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# Age predicts outcomes better than frailty following aneurysmal subarachnoid hemorrhage: A retrospective cohort analysis

Matthew K. McIntyre[a], Chirag Gandhi[b], Andrew Long[a], Alexander Van Hoof[a], Boyi Li[a], Vikas Patel[b], Adil Afridi[a], Mohamed Halabi[a], Meic Schmidt[b], Chad Cole[b], Justin Santarelli[b], Fawaz Al-Mufti[b], Christian A. Bowers[b,*]

[a] *School of Medicine, New York Medical College, 40 Sunshine Cottage Rd, Valhalla, NY, 10595, USA*
[b] *Department of Neurosurgery, Westchester Medical Center, New York Medical College, 100 Woods Road, Valhalla, NY, 10595, USA*

A R T I C L E  I N F O

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A B S T R A C T

*Objective:* Increasing age has been associated with worse outcomes following aneurysmal subarachnoid hemorrhage (aSAH), yet frailty's effect on aSAH outcomes has never been studied. The most common frailty measurement tool is the modified frailty index (mFI). The goal of this study is to compare the effect of frailty versus age as predictors of aSAH outcomes and mortality.

*Patients and methods:* Our institutional aSAH series were retrospectively identified and divided into non-frail (mFI = 0–1) and frail (mFI ≥ 2) cohorts based on admission mFI scores. Primary outcomes were mortality and discharge location. Univariate and multivariate analysis were performed.

*Results:* There were 217 aSAH patients identified and 57 were frail (26.3%). Forty-one (18.9%) patients died and 74 (34%) were discharged home. Frail patients were significantly older ($p < 0.0001$) and had higher Hunt & Hess (HH) ($p = 0.005$) and Fisher ($p = 0.0255$) scores. Frail patients were less likely to receive an intervention (OR = 0.3; 95%CI:0.1–0.6); $p = 0.0056$), be discharged home (OR = 0.32; 95%CI:0.16-0.68; $P = 0.0020$), and were more likely to expire (OR = 2.4; 95%CI:1.2–5; $P = 0.0183$) and develop a complication (OR = 2.6; 95%CI:1.1–6.6; $P = 0.0277$). Multivariate regressions showed that the HH score (OR = 2.7; 95%CI: 1.9–3.0; $P < 0.0001$) followed by age ≥ 65 (OR = 2.7; 95%CI:1.2–6.0; $p = 0.012$) were the only independent predictors of mortality. Likewise, discharge home was best predicted by HH score (OR = 0.24; 95%CI:0.15–0.37; $p < 0.0001$) and age (OR = 0.25; 95%CI:0.1-0.6; $p = 0.003$).

*Conclusion:* Frailty is associated with worse aSAH grades, more complications, and increased mortality, however, increasing age and HH scores were the only independent predictors of aSAH outcomes. This study suggests that HH score and increasing patient age, and not the accumulated co-morbidities at the time of aSAH, better predict outcomes.

## 1. Introduction

The short- and long-term consequences of aneurysmal subarachnoid hemorrhage (aSAH) can be devastating and despite advances in neurocritical care and the less invasive treatment option of endovascular coiling, morbidity and mortality rates remain high [1]. Given the increasing age of our population, several studies have investigated the effect of age on aSAH outcomes, determining that increasing age is one of the most significant predictors of poorer outcomes [2,3]. This effect has mainly been attributed to the accumulating comorbidities over the lifetime, but aside from hypertension, the independent effect of these comorbidities has not been studied [4,5]. Recent studies across the surgical disciplines have investigated the effect of frailty, i.e. a reduced physiologic reserve, on outcomes [6–8]. Frailty is most commonly measured using the modified frailty index (mFI) and has been shown to predict mortality, complications, and discharge location following neurosurgical procedures and across multiple other surgical disciplines [9–11]. Therefore, this study's goals were to determine the effect of frailty on outcomes, complication rates, and mortality rates following aSAH and to compare frailty's effect on age, Hunt & Hess (HH) and Fisher scores. We hypothesized that, like other studies, increasing frailty would be an independent predictor of worse outcomes following aSAH.

* Corresponding author.
*E-mail address:* christian.bowers@wmchealth.org (C.A. Bowers).

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## 2. Patients and methods

### 2.1. Study design and setting

This retrospective cohort study was performed at a quaternary academic medical center with high patient volume (Westchester Medical Center in Valhalla, New York), between June 2014-July 2018 after Institutional Review Board Approval from New York Medical College & Westchester Medical Center. Data was collected for the *a priori* selected variables.

