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The Effect of Frailty on Short-Term Outcomes After Head and Neck Cancer Surgery

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Objective: To determine the relationship between frailty and comorbidity, in-hospital mortality, postoperative complications, length of hospital stay (LOS), and costs in head and neck cancer (HNCA) surgery.

Study Design: Cross-sectional analysis.

Methods: Discharge data from the Nationwide Inpatient Sample for 159,301 patients who underwent ablative surgery for a malignant oral cavity, laryngeal, hypopharyngeal, or oropharyngeal neoplasm in 2001 to 2010 was analyzed using cross-tabulations and multivariate regression modeling. Frailty was defined based on frailty-defining diagnosis clusters from the Johns Hopkins Adjusted Clinical Groups frailty-defining diagnosis indicator.

Results: Frailty was identified in 7.4% of patients and was significantly associated with advanced comorbidity (odds ratio [OR] = 1.5[1.3–1.8]), Medicaid (OR = 1.5[1.3–1.8]), major procedures (OR = 1.6[1.4–1.8]), flap reconstruction (OR = 1.7[1.3–2.1]), high-volume hospitals (OR = 0.7[0.5–1.0]), discharge to a short-term facility (OR = 4.4[2.9–6.7]), or other facility (OR = 5.4[4.5–6.6]). Frailty was a significant predictor of in-hospital death (OR = 1.6[1.1–2.4]), postoperative surgical complications (OR = 2.0[1.7–2.3]), acute medical complications (OR = 3.9[3.2–4.9]), increased LOS (mean, 4.9 days), and increased mean incremental costs ($11,839), and was associated with higher odds of surgical complications and increased costs than advanced comorbidity. There was a significant interaction between frailty and comorbidity for acute medical complications and length of hospitalization, with a synergistic effect on the odds of medical complications and LOS in patients with comorbidity who were also frail.

Conclusion: Frailty is an independent predictor of postoperative morbidity, mortality, LOS, and costs in HNCA surgery patients, and has a synergistic interaction with comorbidity that is associated with an increased likelihood of medical complications and greater LOS in patients with comorbidity who are also frail.

Key Words: Frailty, comorbidity, complications, mortality, surgery, head and neck cancer, Nationwide Inpatient Sample.

Level of Evidence: 2c.

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INTRODUCTION

Gains in life expectancy, along with increased incidence of head and neck cancers (HNCAs), have introduced critical questions regarding the appropriate surgical management of older adults with HNCA given the unique challenges often associated with advanced age, such as comorbidities, polypharmacy, and frailty. Over 45,000 new cases of HNCA are diagnosed in the United States each year, with increased incidence of all cancers with advancing age.[1] Age is associated with worse outcomes among surgical patients, including HNCA patients, with increased rate of complications, length of hospital stay, and mortality.[2–6] However, age alone is a limited indicator of patients' ability to undergo surgical treatment for their oncologic disease and may place older adults at risk of not receiving standard treatments associated with improved survival.[2,7–10]

Beyond age, surgeons increasingly recognize the clinical entity of frailty to better capture the functional status of patients and their ability to undergo surgical resection—an entity that geriatricians have recognized as a key risk factor for poor outcomes for more than two decades.[11] Fried et al. define frailty as a phenotype characterized by decreased ability to restore homeostasis following exposure to a stressor, which thus increases the risk of a negative outcome.[12,13] Numerous measurements attempt to capture a patient's degree of frailty based on clinical assessment of physical function, such as Fried et al.'s frailty phenotype based on five criteria, including unintentional weight loss, exhaustion, decreased grip strength, decreased walking speed, and low physical activity—or a more comprehensive, multidomain assessment, such as

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the Canadian Study of Health and Aging Frailty Index, which documents deficits in physical function along with cognitive, functional, and social status.[12,14,15] Measures of frailty also have been adapted for use with claims data, which utilize frailty-defining diagnoses such as the Johns Hopkins Adjusted Clinical Groups (ACG) frailty-defining diagnosis indicator.[16] The ACG indicator has been further adapted to capture 10 clusters of frailty-defining diagnoses based on the International Classification of Disease, Ninth Revision (ICD-9), codes assigned during admission.[17,18]

