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Impact of Frailty on Clinical Outcomes after Carotid Artery Revascularization

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Background: Frailty has been increasingly recognized as an important risk factor for vascular procedures. To assess the impact of frailty on clinical outcomes and resource utilization in patients undergoing carotid revascularization using a national cohort.

Methods: The 2005-2017 National Inpatient Sample was used to identify patients who underwent carotid endarterectomy (CEA) or carotid stenting (CAS). Patients were classified as frail using diagnosis codes defined by the Johns Hopkins Adjusted Clinical Groups frailty indicator. Multivariable regression was used to evaluate associations between frailty and in-hospital mortality, postoperative stroke, myocardial infarction (MI), hospitalization costs, and length of stay (LOS).

Results: Of 1,426,343 patients undergoing carotid revascularization, 59,158 (4.2%) were identified as frail. Among frail patients, 79.4% underwent CEA and 20.6% underwent CAS. Compared to CEA, a greater proportion of patients undergoing CAS were frail (6.0% vs. 3.8%, $P < 0.001$). Compared to the nonfrail cohort, frail patients had higher rates of mortality (2.2% vs. 0.5%, $P < 0.001$), postoperative stroke (2.6% vs. 1.0%, $P < 0.001$), MI (2.2% vs. 0.8%, $P < 0.001$), and stroke/death (4.4% vs. 1.4%, $P < 0.001$). After adjustment, frailty was associated with increased odds of mortality (AOR = 1.59, 95% CI: 1.30-1.80, $P < 0.001$), stroke (AOR = 1.66, 95% CI: 1.38-1.83, $P < 0.001$), MI (AOR = 1.51, 95% CI: 1.29-1.72, $P < 0.001$), and stroke/death (AOR = 1.62, 95% CI: 1.45-1.81, $P < 0.001$). Furthermore, frailty was associated with increased hospitalization costs ($\beta = +\$5,980$, 95% CI: \$5,490-\$6,470, $P < 0.001$) and LOS ($\beta = +2.6$ days, 95% CI: 2.4-2.8, $P < 0.001$).

Conclusions: Frailty is associated with adverse outcomes and greater resource use for those undergoing carotid revascularization. Risk models should include an assessment of frailty to guide management and improve outcomes for these high-risk patients.

Author Contributions: Ms. Mandelbaum conceptualized and designed the study, collected data, carried out the analyses, drafted the manuscript, and reviewed and revised the manuscript. Dr. Hadaya conceptualized and designed the study, assisted with data analyses, and reviewed and revised the manuscript. Dr. Ulloa reviewed and critically revised the manuscript. Dr. Patel reviewed and critically revised the manuscript. Dr. McCallum assisted with the study design and critically reviewed the manuscript. Dr. De Virgilio assisted with the study design and critically reviewed the manuscript. Dr. Benharash conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

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Abbreviations: CEA, carotid endarterectomy; CAS, carotid artery stenting; NIS, National Inpatient Sample; HCUP, Healthcare Cost and Utilization Project; ICD, International Classification of Diseases; LOS, length of stay; NFRAIL, Nonfrail.

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INTRODUCTION

Carotid artery stenosis accounts for approximately 10% of all ischemic strokes in the United States and primarily affects the elderly.^{1,2} While carotid endarterectomy (CEA) remains the gold standard treatment for patients meeting operative criteria, carotid artery stenting (CAS) has emerged as an alternative, and less invasive option.³ Compared to CEA, transfemoral CAS is associated with reduced odds of perioperative cardiac complications despite higher rates of perioperative stroke.⁴ Nonetheless, short-term follow-up data for both CEA and CAS have shown inferior postoperative outcomes in association with medical comorbidities and advanced age.²⁻⁷

With an estimated 60% of vascular surgical procedures performed in patients >65 years of age, preoperative assessment and the mitigation of perioperative risk is heightened in this population.^{8,9} A growing body of evidence has implicated frailty as an independent risk factor for adverse outcomes following major operations, independent of age.¹¹⁻¹⁸ While an exact definition is lacking, frailty may be related to poor functional reserve as well as an accumulation of comorbidities. Unfortunately, objective frailty instruments, such as measures of gait speed, are not widely adopted in clinical practice owing to their resource intensive nature.¹⁸ Limitations of administrative tools such as the Modified Frailty Index (National Surgical Quality Improvement Program) have motivated several investigators to examine alternatives, such as the binary Johns Hopkins indicator.^{12,17} The Johns Hopkins Adjusted Clinical Groups (ACG) frailty-defining diagnosis indicator utilizes administrative codes to identify frail patients without additional testing.¹⁹ The utility of the Johns Hopkins indicator in predicting outcomes of carotid interventions remains unknown.

The present study characterized the impact of frailty, defined using a coding-based tool, on clinical outcomes and resource utilization following CEA and CAS. We hypothesized frailty to be independently associated with increased mortality, postoperative complications, length of stay, and hospitalization costs.

