**SUPPLEMENTAL DIGITAL CONTENT**

Supplemental Methods

Data source

The study was approved by the University of Florida (UF) Institutional Review Board and Privacy Office. Using UF Integrated Data Repository (UF IDR) we integrated multiple existing clinical and administrative databases at the UF Health Hospital. The administrative database for the UF Health Hospital, established in 1990, provides detailed information for all discharged patients’ demographics, clinical outcomes, hospital charges, insurance status, and physician provider status and identifying number. The final database also contained laboratory data (including daily serum creatinine and other relevant laboratory and microbiology data), pharmacy data and blood bank data, and International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for up to fifty diagnoses and procedures, data on long-term mortality and ICD-10 codes for cause of death received from The Bureau of Vital Statistics at the Florida Department of Health. We performed manual review of medical records to obtain data related to affected artery, SAH severity and treatment, anatomical location of cerebral aneurysm, vasospasm, electrocardiographic findings, cardiac markers, previous cardiac history, clinical indications for ordering echocardiogram and cardiology consult notes when available (review was performed by three neuro-intensivists (EM, PW, AB) and a cardiologist (JP)). We excluded eight patients with known LV systolic dysfunction prior to admission and those deemed to have documented acute coronary disease during hospitalization by JP review.

Patient population

We identified all patients discharged with the primary or secondary diagnosis of SAH International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic code 430 between January 1, 2000 and November 39, 2010 who underwent surgical treatment requiring hospital admission for longer than 24 hours. Patients who were younger than age 18 at the time of admission were excluded. The type of surgical procedure was determined based on primary procedure codes and review of operative notes. We excluded patients with a primary or secondary diagnosis of arteriovenous malformation (ICD-9-CM code 747.81) or head trauma (ICD-9-CM codes 801.00-803.20, 850.5-853.06, and 873.0-873.44) to exclude traumatic SAH as previously reported. [1](#_ENREF_1) In order to limit the current analysis to only those patients with stress cardiomyopathy, eight patients with a known history of heart failure prior to admission or a documented acute coronary disease during hospitalization were excluded. The final cohort consisted of 715 patients.

Echocardiography

For 200 patients in the cohort an echocardiogram was performed for clinically indicated reasons (Supplemental Table S1), most commonly clinical diagnoses of acute LV dysfunction (51/200, 25) , suspected acute ischemic heart disease (39/200), and changes in electrocardiogram or cardiac enzymes (59/200) and arrhythmia (19/200). For each patient JP 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’)).[2](#_ENREF_2) 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 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. [3](#_ENREF_3)

Using Mayo Clinic criteria [4](#_ENREF_4) 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 three groups: 1. No RLVD if no segmental wall motion abnormalities were identified; 2. Classic SCM-apical if the average wall motion score index for apical segments was greater than the score for basal segments; and 3. Variant SCM-basal 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. For patients who were discharged alive after index hospitalization for SAH we used full name, birth date, and Social Security number to search the Social Security Death Index in July 2013 to assess survival through January 31, 2013 (because of an approximate 6-month lag in data reporting) [5](#_ENREF_5) that was also date of data censoring for patients who were last known to be alive allowing at least two years of follow-up time as cohort included patients admitted between 2000 and 2010. ICD-10 codes for primary cause of death were obtained from death certificates from Florida Bureau of Statistics using matching algorithm that utilized full name, date of birth and date of death.

