

Long-Term Outcomes for Different Forms of Stress Cardiomyopathy After Surgical Treatment for Subarachnoid Hemorrhage

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BACKGROUND: Stress-induced cardiomyopathy (SCM) after subarachnoid hemorrhage (SAH) includes predominant apical or basal regional left ventricular dysfunction (RLVD) with concomitant changes in electrocardiogram or increase in cardiac enzymes. We hypothesized that difference in outcome is associated with the type of RLVD after SAH.

METHODS: We studied a single-center retrospective cohort of SAH patients hospitalized between 2000 and 2010 with follow-up until 2013. We classified patients who had an echocardiogram for clinically indicated reasons according to the predominate location of RLVD as classic SCM-apical form and variant SCM-basal form. A Cox proportional hazard model and logistic regression were used to estimate the risk for death and hospital complications associated with different RLVD after adjustment for propensity to undergo echocardiography given clinical characteristics on admission.

RESULTS: Among 715 SAH patients, 28% (200/715) had an echocardiogram for clinical evidence of cardiac dysfunction during hospitalization, the most common being acute left ventricular dysfunction, suspected acute ischemic event, changes in electrocardiogram and cardiac enzymes, and arrhythmia. SCM was present in 59 patients (8% of all cohort and 30% of patients with echocardiogram, respectively) with similar distribution of SCM-basal (25/59) and SCM-apical forms (34/59). SAH patients who had an echocardiogram for clinically indicated reasons had a significantly decreased risk-adjusted long-term survival compared with those without an echocardiogram, regardless of the presence of RLVD. SCM-basal form was associated with cardiac complications (odds ratio, 6.1; 99% confidence interval, 1.8–20.2) and severe sepsis (odds ratio, 5.3; 99% confidence interval, 1.6–17.2).

CONCLUSIONS: SAH patients with echocardiogram for a clinically indicated reason have a decreased long-term survival, regardless of the presence of RLVD. The association between severe sepsis and SCM-basal warrants future studies to determine their potential synergistic effect on left ventricular systolic dysfunction among SAH patients. (Anesth Analg 2016;122:1594–602)

Aneurysmal subarachnoid hemorrhage (SAH) is a sudden and devastating hemorrhagic variant of stroke with a high likelihood of death and, if a patient survives, a high likelihood of severe and long-term disability. Stress-induced cardiomyopathy (SCM), characterized by various forms of transient regional left

ventricular (LV) systolic dysfunction, is a well-documented complication of a multitude of acute stress states and, in particular, neurologic injuries and SAH.^{1–4} This syndrome has previously gone by different names in the literature, including “broken heart syndrome,” tako-tsubo cardiomyopathy,^{5–7} transient LV apical ballooning syndrome,⁸ neurogenic stunned myocardium, and neurogenic stress cardiomyopathy.^{3,9–11} The underlying mechanism, similar to other SCM, includes both excessive circulating catecholamine levels and substantial local release of norepinephrine from myocardial nerve endings after the rupture of an aneurysm, leading to vasoconstriction, dysfunction of the endothelium, and increase in vascular permeability.^{3,9,11,12}

The classic pattern involving the transient dysfunction of predominantly LV apex remains the most commonly reported form of SCM in patients with SAH,^{13,14} but more variant forms, including basal LV dysfunction, are being reported.^{10,15–17} Most studies reporting SCM as an independent predictor of hospital death after SAH include not only patients undergoing surgical treatment for prevention of rebleeding but also those who were not treated surgically, often because of poor prognosis.^{2,18,19} It remains unclear whether certain patterns of regional left ventricular dysfunction (RLVD) are more prevalent or predictive of poor outcomes, including long-term survival and cardiovascular death, depending on whether the patient undergoes surgical treatment for SAH.^{14,20,21}

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In the single-center cohort of patients with SAH with available echocardiographic studies, we aimed to compare short- and long-term outcomes in patients with different patterns of RLVD.

METHODS

Data Source and Patient Population

The study was approved by the University of Florida (UF) IRB and Privacy Office, and the requirement for written informed consent was waived by the IRB. By using the UF Integrated Data Repository, we assembled a single-center cohort of 723 patients aged 18 years or older who underwent surgical treatment for primary diagnosis of SAH between January 1, 2000, and November 30, 2010. Patients with arteriovenous malformation or head trauma were excluded as previously described.²² We performed a manual review of medical records and imaging studies to obtain data related to SAH severity and treatment, anatomical location of cerebral aneurysm, vasospasm, electrocardiographic findings, cardiac markers, cardiac history, clinical indications for ordering echocardiogram, and cardiology consult notes when available. We excluded 8 patients with known LV systolic dysfunction before admission and those deemed to have documented acute coronary disease during hospitalization by review.