### 2.2. Participant selection

SAH patients were identified by reviewing the departmental patient database and by reviewing the digital subtraction angiogram (DSA) institutional database. All individuals who were found to have aSAH were included. Aneurysmal SAH was defined by the presence of an aneurysm on DSA coupled with a non-traumatic SAH presentation based on initial CT or MRI. Exclusion criteria were traumatic, or non-aneurysmal SAH, incomplete or unavailable records, concurrent non-SAH neurosurgical or acute medical illness, non-acute presentation of SAH, or no hemorrhage on imaging. All data were retrospectively collected using the electronic medical record system.

### 2.3. Measures and outcomes

For each patient, the demographics, aneurysm location and size, anticoagulation/antiplatelet (AC/AP) medication use, body mass index (BMI), and smoking history were collected. A modified frailty index (mFI) score was calculated as previously described based on pre-hemorrhage comorbidities and baseline variables are shown in Table 1. Baseline patient information was collected based on the documented patient interview or family member interview for the medical record. Patients were grouped as mFI ≤ 1 (non-frail) or mFI ≥2 (frail). Primary outcomes were discharged home and mortality. Secondary measures were Hunt & Hess (HH) scores, Fisher scores, extra-ventricular drain (EVD) requirement, admission and discharge Glasgow coma scale (GCS) scores, hospital length of stay (LOS), intensive care unit (ICU) LOS, need for tracheostomy, gastrostomy tube, radiographic evidence of vasospasm, and complications including deep vein thrombosis (DVT), pulmonary embolism (PE), pneumonia, intubation, and vasopressor use.

### 2.4. Statistical analysis

Normal distributions were determined using an Anderson-Darling normality test. A *T*-test was used for normally distributed continuous samples and a Mann-Whitney test was used for non-normally distributed continuous samples and data are shown using mean ± standard error of the mean (SEM). A Fisher's exact test was used for binary variables, and odds ratios (OR) are shown with 95% confidence intervals (95% CI). Kaplan-Meier survival curves were generated for both age ≥ 65 and mFI ≥ 2 for Log-Rank analysis. Univariate logistic regressions for mortality and discharge home were performed using the following variables: mFI ≥ 2, age ≥ 65, HH score, Fisher score, aneurysm location and size, treatment type, sex, race, BMI, AC/AP use, and smoking history. Multivariate logistic regressions utilizing the forward conditional method were then performed only using variables significant in corresponding univariate logistic regression. No collinearity was detected in any multivariate analysis, as defined as a variance inflation factor of < 1 or > 10, and therefore both HH and Fisher scores were included in the same multivariate analyses. Statistical analysis was performed using Prism 8.0.1 [12] and IBM SPSS Version 25 [13]. We defined significance at P < 0.05.

## 3. Results

### 3.1. Baseline features and demographics

Between June 2014 and July 2018, 217 aSAH patients were identified (Fig. 1). The majority of patients were white (122/217, 56.2%), female (142/217, 65.4%), and had an average age of 57.6 ± 1.0 (range: 14–98). Age was normally distributed across the sample (A2 = 0.5102; P = 0.1950). The average HH score was 2.9 ± 0.09 while the average Fisher score was 3.7 ± 0.04. 31 (14.3%), 56 (25.8%), 64 (29.5%), 33 (15.2%), and 33 (15.2%) patients had HH scores of 1, 2, 3, 4, or 5, respectively and was not normally distributed across the population (A2 = 7.040; P < 0.0001). The most common aneurysm location was at the anterior communicating artery (72/217, 33.2%) followed by the posterior communicating artery (43/217; 19.8%). Two patients had two aneurysms treated concurrently with endovascular coil embolization; one had both a posterior cerebral artery and a middle cerebral artery aneurysm while the other patient had an anterior communicating and an internal carotid aneurysm.

A total of 57/217 (26.3%) of patients were classified as frail (mFI ≥ 2) while 160/217 (73.7%) were non-frail. The prevalence of variables used to define the mFI are presented in Table 1. As expected, the most prevalent co-morbidity was hypertension (113/217, 52.1%) followed by diabetes mellitus (28/217, 12.9%) and frail patients had significantly more of each of the mFI co-morbidities compared to non-frail individuals (p < 0.0084). Patient baseline characteristics stratified by group are presented in Table 2. The frail group was significantly older (66.0 vs. 54.6 years; p < 0.0001) and had a higher prevalence of anticoagulant/anti-platelet (AC/AP) use (45.6 vs. 16.5%; p < 0.0001) indicating a poorer overall health status. Sex, race, BMI, smoking history, aneurysm location and aneurysm size were not significantly different between the two groups.