Secondary outcomes included following major hospital complications: 1. Prolonged mechanical ventilation (MV) (defined as MV duration of at least 72 hours); 2. Acute kidney injury (AKI); 3. Severe sepsis; 4. Cardiac complications including cardiogenic shock, cardiac arrhythmias, or need for inotropes, 5. Occurrence of vasospasm and 6. Hospital discharge to either home or rehabilitation center. Applying consensus Risk, Injury, Failure, Loss, and End-stage kidney (RIFLE) criteria [6](#_ENREF_6) we defined AKI as at 50% change in serum creatinine from the reference creatinine defined as the minimum of all creatinine values within six months of the admission. [7](#_ENREF_7) For the definition of sepsis we followed the selection criteria developed by the Agency for Healthcare Research and Quality for the patient safety indicators “Postoperative Sepsis”. [8](#_ENREF_8) Organ failure associated with sepsis was identified by adding ICD-9-CM codes for acute organ dysfunction to sepsis diagnosis. [9](#_ENREF_9),[10](#_ENREF_10) We identified cardiogenic shock by ICD-9-CM code 785.51 and arrhythmia using ICD-9-CM codes 426.xx and 427.xx. The need for inotrope therapy (dobutamine and milrinone) was determined from the pharmacy database. Resource utilization was assessed by hospital and ICU length of stay and cost of hospitalization that was estimated by applying the ratio of cost-to-charge for urban hospitals in the South Atlantic division to the amount charged for hospitalization. [11](#_ENREF_11) The cost-to-charge ratio files are provided by Healthcare Cost and Utilization Project (HCUP), a federal-state-industry partnership sponsored by the Agency for Healthcare Research and Quality. The charge information represents the amount that hospitals billed for services but does not reflect how much hospital services actually cost or the specific amounts that hospitals received in payment. The HCUP Cost-to-Charge Ratio Files enable this conversion. Each file contains hospital-specific cost-to-charge ratios based on all-payer inpatient cost for nearly every hospital. Cost information was obtained from the hospital accounting reports collected by the Centers for Medicare and Medicaid Services.[11](#_ENREF_11) We converted all costs to 2010 dollars using the Consumer Price Index for Medical Services to adjust for inflation over the years.

Covariates and Development of High-Dimensional Propensity score

The presence of underlying comorbidities was identified by ICD-9-CM codes based on criteria described by Elixhauser et al. [12](#_ENREF_12) In addition, Charlson-Deyo comorbidity index was calculated for each individual based on the diagnostic codes recorded during hospital admission and higher scores indicate greater comorbid disease. [13](#_ENREF_13) Three investigators with training in neuro-anesthesiology and neurocritical care (AB, EM and PW) independently performed manual review of medical records and imaging studies to obtain data related to affected artery, SAH severity and treatment, anatomical location of cerebral aneurysm and vasospasm. We used modified Fisher grade scores to determine severity of bleeding using admission head computerized tomography: Fisher grade 1 was defined as thin blood, less than 1 mm in cisterns without intraventricular hemorrhage; Fisher grade 2 as thin blood with intraventricular hemorrhage, Fisher grade 3 as thick blood, greater than 1 mm, without intraventricular hemorrhage; and, Fisher grade 4 was defined as thick blood with intraventricular hemorrhage. [14](#_ENREF_14),[15](#_ENREF_15) Hunt-Hess class was additionally obtained for each patient to account for the severity of clinical presentation. [16](#_ENREF_16) 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. The type of pharmacologic therapy (phenylephrine, epinephrine, norepinephrine and vasopressin) routinely used for hyperdynamic augmentation of blood pressure during vasospasm was determined by combining data from the pharmacy database with the manual review of the records.

To account for the potential difference in underlying disease severity between patients with and without echocardiogram we applied high-dimensional propensity score developed specifically for the use with claim and pharmacy data. For each patient up to fifty diagnostic and procedure ICD-9-CM codes where available while all medications dispensed on the day of admission were extracted from the pharmacy database. The propensity score was calculated for each patient to account for the probability of undergoing echocardiography given her clinical characteristics using multistep algorithm that implements high-dimensional proxy adjustment in claims data. The algorithm identifies a large number of covariates in multiple data dimensions, 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. [17](#_ENREF_17) In addition to demographic *d* covariates (age, gender, ethnicity, year of admission year, month of admission, and weekend admission status) we identified *l* categorical or numeric predefined covariates (based on context knowledge we chose SAH severity scores, anatomical location of aneurysm, previous 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 in order to prioritize and select covariates for adjustment by their potential for controlling confounding that is not conditional on exposure and other covariates. 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. The achievement of balance produced by propensity score was assessed by modeling each variable using echocardiography, propensity score, and their interaction in the regression model and p-values for all the variables of interest were all above 0.2.