MATERIALS AND METHODS

Study Design and Population

The National Inpatient Sample (NIS) was used to identify adult (≥ 18 years) patients who underwent carotid artery stenting or endarterectomy between 2005 and 2017. The NIS is the largest, publicly

available, all-payer inpatient database in the United States and is maintained by the Agency for Healthcare Research and Quality (AHRQ) as part of the Healthcare Cost and Utilization Project (HCUP).²⁰ Accurate trend and discharge weights to estimate 97% of all US hospitalizations are obtained from an approximately 20% sample of all inpatient discharges.

International Classification of Diseases, Ninth and Tenth Revisions (ICD-9 and ICD-10) procedure codes were used to identify patients who underwent carotid endarterectomy (ICD-9: 38.12; ICD-10: 03CH0ZZ, 03CJ0ZZ, 03CK0ZZ, 03CL0ZZ) or carotid artery stenting (ICD-9: 00.63; ICD-10: 037H3DZ, 037J3DZ, 037K3DZ, 037L3DZ). To maintain homogeneity, patients with codes for percutaneous coronary intervention (PCI), coronary artery bypass (CABG), endovascular repair of intracranial vessels, or carotid dissections during the same hospitalization were excluded. Patients were identified as symptomatic based on primary diagnoses indicating carotid stenosis or occlusion with cerebral infarction, transient ischemic attack, or amaurosis fugax. This approach has been previously utilized by Giles et al. and Giacobelli et al. in large national datasets, and validated through evaluation of medical records.^{21,22}

The methodology of the Johns Hopkins Adjusted Clinical Groups (ACG) frailty indicators is described in detail elsewhere.¹⁹ Briefly, this binary indicator is considered positive (FRAIL) if any of the diagnoses in the ACG clusters are present (Supplemental Table I). The remaining patients comprised the nonfrail cohort (NFRAIL). Patient demographics included age, gender, race, insurance payer, and median household income quartile. The previously validated Elixhauser Comorbidity Index was used to numerically assess patient comorbidities by tabulating the burden of 30 common chronic conditions.²³ Hospital characteristics included teaching status, geographic region, and bed-size as described in the HCUP data dictionary.²⁰ ICD diagnosis codes were used to identify postoperative stroke (ICD-9: 997.02; ICD-10: I97.811, I97.821) and myocardial infarction (MI) (ICD-9: 410.x; ICD-10: I21.x). Using previously validated volume cut-offs, hospitals were characterized as low (<20 cases/year), medium (20–79 cases/year) and high (≥ 80 cases/year) based on the annual CEA caseload per hospital.^{24,25}

The primary outcomes of interest were in-hospital mortality, stroke, and myocardial infarction (MI), stratified by symptomatic status and procedure type. A composite outcome of postoperative stroke or death was also assessed.^{21,26}

We further evaluated the association of frailty with hospitalization costs and postoperative length of stay (LOS). Hospitalization costs were calculated using cost-to-charge ratios provided by HCUP and inflation-adjusted to the 2017 US Gross Domestic product.

Statistical Analysis

Data analysis was performed using Stata 16.1 (StataCorp, College Station, TX) using survey-specific commands. Appropriate trend and survey weights were used to account for the change in NIS sampling methodology in 2012.²⁷ The significance of time-related variations was assessed using Cuzick's nonparametric test for trends (NP-trend).²⁸ Adjusted Wald and Mann-Whitney tests were used to compare categorical and continuous variables, respectively. Multivariable regression models were fit to assess the association of frailty with mortality, postoperative stroke, myocardial infarction, composite stroke/death, hospitalization costs, and LOS. Following a stepwise backward elimination, additional covariates were removed based on significance. The Stata margins command was used to calculate the average marginal effect on outcomes. Given the adoption of transcatheter aortic valve replacement (TAVR) into clinical practice with the launch of TAVR Surveillance Project in September 2016,^{29–30} a sensitivity analysis was performed to exclude operations during the 2017 calendar year. Statistical significance was set at $\alpha \leq 0.05$. This study was deemed exempt from full review by the Institutional Review Board at the University of California, Los Angeles due to the deidentified nature of the database. Informed consent from individual patients was similarly not obtained.

RESULTS

Of an estimated 1,426,343 patients undergoing carotid artery revascularization, 59,158 (4.2%) comprised the *FRAIL* cohort. Among frail patients, 79.4% underwent CEA and 20.6% underwent CAS (Fig. 1). Compared to the CEA cohort, those who underwent CAS were more likely to be frail (6.0% vs. 3.8%, $P < 0.001$). Symptomatic status was identified in 21.0% of *FRAIL* and 6.9% of *NFRAIL* ($P < 0.001$).