### 3.2. In-hospital outcomes

Frail patients had significantly higher HH (3.3 vs. 2.8; p = 0.0050) and Fisher scores (3.8 vs. 3.6; p = 0.0255) compared to non-frail

**Table 1**
Distribution of the 11 mFI Characteristics Stratified by Frailty. Comparisons between frail and non-frail for each mFI characteristic are shown.

| History of: | Overall (n = 217) | mFI = 0-1 (n = 160) | mFI ≥ 2 (n = 57) | p-value |
|---|---|---|---|---|
| Hypertension on medications | 113 (52.1%) | 60 (37.5%) | 53 (93.0%) | **< 0.0001** |
| Congestive Heart Failure | 5 (2.3%) | 0 (0%) | 5 (8.8%) | **0.0011** |
| Diabetes mellitus | 28 (12.9%) | 3 (1.9%) | 25 (43.9%) | **< 0.0001** |
| History of transient ischemic attack or cerebrovascular accident without neurological deficit | 21 (9.7%) | 2 (1.3%) | 19 (33.3%) | **< 0.0001** |
| Non-independent functional status | 5 (2.3%) | 0 (0%) | 5 (8.8%) | **0.0011** |
| Myocardial Infarction | 7 (3.2%) | 0 (0%) | 7 (12.3%) | **< 0.0001** |
| Peripheral Vascular Disease or ischemic rest pain | 8 (3.7%) | 0 (0%) | 8 (14.0%) | **< 0.0001** |
| Cerebral vascular accident with deficit | 8 (3.7%) | 0 (0%) | 8 (14.0%) | **< 0.0001** |
| Chronic Obstructive Pulmonary Disease, Pneumonia | 11 (5.1%) | 4 (2.5%) | 7 (12.3%) | **0.0084** |
| Previous coronary intervention or angina | 10 (4.6%) | 1 (0.6%) | 9 (15.8%) | **< 0.0001** |
| Impaired Sensorium | 7 (3.2%) | 1 (0.6%) | 6 (10.5%) | **0.0015** |

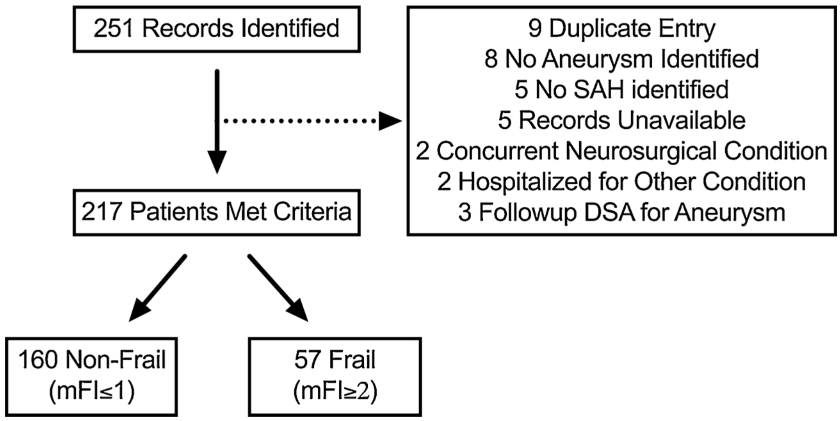


**Fig. 1.** Patient Identification and Selection. DSA = digital subtraction angiography.

patients (Table 3). Frail patients had lower admission GCS scores (12.0 versus 10.7; P = 0.0169), which likely contributed to a higher rate of requiring intubation (OR = 1.9; 95% CI 1.003–3.4; P = 0.0461). Interestingly, frail individuals were less likely to receive any treatment for their aneurysm compared to non-frail individuals (OR = 0.25; 95% CI: 0.11-0.64; P = 0.0056), but the non-treatment rate was low at < 10%. Furthermore, when treatment was initiated, no differences in treatment modality were found between groups. Overall, frail individuals were more likely to develop a complication during the hospital stay (OR = 2.6; 95% CI: 1.1–6.6; P = 0.0277) however no differences in vasospasm rates were noted between groups (P > 0.05). Frail individuals were significantly less likely to be discharged home (OR = 0.32; 95% CI: 0.11-0.68; P = 0.0020). Likewise, frail individuals were more likely to expire during their hospitalization when compared to the non-frail individuals (29.8%; OR = 2.4; 95% CI: 1.2–5.0; P = 0.0183). Other outcomes and complications that were not significantly different between groups are shown in Table 3.