Although frailty is an established risk factor for significant adverse outcomes across surgical specialties, relatively few large-scale studies have explored the extent to which frailty impacts outcomes among HNCA patients, particularly in differentiating the effects of comorbidity and frailty.[19–21] *Comorbidity*, defined as the presence of two or more chronic conditions or diseases, differs from *frailty*, which is a physiological state of vulnerability characterized by changes such as weight loss, fatigue, decreased muscle mass, and changes in gait or cognition, and must be differentiated due to differences in prevention and treatment strategies and overall health care implications.[22] HNCA patients may be at an increased risk of frailty given the symptoms and risk factors associated with HNCA, including unintentional weight loss, malnutrition, and lower rates of social support.[23–25] We examined the rate of frailty and its effects on short-term outcomes among patients undergoing surgical management for HNCA. We hypothesized that frailty would independently increase the risk of postoperative complications, length of hospitalization, and costs in HNCA surgery.

MATERIALS AND METHODS

We conducted a cross-sectional analysis utilizing discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality. The analytic cohort consisted of patients with a diagnosis of oral cavity, laryngeal, hypopharyngeal, or oropharyngeal cancer. As previously described, the NIS is the largest all-payer inpatient care database in the United States, containing data from approximately 8 million hospital stays each year from a stratified sample of 20% of nonfederal U.S. hospitals from participating states.[21,26–30] The NIS database captures information on the index hospital admission, including patient demographic data, primary and secondary diagnoses, primary and secondary procedures, hospital characteristics, and inpatient and discharge mortality rates.[21,27–30] We utilized codes to identify adult patients ($\geq$ 18 years of age) who underwent an ablative procedure for a malignant oral cavity, laryngeal, hypopharyngeal, or oropharyngeal neoplasm for the years 2001 through 2010[21,27–30] (Supporting Table SI). The cohort included oropharyngeal cancer patients undergoing biopsy if neck dissection was the index admission procedure and no other ablative procedure was recorded.[21,27–30] Codes for pedicled or free flap reconstruction were used to identify patients undergoing reconstructive procedures, and codes for previous exposure to therapeutic or other ionizing radiation (V15.3) were used to identify patients with prior irradiation.[21,27–30]

We graded comorbidity using the Romano adaptation of the Charlson comorbidity index, excluding ICD-9 codes for the index cancer diagnosis from the solid tumor category, as previously described.[21,27–33] The NIS does not include cancer staging information, and ICD-9 codes for metastases have been shown to be an unreliable surrogate for disease stage and therefore were excluded.[21,27–30] Codes for specific comorbid illnesses were used to create categories for acute medical and surgical complications (Supporting Table 2). Acute medical complications were derived from codes for acute cardiac events, acute pulmonary edema or failure, acute renal failure, acute hepatic failure, acute cerebrovascular events, sepsis, pneumonia, and UTI assigned at the time of hospital discharge. Surgical complications were derived from codes for complications directly resulting from surgical procedures assigned at the time of hospital discharge, as previously described.[21,27–30] Frailty was defined based on the 10 clusters of frailty-defining diagnoses that comprise the Johns Hopkins ACG frailty-defining diagnosis indicator—a binary variable—using ICD-9 codes assigned during admission[16] (Table I). Frailty-defining diagnoses were distinct from comorbidity diagnoses, with the exception of dementia, for which the ICD-9 codes 290.0 to 290.3 that defined dementia in the frailty index were also part of the definition of dementia in comorbidity coding, but only accounted for 1.5% of cases of dementia as defined by comorbidity.

Frailty, in-hospital death, postoperative complications, length of hospitalization, and costs was examined as dependent variables. Interactions between frailty and comorbidity were investigated. Where independent, frailty was also examined as an independent variable. Other independent variables included were age, sex, race/ethnicity, payer source (commercial or health maintenance organization, Medicare, Medicaid, self-pay, or other), comorbidity, nature of admission (emergent/urgent, or other), procedure severity, flap reconstruction, prior radiation, hospital ownership/control, hospital bed size, hospital location (rural or urban), geographic region, hospital teaching status, and hospital volume. As previously described, procedures were categorized by severity as minor (excision/destruction of lesion, tonsillectomy, and partial glossectomy, with or without neck dissection; and neck dissection alone when performed as the index admission procedure) and major (partial or total laryngectomy, esophagectomy, total glossectomy, pharyngectomy, mandibulectomy, and maxillectomy, with or without neck dissection).[21,27,29,30] The average annual number of HNCA surgery cases performed per year of surgical activity was obtained by calculating the mean of the number of cases performed each year for each individual hospital for the years in which that hospital performed at least one HNCA cancer surgery.[27–29] Hospital volume was stratified by tertiles, which resulted in cutoff values for annual case volume of $\leq$ 14, 15 to 65, and $>$ 65 cases per year.[27–29] The tertiles were classified as low-, intermediate-, and high-volume hospitals.[27–29] The NIS database does not include American Joint Commission on Cancer tumor stage, tumor grade, histological subtype, or outcome after discharge.