Compared to *NFRAIL*, patients in the *FRAIL* group were on average older (73.4 vs. 70.9 years, $P < 0.001$) and had a higher Elixhauser Comorbidity Index (3.1 vs. 2.3, $P < 0.001$) (Table 1). The majority of *FRAIL* were White (82.6%) and insured

by Medicare (78.9%). A greater proportion of the *FRAIL* cohort were admitted nonelectively (51.0% vs. 21.8%, $P < 0.001$) and treated at low-volume (11.2% vs. 8.2%, $P < 0.001$) centers compared to the *NFRAIL* cohort.

FRAIL patients had increased unadjusted rates of in-hospital mortality (2.0% vs. 0.5%, $P < 0.001$) compared to *NFRAIL* (Supplemental Table II). The *FRAIL* group also had greater rates of postoperative stroke (2.6% vs. 1.0%, $P < 0.001$), MI (2.2% vs. 0.8%, $P < 0.001$), and stroke/death (4.4% vs. 1.4%, $P < 0.001$). In both *FRAIL* and *NFRAIL* groups, symptomatic presentation and nonelective admission were associated with higher unadjusted mortality, stroke, MI, and stroke/death rates compared to asymptomatic cases (Supplemental Table II). Compared to CEA, CAS was associated with increased unadjusted rates of mortality, stroke, MI and stroke/death as shown in Table II. Moreover, CAS was associated with increased rates of stroke/death for *FRAIL* patients in both the symptomatic (10.4% vs. 4.5%, $P < 0.001$) and asymptomatic subsets (6.3% vs. 3.4%, $P < 0.001$).

Patients in the *FRAIL* cohort had significantly greater index hospitalization costs (\$23,556 vs. \$12,334, $P < 0.001$), preoperative LOS (2.4 vs. 0.7 days, $P < 0.001$), and overall LOS (7.0 vs. 2.6 days, $P < 0.001$), compared to those in the *NFRAIL* cohort (Supplementary Table III). Symptomatic presentation was also associated with increased costs and LOS among the *FRAIL* cohort. Furthermore, frail patients who underwent CAS incurred increased costs (\$32,768 vs. \$21,884, $P < 0.001$), preoperative LOS (2.2 vs. 2.5 days, $P < 0.001$), and overall LOS (8.1 vs. 6.8 days, $P < 0.001$) compared to CEA.

Multivariable logistic regression models were fit to identify independent predictors of in-hospital mortality, postoperative stroke, MI and the composite endpoint of stroke/death following carotid revascularization. After adjustment, frailty remained an independent predictor of mortality (AOR = 1.59, 95% CI: 1.30–1.80, $P < 0.001$), stroke (AOR = 1.66, 95% CI: 1.38–1.83, $P < 0.001$), MI (AOR = 1.51, 95% CI: 1.29–1.72, $P < 0.001$), and the composite stroke/death (AOR = 1.62, 95% CI: 1.45–1.81, $P < 0.001$). Frail patients had an increased predicted probability of mortality and composite stroke/death at all ages compared to *NFRAIL* patients (Fig. 2). In asymptomatic cases, frailty was significantly associated with mortality (AOR = 2.01, 95% CI: 1.65–2.45, $P < 0.001$), stroke (AOR = 1.77, 95% CI: 1.51–2.09, $P < 0.001$), MI (AOR = 1.52, 95% CI: 1.28–1.81, $P < 0.001$), and composite stroke/death (AOR = 1.93, 95% CI: 1.69–

Table I. Demographics and clinical characteristics of patients undergoing carotid artery revascularization

