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Hypoalbuminemia and Postoperative Outcomes Following Major Salivary Gland Resection

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ABSTRACT

Objective: Hypoalbuminemia (HA) is a proxy for malnutrition that has been associated with postoperative complications in several surgical subspecialties. This study investigates the association between pre-operative HA and complications following major salivary gland (MSG) resection.

Methods: Patients undergoing outpatient, elective MSG resection were extracted from the 2005 to 2020 National Surgical Quality Improvement Program database. Demographics and comorbidities were compared between HA (preoperative serum albumin < 3.5 g/dL) and non-HA cohorts. To determine associations between albumin status and postoperative complications, univariate and multivariable binary logistic regression analyses were performed.

Results: A total of 5774 patients undergoing MSG resection were included, of which 321 (5.6%) had preoperative HA. HA was associated with older age on univariate analysis (65.2 vs. 60.2 years, $p < 0.001$). Multivariable analysis found HA to be independently associated with any surgical complication (OR 2.03, 95% CI 1.09–3.56, $p = 0.019$) and length of stay (LOS) ≥ 90th percentile (OR 1.58, 95% CI 1.04–2.38, $p = 0.032$).

Conclusion: Preoperative HA may be a poor prognostic factor associated with an increased risk of surgical complications and prolonged LOS among patients undergoing MSG resection.

Level of Evidence: 4.

1 | Introduction

Pathologies of the major salivary glands (MSGs) span chronic inflammatory, infectious, neoplastic, and obstructive etiologies [1] and may be treated with surgical resection [1–4]. MSG resections are considered relatively safe procedures, but have been associated with postoperative complications, including facial nerve or other nerve injuries, altered sensation, hematoma, Frey's syndrome, salivary fistula, sialocele, infection, skin necrosis, and poor cosmesis [5–7].

Although malnutrition in surgical patients can be screened with a variety of methods, it is grossly underdiagnosed [8]. Serum albumin levels are frequently used as a surrogate marker to evaluate nutritional status, with hypoalbuminemia (HA), classified as < 3.5 g/dL, suggesting malnutrition [9–13]. Hypoalbuminemia has been associated with postoperative complications following elective bariatric surgery, hip arthroplasty, total joint arthroplasty, metastatic spinal disease surgery, and operative repair of peptic ulcer disease [8, 10, 12, 14–16]. HA has also been frequently correlated with poor postoperative outcomes following head and neck (H&N) surgeries such as thyroidectomy, glossectomy, parathyroidectomy, and microvascular free flap reconstruction [17–20]. In fact, an analysis of head and neck cancer surgeries utilizing the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database associated HA with intensive care unit-level complications, prolonged length of stay (LOS), and adverse discharge disposition; this prior study excluded patients with salivary malignancy [21].

Albumin levels can be used by surgeons to preoperatively screen for malnutrition, but to our knowledge, the relationship between HA and complications following MSG resection has yet to be evaluated with a large, nationally representative cohort. The objective of this study was to evaluate postoperative complications following MSG resection in patients with and without preoperative HA using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP).

2 | Methods

2.1 | Data Source

We queried the 2005–2020 ACS National Surgical Quality Improvement Program (NSQIP), a nationally validated database for data on surgical procedures and 30-day perioperative data collected from > 700 community and academic hospitals in the United States. As the ACS-NSQIP includes de-identified patient data, this study did not require approval from the Institutional Review Boards at Rutgers New Jersey Medical School and the Perelman School of Medicine at the University of Pennsylvania.

2.2 | Inclusion Criteria

Cases were identified with Current Procedural Terminology (CPT) codes for parotidectomy (42415, 42410, 42420, 42425, and 42426), submandibular gland resection (42440), and sublingual gland resection (42450). Patients were excluded if they underwent non-elective or emergent MSG resection, had missing preoperative albumin, had an American Society of Anesthesiology (ASA) Classification of V, or had preoperative sepsis or shock.

2.3 | Variables

Albumin levels documented in the ACS-NSQIP were measured < 30 days before the procedure; hypoalbuminemia was defined as serum albumin < 3.5 g/dL. A total of 19442 patients undergoing outpatient, elective MSG resection in the ACS-NSQIP, 13,647 had unknown albumin level and were excluded from analysis.