Hospital-related charges for each index admission were converted to the organizational cost of providing care using cost-to-charge ratios for individual hospitals. We utilized detailed reports by hospitals to the Centers for Medicare and Medicaid Services to calculate the cost-to-charge ratios, which provide an estimate of the all-payer inpatient cost-to-charge ratio by hospital.[21,27–30] Each patient's charge is multiplied by the cost-to-charge ratio to calculate the cost per admission.[21,27–30,34] Based on the U.S. Bureau of Labor Statistics indices, all costs were adjusted for inflation and results converted to 2016 USD.[21,27–30,35,36] National cost estimates were obtained by reweighting all discharges in order to account for cases for which cost estimates were missing.[21,27–30,34]

We utilized Stata 12 (StataCorp, College Station, Texas, U.S.A.) for all data analyses. Similar to previously described

TABLE I.
Frailty-Defining Diagnoses in The Johns Hopkins ACG Frailty Indicator With Corresponding ICD-9 Codes.

Variable	Diagnoses	ICD9
Malnutrition	Nutritional marasmus	261, 262, 263.8, 263.9, V77.2
	Other severe protein-calorie malnutrition	
Dementia	Senile dementia with delusional or depressive features	290.20, 290.21, 290.3
	Senile dementia with delirium	
Severe vision impairment	Profound impairment, both eyes	369.0, 369.00, 369.01, 369.03, 369.04, 369.06, 369.07, 369.08
	Moderate or severe impairment, better eye/lesser eye: profound	
Decubitus ulcer	Decubitus ulcer	707.0, 707.00, 707.01, 707.02, 707.03, 707.04, 707.05, 707.06, 707.07, 707.09, 707.20, 707.21, 707.22, 707.23, 707.24, 707.25
Incontinence of urine	Incontinence without sensory awareness	788.34, 788.37
	Continuous leakage	
Loss of weight	Abnormal loss of weight and underweight	783.2, 783.21, 783.22, 783.3
	Feeding difficulties and mismanagement	
Fecal incontinence	Incontinence of feces	787.6
Social support needs	Lack of housing	V60.0, V60.1,
	Inadequate housing	V60.2
	Inadequate material resources	
Difficulty in walking	Difficulty in walking	719.7, 781.2
	Abnormality of gait	
Fall	Fall on stairs or steps	E880, E880.0, E880.1, E880.9, E884.3
	Fall from wheelchair	

ACG = Adjusted Clinical Groups; ICD-9 = International Classification of Disease, Ninth Revision.

methodology, associations between variables were analyzed using cross-tabulations, multivariate logistic regression, and multinomial logistic regression modeling.[21,27–30] Data were weighted, applying modified hospital and discharge weights to correct for changes in sampling over time.[21,27–30] Variance estimation was performed using procedures for survey data analysis with replacement.[21,27–30] Strata with one sampling unit were centered at the population mean.[21,27–30] Variables with missing data for more than 10% of the population were coded with a dummy variable to represent the missing data in regression analysis.[21,27–30] We employed multiple logistic regression analysis to evaluate the primary clinical endpoints. Cost and length of stay were analyzed using generalized linear regression modeling with a log link given non-normal distribution. Interactions between frailty and comorbidity were evaluated in regression models. If the interaction was not significant, the interaction was dropped from the model. This protocol was reviewed and approved as exempt by the Johns Hopkins Medical Institutions Institutional Review Board.