Interestingly, older patients (age ≥ 65) had higher HH scores (3.2 vs. 2.8; p = 0.0204) but no differences in Fisher scores (Table 4). Contrary to this, older individuals were significantly less likely to develop vasospasm compared to younger patients (OR = 0.5; 95% CI: 0.3-0.9; p = 0.0274). Similar to frail individuals, elderly patients were significantly less likely to be discharged home (OR = 0.2; 95% CI: 0.1-0.5; p < 0.0001) and were more likely to die (OR = 3.1; 95% CI:1.5–6.1; p = 0.0016) with a 31.4% (22/70) mortality rate. Older patients had no differences in the rate of aneurysm intervention or complications when compared to younger patients. Only 5/22 (2.3%) of frail patients < 65 years died during the stay. Similar to frail patients, Log Rank analysis shows that older individuals have lower survival compared to younger patients [$x^2(1) = 9.710$; p = 0.002]. While frail individuals ≥65 have an initial decrease in survival over the hospital stay, frailty does not negatively impact survival in this ≥65 years group [$x^2(1) = 0.473$; p = 0.492] (Fig. 2). The other outcomes and complications that were not significantly different between groups are shown in Table 4.

### 3.3. Subgroup analysis of low-grade aSAH

A subgroup analysis of low-grade aSAH, i.e. HH grade 1–3, was performed to determine if the effect of mFI on mortality and discharge location were grade-dependent. Among low-grade aSAH, frailty continued to be associated with decreased rates of aneurysm intervention (OR 0.09: 95% CI: 0.007-0.6; P = 0.0342) and discharge home (OR = 0.4; 95% CI: 0.2-0.9; P = 0.0298) (Supplemental Table 1). There also trended to be a non-significant increase in mortality (OR = 3; CI: 0.9–8.8; P = 0.0835) and sepsis development (OR = 3.3; 95% CI: 1.02–12.4; P = 0.0664) in frail patients compared to non-frail patients. Subgroup analysis of those with high-grade, i.e. HH4-5, failed to show differences in aneurysm intervention, discharge home, and mortality (Supplemental Table 2). See Supplemental Tables 1–2 for non-significant differences between groups.

### 3.4. Multivariate analysis for predicting mortality and discharge home

To evaluate the influence of age and mFI on aSAH mortality and discharge home, multivariate logistic regressions were performed initially considering mFI ≥ 2, age ≥ 65, HH score, Fisher score, aneurysm

**Table 2**
Patient Demographics and Frailty. AC/AP = anticoagulant/antiplatelet use. ˆ = not normally distributed.

| | Overall (n = 217) | mFI ≤ 1 (n = 160) | mFI ≥ 2 (n = 57) | P-value |
|---|---|---|---|---|
| Age (years) | 57.6 ± 1.0 | **54.6 ± 1.1** | **66.0 ± 1.7** | **< 0.0001** |
| Female (%) | 142 (65.4%) | 103 (64.3%) | 39 (68.4%) | 0.6292 |
| White (%) | 122 (56.2%) | 88 (55%) | 34 (59.6%) | 0.6413 |
| Body Mass Index (%, kg/$m^2$) ˆ | 27.8 ± 0.5 | 27.4 ± 0.5 | 28.9 ± 0.9 | 0.1759 |
| AC/AP use (%) | 52 (24.0%) | **26 (16.3%)** | **26 (45.6%)** | **< 0.0001** |
| Smoking History (%) | 87 (40.1%) | 62 (38.8%) | 26 (43.9%) | 0.5312 |
| Ruptured Aneurysm location | | | | |
| Anterior Cerebral (%) | 9 (4.1%) | 8 (5%) | 1 (1.8%) | 0.4511 |
| Anterior Communicating (%) | 72 (33.2%) | 54 (33.8%) | 18 (31.6%) | 0.8702 |
| Basilar (%) | 16 (7.4%) | 11 (6.9%) | 5 (8.8%) | 0.7680 |
| Internal Carotid (%) | 23 (10.6%) | 20 (12.5%) | 3 (5.3%) | 0.2079 |
| Middle Cerebral (%) | 31 (14.3%) | 22 (13.8%) | 9 (15.8%) | 0.6665 |
| Posterior Cerebral (%) | 4 (1.8%) | 3 (1.9%) | 1 (1.8%) | > 0.9999 |
| Posterior Communicating (%) | 43 (19.8%) | 28 (17.5%) | 15 (26.3%) | 0.1762 |
| Vertebral (%) | 7 (3.2%) | 4 (2.5%) | 3 (5.3%%) | 0.3825 |
| Other (%) | 14 (6.5%) | 11 (6.9%) | 3 (5.3%) | > 0.9999 |
| Aneurysm Size (mm)ˆ | 6.0 ± 0.2 | 5.9 ± 0.2 | 6.3 ± 0.5 | 0.7804 |