Demographics including age (< 50, 50–59, 60–69, 70–79, and ≥ 80 years), race (White, Black or African American, or other), and sex were analyzed. This study also considered comorbidities and clinical factors such as obesity (body mass index [BMI] > 30), hypertension requiring medication, recent smoking history, diabetes mellitus, primary major salivary gland cancer (MSGC), dyspnea at rest or on exertion, chronic obstructive pulmonary disease, steroid use, disseminated cancer, bleeding disorders, contaminated wound, poor functional status (partially dependent or totally dependent), preoperative wound infection (defined in the ACS-NSQIP as "preoperative evidence of a documented open wound at the time of the principal operative procedure, defined as a breach in the integrity of the skin or separation of skin edges and includes open surgical wounds, with or without cellulitis or purulent exudate,") preoperative weight loss of ≥ 10% body weight within 6 months prior to surgery, current dialysis, congestive heart failure, history of previous cardiac surgery, previous percutaneous coronary intervention, and admission status (inpatient or outpatient). ASA Classification (I–IV) was used as a surrogate for disease severity. The International Classification of Diseases (ICD) 9th (ICD-9) and 10th (ICD-10) editions were used to identify cancer of the parotid (142.0 and C07), submandibular (142.1 and C08.0), and sublingual (142.0 and C08.1) glands. The following CPT codes were used to define concurrent neck dissection: 42426, 38542, 38700, 38720, and 38724.

The primary endpoints in this study were postoperative complications, of which surgical complications included surgical site infections (superficial incisional, deep incisional, and organ space), graft failure, blood transfusions (≥ 1-unit RBCs within 72 h post-surgery), and wound disruptions/dehiscence within 30 days following operation; medical complications included mechanical ventilation > 48 h, re-intubation, pulmonary embolism, pneumonia, urinary tract infection, renal insufficiency, acute renal failure, cardiac arrest, myocardial infarction (MI), peripheral nerve injury, cerebrovascular accident, deep vein thrombosis, and sepsis/septic shock. Unplanned readmissions, re-operations, and length of stay (LOS) were also analyzed. Prolonged operative time and LOS were defined as ≥ 90th percentile (90th percentile of operative time: 266 min, 90th percentile of LOS: 2 days).

2.4 | Statistical Analysis

Univariate analysis using Pearson chi-square analysis and Fisher exact tests (following exclusion of patients with missing data for specific comorbidities) was conducted to compare rates of demographics, comorbidities, and perioperative complications in patients with and without HA. Determination of percentages in chi square analysis only considered known values, accounting for variability across categorial variables. Demographics and comorbidities significantly associated with HA were included as covariates in the multivariable binary logistic regression models with postoperative complications as outcomes. Adjusted odds ratio (OR) and confidence intervals were calculated. Comorbidities in the ACS-NSQIP with low incidence in our cohort ($N < 15$) were omitted from analysis (alcohol consumption, ventilator dependence, past pneumonia, ascites, esophageal varices, history of MI, angina, peripheral vascular disease, rest pain, acute renal failure, impaired sensorium, coma, hemiplegia, prior transient ischemic attack, prior cerebrovascular accident, CNS tumor, paraplegia, quadriplegia, pre-op blood transfusion, chemotherapy, radiotherapy, systemic sepsis, prior operation within 30 days, and emergency case). A

TABLE 1 | Univariate analysis comparing demographics and comorbidities of patients with and without HA undergoing MSG resection.

Characteristic	*N*	Overall *N* = 5774[a]	Hypoalbuminemia *N* = 321[a]	Normoalbuminemia *N* = 5453[a]	*p*[b]
Sex	5773				**0.015**
Female		2727 (47%)	139 (43%)	2588 (47%)	
Male		3046 (53%)	181 (56%)	2865 (53%)	
Age	5774				**< 0.001**
< 50		1205 (21%)	42 (13%)	1163 (21%)	
50–59		1296 (22%)	59 (18%)	1237 (23%)	
60–69		1628 (28%)	89 (28%)	1539 (28%)	
70–79		1135 (20%)	75 (23%)	1060 (19%)	
≥ 80		510 (8.8%)	56 (17%)	454 (8.3%)	
Race	5774				0.4
Black or African American		515 (8.9%)	35 (11%)	480 (8.8%)	
Other		988 (17%)	54 (17%)	934 (17%)	
White		4271 (74%)	232 (72%)	4039 (74%)	
ASA class	5769				**< 0.001**
1-No disturbance		288 (5.0%)	6 (1.9%)	282 (5.2%)	
2-Mild disturbance		2546 (44%)	69 (21%)	2477 (45%)	
3-Severe disturbance		2755 (48%)	214 (67%)	2541 (47%)	
4-Life threatening		180 (3.1%)	32 (10.0%)	148 (2.7%)	
Body mass index levels	5774				**< 0.001**
0 (< 18.5)		88 (1.5%)	12 (3.7%)	76 (1.4%)	
1 (18.5–24.9)		1216 (21%)	66 (21%)	1150 (21%)	
2 (25.0–29.9)		1959 (34%)	100 (31%)	1859 (34%)	
3 (30.0–34.9)		1349 (23%)	55 (17%)	1294 (24%)	
4 (35.0–39.9)		670 (12%)	43 (13%)	627 (11%)	
5 (≥ 40)		492 (8.5%)	45 (14%)	447 (8.2%)	
Admission status	5774				**< 0.001**
Inpatient		1700 (29%)	125 (39%)	1575 (29%)	
Outpatient		4074 (71%)	196 (61%)	3878 (71%)	
Location of resection	5774				0.5
Parotid		4885 (85%)	274 (85%)	4611 (85%)	
Sublingual		33 (0.6%)	0 (0%)	33 (0.6%)	
Submandibular		856 (15%)	47 (15%)	809 (15%)	
Concurrent neck dissection	5774	707 (12%)	54 (17%)	653 (12%)	**0.010**
Comorbidities					
Obesity	5774	2511 (43%)	143 (45%)	2368 (43%)	0.7