RESULTS

There were 159,301 cases in 2001 to 2010 (Table II). The majority of patients were male, White, and the mean age was 62 years (range, 18–104). Frailty was present in 7.4% of all patients and was significantly more common in patients with larynx or hypopharynx tumors, aged $\geq$ 65 years, with Medicare or Medicaid insurance coverage, and with comorbidity. Comorbid conditions were significantly more common in frail patients (52.8%) than in non-frail patients (37.1%; $P < 0.001$). Frail patients were more likely to be admitted urgently or emergently, undergo major procedures, undergo flap reconstruction, and sustain postoperative medical and surgical complications. The incidence of nonstandard discharge and mortality were higher in frail patients. Multiple logistic regression analysis of variables associated with frailty are shown in Table III. After controlling for all other variables, frailty was significantly associated with an increased likelihood of urgent or emergent admission, major surgical procedures, flap reconstruction, advanced comorbidity, Black race/ethnicity, Medicaid, and nonstandard discharge. Frailty was associated with decreased odds of laryngeal primary site disease and high-volume hospital care, whereas sex and age were not significantly associated with frailty.

Multiple logistic regression analysis of independent variables associated with the risk of in-hospital death and postoperative complications are shown in Table IV. After controlling for the effects of all variables, independently significant factors associated with an increased risk of in-hospital death were age > 80 years, Medicare or Medicaid insurance, urgent or emergent admission, major procedures, flap reconstruction, frailty, and comorbidity, whereas high-volume hospital care was associated with decreased odds of mortality. Comorbidity was associated with greater odds of in-hospital death than frailty. The odds of postoperative surgical complications were significantly higher for urgent or emergent admission, Medicaid, major procedures, flap reconstruction, frailty, and comorbidity, and were lower for laryngeal primary site disease. Frailty was associated with greater odds of

TABLE II.
Demographic Characteristics.

	All Patients (N = 159,301)	Non-Frail (N = 147,578)	Frail (N = 11,723)	*P* Value
Primary site				<0.0001
Oral cavity	37.5%	37.8%	34.4%	
Larynx	27.1%	26.5%	34.2%	
Hypopharynx	3.6%	3.3%	6.6%	
Oropharynx	31.8%	32.4%	24.8%	
Age group				<0.0001
≤ 40 years	4.0%	4.1%	2.5%	
40–64 years	54.6%	54.9%	51.1%	
65–80 years	33.8%	33.4%	38.2%	
> 80 years	7.6%	7.6%	8.2%	
Race/ethnicity				0.0037
White	60.6%	60.9%	56.9%	
Black	6.7%	6.4%	10.8%	
Hispanic	4.2%	4.3%	3.1%	
Asian or Pacific Islander	1.4%	1.5%	0.6%	
Native American	0.3%	0.3%	0.1%	
Other	2.0%	2.0%	2.0%	
Unknown	24.8%	24.6%	26.5%	
Sex				0.6040
Male	70.0%	70.0%	70.6%	
Female	30.0%	30.0%	29.4%	
Payor				<0.0001
Private	42.0%	40.9%	27.8%	
Medicare	10.8%	41.5%	48.9%	
Medicaid	39.9%	10.3%	16.8%	
Self-pay	3.7%	3.7%	2.8%	
No charge	0.5%	0.5%	0.3%	
Other	3.1%	3.1%	3.4%	
Nature of admission				<0.0001
Elective	83.8%	84.6%	74.5%	
Emergency/urgent	16.2%	15.4%	25.5%	
Comorbidity				<0.0001
0	61.7%	62.9%	47.2%	
1	26.2%	25.5%	33.8%	
2	8.3%	7.9%	13.1%	
≥ 3	3.8%	3.7%	5.9%	
Procedure severity				<0.0001
Minor	50.3%	51.9%	30.6 %	
Major	49.7%	48.1%	69.4%	
Flap reconstruction				<0.0001
No	89.7%	90.5%	80.5%	
Yes	10.3%	9.5%	19.5%	
Hospital volume				0.1699
Low (6–14 cases/year)	33.6%	33.5%	33.7%	
Intermediate (15–65 cases/year)	33.1%	32.8%	37.7%	
High (> 65 cases/year)	33.3%	33.7%	28.6%	
Hospital bed size				0.0059
Small	10.6%	10.9%	6.8%	
Medium	16.7%	16.8%	15.8%	
Large	72.7%	72.3%	77.4%	

TABLE II.
(*Continued*)

