalizations in December; to calculate 60-day rates, we excluded index hospitalizations in November and December; and to calculate 90-day rates, we excluded index hospitalizations in October, November, and December. We compared rates of ischemic and hemorrhagic stroke after cardiac procedures with rates following common noncardiac surgeries and medical admissions.

Additionally, we performed 2-way comparisons of CABG versus PCI and TAVR versus SAVR. For this analysis, we used all available follow-up data and measured time from discharge from the index hospitalization to admission for stroke. Because only the month of admission, and not the exact date, is available in the Nationwide Readmissions Database, for those without the event of interest, we calculated the maximum observed follow-up period as the number of days from the midpoint of the month of index admission to December 31, 2013. We assumed full capturing of mortality and no loss to follow-up because all outcomes studied were highly likely to result in hospitalization. For each comparison, we created Kaplan–Meier curves of the cumulative risk of ischemic and hemorrhagic stroke, stratified by index admission type. We performed Cox regression, reporting hazard ratio and 95% confidence intervals separately for the outcomes of ischemic and hemorrhagic stroke. We ran an unadjusted model, and then adjusted for risk of mortality, based on the subclass assigned by 3M's APR-DRG software, based on likelihood of dying, with 1=minor, 2=moderate, 3=major, and 4=extreme. In a separate model, we adjusted for severity of illness, based on the subclass assigned by 3M's APR-DRG software and classified similarly as the APR-DRG risk of mortality. In another model, we adjusted for vascular risk factors during the index admission, including age, atrial fibrillation or atrial flutter, carotid artery disease, coagulation disorders, congestive heart failure, coronary artery disease, diabetes mellitus, hypertension, hypercholesterolemia, obesity, peripheral artery disease, renal failure, smoking history, and stroke history. The fully adjusted model was adjusted for vascular risk factors, hospital bed size, teaching hospital status, income quartile of patient's ZIP code, and National Center for Health Statistics urban-rural location classification, all measured at the time of index admission. The proportional hazards assumption was not violated in these models. Analyses were performed in SAS (version 9.4; SAS Institute Inc, Cary, NC) and R (version 3.3.1; R Foundation for Statistical Software, Vienna, Austria).

Results

Table 1 lists baseline characteristics of the study population at the time of index event. There were 653 216 patients in the cardiac procedure group, 1 198 209 in the noncardiac surgery group, and 968 224 in the medical group. Noncardiac surgery patients were younger, had fewer vascular risk factors, and had lower estimated risk of mortality and illness severity than the cardiac procedure and medical groups. Among cardiac procedure patients, males outnumbered females, and vascular risk factors were more common than in the other groups. The most common cardiac procedures were cardiac catheterization (191 400 for the ischemic stroke analysis and 193 963 for hemorrhagic stroke) and permanent pacemaker placement (61 841 for the ischemic stroke analysis and 63 071 for hemorrhagic stroke).

Following cardiac procedures, noncardiac surgeries, and medical admissions, readmission rates for ischemic and hemorrhagic stroke increased from the 30-, 60-, to 90-day periods following all index events, suggesting a progressive, and not stepwise, risk in the intermediate follow-up period. In the cardiac surgery group, readmission rate for ischemic stroke was highest after TAVR and lowest after LAA closure (Figure 1A). Notably, aside from LAA closure and ablation, the ischemic stroke readmission rate following cardiac procedures was still higher than the highest-risk noncardiac surgery (Figure 2). The ischemic stroke readmission rates following SAVR, cardiac catheterization, LVAD, and TAVR were all higher than rates following admission for UTI, pneumonia (PNA), and COPD (Figure 2). Hemorrhagic stroke readmission rates were highest after LVAD and lowest following implantable cardioverter defibrillator placement (Figure 1B).