Statistical Analysis

 The analytical plan followed the STROBE recommendations. [18](#_ENREF_18) Patients were stratified into groups based on RLVD (SCM-Apical, SCM-Basal and no RLVD). Patients who did not have any echocardiography for clinically indicated reason were analyzed as a separate group. Frequencies of categorical variables were reported as a percentage and the Pearson χ2 test or Fisher's exact test was applied as appropriate to test for association between categorical variables. For continuous variables, means (standard deviation) were reported for variables that exhibited a normal distribution and compared using Student’s T-test or analysis of variance (ANOVA), when appropriate whereas continuous variables that did not satisfy the normality assumptions were reported as medians, 25th and 75th percentiles and the Kruskal-Wallis test was used for comparisons. Kolmogorov-Smirnov test was performed to test the normality of distribution.

For the survival analysis, survival was calculated from the admission date to the date of death from any cause or the date of data censoring. A Cox proportional hazard model was used to estimate hazard ratios (HR) with 99% confidence intervals (99% CI) for death associated with different RLVD groups, after adjustment for propensity to undergo echocardiography given her clinical characteristics on admission. We plotted adjusted survival curves by RLVD groups based on a stratified Cox model adjusted for propensity scores. [19](#_ENREF_19) The proportional-hazards assumption for all models was tested within the PROC PHREG module.

Separate multivariable logistic regression analyses were used to estimate odds ratios (OR) with 99% CI for each secondary outcome associated with different RLVD groups, after adjustment for propensity to undergo echocardiography given her clinical characteristics on admission using propensity described propensity score. 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 standard deviations 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 (AUC) with 99% CI was used to assess model discrimination and Hosmer-Lemeshow test p-value was used for goodness of fit. Bonferroni method was used to adjust for multiple comparisons. Statistical analyses were performed with SAS (version 9.3, Cary, NC).

Table S1. Clinical indications for ordering echocardiogram

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Clinical Indications for ordering echocardiogram | All Cohort(n=200) | No RLVD (n=141) | SCM-Apical (n=34) | SCM-Basal (n=25) |
| Changes in electrocardiogram or cardiac enzymes, n (%) | 58 (29) | 41 (29) | 11 (32) | 6 (24) |
| Acute left ventricular dysfunction or heart failure, n (%) | 51 (26) | 25 (18) | 16 (47) | 10 (40) |
| Suspected acute ischemic heart disease, n (%) | 39 (20) | 31 (22) | 3 (9) | 5 (20) |
| New onset arrhythmia, n (%)1 | 19 (9) | 11 (8) | 4 (12) | 4 (16) |
| Suspected valvular disease, n (%) | 22 (11) | 22 (16) | 0 (0) | 0 (0) |
| Other, n (%) | 11 (5) | 11 (8) | 0 (0) | 0 (0) |

1 Including atrial fibrillation and flutter, supraventricular tachycardia and ventricular tachycardia.

Table S2. Clinical characteristics of 715 patients with subarachnoid hemorrhage.

|  |  |
| --- | --- |
|  Variables | Values |
| Days between surgical procedure and echocardiogram, median (25th, 75th) | 5 (2,11) |
| Echocardiographic findings, n (%) |  |
| Echocardiography not performed (no clinical indication) | 515 (62) |
| Echocardiography performed for clinical indication  | 200 (28) |
| Stress-induced cardiomyopathy | 59 (8) |
| Classic Apical cardiomyopathy | 34 (5) |
| Variant Basal cardiomyopathy | 25 (3) |
| No regional left ventricular dysfunction | 141 (20) |
| Baseline Characteristics |  |
| Age, mean (standard deviation) | 54 (13) |
| Female gender, n (%) | 491 (69) |
| African American ethnicity, n (%) | 122 (17) |
| Coronary artery disease, n (%) | 53 |
| Hyperlipidemia, n (%) | 72 |
| Chronic kidney disease, n (%) | 42 (6) |
| End-stage renal disease, n (%) | 5 (0.7) |
| Charlson Comorbidity Index, median (25th, 75th) | 2 (1, 2) |
| Surgery type, n (%) |  |
| Microsurgical Clipping | 514 (72) |
| Endovascular Coiling | 144 (20) |
| Primary outcomes |  |
| Hospital mortality, n (%) | 110 (15) |
| One-year cumulative survival, % | 78 |
| Five-year cumulative survival, % | 72 |
| Ten-year cumulative survival, % | 66 |
| Hospital Complications, n (%) |  |
| Mechanical ventilation ≥ 72 hours,  | 420 (59) |
| Cardiac complications | 175 (24) |
| Acute kidney injury | 130 (18) |
| Severe Sepsis | 85 (12) |
| Vasospasm | 264 (37) |
| Resource Utilization, median (25th, 75th) |  |
| Days in intensive care unit | 12 (6, 17) |
| Days in hospital | 20 (13, 33) |
| Hospital cost ($1000) | 66 (41, 110) |
| Hospital Disposition, n (%) |  |
| Home  | 256 (42) |
| Rehabilitation center  | 197 (33) |
| Nursing home | 84 (14) |
| Long-term acute care hospital | 60 (10) |