	All Patients (N = 159,301)	Non-Frail (N = 147,578)	Frail (N = 11,723)	*P* Value
Hospital teaching status				0.6565
Nonteaching hospital	21.0%	21.0%	20.3%	
Teaching hospital	79.0%	79.0%	79.7%	
Hospital ownership/control				0.3499
Government, nonfederal	24.9%	24.9%	24.8%	
Private, nonprofit	69.0%	69.1%	67.2%	
Private, for profit	6.1%	6.0%	8.0%	
Geographic region				0.0113
Northeast	20.8%	21.2%	16.2%	
Midwest	23.8%	23.4%	28.5%	
South	37.7%	37.4%	41.8%	
West	17.7%	18.0%	13.5%	
Hospital location				0.6011
Rural	4.6%	4.6%	4.9%	
Urban	95.4%	95.4%	95.1%	
Postoperative complications				
Acute cardiac event	9.8%	9.3%	16.0%	<0.0001
Acute pulmonary edema/failure	3.8%	3.0%	14.7%	<0.0001
Acute cerebrovascular event	0.5%	0.5%	1.1%	0.0004
Acute renal failure	1.4%	1.1%	4.8%	<0.0001
Acute hepatic failure	<0.1%	<0.1%	0.1%	0.0902
Pneumonia	6.4%	5.4%	20.1%	<0.0001
Sepsis	1.0%	0.7%	4.3%	<0.0001
Urinary tract infection	1.9%	1.6%	5.4%	<0.0001
Surgical complications	10.8%	9.9%	22.3%	<0.0001
Disposition				<0.0001
Routine	57.3%	59.8%	25.5%	
Short-term hospital care	0.8 %	0.7%	1.7%	
Other facility	11.0%	9.5%	30.0%	
Home health care	29.9%	29.0%	40.3%	
AMA	0.1%	0.1%	0.2%	
Died in hospital	0.9%	0.8%	2.2%	

postoperative surgical complications than comorbidity. Acute medical complications were significantly associated with increasing age, urgent or emergent admission, Medicare or Medicaid, major surgical procedures and pedicled or free flap reconstruction, frailty, and comorbidity, whereas oropharynx primary site, female sex, and high-volume hospital care was significantly associated with lower odds of acute medical complications. There was a significant interaction between frailty and comorbidity for acute medical complications, with a synergistic effect in patients with low or moderate comorbidity who also were frail. This interaction was not significant for in-hospital mortality or surgical complications.

Multivariate generalized linear regression analyses of independent variables predictive of length of hospital stay and hospital-related costs are shown in Table V, with mean values representing the change in the value of the intercept mean. Urgent or emergent admission, age $\geq$ 65 years, hypopharyngeal primary site disease, major surgical procedures, pedicled or free flap reconstruction, comorbidity, and Black or Hispanic race/ethnicity and noncommercial insurance were significantly associated with greater length of hospitalization. There was a significant interaction between frailty and comorbidity for length of stay, with a synergistic effect in patients with comorbidity who also were frail. Hospital costs were significantly associated with laryngeal cancer, urgent/emergent admission, Black or Hispanic race/ethnicity, major procedures and flap reconstruction, increased hospital volume, Medicare or Medicaid, frailty, and comorbidity. The interaction between frailty and comorbidity was not significant for hospital costs, with frailty an independent predictor of cost and associated with significantly increased costs compared to advanced comorbidity, after controlling for all other variables.

DISCUSSION

In this study of a large national cohort of HNCA patients, frailty was independently associated with several significant adverse short-term outcomes, including

TABLE III.
Multivariate Logistic Regression Analysis of Variables Significantly Associated With Frailty.

Variable	Odds Ratio	95% CI	*P* Value
Larynx primary site	0.85	0.74 to 0.98	0.031
Black race/ethnicity	1.26	1.06 to 1.50	0.009
Major procedure	1.59	1.37 to 1.84	<0.001
Pedicled or free flap reconstruction	1.71	1.40 to 2.09	<0.001
Urgent/emergent admission	1.65	1.43 to 1.91	<0.001
High-volume hospital	0.66	0.45 to 0.96	0.034
Medicaid	1.52	1.27 to 1.83	<0.001
Comorbidity score 1	1.37	1.20 to 1.56	<0.001
Comorbidity score 2	1.49	1.25 to 1.78	<0.001
Comorbidity score $\geq$ 3	1.33	1.04 to 1.70	0.010
Discharge to short-term hospital	4.40	2.90 to 6.65	<0.001
Discharge to other facility	5.42	4.47 to 6.55	<0.001
Home healthcare	2.70	2.29 to 3.18	<0.001

in-hospital mortality, postoperative medical and surgical complications, increased length of hospitalization, and increased cost. Compared to comorbidity, frailty was a greater predictor of postoperative surgical complications and increased costs than comorbidity. In this study, frailty interacted significantly with comorbidity, increasing the odds of acute medical complications and increased length of hospitalization synergistically.