Echocardiography

For 200 patients in the cohort, an echocardiogram was performed for clinically indicated reasons (Supplemental Digital Content, Supplemental Table S1, <http://links.lww.com/AA/B384>), most commonly clinical diagnoses of acute LV dysfunction (26%), suspected acute ischemic heart disease (26%), changes in electrocardiogram or cardiac enzymes (29%), and arrhythmia (10%). For each patient, 1 author independently reviewed data in the UF echocardiography database using the standard American Society of Echocardiography 17-segment model for systolic function to determine LV ejection fraction, wall motion abnormalities, and LV inflow data (early filling velocities [E], atrial filling velocities [A], deceleration time [DT], mitral annular tissue Doppler early diastolic peak velocity [E']).²³ All segments were scored based on contractility: 1 normal, 1.5 mild hypokinesis, 2 moderate hypokinesis, 2.5 severe hypokinesis, 3 akinesis, 4 dyskinesis, and 5 aneurysmal. A wall motion score index was calculated by dividing the sum of wall motion scores by the number of visualized segments. Diastolic function was assessed by measuring pulsed-wave Doppler of mitral valve peak velocity of early and late diastolic flow, early flow deceleration time, and duration of late flow. The E:A ratio was calculated from the mean E and A of 3 heart cycles.²⁴

By using Mayo Clinic criteria,¹⁴ patients were considered to have SCM if they had any type of new RLVD extending beyond a single epicardial vascular distribution, an absence of obstructive coronary disease, and new electrocardiographic abnormalities (either ST segment elevation and/or T-wave inversion) or modest elevation in cardiac biomarkers. We classified patients into 3 groups: (1) no RLVD if no segmental wall motion abnormalities were identified, (2) classic SCM-apical form if the average wall motion score

index for apical segments was greater than the score for basal segments, and (3) variant SCM-basal form if the average wall motion score index for basal segments was greater than the score for apical segments. Patients without clinically indicated echocardiogram during hospitalization were considered as a separate group.

Outcomes

Primary outcome was hospital and long-term survival. The date and cause of death were determined using hospital records, Social Security Death Index, and Florida Bureau of Statistics (Supplemental Digital Content, Supplemental Methods, <http://links.lww.com/AA/B384>). Secondary outcomes included prolonged mechanical ventilation with duration of at least 72 hours, acute kidney injury, severe sepsis, cardiac complications (cardiogenic shock, cardiac arrhythmias, or need for inotropes), vasospasm, and discharge to either home or rehabilitation center. Applying consensus Risk, Injury, Failure, Loss, and End-stage kidney criteria,²⁵ we defined acute kidney injury as at least 50% change in serum creatinine from the reference creatinine value, defined as the minimum of all serum creatinine values within 6 months of the admission.²⁶ Sepsis and cardiac complications were defined by applying the selection criteria developed by the Agency for Healthcare Research and Quality to *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnostic codes.²⁷ Development of vasospasm was determined based on the clinical and radiographic diagnosis in the medical records. The need for inotropic therapy (dobutamine and milrinone) was determined from the pharmacy database. Resource utilization was assessed by hospital and ICU length of stay, whereas cost of hospitalization was estimated using the ratio of cost-to-charge for urban hospitals in the South Atlantic division²⁸ and was adjusted for inflation (Supplemental Digital Content, Supplemental Methods, <http://links.lww.com/AA/B384>).

Covariates and Development of High-Dimensional Propensity Score

The presence of underlying comorbidities was identified by ICD-9-CM codes and Charlson-Deyo Comorbidity Index.^{29,30} We used modified Fisher grade scores to determine the severity of bleeding by using admission head computerized tomography.^{31,32} Hunt-Hess class was additionally obtained for each patient to account for the severity of clinical presentation.³³ Surgical treatment of SAH was defined by primary or secondary ICD-9-CM procedure codes for microvascular neurosurgical clipping (39.51 and 39.52) or endovascular coiling (39.72 and 39-79) and was confirmed by the manual review of medical records.