Table S3. Clinical characteristics and unadjusted outcomes among subarachnoid hemorrhage patients stratified by the left ventricular function.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  Variables | No Echocardiography(n=515) | No RLVD(n=141) | SCM-Apical(n=34) | SCM-Basal(n=25) |
| Age, mean (standard deviation) | 53 (13) | 56 (14) | 61 (10) a | 57 (13) |
| Female gender, n (%) | 352 (68) | 93 (66) | 30 (88) | 16 (64) |
| African American ethnicity, n (%) | 91(18) | 28 (20) | 0 (0) a,b | 3 (12) |
| Coronary artery disease, n (%) | 31 (6) | 15 (10) | 4 (12) | 3 (12) |
| Hyperlipidemia, n (%) | 37 (7) | 25 (18) a | 3 (9) | 7 (28) a |
| Chronic kidney disease, n (%) | 28 (5) | 9 (6) | 0 (0) | 5 (20) |
| End-stage renal disease, n (%) | 4 (1) | 0 (0) | 0 (0) | 1 (4) |
| Charlson comorbidity Index, median (25th, 75th) | 1 (1, 2) | 2 (1, 3) a | 2 (1, 3) a | 2 (2, 3) a |
| Fisher Grade ≥ 3, n (%) | 400 (78) | 122 (87) | 32 (94) | 23 (92) |
| Hunt and Hess Grade, n (%) |  |  |  |  |
| 1-2 | 256 (50) | 57 (40) | 4 (12) a, b | 5 (20) |
| 3 | 163 (32) | 39 (28) | 13 (38) | 7 (28) |
| 4-5 | 95 (18) | 45 (32) a | 17 (50) a | 13 (52) a |
| Surgery type, n (%) |  |  |  |  |
| Microsurgical Clipping | 386 (75) | 91 (64) | 23 (68) | 14 (56) |
| Endovascular Coiling | 83 (16) | 43 (31) a | 10 (29) | 8 (32) |
| Affected artery, n (%) |  |  |  |  |
| Anterior circulation | 292 (58) | 80 (57) | 17 (52) | 11 (44) |
| Posterior circulation | 166 (33) | 49 (35) | 16 (48) | 10 (40) |
| Patients with measured CK panel, n (%) | 184 (36) | 104 (73) a | 32 (97) a, b | 22 (88) a |
| Elevated peak CK, n (%) | 91 (18) | 52 (37) a | 20 (59) a | 12 (48) a |
| Elevated peak CK-Mb, n (%) | 89 (17) | 73 (52) a | 28 (82) a, b | 18 (72) a |
| Peak CK U/L, median (25th, 75th) | 123 (55, 279) | 140 (77, 256) | 187 (121, 454) | 174 (64, 507) |
| Peak CK-Mb ng/mL, median (25th, 75th) | 3.0 (2.0, 5.0) | 4.0 (2.8, 6.4) | 7.2 (3.8, 14.1)a, b | 4.9 (3.4, 19.4) a, b |
| Patients with measured Troponin T, n (%) | 160 (31) | 97 (69) a | 27 (79) a | 18 (72) a |
| Elevated peak Troponin T, n (%) | 27 (5) | 40 (28)a | 23 (68) a, b | 13 (52) a |
| Peak Troponin T ng/mL, median (25th, 75th) | <0.03 (<0.03, <0.03) | <0.03 (<0.03, 0.08) | 0.09 (0.04, 0.26) a, b | 0.28 (<0.03, 0.61) a, b |
| Ejection fraction %, mean (standard deviation) | Not available  | 61 (6) | 37 (14) b | 45 (14) b |
| Resource Utilization, median (25th, 75th) |  |  |  |  |
| Days in intensive care unit | 10 (6, 15) | 15 (10, 22) a | 19 (15, 21)a | 20 (15, 27) a |
| Days in Hospital | 17 (12, 28) | 26 (15, 44) a | 36 (25, 50) a | 38 (21, 48) a |
| Hospital cost ($1000) | 56 (36, 89) | 96 (57, 145) a | 124 (92, 145) a | 133 (93, 149) a |
| Hospital complications, n (%) |  |  |  |  |
| Mechanical ventilation ≥ 72 hours | 257 (50) | 107 (76) a | 32 (94) a | 24 (96) a |
| Cardiac complications | 80 (16) | 58 (41) a | 20 (59) a | 17 (68) a |
| Acute kidney injury | 73 (14) | 42 (29) a | 7 (21) | 8 (32) |
| Severe Sepsis | 44 (9) | 20 (14) | 9 (26) a | 12 (48) a, b |
| Vasospasm | 172 (33) | 60 (43) | 18 (53) | 14 (56) |
| Discharge to Home or Rehabilitation Center, n (%) | 358 (79) | 67 (63) a | 21 (70) | 7 (41) a |
| Survival |  |  |  |  |
| Hospital mortality, n (%) | 64 (12) | 34 (24) a | 4 (12) | 8 (32) |
| One-year cumulative survival, % | 83 | 62 a | 75 a, b | 60 a, b |
| Five-year cumulative survival, % | 77 | 56 a | 64 a, b | 60 a, b |
| Ten-year cumulative survival, % | 73 | 52 a | 48 a, b | 45 a, b |