(Continues)

TABLE 1 | (Continued)

Characteristic	N	Overall $N = 5774$[a]	Hypoalbuminemia $N = 321$[a]	Normoalbuminemia $N = 5453$[a]	p[b]
Hypertension medication use	4570	2372 (52%)	143 (59%)	2229 (52%)	**0.021**
Cigarettes	5774	1431 (25%)	87 (27%)	1344 (25%)	0.3
Diabetes mellitus	5774	1150 (20%)	89 (28%)	1061 (19%)	**<0.001**
Primary MSG cancer	5774	687 (12%)	42 (13%)	645 (12%)	0.5
Dyspnea	5774	361 (6.3%)	43 (13%)	318 (5.8%)	**<0.001**
Chronic obstructive pulmonary disease	5774	322 (5.6%)	37 (12%)	285 (5.2%)	**<0.001**
Steroid use	5774	254 (4.4%)	23 (7.2%)	231 (4.2%)	**0.013**
Disseminated cancer	5774	172 (3.0%)	20 (6.2%)	152 (2.8%)	**<0.001**
Bleeding disorder	5774	166 (2.9%)	14 (4.4%)	152 (2.8%)	0.10
Contaminated wound	4682	120 (2.6%)	13 (5.1%)	107 (2.4%)	**0.008**
Poor functional status	5745	74 (1.3%)	17 (5.3%)	57 (1.1%)	**0.001**
Wound infection	5774	47 (0.8%)	9 (2.8%)	38 (0.7%)	**<0.001**
Weight loss	5774	33 (0.6%)	7 (2.2%)	26 (0.5%)	**0.002**
Dialysis	5774	29 (0.5%)	13 (4.0%)	16 (0.3%)	**<0.001**
Congestive heart failure	5774	25 (0.4%)	3 (0.9%)	22 (0.4%)	0.2
Previous cardiac surgery	371	23 (6.2%)	4 (14%)	19 (5.5%)	0.084
Previous percutaneous coronary intervention	371	21 (5.7%)	2 (7.1%)	19 (5.5%)	0.7

Note: Bold values are statistically significant ($p < 0.05$).
[a] n (%).
[b] Fisher's exact test; Pearson's Chi-squared test.

sensitivity analysis adjusting for HA as a continuous variable was performed to evaluate the impact of incremental increases in albumin on surgical outcomes. A secondary sensitivity analysis was performed to compare demographics, comorbidities, and postoperative complications between patients who did and did not have preoperative albumin levels documented in the ACS-NSQIP. Statistical significance was set to $p < 0.05$. R Studio Version 2023.03.1 was used to conduct all statistical analyses.