**Table 3**
Hospital Course and Frailty. HH = Hunt & Hess, LOS = length of stay, ICU = intensive care unit, EVD = external ventricular drain, VPS = ventriculoperitoneal shunt, GCS = Glasgow Coma Scale. ^ = not normally distributed.

| | mFI ≤ 1 (n = 160) | mFI ≥ 2 (n = 57) | OR (95% CI) | P-value |
|---|---|---|---|---|
| **HH Score^** | **2.8 ± 0.1** | **3.3 ± 0.2** | – | **0.0050** |
| **Fisher Score^** | **3.6 ± 0.1** | **3.8 ± 0.1** | – | **0.0255** |
| Hospital LOS (days)^ | 21.1 ± 1.0 | 19.9 ± 2.0 | – | 0.3379 |
| ICU LOS (days)^ | 17.3 ± 0.7 | 16.5 ± 1.5 | – | 0.4901 |
| EVD Required | 118 (73.8%) | 46 (80.7%) | 1.5 (0.7-3.2) | 0.3701 |
| VPS Required | 13 (8.1%) | 5 (8.8%) | 1.1 (0.4-3.1) | > 0.9999 |
| Vasospasm | 91 (56.9%) | 33 (57.9%) | 1.0 (0.6-1.9) | > 0.9999 |
| **Admission GCS^** | **12.0 ± 0.3** | **10.7 ± 0.6** | – | **0.0169** |
| Discharge GCS^ (without deaths) | 14.1 ± 0.2 | 13.9 ± 0.4 | – | 0.4309 |
| Tracheostomy | 34 (21.3%) | 14 (24.6%) | 1.2 (0.6-2.4) | 0.5835 |
| Gastrostomy | 38 (23.8%) | 15 (26.3%) | 1.1 (0.6-2.3) | 0.7213 |
| **Aneurysm Intervention** | **151 (94.4%)** | **46 (80.7%)** | **0.25 (0.11-0.64)** | **0.0056** |
| Clip | 18 (11.9%) | 4 (8.7% | 0.70 (0.2-2.0) | 0.7893 |
| Coil | 136 (90.0%) | 41 (89.1%) | 0.9 (0.3-2.4) | 0.7870 |
| Pipeline | 3 (2.0%) | 1 (2.2%) | 1.1 (0.1-7.5) | > 0.9999 |
| Discharge Location | | | | |
| **Home** | **64 (40.0%)** | **10 (17.5%)** | **0.32 (0.16-0.68)** | **0.0020** |
| Rehab | 67 (41.9%) | 27 (47.4%) | 1.2 (0.7-2.3) | 0.5343 |
| Nursing Home /Hospice | 3 (1.9%) | 3 (5.3%) | 2.9 (0.7-12.7) | 0.1873 |
| **Death** | **24 (15.0%)** | **17 (29.8%)** | **2.4 (1.2-5.0)** | **0.0183** |
| Transferred | 2 (1.3%) | 0 (0.0%) | 0 (0-6.1) | > 0.9999 |
| Any complication | **117 (73.1%)** | **50 (87.7%)** | **2.6 (1.1-6.6)** | **0.0277** |
| Urinary Tract Infection | 40 (25.0%) | 17 (29.8%) | 1.3 (0.6-2.5) | 0.4872 |
| Sepsis | 13 (8.1%) | 6 (10.5%) | 1.3 (0.5-3.6) | 0.5902 |
| Intubated | **79 (49.4%)** | **37 (64.9%)** | **1.9 (1.003-3.4)** | **0.0461** |
| Vasopressor | 64 (40.0%) | 21 (36.8%) | 0.88 (0.46-1.66) | 0.7528 |
| Pneumonia | 44 (27.5%) | 12 (21.1%) | 0.70 (0.35-1.48) | 0.3822 |
| Deep vein thrombosis | 10 (6.3%) | 5 (8.8%) | 1.4 (0.5-4.1) | 0.5472 |
| Pulmonary Embolism | 2 (1.3%) | 1 (1.8%) | 1.4 (0.1-12.3) | > 0.9999 |

location and aneurysm size, treatment type, sex, race, BMI, AC/AP use, and smoking history. Interestingly the HH score (OR = 2.7; 95% CI: 1.9–3.0; P < 0.0001) followed by age≥65 (OR = 2.7; 1.2–6.0; p = 0.012) were the only independent predictors of mortality (Table 5). Likewise, the independent predictors of discharge home were HH score (OR = 0.24; 95%CI: 0.15-0.37; p < 0.0001) followed by age