Among the noncardiac surgery group, ischemic stroke readmission rates were highest following cystectomy and lowest after knee surgery (Figure 2). Hemorrhagic stroke

Table 1. Baseline Characteristics of Study Population at Index Event

	Type of Index Admission		
	Cardiac Procedure	Noncardiac Surgery	Medical
No. of participants	653 216	1 198 209	968 224
Age, y, mean (SD)	66.1 (13.3)	60.8 (15.9)	70.0 (16.6)
Male, N (%)	402 150 (61.6)	527 898 (44.1)	424 514 (43.8)
Median income for ZIP code, N (%)			
$0 to 25 000	178 328 (27.8)	261 134 (22.2)	294 881 (31.0)
$25 001 to 30 000	170 203 (26.5)	304 869 (25.9)	261 197 (27.4)
$30 001 to 35 000	156 100 (24.3)	314 240 (26.7)	222 633 (23.4)
$35 001+	137 297 (21.4)	297 954 (25.3)	173 919 (18.3)
APRDRG mortality risk, N (%)			
Minor likelihood	245 606 (37.6)	913 019 (76.2)	242 980 (25.1)
Moderate likelihood	215 246 (33.0)	196 344 (16.4)	370 228 (38.2)
Major likelihood	140 659 (21.5)	68 802 (5.7)	298 987 (30.9)
Extreme likelihood	51 682 (7.9)	20 017 (1.7)	55 970 (5.8)
APRDRG illness severity subclass, N (%)			
No or minor loss of function	169 030 (25.9)	556 375 (46.4)	110 129 (11.4)
Moderate loss of function	259 498 (39.7)	488 636 (40.8)	427 588 (44.2)
Major loss of function	170 850 (26.2)	125 544 (10.5)	375 699 (38.8)
Extreme loss of function	53 815 (8.2)	27 627 (2.3)	54 749 (5.7)
Atrial fibrillation or atrial flutter, N (%)	194 184 (29.7)	78 342 (6.5)	228 772 (23.6)
Carotid artery disease, N (%)	17 292 (2.7)	6370 (0.5)	11 527 (1.2)
Coagulation disorder, N (%)	45 482 (7.0)	33 738 (2.8)	55 969 (5.8)
Congestive heart failure, N (%)	196 101 (30.0)	42 948 (3.6)	406 681 (42)
Coronary artery disease, N (%)	469 046 (71.8)	143 922 (12.0)	322 361 (33.3)
Diabetes mellitus, N (%)	231 554 (35.5)	224 071 (18.7)	329 649 (34.1)
Hypertension, N (%)	383 991 (58.8)	587 146 (49.0)	451 320 (46.6)
Hyperlipidemia, N (%)	406 639 (62.3)	395 659 (33.0)	367 786 (38.0)
Obesity, N (%)	114 316 (17.5)	201 452 (16.8)	134 280 (13.9)
Peripheral artery disease, N (%)	57 954 (8.9)	32 048 (2.7)	70 382 (7.3)
Renal failure, N (%)	80 931 (12.4)	46 997 (3.9)	142 773 (14.8)
Smoking history, N (%)	242 604 (37.1)	287 774 (24.0)	328 676 (34.0)
Stroke history, N (%)	37 277 (5.7)	20 775 (1.7)	58 311 (6.0)
Primary expected payer, N (%)			
Medicare	383 730 (58.8)	564 046 (47.1)	692 216 (71.6)
Medicaid	46 695 (7.2)	83 759 (7.0)	87 374 (9.0)
Private insurance	165 373 (25.4)	442 526 (37.0)	122 237 (12.6)
Self-pay	29 633 (4.5)	37 442 (3.1)	34 680 (3.6)
No charge	4608 (0.7)	5529 (0.5)	4734 (0.5)
Other	22 385 (3.4)	63 755 (5.3)	2587 (2.7)
Length of stay, day, mean (SD)	5.5 (7.4)	4.2 (5.8)	4.8 (5.6)

APRDRG indicates All Patient Refined Diagnosis Related Group.