3 | Results

A total of 5774 patients undergoing MSG resection were included in this analysis, of which 5.56% ($N = 321$) had preoperative HA (Table 1). The average preoperative albumin level was 4.14 g/dL (SD = 0.43; Figure 1). 4885 (85%) patients underwent parotid gland resection, 856 (15%) underwent submandibular gland resection, and 33 (0.6%) underwent sublingual gland resection. The mean patient age was 60.4 years (SD = 14.4) across the whole cohort, 65.2 (SD = 13.6) among patients with HA, and 60.2 (SD = 14.4) years among patients without HA, respectively ($p < 0.001$; Figure 2). Patients with and without HA had significant differences in age ($p < 0.001$), ASA class ($p < 0.001$), and BMI ($p < 0.002$). HA was significantly associated with hypertension medication use ($p = 0.021$), diabetes mellitus ($p < 0.001$), concurrent neck dissection ($p = 0.010$), dyspnea ($p < 0.001$), chronic obstructive pulmonary disorder ($p < 0.001$), steroid use ($p = 0.013$), disseminated cancer ($p < 0.001$), wound classification ($p = 0.008$), poor functional status ($p < 0.001$), wound infection ($p < 0.001$), weight loss ($p = 0.002$), and dialysis ($p < 0.001$). Median operative time was 124 min (IQR 83–184) median and LOS was 1 day (IQR 0–1) across the cohort.

Patients with HA had higher rates of surgical complication (7.2% vs. 3.4%, $p < 0.001$), deep surgical site infection (1.2% vs. 0.3%, $p = 0.022$), blood transfusions (2.8% vs. 1.0%, $p = 0.008$), any medical complication (3.4% vs. 1.4%, $p = 0.016$), pneumonia (2.2% vs. 0.4%, $p < 0.001$), mechanical ventilation > 48 h (0.9% vs. 0.1%, $p = 0.020$), any complication (10.0% vs. 4.6%, $p < 0.001$), LOS ≥ 90th percentile (32% vs. 19%, $p < 0.001$), unplanned readmission (100% vs. 79%, $p = 0.043$), and discharge not to home (3.7% vs. 1.2%, $p < 0.001$). Rates of all complications across both cohorts are detailed in Table 2.

On multivariable analysis, following adjustment for demographics and comorbidities significantly associated with HA on univariable analysis, HA was independently associated with surgical complications (OR 2.03, 95% CI 1.09–3.56, $p = 0.019$; Table 3) and prolonged LOS (OR 1.58, 95% CI 1.04–2.38, $p = 0.032$). Hypoalbuminemia was not significantly associated