**Table 4**
Hospital Course and Age. HH = Hunt & Hess, LOS = length of stay, ICU = intensive care unit, EVD = external ventricular drain, VPS = ventriculoperitoneal shunt, GCS = Glasgow Coma Scale. ^ = not normally distributed.

| | Age < 65 years (n = 147) | Age ≥ 65 years (n = 70) | OR (95% CI) | P-value |
|---|---|---|---|---|
| **HH Score^** | **2.8 ± 0.1** | **3.2 ± 0.1** | – | **0.0204** |
| Fisher Score^ | 3.6 ± 0.05 | 3.7 ± 0.08 | – | 0.0703 |
| Hospital LOS (days)^ | 21.0 ± 1.0 | 20.4 ± 1.7 | – | 0.3263 |
| ICU LOS (days)^ | 17.3 ± 0.8 | 16.7 ± 1.3 | – | 0.3016 |
| EVD Required | 106 (72.1%) | 58 (82.9%) | 1.9 (0.9-3.8) | 0.0933 |
| VPS Required | 12 (8.2%) | 6 (8.6%) | 1.1 (0.4-2.9) | > 0.9999 |
| **Vasospasm** | **92 (62.6%)** | **32 (45.7%)** | **0.5 (0.3-0.9)** | **0.0274** |
| Admission GCS^ | 12.0 ± 0.4 | 11.1 ± 0.5 | – | 0.0889 |
| Discharge GCS^ (without deaths) | 14.3 ± 0.2 | 13.6 ± 0.4 | – | 0.0291 |
| Tracheostomy | 33 (22.5%) | 15 (21.4%) | 0.9 (0.5-1.9) | > 0.9999 |
| Gastrostomy | 33 (22.5%) | 20 (28.6%) | 1.4 (0.7-2.6) | 0.3981 |
| Aneurysm Intervention | 137 (93.2%) | 60 (85.7%) | 0.4 (0.2-1.1) | 0.0836 |
| Clip | 14 (9.5%) | 8 (11.4%) | 1.2 (0.5-3.1) | 0.6391 |
| Coil | 123 (83.7%) | 54 (77.1%) | 0.7 (0.3-1.3) | 0.2645 |
| Pipeline | 4 (2.7%) | 0 (0.0%) | 0 (0-2.1) | 0.3075 |
| Discharge Location | | | | |
| **Home** | **64 (43.5%)** | **10 (14.3%)** | **0.2 (0.1-0.5)** | **< 0.0001** |
| Rehab | 59 (40.1%) | 35 (50%) | 1.5 (0.9-2.6) | 0.1889 |
| Nursing Home /Hospice | 3 (2.0%) | 3 (4.3%) | 2.1 (0.5-9.4) | 0.3902 |
| **Death** | **19 (12.9%)** | **22 (31.4%)** | **3.1 (1.5-6.1)** | **0.0016** |
| Transferred | 2 (1.4%) | 0 (0.0%) | 0 (0-4.5) | > 0.9999 |
| Any complication | 109 (74.2%) | 58 (82.0%) | 1.7 (0.8-3.4) | 0.1713 |
| Urinary Tract Infection | 38 (25.9%) | 19 (27.1%) | 1.1 (0.6-2.0) | 0.8697 |
| Sepsis | 10 (6.8%) | 9 (12.9%) | 2.0 (0.8-5.2) | 0.1970 |
| Intubated | 73 (49.7%) | 43 (61.4%) | 1.6 (0.9-2.9) | 0.1117 |
| Vasopressor | 62 (42.2%) | 23 (32.9%) | 0.7 (0.4-1.2) | 0.2341 |
| Pneumonia | 35 (23.8%) | 21 (30%) | 1.4 (0.7-2.5) | 0.4068 |
| DVT | 11 (7.5%) | 4 (5.7%) | 0.7 (0.3-2.2) | 0.7787 |
| PE | 2 (1.4%) | 1 (1.4%) | 1.1 (0.07-9.2) | > 0.9999 |

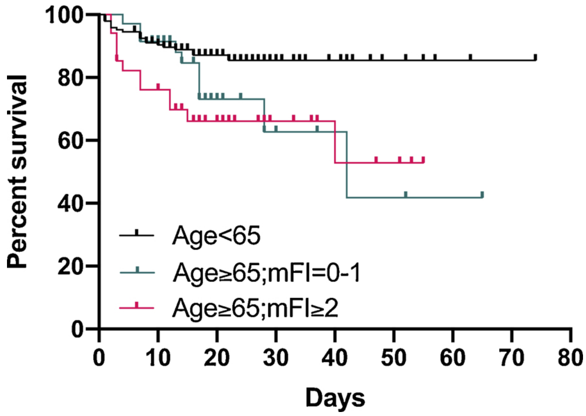


**Fig. 2.** Kaplan-Meier Survival Curve with Mentel-Cox Log Rank Regression. Those age ≥ 65 years have a significantly decreased survival [$x^2(1) = 9.710$; p = 0.002] but among those ≥65 years there is no effect of frailty on survival [x2(1) = 0.473; p = 0.492]. Tics represent censored data (i.e. patient discharge not due to death).