| | All patients (N = 1,426,343) | FRAIL (N = 59,158) | NFRAIL (N = 1,367,185) | P-value |
|---------------------------------|------------------------------|--------------------|------------------------|---------|
| Age (years ± SD) | 70.9 ± 9.7 | 73.4 ± 10.4 | 70.8 ± 9.6 | <0.001 |
| Elixhauser index (score ± SD) | 2.4 ± 1.6 | 3.1 ± 2.0 | 2.3 ± 1.6 | <0.001 |
| Surgery type (%) | | | | <0.001 |
| CEA ^a | 84.9 | 77.6 | 85.2 | |
| CAS ^b | 15.1 | 22.4 | 14.8 | |
| Symptomatic (%) | 7.8 | 21.2 | 7.1 | <0.001 |
| Nonelective (%) | 23.1 | 51.0 | 21.8 | <0.001 |
| Female (%) | 41.4 | 42.0 | 41.4 | 0.182 |
| Race (%) | | | | <0.001 |
| White | 87.3 | 82.6 | 87.5 | |
| Black | 4.6 | 7.7 | 4.4 | |
| Hispanic | 4.5 | 5.7 | 4.4 | |
| Asian | 1.1 | 1.2 | 1.1 | |
| Other ^c | 2.5 | 2.7 | 2.5 | |
| Insurance coverage (%) | | | | <0.001 |
| Medicare | 72.7 | 78.9 | 72.4 | |
| Medicaid | 3.7 | 4.9 | 3.6 | |
| Private | 20.4 | 12.2 | 20.8 | |
| Other ^d | 3.2 | 3.9 | 3.2 | |
| Income quartile (%) | | | | 0.026 |
| <25th | 26.9 | 27.9 | 26.9 | |
| 25th–50th | 28.8 | 28.5 | 28.9 | |
| 50th–75th | 24.8 | 23.7 | 24.9 | |
| 75th > | 19.4 | 19.9 | 19.4 | |
| Hospital region (%) | | | | 0.014 |
| Northeast | 16.0 | 14.4 | 16.0 | |
| Midwest | 24.8 | 25.2 | 24.8 | |
| South | 43.3 | 44.2 | 43.3 | |
| West | 15.9 | 16.3 | 15.9 | |
| Teaching status (%) | | | | <0.001 |
| Rural, nonteaching | 7.1 | 5.3 | 7.2 | |
| Urban, nonteaching | 39.1 | 32.9 | 39.4 | |
| Urban, teaching | 53.7 | 61.8 | 53.4 | |
| Bed size (%) | | | | 0.294 |
| Small | 10.7 | 10.6 | 10.7 | |
| Medium | 24.3 | 25.1 | 24.2 | |
| Large | 65.1 | 64.3 | 65.1 | |
| Hospital volume (%) | | | | <0.001 |
| Low | 8.3 | 11.2 | 8.2 | |
| Medium | 43.2 | 46.6 | 43.0 | |
| High | 48.5 | 42.2 | 48.8 | |
| Comorbidities | | | | |
| Congestive heart failure | 9.1 | 16.1 | 8.8 | <0.001 |
| Coronary artery disease | 44.1 | 39.9 | 44.3 | <0.001 |
| Coagulopathy | 1.4 | 3.4 | 1.3 | <0.001 |
| Liver disease | 0.8 | 1.4 | 0.8 | <0.001 |
| Chronic kidney disease | 9.5 | 15.4 | 9.3 | <0.001 |
| Pulmonary circulation disorders | 1.4 | 2.5 | 1.3 | <0.001 |

^aCEA indicates carotid endarterectomy.^bCAS indicates carotid artery stenting.^cIndicates a combined group of Native American and other races as defined by NIS.^dIndicates a combined insurance status including self-pay, uninsured, and other.

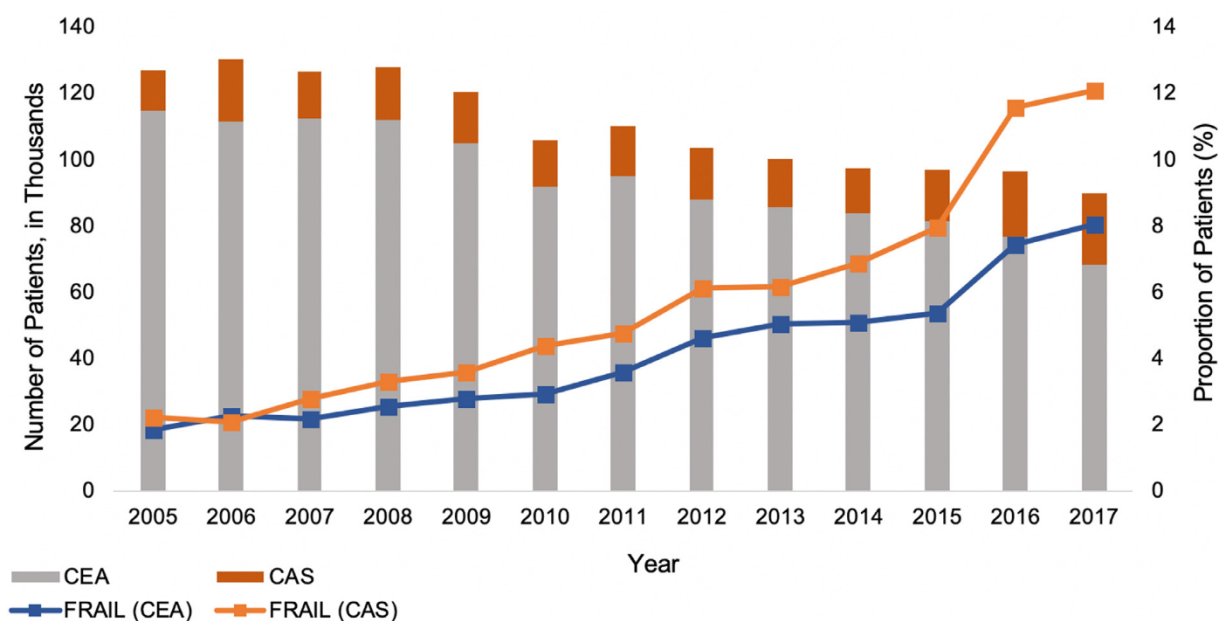


Fig. 1. Annual carotid revascularization caseload and percentage frail by operation.