To account for the potential difference in underlying disease severity between patients, with and without echocardiogram for each patient, we calculated the probability of undergoing echocardiography given clinical characteristics using high-dimensional propensity score calculated with multistep algorithm that implements proxy adjustment using multiple data dimensions. The algorithm eliminates covariates with very low prevalence and minimal potential for causing bias and then uses propensity score techniques

to adjust for a large number of target covariates.³⁴ In addition to demographic and practice-related d covariates (age, sex, ethnicity, year of admission, month of admission, and weekend admission status), we identified l categorical or numeric predefined covariates (based on the context knowledge, we chose SAH severity scores, anatomical location of aneurysm, history of cardiac disease, and Charlson Comorbidity Index) and multiple empirical k covariates from several data dimensions (secondary ICD-9-CM diagnostic codes, inpatient procedures, and drugs dispensed on the first admission day). We assessed recurrence of codes to prioritize and select covariates for adjustment by their potential for controlling confounding that is not conditional on exposure and other covariates. By using multivariable logistic regression, a propensity score was estimated for each subject as the predicted probability of exposure (having echocardiogram) conditional on all $d + l + k$ covariates. We varied the number of empirical covariates for inclusion in the propensity score modeling as a sensitivity analysis.

Statistical Analysis

The analytical plan followed the STROBE recommendations.³⁵ The survival time was calculated from the admission date to the date of death from any cause. A Cox proportional hazard model was used to estimate hazard ratios (HRs) with 99% confidence intervals (CIs) for death associated with different RLVD groups, after adjustment for propensity to undergo echocardiography by entering propensity score calculated for each patient into each model as a continuous variable. Separate multivariable logistic regression analyses were used to estimate odds ratios (ORs) with 99% CI for each hospital complication associated with different RLVD groups, after adjustment for propensity to undergo echocardiography. As a sensitivity analysis, we formed matched sets of patients, with and without echocardiography, who have a similar propensity score value. Patients were matched on the logit of the propensity score using a caliper of 0.2 SDs of the logit of the propensity score. A Cox proportional hazards model was fit to matched sample where the model contained echocardiography status as the sole predictor variable, stratified on the matched pairs. Area under the receiver operating curve with 99% CI and Hosmer-Lemeshow test was used to assess model discrimination and goodness of fit. Bonferroni method was used to adjust for multiple comparisons. Statistical analyses were performed with SAS (version 9.3, SAS Institute Inc., Cary, NC).

RESULTS

Clinical Characteristics of the Cohort and Prevalence of Stress Cardiomyopathy

Among 715 SAH patients, 28% (200/715) had an echocardiogram for clinical evidence of cardiac dysfunction during hospitalization, the most common being acute LV dysfunction, suspected acute ischemic event, changes in electrocardiogram and cardiac enzymes, and arrhythmia (Supplemental Digital Content, Supplemental Table S1, <http://links.lww.com/AA/B384>). Among them, 30% (59/200) had evidence of SCM with almost equal distribution of variant SCM-basal (25/59) and classic SCM-apical forms (34/59). The majority of patients in the cohort were

middle-aged females with low comorbidity index, and 92% of them underwent surgical treatment for SAH (Table 1; Supplemental Digital Content, Supplemental Table S2 and S3, <http://links.lww.com/AA/B384>).

Patients with SCM were more likely to have multiple comorbidities ($P = 0.0004$) and to present with more severe bleeding ($P = 0.01$). African American patients were less likely to have either form of cardiomyopathy ($P = 0.01$). Up to 52% of patients with no RLVD had elevated cardiac biomarkers, most often creatine kinase composed of muscle and brain subunits. Ejection fraction was significantly lower in patients with each type of SCM compared with patients with no RLVD ($P < 0.0001$). In the subset of 48 patients with echocardiographic evaluation of LV diastolic function, we observed a trend toward impaired LV diastolic function in the SCM group with significantly lower E ($P = 0.004$) and E' ($P = 0.02$) compared with patients without RLVD (Supplemental Digital Content, Supplemental Table S4, <http://links.lww.com/AA/B384>). Only 5 patients had repeated echocardiogram: 4 patients with apical SCM and 1 patient with basal SCM had subsequent normal echocardiogram within 10 days of first testing.

Short- and Long-Term Survival and Cause of Death

The median follow-up time was 7.6 years with a maximum follow-up of 13 years. Patients with either form of SCM had lower 1-, 5-, and 10-year survival compared with patients who did not have echocardiogram, but so did the patients whose clinically indicated echocardiogram had no RLVD (Table 1; Supplemental Digital Content, Supplemental Table S3, <http://links.lww.com/AA/B384>).