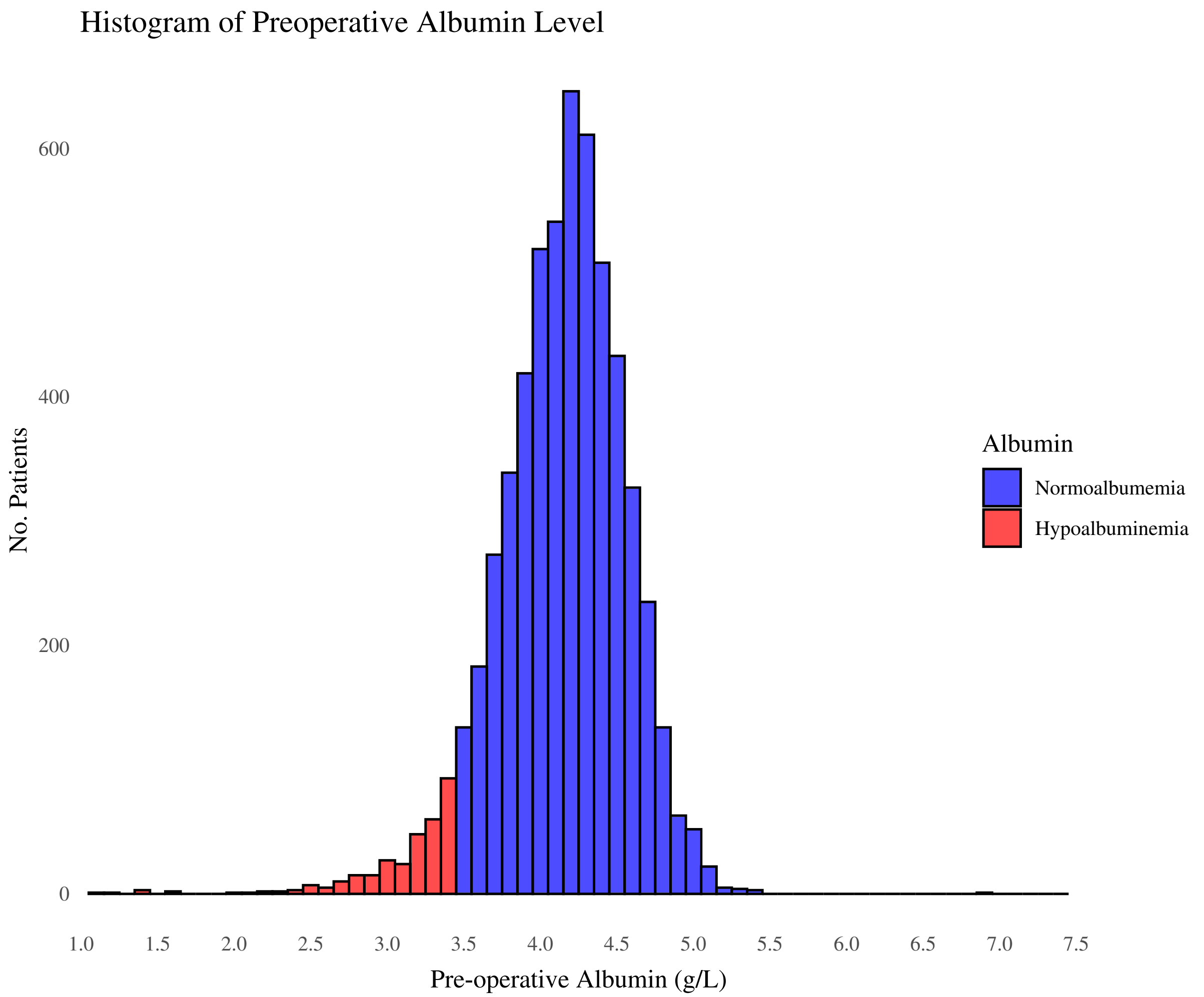

FIGURE 1 | Distribution of preoperative albumin levels.

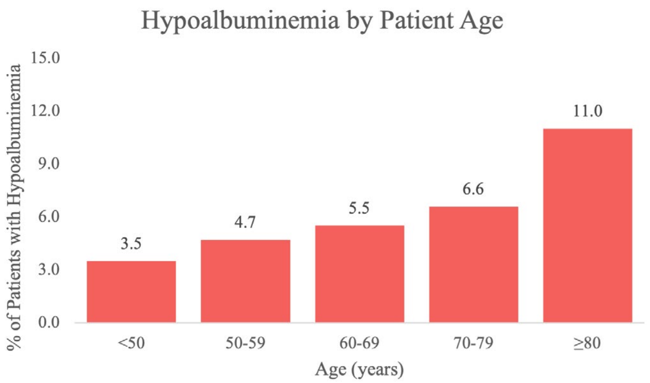

FIGURE 2 | Frequency of hypoalbuminemia by patient age.

with any medical complication (OR 1.19, 95% CI 0.45–2.74, $p=0.7$; Table 4), prolonged operative time (OR 0.76, 95% CI 0.43–1.29, $p=0.3$), re-operation (OR 0.92, 95% CI 0.34–2.09, $p=0.9$), and discharge not to home (OR 1.89, 95% CI 0.78–4.10, $p=0.13$) on multivariable analysis (Table 5). Neck dissection (OR 3.05, 95% CI 1.94–4.74, $p<0.001$), contaminated wound (OR 2.73, 95% CI 1.19–5.66, $p=0.011$), and wound infection (OR 3.85, 95% CI 1.40–9.57, $p=0.005$) remained associated with experiencing any surgical complication. Male sex (OR 2.30, 95% CI 1.19–4.76, $p=0.018$), ≥80+ years of age (OR 5.23, 95% CI 1.69–20.1, $p=0.007$), outpatient status (OR 0.35, 95% CI 0.19–0.64, $p<0.001$), and wound infection (OR 6.82, 95% CI 1.94–21.1, $p=0.001$) remained associated with experiencing any medical complication.

Table 6 compares rates of any medical or surgical complication by age and comorbidity status. Across age groups, patients between 70 and 79 years had the highest incidence of any complication (i.e., medical or surgical) (6.2%). Rates of any complication was highest among patients with preoperative wound infection (32%), poor functional status (20%), and dialysis (17%).

3.1 | Hypoalbuminemia Sensitivity Analyses

Sensitivity analysis adjusting for HA as a continuous variable on multivariable analysis, also adjusting for demographics and comorbidities significantly associated on univariate analysis, are shown in Supplemental Tables S1–S3. Pre-operative serum albumin remained significantly associated with any surgical complication (OR 0.64, 95% CI 0.43–0.98, $p=0.034$). There was no association between preoperative albumin and any medical complication (OR 0.92, 95% CI 0.49–1.76, $p=0.8$), prolonged operative time (OR 1.35, 95% CI 0.99–1.84, $p=0.061$), prolonged

TABLE 2 | Univariate analysis comparing rates of postoperative complications in patients with and without HA.