Table II. Unadjusted outcomes for *FRAIL* and *NFRAIL* stratified by carotid endarterectomy (CEA) and carotid artery stenting (CAS), and symptomatic status

| | <i>FRAIL</i> (N = 59,158) | <i>NFRAIL</i> (N = 1,367,185) | P-value |
|---------------------------------|---------------------------|-------------------------------|---------|
| CEA ^a , asymptomatic | | | |
| Mortality | 500 (1.3) ^c | 2,832 (0.3) | <0.001 |
| Stroke | 883 (2.3) | 8,930 (0.8) | <0.001 |
| MI | 757 (2.0) | 7,610 (0.7) | <0.001 |
| Stroke/Death | 1,300 (3.4) | 10,962 (1.0) | <0.001 |
| CEA, symptomatic | | | |
| Mortality | 146 (1.7) | 753 (1.0) | 0.016 |
| Stroke | 265 (3.0) | 2,015 (2.8) | 0.559 |
| MI | 215 (2.4) | 1,088 (1.5) | 0.002 |
| Stroke/Death | 392 (4.5) | 2,591 (3.6) | 0.055 |
| CAS ^b , asymptomatic | | | |
| Mortality | 272 (3.2) | 1,564 (0.9) | <0.001 |
| Stroke | 282 (3.3) | 2,379 (1.4) | <0.001 |
| MI | 166 (1.9) | 1,858 (1.1) | <0.001 |
| Stroke/Death | 535 (6.3) | 3,688 (2.2) | <0.001 |
| CAS, symptomatic | | | |
| Mortality | 270 (7.4) | 1,516 (6.9) | 0.599 |
| Stroke | 127 (3.5) | 689 (3.1) | 0.618 |
| MI | 154 (4.2) | 701 (3.2) | 0.140 |
| Stroke/Death | 377 (10.4) | 2,102 (9.6) | 0.486 |

^aCEA indicates carotid endarterectomy.

^bCAS indicates carotid artery stenting.

^cData are total number (%).

2.21, $P < 0.001$) (Supplemental Table IV). Among symptomatic cases, no significant association was found between frailty and mortality (AOR=0.98, 95% CI: 0.75–1.29, $P = 0.882$), stroke (AOR=1.23, 95% CI: 0.94–1.61, $P = 0.130$), or composite

stroke/death (AOR=1.11, 95% CI: 0.91–1.36, $P = 0.299$). However, frail patients with symptomatic disease had increased odds of MI (AOR=1.43, 95% CI: 1.08–1.88, $P = 0.012$). Furthermore, in elective admissions, frailty was associated with

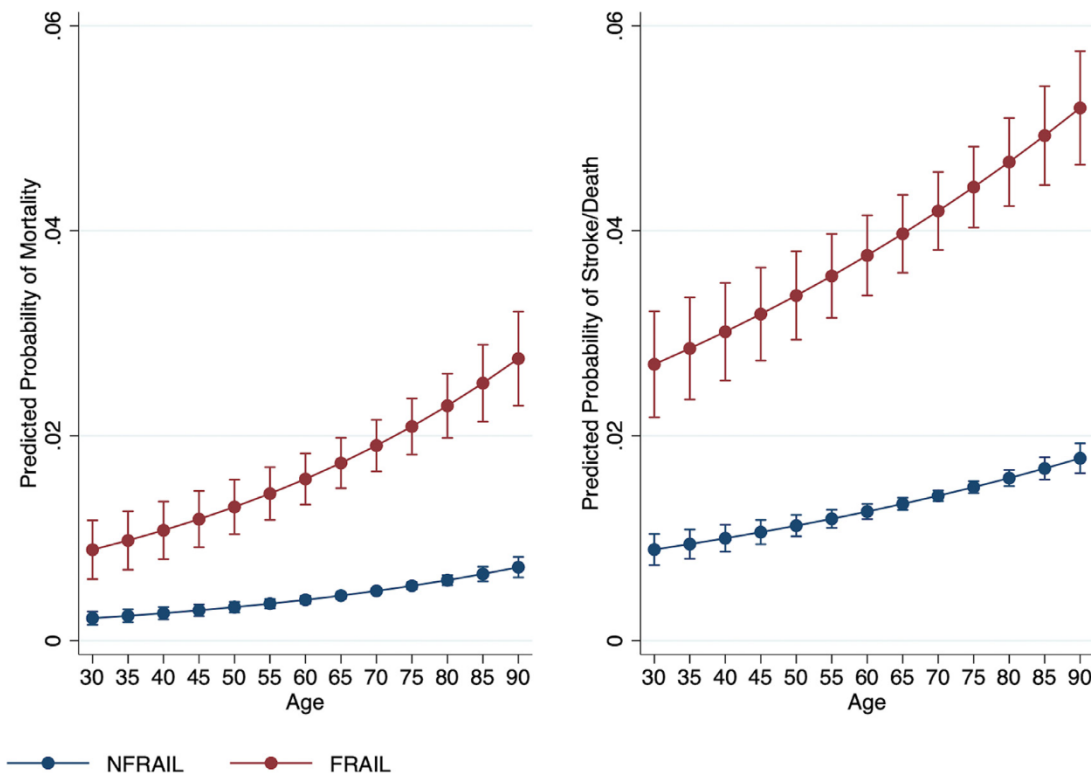


Fig. 2. Predicted probability of mortality (Panel A) or stroke/death (Panel B) by age and frailty status.

increased likelihood of all evaluated outcomes. Among nonelective cases, frail status was linked to a greater likelihood of in-hospital mortality, MI, and composite stroke/death, but not postoperative stroke (Supplementary Table IV). Several other patient and hospital characteristics were associated with inferior outcomes in patients undergoing carotid revascularization (Table III).