Overall, 7.4% of the cohort were frail, which can be compared to similar rates of frailty in other studies of surgical patients in whom estimates range from 8.6% to 28%, with higher rates of frailty seen in studies restricted to cohorts comprised of older adults only.[19,37,38] Frailty was more common in older patients and the rates of comorbid conditions, nonstandard discharge, and mortality were higher among frail patients, highlighting the complexity and additional resources often required to care for frail patients. In this study, frailty was independently associated with Black race/ethnicity and Medicaid status, which is similar to studies of frailty in a general older adult population.[12] The association between frailty, Black race/ethnicity, and Medicaid status may represent an additional risk factor for adverse outcomes among an already at-risk disadvantaged population.

Frailty is a known risk factor for mortality and postoperative complications among older surgical patients across specialties. Increased rates of mortality have been documented among frail general surgery patients as well as HNCA patients.[21,37] Similarly, frailty has been shown to increase the risk of postoperative complications among older adults undergoing general surgery, colorectal procedures, cardiac surgery, or head and neck oncologic procedures.[19,21,38,39] When considering the risk of mortality and postoperative complications, the effects of comorbidity and frailty are closely related. We found that comorbidity was associated with greater odds of in-hospital mortality than frailty, whereas frailty was associated with greater odds of postoperative surgical complications than comorbidity. We found a significant interaction between frailty and comorbidity that synergistically increased the odds of acute medical complications in HNCA surgical patients, suggesting that frailty significantly modifies the impact of comorbidities in the acute postoperative period. HNCA surgical patients may experience malnutrition, weight loss, and low social support, all of which are frailty-defining conditions that may contribute to increased risk of complications in the immediate postoperative period, beyond comorbidities.[23–25]

Besides mortality and postoperative complications, frailty is associated with increased length of hospitalization and costs. In this study, frailty increased the length of hospitalization by a mean of almost 5 days, which is greater than other studies of HNCA patients.[21] Among patients who also were frail, comorbidity synergistically increased the length of hospitalization. Studies of general surgery patients also document increased length of hospitalization, with frail patients having 65% to 89% longer stays in one study.[19,39] Increased length of hospital stay may be secondary to greater care needs that may need to be addressed prior to discharge, greater delays in return to baseline function, or relapse due to frailty not captured by complication codes. With increased length of hospitalization and postoperative complications, we found that frailty equated to an increase in mean incremental cost of over $11,000, which is nearly double the amount reported in other studies of HNCA patients.[21]

Our study has several limitations, primarily related to the use of hospital-level discharge data via the NIS database. Given the NIS database's focus on inpatient care, only limited follow-up data are available and are restricted to the index admission and a 30-day postoperative window, confining analysis to short-term effects and outcomes. No information on survival rates are available, and we are unable to assess long-term outcomes to understand differences in outcomes and survival of HNCA patients by frailty status. As noted in previous work with the NIS database, the database lacks information on prior surgery or chemotherapy, as well as the grade, subtype, or stage of HNCA, which may impact the extent of surgery, likelihood of complications, and length of hospital stay. Other important quality indicators, such as readmission, are not available. Similarly, there may be differences between patients, extent of disease, and case mix, in general, not captured in administrative databases that rely on discharges diagnoses, such as the NIS database. Rates of postoperative complications may not be accurately captured given that not all postoperative complications may be detected by discharge. Frailty may be underestimated due to undercoding of frailty-defining diagnoses, which may not be recognized and coded by administrative personnel, and because the use of interventions known to mitigate the effect of frailty-defining diagnoses are not described in ICD-9 coding and thus cannot be determined. The use of a binary definition of frailty does not allow evaluation of the effect of different degrees of frailty. Another potential limitation is that the cost analysis was based on hospital-related charges, adjusted for institutional

TABLE IV.
Multivariate Logistic Regression Analysis of Variables Significantly Associated With Risk of In-Hospital Death and Postoperative Complications.