Characteristic	Overall $N=5774$[a]	Hypoalbuminemia $N=321$[a]	Normoalbuminemia $N=5453$[a]	p[b]
Any surgical complication	211 (3.7%)	23 (7.2%)	188 (3.4%)	**<0.001**
Superficial SSI	106 (1.8%)	8 (2.5%)	98 (1.8%)	0.4
Deep SSI	20 (0.3%)	4 (1.2%)	16 (0.3%)	**0.022**
Organ space SSI	17 (0.3%)	2 (0.6%)	15 (0.3%)	0.2
Wound dehiscence	22 (0.4%)	3 (0.9%)	19 (0.3%)	0.12
Blood transfusion	63 (1.1%)	9 (2.8%)	54 (1.0%)	**0.008**
Graft failure	2 (0.2%)	0 (0%)	2 (0.2%)	>0.9
Any medical complication	89 (1.5%)	11 (3.4%)	78 (1.4%)	**0.016**
Pneumonia	27 (0.5%)	7 (2.2%)	20 (0.4%)	**<0.001**
Re-intubation	20 (0.3%)	3 (0.9%)	17 (0.3%)	0.10
Pulmonary embolism	6 (0.1%)	0 (0%)	6 (0.1%)	>0.9
Ventilation >48 h	11 (0.2%)	3 (0.9%)	8 (0.1%)	**0.020**
Renal insufficiency	3 (<0.1%)	0 (0%)	3 (<0.1%)	>0.9
Acute renal failure	3 (<0.1%)	1 (0.3%)	2 (<0.1%)	0.2
Urinary tract infection	12 (0.2%)	2 (0.6%)	10 (0.2%)	0.14
Cerebrovascular accident	14 (0.2%)	0 (0%)	14 (0.3%)	>0.9
Peripheral nerve injury	0 (0%)	0 (0%)	0 (0%)	
Cardiac arrest	5 (<0.1%)	1 (0.3%)	4 (<0.1%)	0.2
Myocardial infarction	9 (0.2%)	2 (0.6%)	7 (0.1%)	0.086
Deep vein thrombosis	9 (0.2%)	2 (0.6%)	7 (0.1%)	0.086
Sepsis	9 (0.2%)	0 (0%)	9 (0.2%)	>0.9
Septic shock	5 (<0.1%)	1 (0.3%)	4 (<0.1%)	0.2
Coma	0 (0%)	0 (0%)	0 (0%)	
Any complication	282 (4.9%)	32 (10.0%)	250 (4.6%)	**<0.001**
Prolonged Op time	580 (10%)	36 (11%)	544 (10.0%)	0.5
Prolonged LOS	1114 (19%)	103 (32%)	1011 (19%)	**<0.001**
Unplanned readmission	130 (81%)	16 (100%)	114 (79%)	**0.043**
Re-operation	130 (2.3%)	9 (2.8%)	121 (2.2%)	0.5
Discharge not to home	76 (1.3%)	12 (3.7%)	64 (1.2%)	**<0.001**

Note: Bolded complications indicate infectious etiology. Bold values are statistically significant ($p < 0.05$).
[a] *n* (%).
[b] Pearson's Chi-squared test; Fisher's exact test.

LOS (OR 0.84, 95% CI 0.65–1.08, $p=0.2$), re-operation (OR 0.72, 95% CI 0.42–1.28, $p=0.3$), and discharge not to home (OR 0.662, 95% CI 0.33–1.18, $p=0.14$).

Tables S4, S5 compare demographics and comorbidities and postoperative complications between patients with known and unknown preoperative albumin levels, respectively. Patients with known preoperative albumin levels had higher rates of various preoperative comorbidities including obesity ($p<0.001$), hypertension medication use ($p<0.001$), cigarette use ($p=0.006$), diabetes mellitus ($p<0.001$), primary MSG cancer ($p=0.003$), dyspnea ($p<0.001$), chronic obstructive pulmonary disease ($p<0.001$), steroid use ($p<0.001$), disseminated cancer ($p<0.001$), bleeding disorder ($p<0.001$), preoperative contaminated wound ($p=0.033$), poor functional status ($p<0.001$), preoperative weight loss ($p=0.012$), dialysis use ($p=0.032$), congestive heart failure ($p=0.011$), previous cardiac surgery ($p=0.012$), and previous percutaneous coronary intervention ($p=0.045$). Rates of preoperative wound infection were similar between groups. Patients with known preoperative

TABLE 3 | Multivariable binary logistic regression models identifying factors associated with any surgical complication following MSG resection.