Furthermore, frailty was associated with increased costs ($\beta = +\$5,980$, 95% CI: \$5,490–\$6,470, $P < 0.001$) and overall LOS ($\beta = +2.6$ days, 95% CI: 2.4–2.8, $P < 0.001$). Exclusion of procedures during the 2017 calendar year for sensitivity analysis did not alter the findings reported above.

A subset analysis was performed to assess the interaction of frailty and procedure type on outcomes. Similar average marginal effects on mortality as well as the composite endpoint of stroke/death were observed in frail patients who underwent CEA versus CAS (Fig. 3).

DISCUSSION

With increased emphasis on value-based healthcare delivery, accurate identification of risk factors, and perioperative risk reduction are particularly relevant. Traditional risk factors aside, frailty has

recently garnered attention as an independent predictor of inferior outcomes in a multitude of operations. Given the complexities associated with traditional frailty assessment tools, we utilized a coding-based frailty instrument in a large national cohort of patients undergoing carotid interventions and made several important observations. While the proportion of patients identified as frail steadily increased in both cohorts, frailty and symptomatic presentation appear more prevalent among patients receiving a carotid stent compared to endarterectomy. Frailty was independently associated with increased odds of perioperative MI, stroke, in-hospital death, as well as greater postoperative LOS and hospitalization costs for both modalities. Compared to symptomatic disease, frailty was found to have a greater impact on outcomes of patients with asymptomatic carotid stenosis. These findings warrant further discussion.

Convincing evidence on the association of frailty with postoperative outcomes has motivated the incorporation of this variable into multiple risk prediction models including the NSQIP mFI.^{8–10,31,32} However, measures of frailty are highly varied and range from assessment of physical performance and sarcopenia to an inventory of chronic conditions. A binary tool based on the presence of several clusters

Table III. Multivariable analysis of factors associated with mortality following carotid endarterectomy and stenting

| | AOR | 95% CI | P-value |
|--|-----------|-----------|---------|
| Frailty | 1.53 | 1.30–1.80 | <0.001 |
| Type of procedure | | | |
| CEA ^a | Reference | | |
| CAS ^b | 3.15 | 2.81–3.52 | <0.001 |
| Symptomatic status | | | |
| Asymptomatic | Reference | | |
| Symptomatic | 1.98 | 1.71–2.28 | <0.001 |
| Age (per year increment) | 1.02 | 1.01–1.03 | 0.075 |
| Elixhauser index (per 1-point increment) | 1.18 | 1.17–1.27 | <0.001 |
| Sex | | | |
| Male | Reference | | |
| Female | 1.03 | 0.91–1.15 | 0.654 |
| Admission status | | | |
| Nonelective | Reference | | |
| Elective | 0.35 | 0.30–0.39 | <0.001 |
| Race | | | |
| White | Reference | | |
| Black | 1.21 | 0.99–1.48 | 0.061 |
| Hispanic | 1.25 | 1.00–1.58 | 0.045 |
| Asian | 1.62 | 1.12–2.38 | 0.009 |
| Other ^c | 1.03 | 0.81–1.30 | 0.812 |
| Insurance coverage | | | |
| Private | Reference | | |
| Medicare | 1.36 | 1.07–1.73 | 0.013 |
| Medicaid | 0.96 | 0.80–1.15 | 0.647 |
| Other ^d | 1.44 | 1.11–1.87 | 0.006 |
| Hospital region | | | |
| Northeast | Reference | | |
| Midwest | 1.01 | 0.84–1.22 | 0.908 |
| South | 1.02 | 0.87–1.18 | 0.847 |
| West | 1.10 | 0.92–1.32 | 0.308 |
| Teaching Status | | | |
| Rural, nonteaching | Reference | | |
| Urban, nonteaching | 1.18 | 0.88–1.58 | 0.271 |
| Urban, teaching | 1.40 | 1.04–1.87 | 0.024 |
| Bed size | | | |
| Small | Reference | | |
| Medium | 1.06 | 0.85–1.33 | 0.598 |
| Large | 1.32 | 1.07–1.62 | 0.01 |
| Hospital volume | | | |
| Low | Reference | | |
| Medium | 0.86 | 0.72–1.02 | 0.089 |
| High | 0.81 | 0.67–0.98 | 0.032 |
| Comorbidities | | | |
| Congestive heart failure | 2.12 | 1.81–2.46 | <0.001 |
| Coronary artery disease | 0.58 | 0.51–0.65 | <0.001 |
| Coagulopathy | 2.20 | 1.75–2.77 | <0.001 |
| Liver disease | 2.78 | 2.04–3.79 | <0.001 |
| Chronic kidney disease | 0.97 | 0.83–1.13 | 0.679 |
| Pulmonary circulation disorders | 1.08 | 0.82–1.43 | 0.569 |

^aCEA indicates carotid endarterectomy.