Variable	Odds Ratio	95% CI	*P* Value
In-hospital death			
Age > 80 years	1.66	1.19 to 2.31	0.003
Medicare	1.83	1.16 to 2.88	0.010
Medicaid	1.93	1.19 to 3.13	0.007
Major procedure	1.98	1.42 to 2.76	<0.001
Pedicled or free flap reconstruction	2.44	1.77 to 3.38	<0.001
Urgent/emergent admission	1.66	1.19 to 2.31	0.003
High-volume hospital	0.60	0.40 to 0.90	0.014
Frail	1.62	1.12 to 2.36	0.011
Comorbidity score 1	2.01	1.45 to 2.79	<0.001
Comorbidity score 2	4.64	3.20 to 6.73	<0.001
Comorbidity score ≥ 3	6.20	4.05 to 9.49	<0.001
Postoperative surgical complications			
Larynx primary site	0.77	0.70 to 0.85	<0.001
Major procedure	2.28	2.07 to 2.50	<0.001
Pedicled or free flap reconstruction	2.38	2.06 to 2.74	<0.001
Urgent/emergent admission	1.17	1.01 to 1.37	0.036
Medicaid	1.25	1.08 to 1.46	0.003
Frail	2.00	1.74 to 2.31	<0.001
Comorbidity score 1	1.16	1.05 to 1.30	0.004
Comorbidity score 2	1.26	1.04 to 1.52	0.015
Comorbidity score ≥ 3	1.26	1.04 to 1.53	0.019
Acute medical complications			
Oropharynx primary site	0.90	0.81 to 0.98	0.026
Age 40 to 64 years	1.40	1.05 to 1.87	0.024
Age 65 to 80 years	2.82	2.08 to 3.82	<0.001
Age > 80 years	4.62	3.32 to 6.43	<0.001
Medicare	1.21	1.09 to 1.35	<0.001
Medicaid	1.40	1.23 to 1.60	<0.001
Major procedure	1.52	1.40 to 1.64	<0.001
Pedicled or free flap reconstruction	1.66	1.47 to 1.88	<0.001
Urgent/emergent admission	1.43	1.26 to 1.62	<0.001
Female sex	0.91	0.84 to 0.98	0.026
High-volume hospital	0.81	0.70 to 0.94	0.006
Nonfrail, comorbidity score 1	2.32	2.14 to 2.52	<0.001
Nonfrail, comorbidity score 2	5.07	4.53 to 5.68	<0.001
Nonfrail, comorbidity score ≥ 3	8.71	7.49 to 10.12	<0.001
Frail, comorbidity score 0	3.94	3.16 to 4.93	<0.001
Frail, comorbidity score 1	5.23	4.43 to 6.18	<0.001
Frail, comorbidity score 2	11.07	8.30 to 14.76	<0.001
Frail, comorbidity score ≥ 3	16.02	10.43 to 24.60	<0.001

CI = confidence interval.

expense-to-revenue ratios, and did not include physician-related costs because these data are not contained in the NIS database.

Nevertheless, these data demonstrate that a claims-based measure of frailty is a significant and independent predictor of adverse short-term outcomes for HNCA surgical patients. Further, frailty, independent of comorbidity, increases the risk of postoperative surgical complications and hospital-related costs, and synergistically increases the risk acute medical complications and length of hospitalization. Understanding the contribution and interaction of both frailty and comorbidity may aid in surgical decision making, optimizing patients preoperatively, and tailoring interventions to the needs of patients with comorbidities, who are frail, or both. For example, perioperative interventions for patients with comorbidities may

TABLE V.
Generalized Linear Regression Analysis of Length of Stay and Hospital Costs.