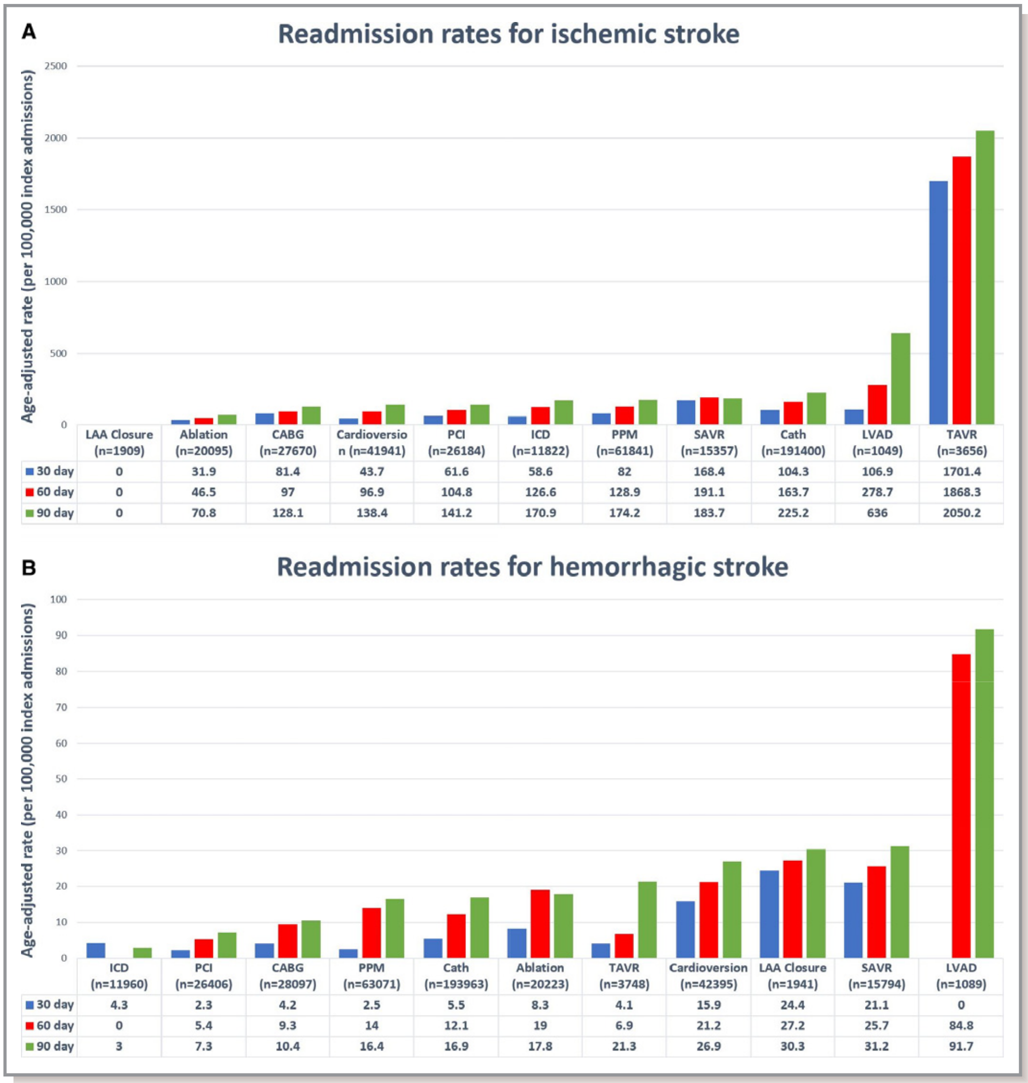

Figure 1. Readmission rates for ischemic (A) and hemorrhagic (B) stroke after cardiac procedures. CABG indicates coronary artery bypass graft; Cath, cardiac catheterization; ICD, implantable cardioverter defibrillator placement; LAA closure, left atrial appendage closure; LVAD, left ventricular assist device placement; PCI, percutaneous coronary intervention; PPM, permanent pacemaker placement; Surgical AVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

readmission rates were highest following thyroid surgery and lowest after appendectomy (Figure 2). After medical index admissions, ischemic stroke readmission rates were highest for CHF, comparable with that observed following LVAD, and lowest for COPD, comparable with rates following ablation (Figure 2). Hemorrhagic stroke readmission rates were also highest following admission for CHF and lowest for COPD. Hemorrhagic stroke readmission rates following UTI and pneumonia were comparable to those following CABG, cardioversion, and PCI (Figure 2).