By using a high-dimensional propensity score model with an area under the receiver operating curve of 0.78 (95% CI, 0.73–0.83), we further adjusted for 60 admission covariates to account for the propensity to undergo echocardiogram that may have reflected underlying severity of disease as a confounder (Table 2). In the multivariable Cox regression analysis, the propensity score-adjusted risk of death remained significantly higher for patients who underwent echocardiography for clinically indicated reason regardless of the presence of RLVD (HR, 1.70; 99% CI, 1.13–2.54, $P = 0.0007$). For patients with SCM, the association was not significant (HR, 1.43; 99% CI, 0.75–2.59, $P = 0.13$) when compared with patients without an echocardiogram after adjusting for propensity score (Table 3 and Fig. 1). When compared with patients who did not have an echocardiogram, the risk of death was higher for those with no RLVD (HR, 1.80; 99% CI, 1.17–2.74; Table 3). There was no evidence of significant difference in adjusted HR between patients with different types of SCM and those with no RLVD (data not shown). Sensitivity analysis performed running Cox proportional hazards model on the propensity score-matched sample gave similar result as the model that included propensity score as a continuous variable with HR of 1.63 (99% CI, 1.15–2.31). Twenty-one percent of all patients with cardiomyopathy and 15% of patients without cardiomyopathy died in the hospital ($P = 0.27$). Among patients with SCM, the most common primary causes of death after hospital discharge were neoplastic disease (29%), cerebrovascular disease (24%), and cardiovascular disease (17%).

Table 1. Clinical Characteristics and Unadjusted Outcomes Among Subarachnoid Hemorrhage Patients Stratified by the Echocardiographic Findings

Variables	No echocardiography (n = 515)	No RLVD (n = 141)	Stress cardiomyopathy (n = 59)
Age (y), mean (SD)	53 (13)	56 (14)	59 (12) ^a
Female sex, n (%)	352 (68)	93 (66)	46 (78)
African American ethnicity, n (%)	91 (18)	28 (20)	3 (5) ^{a,b}
Coronary artery disease, n (%)	31 (6)	15 (10)	7 (12)
Hyperlipidemia, n (%)	37 (7)	25 (18) ^a	10 (18)
Chronic kidney disease, n (%)	28 (5)	9 (6)	5 (9)
Charlson Comorbidity Index, median (25th–75th)	1 (1–2)	2 (1–3) ^a	2 (1–3) ^a
Fisher grade ≥ 3, n (%)	400 (78)	122 (87)	55 (93)
Hunt and Hess Grade, n (%)			
1–2	256 (50)	57 (40)	9 (15) ^{a,b}
3	163 (32)	39 (28)	20 (34)
4–5	95 (18)	45 (32) ^a	30 (51) ^a
Surgery type, n (%)			
Microsurgical clipping	386 (75)	91 (64)	37 (63)
Endovascular coiling	83 (16)	43 (31) ^a	18 (31)
Affected artery, n (%)			
Anterior circulation	292 (58)	80 (57)	28 (50)
Posterior circulation	166 (33)	49 (35)	26 (45)
Ejection fraction (%), mean (SD)	Not available	61 (6)	40 (15) ^b
Peak CK (U/L), median (25th–75th)	123 (55–279)	140 (77–256)	187 (92–471)
Peak CK-Mb (ng/mL), median (25th–75th)	3.0 (2.0–5.0)	4.0 (2.8–6.4)	6.4 (3.6–15.0) ^{a,b}
Peak troponin T (ng/mL), median (25th–75th)	<0.03 (<0.03–<0.03)	0.03 (<0.03–0.09)	0.13 (0.04–0.55) ^{a,b}
Resource utilization, median (25th–75th)			
Days in intensive care unit	10 (6–15)	15 (10–22) ^a	19 (15–23) ^a
Days in hospital	17 (12–28)	26 (15–44) ^a	35 (22–48) ^a
Hospital cost (\$1000)	56 (36–89)	96 (57–145) ^a	133 (92–147) ^a
Hospital complications, n (%)			
Mechanical ventilation ≥72 h	257 (50)	107 (76) ^a	56 (95) ^{a,b}
Cardiac complications	80 (16)	58 (41) ^a	37 (63) ^a
Acute kidney injury	73 (14)	42 (29) ^a	15 (26)
Severe sepsis	44 (9)	20 (14)	21 (37) ^{a,b}
Vasospasm	172 (33)	60 (43)	32 (54) ^a
Discharge to home or rehabilitation center, n (%)	358 (79)	67 (63) ^a	28 (60) ^a
Unadjusted survival			
Hospital mortality, n (%)	64 (12)	34 (24) ^a	12 (20)
1-y cumulative survival (%)	83	62 ^a	68 ^{a,b}
5-y cumulative survival (%)	77	56 ^a	62 ^{a,b}
10-y cumulative survival (%)	73	52 ^a	47 ^{a,b}

CK = creatine kinase; CK-Mb = CK composed of muscle and brain subunits; RLVD = regional left ventricular systolic dysfunction.