Variable	Estimate	95% CI	*P* Value	Mean
Length of stay (days)				
Intercept	1.1055	0.9260 to 1.2849	<0.001	7.6
Hypopharynx primary site	0.1613	0.1004 to 0.2221	<0.001	1.2
Urgent/emergent admission	0.2529	0.2078 to 0.2981	<0.001	1.9
Age 65 to 80 years	0.0725	0.0107 to 0.1343	0.021	0.6
Age > 80 years	0.0824	0.0104 to 0.1544	0.025	0.6
Black race/ethnicity	0.1332	0.0763 to 0.1900	<0.001	1.1
Hispanic race/ethnicity	0.1080	0.0404 to 0.1755	0.002	0.9
Major procedure	0.6198	0.5861 to 0.6535	<0.001	4.7
Pedicled or free flap reconstruction	0.4545	0.4058 to 0.5031	<0.001	3.5
Medicare	0.1042	0.0660 to 0.1423	<0.001	0.8
Medicaid	0.1934	0.2420 to 0.3447	<0.001	2.2
Self-pay	0.1945	0.1007 to 0.2882	<0.001	1.5
Nonfrail, comorbidity score 1	0.1568	0.1274 to 0.1862	<0.001	1.2
Nonfrail, comorbidity score 2	0.2894	0.2411 to 0.3377	<0.001	2.2
Nonfrail, comorbidity score ≥3	0.3753	0.3042 to 0.4463	<0.001	2.9
Frail, comorbidity score 0	0.6496	0.5743 to 0.7249	<0.001	4.9
Frail, comorbidity score 1	0.6031	0.5424 to 0.6638	<0.001	4.6
Frail, comorbidity score 2	0.7912	0.6747 to 0.9078	<0.001	6.0
Frail, comorbidity score ≥3	0.9300	0.7420 to 1.1179	<0.001	7.1
Hospital costs (2016 USD)				
Intercept	9.3232	9.0404 to 9.6060	<0.001	$22,980
Larynx primary site	−0.2128	−0.2559 to −0.1698	<0.001	−$4,891
Urgent/emergent admission	0.1288	0.0629 to 0.1948	<0.001	$2,961
Black race/ethnicity	0.0751	0.0104 to 0.1399	0.023	$1,785
Hispanic race/ethnicity	0.2451	0.1700 to 0.3203	<0.001	$6,321
Female sex	−0.0303	−0.0546 to −0.0060	0.014	−$697
Major procedure	0.5980	0.5674 to 0.6286	<0.001	$13,742
Pedicled or free flap reconstruction	0.4896	0.4418 to 0.5375	<0.001	$11,252
Intermediate-volume hospital	0.1226	0.0279 to 0.2174	0.011	$1,630
High-volume hospital	0.1596	0.0491 to 0.2700	0.005	$2,819
Medicare	0.0488	0.0075 to 0.0901	0.020	$3,668
Medicaid	0.2109	0.1614 to 0.2604	<0.001	$4,847
Frail	0.5152	0.4619 to 0.5685	<0.001	$11,839
Comorbidity score 1	0.1144	0.0852 to 0.1436	<0.001	$2,630
Comorbidity score 2	0.2723	0.2241 to 0.3205	<0.001	$6,258
Comorbidity score ≥ 3	0.3765	0.3080 to 0.4451	<0.001	$8,653

CI = confidence interval.

focus on polypharmacy, balancing potentially incompatible treatments for multiple diseases and prioritizing treatments, whereas frailty-focused interventions may incorporate prehabilitation therapy, nutrition services, and involvement of geriatric providers throughout the perioperative period.[22,40,41] Targeted interventions require accurate preoperative identification of the frail phenotype, which should be a routine part of preoperative assessment and is feasible in a busy surgical practice.[19] For example, Makary et al. integrated a standardized frailty assessment into routine preoperative assessment, which consisted of a combination of self-report questions of recent weight loss; feelings of exhaustion; and physical activity as well as physical assessments, including grip strength and gait speed.[19] When identified, frailty should be incorporated into discussions of surgery, surgical decision making, and preoperative planning. Although studies document the negative effects of both comorbidity and frailty across surgical specialties, few studies have characterized the effects of frailty separate from comorbidity among HNCA patients, and add to our growing understanding of the surgical care of older HNCA patients. An awareness of the impact of frailty is required to test the effect of targeted interventions on HNCA surgical outcomes.

CONCLUSION

In a large cohort of HNCA surgical patients, we found that frailty was an independent predictor of in-hospital mortality, postoperative surgical complications, and increased costs, and has a synergistic interaction with comorbidity associated with increased likelihood of medical complications and greater LOS in patients with comorbidity who are also frail. Growing emphasis on outcomes, and associated reporting and reimbursement, add to the importance of documentation, assessment, and intervention required to improve the care of older adults. With increasing incidence of HNCA and a growing older adult population, clinical awareness of the impact of geriatric syndromes, such as frailty, must inform practice and policy.

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