In direct comparison of CABG versus PCI, there was no statistically significant difference in hazards of ischemic or hemorrhagic stroke in both unadjusted and adjusted models (Table 2). There was, however, a consistently elevated cumulative risk of ischemic and hemorrhagic stroke after TAVR compared with SAVR (Figure 3A and 3B) that was also observed in unadjusted and adjusted Cox models (Table 2). The hazard ratio for ischemic stroke after TAVR, compared with SAVR, in fully adjusted Cox models, was 1.86 (95% confidence interval, 1.12–3.08; P=0.016) and 6.17 (95% confidence interval, 1.97–19.33; P=0.0018) for hemorrhagic stroke.

Discussion

This study demonstrates elevated readmission rates for ischemic and hemorrhagic stroke in the intermediate 30-, 60-, and 90-day risk periods following common cardiac procedures relative to noncardiac procedures and common

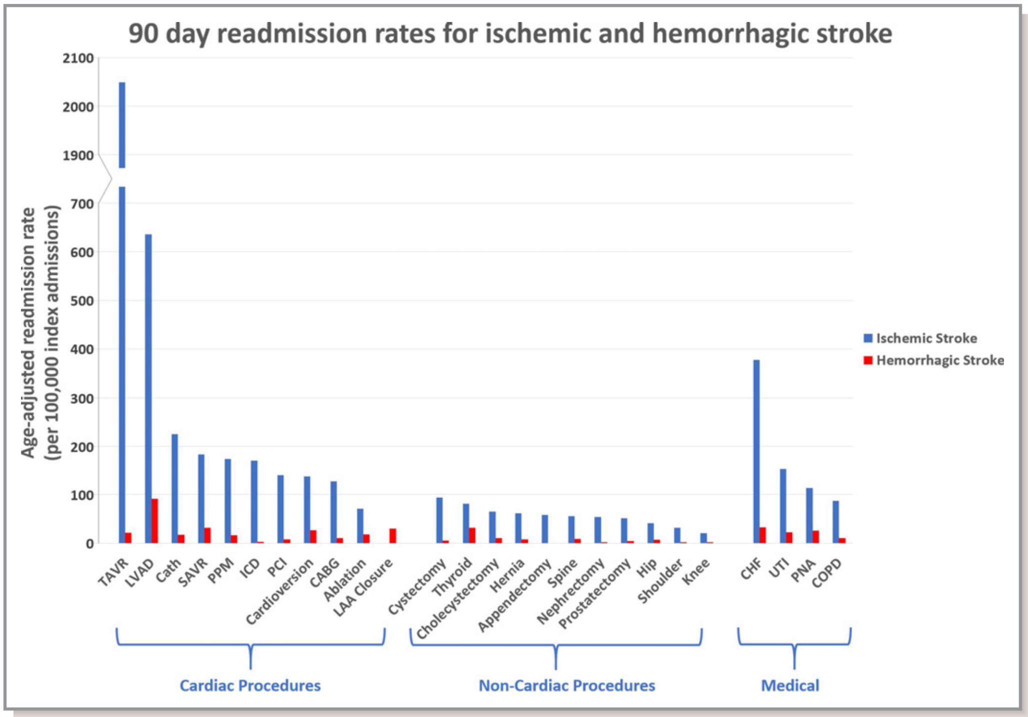

Figure 2. Ninety-day age-adjusted readmission rates for ischemic and hemorrhagic stroke by index event. CABG indicates coronary artery bypass graft; Cath, cardiac catheterization; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; ICD, implantable cardioverter defibrillator placement; LAA closure, left atrial appendage closure; LVAD, left ventricular assist device placement; PCI, percutaneous coronary intervention; PNA, pneumonia; PPM, permanent pacemaker placement; Surgical AVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement; UTI, urinary tract infection.

medical admissions. Ischemic stroke risk was highest following TAVR and LVAD, and hemorrhagic stroke risk was highest following LVAD, SAVR, and LAA closure. Aside from LAA closure, all cardiac procedures were associated with a higher readmission risk for stroke than noncardiac procedures. The ischemic stroke readmission rates following SAVR, cardiac catheterization, permanent pacemaker placement, and implantable cardioverter defibrillator placement were all higher than rates following admission with UTI, pneumonia, and COPD. Ischemic stroke readmission rates following LVAD and TAVR were higher than rates following admission with CHF. These results suggest that the cardiac procedures and postoperative management confer additional vulnerability to patients who have many concurrent vascular risk factors in the intermediate risk period.