P < 0.05 after Bonferroni correction comparing with

^ano echocardiography and

^bno RLVD groups. In this case, $\alpha < 0.0167$ was considered statistically significant.

Table 2. Variations in Covariate Adjustment for the Propensity Score for Having Echocardiography

Covariates included in propensity score model	Covariates list	Number of covariates adjusted	c-Statistic of propensity score model (99% CI)
Demographic and practice related (d)	Age, sex, ethnicity, year of admission, month of admission, weekend admission status.	d = 6	0.64 (0.59–0.70)
Demographic and practice related + predefined (l)	+ Hunt Hess score, anatomical location of aneurysm, history of cardiac disease, Charlson Comorbidity Index	d = 6, l = 4	0.70 (0.64–0.76)
Demographic and practice related + predefined + empirical (k)	+ diagnostic codes, inpatient procedures, drugs dispensed on the first admission day ^a	d = 6, l = 4, k = 50	0.78 (0.73–0.83)

CI = confidence interval.

^aEmpirical variables included full *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnostic and inpatient procedure codes and drugs dispensed on the first admission day. We aggregated RxNorms to group drugs organized according to the US Department of Veterans Affairs National Drug File-Reference Terminology.

Major Complications and Resource Utilization

Major hospital complications, including prolonged mechanical ventilation, severe sepsis, and cardiac complications, were more common in patients with SCM (Table 1). The multivariate analysis did not demonstrate a statistically

significant association between SCM and vasospasm. Interestingly, among patients with vasospasm, patients with SCM-apical and SCM-basal had a higher use of vasopressors and inotropes (35% and 57%, respectively) compared with patients with no echocardiogram or no RLVD

Table 3. High-Dimensional Propensity Score-Adjusted Association Between Stress Cardiomyopathy and Survival

Model	Hazard ratio (99% confidence interval)				
	Echocardiography versus no echocardiography	No RLVD versus no echocardiography	SCM versus no echocardiography	SCM-apical versus no echocardiography	SCM-basal versus no echocardiography
Unadjusted model	2.08 (1.46–2.95)	2.12 (1.41–3.11)	2.02 (1.14–3.34)	1.84 (0.87–3.45)	2.30 (0.96–4.64)
Adjusted for propensity for having echocardiogram	1.70 (1.13–2.54)	1.80 (1.17–2.74)	1.43 (0.75–2.59)	1.26 (0.54–2.59)	1.70 (0.68–3.63)

The propensity score was calculated for each patient as the probability of undergoing echocardiography using multistep algorithm that implements high-dimensional proxy adjustment using 60 clinical variables.

RLVD = regional left ventricular dysfunction; SCM = stress cardiomyopathy.

(9% and 13%, respectively, $P < 0.0001$). Even after adjustment with high-dimensional propensity score, patients with SCM had higher adjusted odds for cardiac complications (OR, 5.3; 99% CI, 2.3–12.3) and severe sepsis (OR, 3.0; 99% CI, 1.2–7.6) compared with patients who did not have an echocardiogram (Table 4). The odds of having cardiac complications (OR, 6.1; 99% CI, 1.8–20.2) and severe sepsis (OR, 5.3; 99% CI, 1.6–17.2) for patients with variant cardiomyopathy-basal form were significantly higher compared with those with no echocardiogram. When analysis was limited only to patients who had an echocardiogram, the adjusted OR for severe sepsis was significantly higher in all patients with SCM (OR, 2.7; 99% CI, 1.04–7.3) and particularly those with cardiomyopathy-basal compared with patients with no RLVD (OR, 4.8; 99% CI, 1.4–16.3; Table 5).