(OR = 0.25; 95%CI:0.1-0.6; p = 0.003) and race (OR = 2.2; 95%CI: 1.01–4.6; p = 0.046). The mFI, Fisher score, aneurysm size and location, treatment type, sex, BMI, AC/AP use, or smoking history were not independently predictive of mortality or discharge home.

## 4. Discussion

In this retrospective cohort study, we show that frailty and increased age were both associated with decreased survival and decreased rates of discharge home. Frailty, but not age ≥ 65, was associated with small but statistically significant increased complication rates, particularly the need for intubation, and decreased rates of intervention for aneurysm treatment. Interestingly, while HH score was the strongest predictor of survival and discharge home, increasing age, and not increasing frailty, was another independent predictor of these endpoints.

To date, others have examined the effect of underlying comorbidities on aSAH outcomes [14,15]. Yue et al. [5] showed that among 173 patients 60 years or older, age, history of hypertension, history of smoking, HH, and aneurysm size were independently predictive of poor outcome at 3 months post-hemorrhage. This group also showed that certain objective findings such as anemia and a low BMI may also carry predictive value, but they did not find any association between diabetes, heart, renal or liver disease, or alcohol consumption with poor outcomes [5]. In line with this, we also found that frailty, but not age ≥ 65, was associated with increased rates of complications, primarily intubation, following aSAH. However, we went on to show that while frail individuals present with more severe hemorrhages, as measured by elevated HH and Fisher scores, have increased mortality, and decreased rates of discharge home compared to non-frail patients, this effect appears to be a function of age and not the underlying increased comorbidities, as is often supposed when increasing frailty is found to be associated with worse outcomes after initial univariate analysis.

Several prior studies have shown that, in addition to traditional measures of aSAH severity such as HH and Fisher scores, increasing age is one of the strongest independent predictors of poor clinical outcomes, including increased complications and increased mortality following aSAH [3,16–18]. Conversely, recent studies throughout the surgical literature have questioned the influence of age itself versus the presence of underlying accumulated co-morbid conditions as predictors of outcomes [6,19]. These studies have argued that frailty is prognostic of poorer outcomes and increased mortality independent of age [6,19]. The most common measurement of these co-morbidities is the modified frailty index (mFI), which is associated with a 3–5 increased odds of mortality following neurosurgical procedures [8]. Specifically, prior studies have shown that frailty is associated with worse outcomes and increased mortality following meningioma resection [10], spinal surgery [9], and intraparenchymal hemorrhage [20] among other pathologies. We, therefore, hypothesized that frailty would be an independent predictor of discharge home and mortality following an aSAH, but we were surprised to discover that increasing age was an independent predictor of these outcomes in multivariate analysis while frailty was not significant after multivariate analysis.

Others have argued that the effect of age on aSAH outcomes may be

**Table 5**
Univariate and Multivariate Logistic Regression for Predictors of Mortality and Discharge Home. Only variables significant in univariate logistic regression were included for multivariate analysis. n.s. = not significant.