In a Japanese nation-wide benchmarking project examining 30-day postoperative complications for CABG, valve operations, and thoracic aortic operations, risk of stroke was highest following thoracic aortic operation (6.8%), valve operation (1.8%), and CABG (1.5%).[1] Different risk periods and subtype of stroke were not examined. Also, this study did not examine rates after a number of important cardiac procedures and did not compare rates with those after medical admissions and noncardiac surgeries. Finally, results may not be generalizable to the US population, whereas the current study includes data from half of all US hospitalizations in 2013.

With the advent of minimally invasive transcatheter approaches, researchers have paid great attention to outcomes following aortic valve replacement and attempted to risk stratify candidates for replacement based on symptom severity and medical comorbidities. Reported rates of stroke after aortic valve replacement vary dramatically, are registry based, and likely do not take into account an even higher incidence of silent stroke.[15] The American College of Cardiology recently published an expert consensus decision pathway for TAVR in adults with aortic stenosis, acknowledging that although TAVR is used for higher-risk patients, it will increasingly be offered to lower-risk patients.[16] We directly compared TAVR and SAVR and found an almost 90% increased risk of ischemic stroke with TAVR compared with SAVR, and more than 6-fold increased risk of hemorrhagic stroke. The Nordic Aortic Valve Intervention Trial showed no difference in stroke or transient ischemic attack at 30 days or 1 year in patients undergoing TAVR versus SAVR, regardless of predicted risk of death following surgery.[17] Similarly, the PARTNER (Placement of Aortic Transcatheter Valves) 2 Trial showed no difference in stroke risk in intermediate-risk

Table 2. Unadjusted and Adjusted Cox Regression Models Testing 2-Way Comparisons for Risk of Ischemic and Hemorrhagic Stroke

	Ischemic Stroke			Hemorrhagic Stroke		
	Hazard Ratio	95% CI	*P* Value	Hazard Ratio	95% CI	*P* Value
Coronary artery bypass graft vs percutaneous coronary intervention (reference)						
Unadjusted model	0.89	0.70 to 1.13	0.34	1.02	0.14 to 7.27	0.98
Adjusted for risk of mortality*	0.80	0.63 to 1.03	0.08	1.20	0.60 to 2.41	0.6
Adjusted for severity of illness†	0.74	0.58 to 0.95	0.017	1.21	0.59 to 2.46	0.6
Adjusting for vascular risk factors‡	0.83	0.65 to 1.07	0.14	1.24	0.61 to 2.55	0.55
Adjusting for additional vascular risk factors§	0.80	0.62 to 1.04	0.10	1.12	0.52 to 2.38	0.78
Fully adjusted‖	0.80	0.62 to 1.05	0.11	1.09	0.51 to 2.34	0.8
Transcatheter aortic valve replacement vs surgical aortic valve replacement (reference)						
Unadjusted model	2.28	1.52 to 3.41	<0.0001	6.53	2.67 to 15.97	<0.0001
Adjusted for risk of mortality*	2.13	1.40 to 3.22	0.0004	5.38	2.20 to 13.20	0.0002
Adjusted for severity of illness†	2.34	1.40 to 3.91	0.001	3.03	0.98 to 9.30	0.053
Adjusted for vascular risk factors‡	1.85	1.15 to 2.96	0.01	4.53	1.53 to 13.45	0.006
Adjusting for additional vascular risk factors§	1.75	1.07 to 2.86	0.026	4.59	1.53 to 13.74	0.007
Fully adjusted‖	1.86	1.12 to 3.08	0.016	6.17	1.97 to 19.33	0.0018

CI indicates confidence interval.
*Adjusted for 3M's All Patient Refined Diagnosis Related Group (APR-DRG) Risk of Mortality, classified as: 1=minor, 2=moderate, 3=major, 4=extreme.
†Adjusted for 3M's All Patient Refined Diagnosis Related Group (APR-DRG) Severity of Illness Subclass, classified as 1=minor, 2=moderate, 3=major, 4=extreme.
‡Adjusted for age, atrial fibrillation or atrial flutter, diabetes mellitus, hypertension, hypercholesterolemia, and smoking history.
§Adjusted for age, atrial fibrillation or atrial flutter, diabetes mellitus, hypertension, hypercholesterolemia, smoking history, coronary artery disease, cerebrovascular disease, peripheral arterial disease, coagulation disorders, carotid artery disease, and obesity.
‖Adjusted for all vascular risk factors as well as: hospital bed size, teaching hospital status, income quartile of patient's ZIP code, and National Center for Health Statistics urban-rural location classification.