DISCUSSION

In a single-center cohort, we have demonstrated that 28% of SAH patients undergoing surgical treatment had clinical evidence of cardiac dysfunction requiring evaluation with echocardiography. Among those patients, one-third had SCM with similar distribution of classic, predominately apical RLVD and variant, predominately basal RLVD forms. Our study adds to the evidence that the variant form may be as common as the more frequently reported classic form while confirming the previously reported rates of SCM in SAH patients between 3% and 28%.^{2,4,9,18,19,36–39} After adjustment with high-dimensional propensity score regression, in spite of the increase in hospital complications and resource utilization, short- and long-term survivals were not different between patients with either SCM form in comparison with patients without RLVD but were lower compared with patients who did not have clinical cardiac dysfunction requiring an echocardiographic evaluation. We observed no difference in cardiovascular-specific mortality rate after discharge. Our finding corroborates recent reports of favorable long-term prognosis for SCM patients with cardiovascular mortality comparable with age- and sex-matched population and recurrence rate of 10% over 4 years.^{4,6,14,20,21}

Even after adjustment with high-dimensional propensity score, the risk of death remained significantly higher in those who had an echocardiogram, regardless of whether the echocardiogram showed normal or abnormal RLVD. Most patients tested with echocardiography had clinical evidence of cardiac dysfunction, manifesting with LV dysfunction, chest pain, electrocardiographic changes, or arrhythmia. The proportion of SAH patients in our cohort requiring echocardiogram for clinically indicated reasons is similar to other cohort reports, ranging from 30%

to 44%.^{9,36,39} This suggests that there were hemodynamic or arrhythmic abnormalities that prompted ordering the echocardiogram that were not captured in our propensity score or available structured electronic clinical data and often are only present in clinical text notes. Alternatively, it is possible that our assessment of RLVD using qualitative assessment of LV segmental wall motion was not sensitive enough to detect clinically relevant ventricular dysfunction that prompted the order for an echocardiogram. The subtle abnormalities of systolic function not appreciated with qualitative assessment that led to clinical instability may have been appreciated with more sophisticated measures. Strain analysis with automated software has identified LV systolic dysfunction despite normal qualitative wall motion and ejection fraction in patients with heart failure.⁴⁰ In addition, in patients with severe aortic stenosis, quantitative measures of LV longitudinal strain are abnormal, despite a normal ejection fraction.⁴¹ Future studies evaluating the use of advanced evaluation of LV systolic function in SAH patients are warranted.

Patients with SCM had significantly increased odds for developing cardiac complications, implying that cardiomyopathy had a functional significance as it has been shown in patients with different causes of SCM.^{42,43} Severe sepsis was significantly more common in those with SCM even after adjustment for other clinical factors. Although prolonged intubation among SAH patients with SCM has been reported,⁹ the increased occurrence of severe sepsis is intriguing and may indicate a potential overlap in pathophysiology between the 2 conditions.⁴⁴ Thus, SCM in SAH patients is associated with higher burden of cardiac and noncardiac complications that may lead to significantly increased resource utilization and hospital cost similar to patients with SCM associated with other conditions.^{4,14}

The prevalence of vasospasm was not different between the patients with SCM and those without RLVD. Previous reports suggest that severe RLVD is a risk factor for delayed cerebral ischemia from vasospasm, but not vasospasm itself.^{9,38} In SCM patients with low cardiac output, the blood pressure goals for hemodynamic augmentation⁴⁵ can be difficult to achieve, which is consistent with our finding of increased use of inotropes and vasopressors in patients with SCM and vasospasm. Because catecholamine toxicity is the postulated mechanism for the cardiomyopathy, the administration of catecholamine-based vasopressors and inotropes could worsen the disease process and affect survival.

The retrospective nature of our study limits our evaluation of the functional outcomes of the patients with tools such as Modified Rankin Scale. We used discharge to a