^bCAS indicates carotid artery stenting.

^cIndicates a combined group of Native American and other races as defined by NIS.

^dIndicates a combined insurance status including self-pay, uninsured, and other.

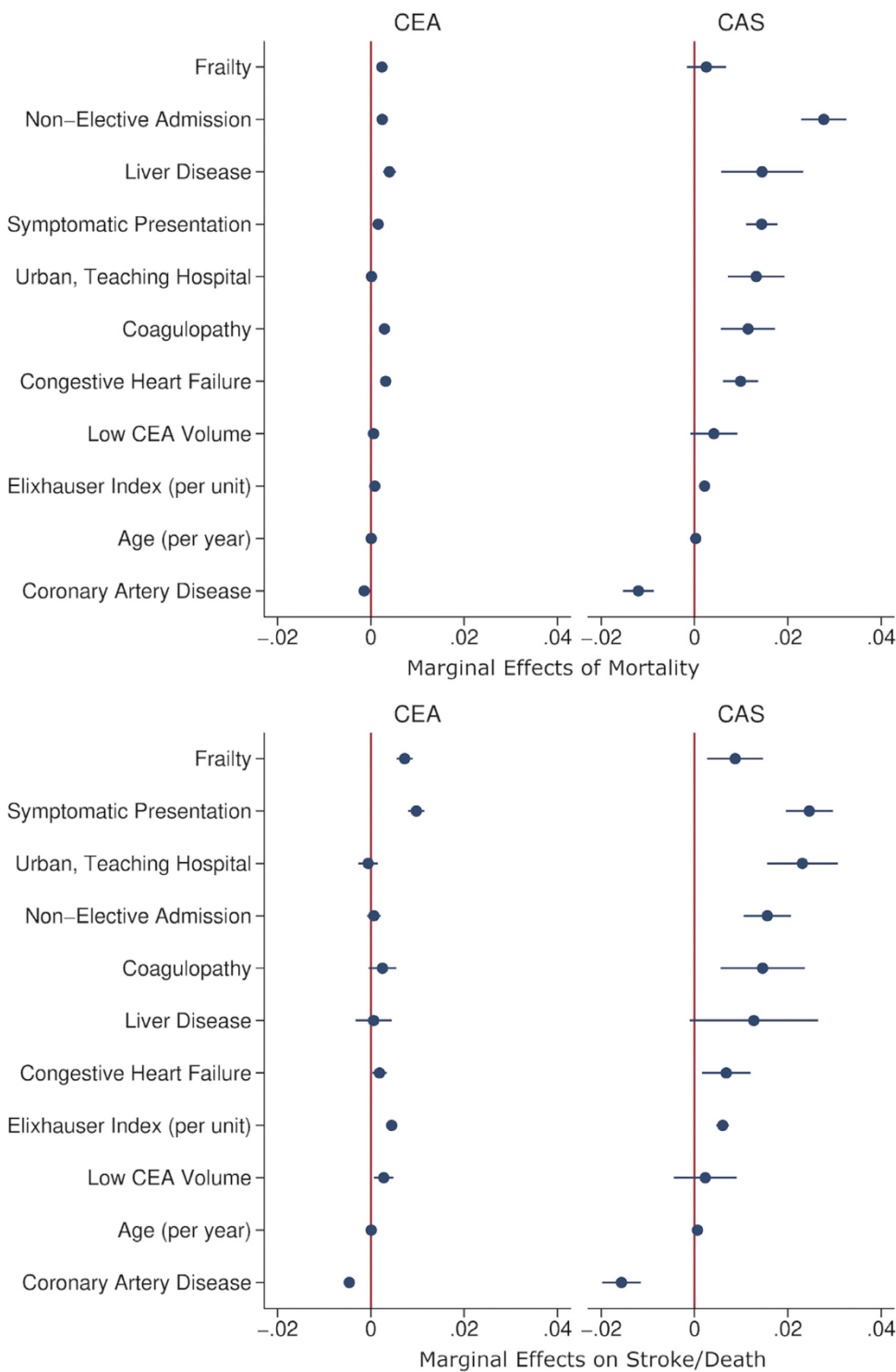


Fig. 3. Average marginal effects of frailty and covariates on mortality (Panel A) and stroke/death (Panel B) following CEA or CAS.

of chronic conditions, the ACG frailty tool, provides an administrative alternative that may be derived automatically. The present study demonstrates patients considered frail using a derivative of

the ACG methodology to have inferior clinical outcomes and increased costs following carotid revascularization. Given the coding-based nature of this method and validation using a national

cohort, such an indicator may provide additional discriminatory power and better inform decision-making among vulnerable and frail patients.