patients at 30 days and 1 year.[5,18] The similar risk following TAVR and SAVR in the PARTNER trials could be attributed to close follow-up these patients received as study participants. Our results may reflect the real-world reality for the majority of patients who are not followed closely in a clinical trial, and highlight a need for closer follow-up in the vulnerable intermediate risk period. Our results may also reflect the fact that more high-risk patients are offered TAVR than SAVR at present, but the elevated stroke risk following TAVR persisted even after adjustment for risk factors and estimates of mortality and illness severity.

In high-risk patients, Adams et al showed comparable stroke risk at 30 days (4.9% in TAVR and 6.2% in SAVR; P=0.46) and 1 year (8.8% and 12.6%; P=0.10). Also, in high-risk patients in The CoreValue US High-Risk Pivotal Trial, stroke risk following TAVR at 30 days, 1 year, and 2 years was 4.9%, 8.7%, and 10.9%, respectively, and 6.2%, 12.5%, and 16.6%, respectively, for SAVR.[4] This study distinguished between hemorrhagic and ischemic stroke and found higher overall rates of ischemic than hemorrhagic stroke following TAVR and SAVR.

We, too, found higher rates of ischemic stroke than hemorrhagic stroke following TAVR and SAVR. However, our study accords more with the results of Smith et al, who found a higher stroke incidence in the high-risk transcatheter group with major stroke 30-day rates of 3.8% in the transcatheter group and 2.1% in the surgical group (P=0.20) and 5.1% and 2.4%, respectively, at 1 year (P=0.07).[7] There was, however, no distinction between stroke subtypes and no examination of the intermediate risk period. It is possible that some of our difference is attributable to an inability to stratify by surgical risk and a larger sample size. In another study, there was an early stroke rate (2–30 days) of 3% and a higher late stroke rate in the 31- to 730-day late period.[3] While these risk periods do not accord with our 30-, 60-, and 90-day intermediate risk periods, they do suggest an incremental increase in risk of stroke with time following TAVR. In another study, 17.9% with TAVR were readmitted within 30 days, and of those, 3.6% were readmitted with stroke or transient ischemic attack.[19] However, this study did not examine the intermediate risk period beyond 30 days, compare readmission rates with other procedures or medical admissions, or distinguish between ischemic and hemorrhagic stroke.

LVAD is known to be associated with a high risk of stroke. Most past studies compare outcomes with different devices within single centers.[8–10] Using administrative claims data

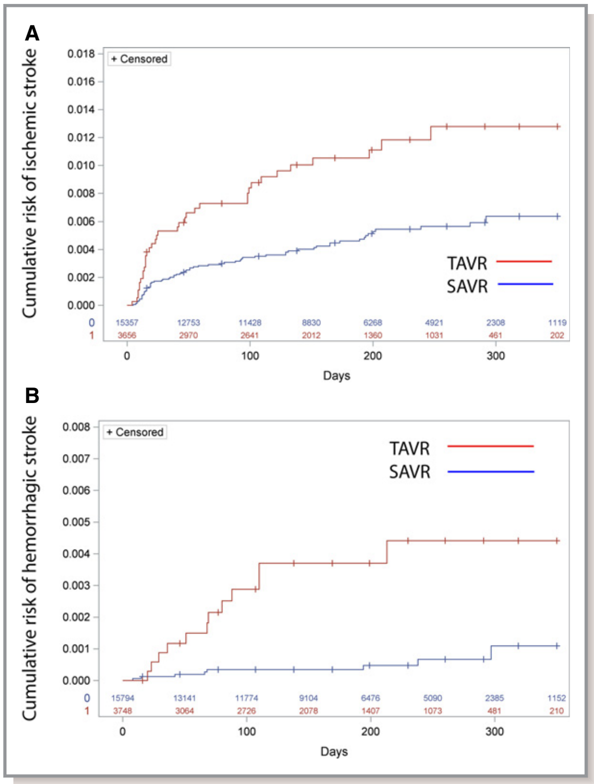

Figure 3. A, Cumulative risk of ischemic stroke following transcatheter aortic valve replacement vs surgical aortic valve replacement. B, Cumulative risk of hemorrhagic stroke following transcatheter aortic valve replacement vs surgical aortic valve replacement. SAVR indicates surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