Predictors of any surgical complications	OR[a]	95% CI[a]	*p*
Sex			
Female	—	—	
Male	1.41	0.93, 2.15	0.11
Age			
< 50	—	—	
50–59	1.10	0.59, 2.11	0.8
60–69	0.57	0.29, 1.14	0.10
70–79	0.74	0.37, 1.49	0.4
≥ 80	0.60	0.27, 1.33	0.2
ASA classification			
1-No disturbance	—	—	
2-Mild disturbance	1.11	0.38, 4.77	0.9
3-Severe disturbance	1.76	0.58, 7.66	0.4
4-Life threatening	2.95	0.76, 14.7	0.14
Body mass index levels			
0 (< 18.5)	1.36	0.29, 4.48	0.7
1 (18.5–24.9)	—	—	
2 (25.0–29.9)	1.12	0.67, 1.93	0.7
3 (30.0–34.9)	0.92	0.52, 1.66	0.8
4 (35.0–39.9)	0.70	0.32, 1.47	0.4
5 (≥ 40)	0.87	0.37, 1.90	0.7
Admission status			
Inpatient	—	—	
Outpatient	0.67	0.44, 1.01	0.053
Hypoalbuminemia	2.03	1.09, 3.56	**0.019**
Concurrent neck dissection	3.05	1.94, 4.74	**< 0.001**
Comorbidities			
Hypertension medication use	1.32	0.85, 2.07	0.2
Diabetes mellitus	0.86	0.52, 1.39	0.6
Dyspnea	1.51	0.78, 2.77	0.2
Chronic obstructive pulmonary disease	1.87	0.97, 3.42	0.052
Steroid use	1.40	0.65, 2.75	0.4
Disseminated cancer	1.71	0.79, 3.36	0.14
Contaminated wound	2.73	1.19, 5.66	**0.011**
Poor functional status	0.62	0.09, 2.34	0.5
Wound infection	3.85	1.40, 9.57	**0.005**
Weight loss	1.26	0.17, 5.80	0.8
Dialysis	0.74	0.04, 4.23	0.8

Note: Bold values are statistically significant ($p < 0.05$).
[a]OR = odds ratio, CI = confidence interval.

albumin levels had higher rates of postoperative complications including any surgical complication, any medical complication, any complication (i.e., medical or surgical), prolonged operative time, prolonged LOS, re-operation, and non-home discharge ($p < 0.01$). Rates of superficial SSI, deep SSI, organ space SSI, wound dehiscence, graft failure, pulmonary embolism, ventilator dependence, renal insufficiency, acute renal failure, urinary tract infection, cardiac arrest, myocardial infarction, deep vein thrombosis, sepsis, and unplanned readmissions were similar.

4 | Discussion

Previous studies have associated HA with adverse surgical outcomes following H&N surgery (i.e., thyroidectomy, glossectomy, parathyroidectomy, and microvascular free flap reconstruction) and across other surgical procedures such as pancreaticoduodenectomy, bariatric surgery, hip arthroplasty, total joint arthroplasty, lower extremity orthopedic trauma surgery, metastatic spinal disease surgery, and operative repair of peptic ulcer [8, 10, 12, 14–18, 20, 21–26]. Moreover, HA has been associated with poor prognosis in hospitalized patients regardless of treatment and increased morbidity and mortality following surgery [27, 28]. In this study, we utilized the ACS-NSQIP to investigate the association between HA and postoperative complications following MSG resection. Preoperative HA was found to be independently associated with any surgical complication and prolonged LOS following adjustment for demographics and related comorbidities.

Because of its association with bioavailable protein energy and inflammation, albumin levels offer a viable measure of nutrition [29, 30]. Although HA is reported in up to 50% of admitted patients and our study identifying a correlation with inpatient status, this finding was present in only 5.56% of our cohort. We also observed increasing incidence of HA with older age, consistent with other studies [8, 31, 32]. Moreover, the lack of association between HA and race is not surprising given the mixed findings in the existing literature and the lack of consensus on which racial groups might be at risk for HA [33, 34]. Malnutrition has a multifaceted and complex etiology, as evidenced by our observation of various comorbidities being linked to HA, consistent with findings from previous studies [12, 16, 35]. Beyond malnutrition, HA also indicates inflammation, which has been associated with poor responses to surgical and medical treatments, diminished quality of life, and reduced longevity [36, 37]. An ACS-NSQIP analysis of 65,192 patients undergoing outpatient procedures across all surgical

TABLE 4 | Multivariable binary logistic regression models identifying factors associated with any medical complication following MSG resection.