The effect of frailty across treatment groups speaks to its influence on outcomes and prognostic power. The efficacy of carotid interventions based on the NASCET and ACAS trials of the 1990s has been predicated on long-term survival and minimal peri-procedural risk.^{33–34} Therefore, factors predisposing patients to shorter life expectancy, including advanced age and chronic kidney disease, have been considered by many as contraindications to intervention in asymptomatic patients.^{35–36} In our cohort, neither age nor chronic kidney disease were associated with increased mortality on multivariable analysis. However, frailty was strongly associated with risks of in-hospital mortality, stroke, MI, and composite endpoints following intervention. This finding demonstrates the potential utility of frailty tools in preoperative risk assessment to potentially minimize adverse outcomes in high-risk patients.

In the present analysis, frailty remained a significant predictor of inferior outcomes in asymptomatic patients. However, frail status was not associated with increased mortality or postoperative stroke after adjustment in patients with symptomatic disease. Given its large magnitude of impact, symptomatic status may overshadow the association of frailty with death and yield the present observation. Nonetheless, the ACAS trial of 1995 established a threshold of <3% stroke/death for CEA to be considered an effective intervention for asymptomatic patients presenting with carotid stenosis.³⁴ The present study found the stroke/death rate for frail asymptomatic patients was 3.4% and 6.3% for patients who underwent CEA and CAS, respectively. Due to the potential for coding inaccuracies for symptomatic disease, we explored elective admission as a proxy for asymptomatic cases and observed similar findings in frail patients admitted electively. This observation suggests that the risks associated with a carotid stenting may outweigh the benefits for frail asymptomatic patients and is in line with the Society for Vascular Surgery guidelines on reserving CAS for symptomatic patients with stenosis of 50% to 99% at high risk for CEA. While the overall decision to intervene on asymptomatic cases of carotid stenosis is multifaceted, particular attention to frailty is needed to ensure informed and shared decision-making.

Frailty was associated with inferior outcomes for both CEA and CAS. Transfemoral carotid stenting has traditionally been associated with higher

rates of perioperative stroke, while conferring less cardiac risk than CEA.³ In our cohort, CAS was associated with higher unadjusted rates of mortality, postoperative stroke and MI. However, this study found the overall effect size of frailty on mortality and the composite outcome of stroke/death was similar between patients undergoing CEA with those undergoing CAS. This observation may in part be explained by a reduced ability to accommodate the hemodynamic changes associated with carotid clamping and general anesthesia for CEA. Prospective studies to determine optimal treatment strategies for frail patients with asymptomatic versus symptomatic carotid stenosis are warranted.

In the present study, frailty was associated with increased hospitalization costs and longer postoperative LOS. Consistent with our findings, several national studies have reported higher costs and LOS in frail patients undergoing cardiac, vascular, and head and neck surgical procedures.^{12,17,37–38} To date, this is the first study that evaluated the effect of frailty on resource utilization following carotid interventions. We found that frailty resulted in approximately twice the costs and prolonged postoperative LOS by almost 3 days when compared to nonfrail patients. Increased costs and postoperative LOS are likely attributed to greater incidence of complications associated with a high-risk population as well as difficulty managing patients with an accumulation of several comorbidities. The impact of frailty on hospitalization costs and postoperative LOS may better refine benchmarks and inform resource allocation.

The present study has several important limitations including those inherent to its retrospective design. The NIS is an administrative database and diagnoses and procedures are identified by ICD codes, which are influenced by provider and hospital practices. The increasing proportion of frail patients in this cohort may be a result of improved coding practices over time. Additionally, this study found approximately 92% of patients who received CEA or CAS had asymptomatic presentation, likely reflecting an inability to document recency of symptoms or potential inaccuracy in diagnosis codes. Nevertheless, this study used specific codes that identify carotid stenosis with or without symptoms to stratify the patient population. To characterize iatrogenic stroke outcomes, we also utilized ICD codes that specify stroke events as a postoperative complication. Furthermore, the results of clinical-level data, such as imaging and laboratory studies,

could not be captured in the NIS. As the NIS reports only inpatient hospitalizations, this study was further limited to outcomes at the index hospitalization with no data on readmissions or long-term outcomes. In addition, we were only able to capture transfemoral stent procedures and thus have no data on the impact of frailty on transcarotid stent operations. Nonetheless, we used the largest available all payer database to report on nationally representative outcomes.

CONCLUSIONS

In summary, frailty is associated with significantly increased odds of in-hospital mortality, stroke, and MI among patients undergoing carotid revascularization. Frail patients are at greater risk for increased hospitalization costs and prolonged length of stay. Preoperative evaluation for carotid intervention should include an assessment of frailty.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.avsg.2020.12.039](https://doi.org/10.1016/j.avsg.2020.12.039).

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