| | Characteristic | Univariate OR (95% CI) | P-value | Multivariate OR (95% CI) | P-value |
|---|---|---|---|---|---|
| Mortality | mFI ≥ 2 | 2.4 (1.2-4.9) | 0.016 | n.s. | n.s. |
| | Hunt & Hess Score | 2.7 (1.9-3.9) | < 0.0001 | 2.7 (1.9-3.0) | < 0.0001 |
| | Fisher Score | 6.6 (1.6-26.7) | 0.008 | n.s. | n.s. |
| | Aneurysm Location | n.s. | n.s. | – | – |
| | Treatment Type | n.s. | n.s. | – | – |
| | Age ≥ 65 | 3.1 (1.5-6.2) | 0.002 | 2.7 (1.2-6.0) | 0.012 |
| | Sex | n.s. | n.s. | – | – |
| | Race | n.s. | n.s. | – | – |
| | BMI | 0.92 (0.86-0.98) | 0.010 | n.s. | n.s. |
| | AC/AP Use | n.s. | n.s. | – | – |
| | Smoking history | n.s. | n.s. | – | – |
| | Aneurysm Size | n.s. | n.s. | – | – |
| Discharge Home | mFI ≥ 2 | 0.32 (0.15-0.68) | 0.003 | n.s. | n.s. |
| | Hunt & Hess Score | 0.25 (0.17-0.38) | < 0.0001 | 0.24 (0.15-0.37) | < 0.0001 |
| | Fisher Score | 0.44 (0.28-0.69) | 0.0003 | n.s. | n.s. |
| | Aneurysm Location | n.s. | n.s. | – | – |
| | Treatment Type | n.s. | n.s. | – | – |
| | Age ≥ 65[a] | 0.22 (0.1-0.46) | < 0.0001 | 0.25 (0.1-0.61) | 0.003 |
| | Sex | n.s. | n.s. | – | – |
| | Race | 1.9 (1.1-3.3) | 0.029 | 2.2 (1.01-4.6) | 0.046 |
| | BMI | n.s. | n.s. | – | – |
| | AC/AP Use | n.s. | n.s. | – | – |
| | Smoking history | n.s. | n.s. | – | – |
| | Aneurysm size | 0.83 (0.74-0.93) | 0.001 | n.s. | n.s. |

a result of decreased vascular reserve in the elderly, leading to a decrease in compensatory autoregulation following an insult [4,21]. It is interesting to consider these impaired autoregulatory mechanisms in the context of our finding of decreased rates of vasospasm in the elderly despite increased rates of mortality and poor outcomes in this group. Others have also noted this relatively lower rate of vasospasm in the elderly, a finding that warrants further study [22]. Together this suggests that age itself, rather than frailty, may influence aSAH outcomes possibly due to decreased cerebrovascular functional reserve.

The finding of age, rather than frailty, as a predictor of aSAH outcomes in our multivariate analysis is curious given our recent work examining angiogram-negative subarachnoid hemorrhages (ANSAH) during the same period as this study. In that study, we found that following ANSAH, the mFI was a superior predictor of mortality and discharge home compared to HH score, Fisher score, and age [25]. The difference may be attributed to the lower mortality rates in ANSAH patients compared to aSAH patients and that the grading systems used for aSAH may not apply to ANSAH patients. In line with ANSAH patients having lower mortality rates, our data trended to show that the effect of frailty on our primary endpoints was driven by the low-grade aSAH group. Patients with low HH scores generally have good prognoses compared to those with high-grade aSAH regardless of underlying comorbidities. However, we show that frail patients in this low-grade aSAH group are at a disadvantage. Furthermore, frail patients have significantly higher HH scores, that may explain why the HH score itself was the best predictor of mortality and discharge home overall.

## 5. Limitations

The main limitation of this study was its retrospective design. A prospective analysis is needed to ensure unbiased data acquisition, especially in the case of the mFI variables. Second, due to the limitations of our medical record system, we were unable to calculate modified Rankin scale or Glasgow outcome scores for our cohort. Prospective analyses, including those initiated at our institution, will likely better capture the true effect of frailty and age on aSAH prognosis and outcomes. Third, there is no consensus on the threshold of mFI that should be used clinically and studies of frailty are incredibly disparate with innumerable different ways to categorize the different levels of frailty, from mFI = 1, 2, or > 3, and others even divide the mFI by 11 to create non-whole number thresholds [23]. While the clinically significant threshold will vary by pathology, large prospective cohort studies are needed set this standardized cutoff especially within the various surgical subspecialties. Finally, while the mFI is the most commonly used measure of frailty, there are other measures of the decreased physiologic reserve including some interesting surrogate markers for frailty such as temporalis thickness [24] and various laboratory values [10] that may prove to be helpful in aSAH prognostication or other pathology subsets down the road.

## 6. Conclusion

Aneurysmal SAH is associated with high rates of morbidity and mortality. Recent studies have investigated the effect of the mFI on outcomes across a multitude of surgical disciplines, typically finding that increasing mFI is associated with worse outcomes than age alone. In this study, we surprisingly found that aSAH patients with high mFI scores, present with worse hemorrhages, have more complications, and have decreased rates of survival compared to non-frail patients. However, in multivariate analysis, the two major predictors of our primary endpoints, of mortality and discharge home, were HH score and age. This data supports the prioritization of age rather than the effect of multiple comorbidities in the decision-making algorithm and prognostication following an aSAH.

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## Declaration of Competing Interest

The authors report no conflicts of interest.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.clineuro.2019.105558.

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