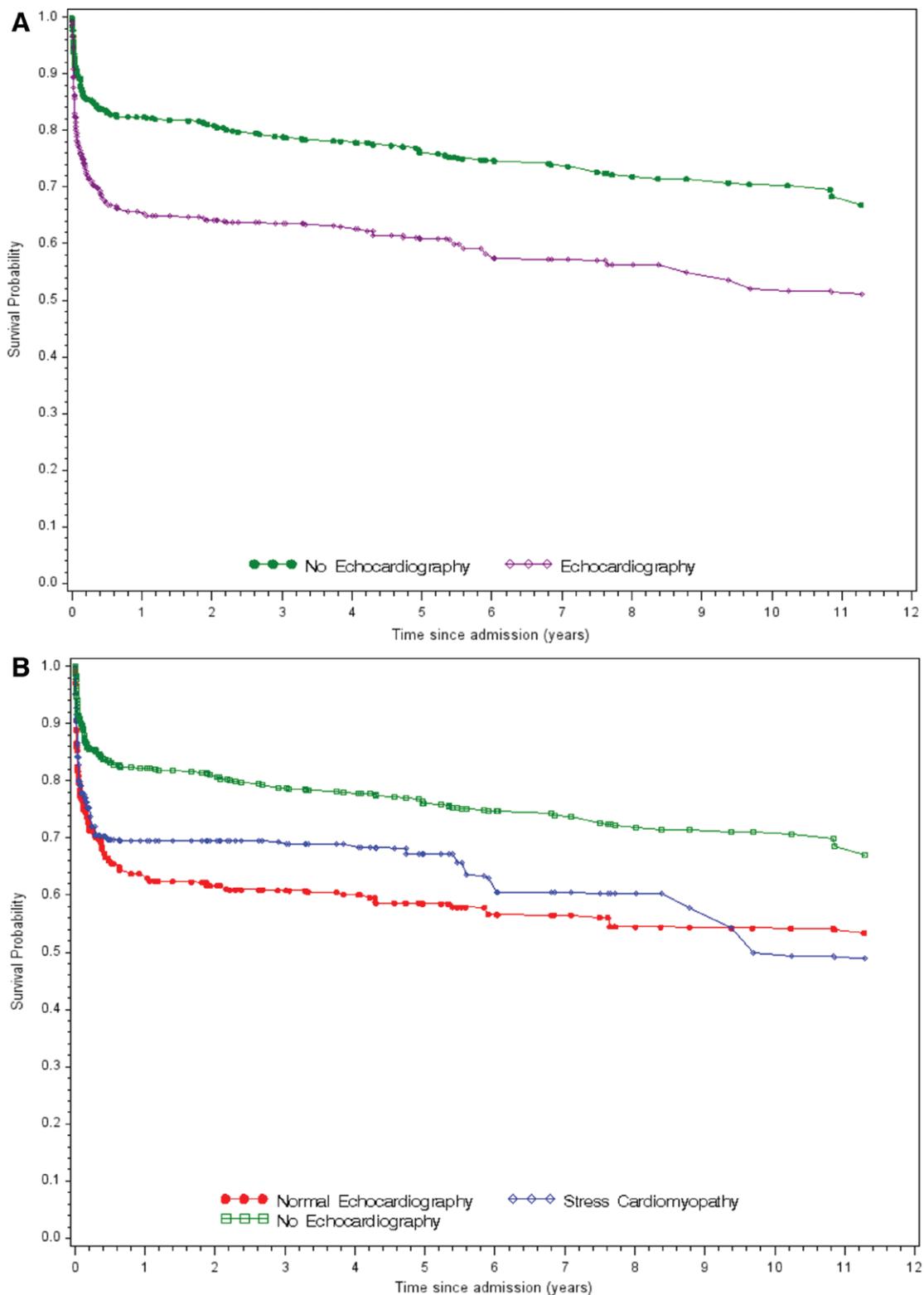


Figure 1. High-dimensional propensity score-adjusted survival curves for patients with and without echocardiogram (A) and patients with an echocardiogram stratified by regional left ventricular dysfunction (B). $P < 0.05$ by log-rank test.

rehabilitation center or to home as a surrogate for a moderate disability or less but were unable to demonstrate significance in the negative association between SCM and this outcome. A sample size larger than in our study would be required to further test the recent observation of

greater incidence of poor outcome and death in patients with midventricular wall motion abnormalities, a subgroup of basal SCM.¹⁹

This was a retrospective cohort; hence, we can neither make the causal inference nor exclude bias from

Table 4. High-Dimensional Propensity Score-Adjusted Association Between Stress-Induced Cardiomyopathy and Hospital Complications

Outcomes	Adjusted odds ratio (99% confidence intervals)				AUC (99% confidence interval) ^a
	Echocardiography versus no echocardiography	SCM versus no echocardiography	SCM-apical versus no echocardiography	SCM-basal versus no echocardiography	
Mechanical ventilation ≥72 h	1.6 (0.9–3.01)	4.0 (0.8–2.7)	3.7 (0.5–28.5)	4.6 (0.3–74.8)	0.82 (0.79–0.86)
Cardiac complications	3.0 (1.8–5.2)	5.3 (2.3–12.3)	4.7 (1.6–13.6)	6.1 (1.8–20.2)	0.75 (0.69–0.81)
Acute kidney injury	1.7 (0.9–3.0)	1.2 (0.5–3.2)	0.9 (0.3–3.2)	1.7 (0.5–5.9)	0.66 (0.59–0.73)
Severe sepsis	1.6 (0.8–3.2)	3.0 (1.2–7.6)	1.8 (0.5–6.1)	5.3 (1.6–17.2)	0.70 (0.62–0.78)
Vasospasm	1.3 (0.8–2.1)	1.5 (0.7–3.4)	1.3 (0.5–3.7)	1.7 (0.6–5.3)	0.62 (0.56–0.68)
Discharge to home or rehabilitation center	0.6 (0.4–1.0)	0.8 (0.3–1.7)	1.5 (0.5–4.3)	0.3 (0.1–1.1)	0.68 (0.63–0.74)

AUC = area under the curve; SCM = stress cardiomyopathy.