from New York, California, and Florida, there was an 8.7% annual risk of stroke following LVAD (5.5% ischemic, 3.1% hemorrhagic).[20] This annual incidence of stroke was similar in another single-center study.[9] While intermediate risk (up to 90 days) and annual risk are not directly comparable, the current study also suggests that in the intermediate risk period, patients were readmitted more commonly with ischemic than hemorrhagic stroke after LVAD.

In previous studies of PCI and CABG, subsequent stroke risk was found to be low. A retrospective cohort study in California demonstrated 1-year stroke rates of 1.4% to 1.7% for CABG, 1.2% to 1.6% for PCI performed in patients with acute coronary syndrome, and 1% to 1.2% for PCI performed in patients without acute coronary syndrome.[6] In a retrospective cohort study in Europe comparing 30-day and 5-year outcomes after PCI and CABG in patients aged ≤50 years, 30-day stroke rate was 0% in the PCI group (n=1617) and 0.7% after CABG (n=592). After 1 year, 99.6% were stroke free after PCI and 99.3% after CABG.[2] The current study compares the risk following PCI and CABG to the risk following common medical diagnoses, with a risk of readmission similar to that following admission for UTI and pneumonia and lower than CHF. We also directly compared stroke risk after CABG and PCI, and found an unadjusted increased risk of ischemic stroke after CABG that reversed after adjustment for estimated risk of mortality and illness severity. However, after full adjustment, hazards were similar for ischemic and hemorrhagic stroke.

Most literature focuses on the perioperative and long-term risk periods following cardiac surgery, whereas the current study uniquely examines the intermediate risk period. This risk period has been highlighted by the Centers for Medicare & Medicaid Services, which has instituted significant penalties for readmissions within 30 days. There may also be implications for targeted treatments that apply only during the intermediate period of risk. For example, a recent study examining randomized trials of aspirin after transient ischemic attack or ischemic stroke suggested that the intermediate risk period (6–12 weeks) is most important in secondary prevention.[11] We suggest that there may be similar opportunities to target patients in the intermediate postoperative period after cardiac surgery. Further study could identify postoperative interventions and monitoring that could lower the risk of ischemic and hemorrhagic stroke following many common cardiac procedures.

There are several limitations to this study. First, there may be misclassification of variables based on *ICD-9CM* codes, and comorbidities may be incomplete. We could not adjust for stroke severity, preprocedural risk, or medications. Second, we could not fully observe out-of-hospital mortality. There are several strengths of this study. We used data from a large, nationally representative, and contemporary data set. Patients were not selected by enrollment in a device registry or from a single center. Additionally, it is imperative to distinguish between ischemic and hemorrhagic stroke outcomes because the management and risk-factor profiles differ for each. The current study is unique because it highlights the intermediate risk period, which has been understudied to date. Rather than focusing on 1 or 2 cardiac procedures, we examined several common cardiac procedures and noncardiac procedures, and we contextualized rates to those following common medical admissions.

In summary, we demonstrated elevated readmission rates for ischemic and hemorrhagic stroke in the intermediate 30-, 60-, and 90-day risk periods following common cardiac procedures. Furthermore, our data suggest an elevated risk of stroke after TAVR compared with SAVR and similar risks following CABG and PCI. Further study is required to better understand mechanisms of increased intermediate risk for these vulnerable patients that may allow the development of targeted interventions during this risk period. Additionally, patients might benefit from the development of a risk index calculator for stroke risk following cardiac and noncardiac surgeries, similar to the Revised Cardiac Risk Index used to calculate the risk of cardiac complications following noncardiac surgery.

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Disclosures

None.

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