Abbreviations. RLVD, regional left ventricular dysfunction; CK, creatine kinase; CK-Mb, creatine kinase comprised of M (muscle) and B (brain) subunits.

a P-value<0.05 after Bonferroni correction comparing to a no echocardiography group and b to no RLVD group. In this case, α<0.01 was considered statistically significant.

Table S4. Diastolic function among patients with subarachnoid hemorrhage stratified by the left ventricular function.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variables | No RLVD(n=36) | Stress cardiomyopathy(n=12) | SCM-Apical(n=3) | SCM-Basal(n=9) |
| Diastolic abnormalities, n (%) a, b |  |  |  |  |
| None | 30 (83) | 6 (50) | 2 (67) | 4 (44) |
| Impaired Relaxation Pattern | 5 (14) | 2 (17) | 0 (0) | 2 (22) |
| Pseudonormal Pattern | 1 (3) | 3 (25) | 1 (33) | 2 (22) |
| Restrictive Pattern | 0 (0) | 1 (8) | 0 (0) | 1 (11) |
| E, median (25th, 75th) a, b | 106 (96, 122) | 85 (84, 99) | 86 (80, 95) | 85 (84, 102) |
| A, median (25th, 75th) | 71 (58, 91) | 78 (59, 85) | 36 (32, 74) | 82 (72, 86) |
| DT, median (25th, 75th) | 209 (183, 236) | 193 (150, 238) | 175 (141, 205) | 215 (158, 246) |
| E', median (25th, 75th) a | 12 (9, 14) | 7 (6, 12) | 8 (6, 12) | 7 (6, 12) |

Abbreviations. A, atrial filling velocities; SCM, stress cardiomyopathy; DT, deceleration time; E, early filling velocities; E', mitral annular tissue Doppler early diastolic peak velocity; RLVD, regional left ventricular dysfunction.

a P-value<0.05 for comparing no RLVD and stress cardiomyopathy group.

b P-value<0.05 for comparing 3 groups (no RLVD, SCM-Apical and SCM-Basal)

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