^aAUC indicates area under the receiver operator curve for each multivariable logistic regression model used to estimate odds ratios while adjusting for propensity for having echocardiogram with multistep algorithm implementing 60 clinical variables. Hosmer-Lemeshow goodness-of-fit test *P* values for all models were nonsignificant indicating good fit.

Table 5. High-Dimensional Propensity Score-Adjusted Association Between Stress Cardiomyopathy and Hospital Complications Among Subarachnoid Hemorrhage Patients Who Had Echocardiogram

Outcomes	Odds ratio (99% confidence interval)			AUC ^a (99% confidence interval)
	SCM versus no RLVD	SCM-apical versus no RLVD	SCM-basal versus no RLVD	
Mechanical ventilation ≥72 h	3.1 (0.6–17.1)	2.8 (0.4–22.2)	3.7 (0.2–60.1)	0.84 (0.75–0.93)
Cardiac complications	2.2 (0.9–5.2)	2.0 (0.7–5.7)	2.5 (0.8–8.6)	0.66 (0.56–0.76)
Acute kidney injury	0.7 (0.3–1.9)	0.5 (0.2–1.9)	1.0 (0.3–3.4)	0.61 (0.50–0.72)
Severe sepsis	2.7 (1.04–7.3)	1.6 (0.5–5.8)	4.8 (1.4–16.3)	0.70 (0.58–0.83)
Vasospasm	1.4 (0.6–3.3)	1.3 (0.5–3.7)	1.7 (0.5–5.2)	0.57 (0.47–0.68)
Discharge to home or rehabilitation center	1.2 (0.5–2.7)	2.2 (0.7–6.4)	0.5 (0.1–1.7)	0.66 (0.55–0.75)

AUC = area under the receiver operating curve; RLVD = regional left ventricular dysfunction; SCM = stress cardiomyopathy.

^aAUC indicates area under receiver operator curve of each multivariable model adjusted for high-dimensional propensity score. Hosmer Lemeshow goodness of fit test *P* values were nonsignificant for all models indicating good fit.

unmeasured factors. The reported prevalence for SCM needs to be interpreted cautiously, because we cannot exclude the possibility of undiagnosed SCM in patients without echocardiogram. We attempted to control for selection bias with multivariable statistical methods and the use of high-dimensional propensity score specifically designed for risk adjustment in claims data³⁴ to offset the potential confounding effect of disease severity and clinical evidence of cardiac dysfunction on the probability of having echocardiogram. Although intriguing, the finding that patients with clinical evidence of cardiac dysfunction had worse outcomes regardless of the echocardiographic findings of SCM needs to be interpreted in the context of small sample size and retrospective study design. Although we assessed comorbidities, sepsis, and cardiac complications using validated approach with ICD-9-CM codes,^{29,46} the subtle differences in coding definitions may lead to risk underassessment. The inability to observe significant difference, rather than trend, in worse diastolic dysfunction among SCM patients may reflect the small sample size of patients with available diastolic function measurements. Although this is a single-institution report, it comprises a cohort of SAH patients obtained over 10 years with outcomes comparable with that reported in the literature.

CONCLUSIONS

Among SAH patients who had an echocardiogram for clinically indicated reasons, variant basal SCM is almost as common as classic apical form. Although we observed

no difference in long-term survival among patients with SCM and those without RLVD, patients who had echocardiogram for clinically evident cardiac dysfunction had significantly decreased long-term survival compared with patients with no echocardiogram, even after adjusting for multiple clinical factors with high-dimensional propensity score. This may suggest that clinical events that prompt the order of an echocardiogram, and possibly subtle RLVD that is not detected with qualitative assessments of LV systolic function, have important prognostic implications. The significant association between severe sepsis and SCM warrants future studies to determine whether these complications may augment LV systolic dysfunction among SAH patients. ■

DISCLOSURES

Name: Azra Bihorac, MD, MS.

Contribution: This author helped design the study, conduct the study, analyze the data, write the manuscript, and revise the manuscript for important intellectual content.

Attestation: Azra Bihorac has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.

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