Predictors of any medical complications	OR[a]	95% CI[a]	*p*
Sex			
Female	—	—	
Male	2.30	1.19, 4.76	**0.018**
Age			
< 50	—	—	
50–59	0.86	0.24, 3.49	0.8
60–69	0.65	0.18, 2.66	0.5
70–79	2.00	0.65, 7.58	0.3
≥ 80	5.23	1.69, 20.1	**0.007**
ASA classification			
1-No disturbance	—	—	
2-Mild disturbance	Inf	0-Inf	> 0.9
3-Severe disturbance	Inf	0-Inf	> 0.9
4-Life threatening	Inf	0-Inf	> 0.9
Body mass index levels			
0 (< 18.5)	0.81	0.04, 5.30	0.9
1 (18.5–24.9)	—	—	
2 (25.0–29.9)	1.02	0.47, 2.30	> 0.9
3 (30.0–34.9)	0.81	0.33, 2.00	0.6
4 (35.0–39.9)	1.57	0.56, 4.23	0.4
5 (≥ 40)	1.72	0.49, 5.40	0.4
Admission status			
Inpatient	—	—	
Outpatient	0.35	0.19, 0.64	**< 0.001**
Hypoalbuminemia	1.19	0.45, 2.74	0.7
Concurrent neck dissection	1.01	0.51, 1.93	> 0.9
Comorbidities			
Hypertension medication use	1.00	0.53, 1.96	> 0.9
Diabetes mellitus	1.10	0.55, 2.13	0.8
Dyspnea	1.03	0.37, 2.49	> 0.9
Chronic obstructive pulmonary disease	1.28	0.48, 3.00	0.6
Steroid use	1.28	0.36, 3.48	0.7
Disseminated cancer	1.81	0.64, 4.37	0.2
Contaminated wound	1.72	0.40, 5.42	0.4
Poor functional status	2.85	0.76, 8.45	0.081
Wound infection	6.82	1.94, 21.1	**0.001**
Weight loss	1.02	0.04, 9.14	> 0.9
Dialysis	0.00		> 0.9

Note: Bold values are statistically significant ($p < 0.05$).
[a]OR = odds ratio, CI = confidence interval.

specialties identified HA as the most significant predictor of 30-day mortality, along with infection, major complications, and readmission [38]. Moreover, previous studies have elucidated the effect of HA within H&N surgery, but excluded patients with MSG cancer. In one such study, patients with HA had poorer overall survival, higher rates of wound infection, and increased risk of ICU-level complications [21, 39]. HA has also been linked to wound dehiscence in patients with oral cavity squamous cell carcinoma, increased mortality in laryngeal squamous cell carcinoma, and increased complications following H&N free flap reconstruction [20, 30, 40].

Our analysis found that patients with HA were more than twice as likely to experience surgical complications (OR 2.03, 95% CI 1.09–3.56) compared with non-HA patients following MSG resection. This finding is consistent with prior studies across various surgical specialties. HA was associated with a significantly increased risk of wound infections following surgery for oral cavity cancer. However, this study assessed postoperative hypoalbuminemia, which could be a result of infection, and used a more stringent cutoff of ≤ 2.8 g/dL to define HA [41]. A similar study identified early postoperative hypoalbuminemia < 2.5 g/dL as a significant risk factor for increased SSIs following oral cancer surgery [18]. Other studies have found preoperative HA to be associated with SSI following total joint arthroplasty, surgical wound dehiscence following posterior lumbar interbody fusion, and wound infection in H&N cancer surgery [21, 41, 42]. As a marker of inflammation, HA can indicate impaired immune function that impairs the wound-healing process, especially in the postoperative environment characterized by high physiological stress [36, 43–45].

In our study, there was, however, a lack of association between HA and medical complications. These mixed findings in our study are similar to an existing report on transcervical Zenker diverticulectomy that found no associations between HA and mortality, any medical complication, and LOS [35]. Another study of patients undergoing pancreaticoduodenctomy found no differences between complications and 30-day mortality with and without postoperative HA [46]. Likewise, preoperative HA was not associated with 30-day overall complications, surgical complications, medical complications, or mortality following surgery for the treatment of pressure ulcers [47].

Our study also found that HA was not significantly associated with non-home discharge. This contrasts with previous studies of H&N surgery and pancreaticoduodenectomy,

TABLE 5 | Multivariable binary logistic regression models of the association between hypoalbuminemia and adverse postoperative outcomes following MSG resection.

Complication	OR[a]	95% CI[a]	*p*
Prolonged Op-time	0.76	0.43, 1.29	0.3
Prolonged LOS	1.58	1.04, 2.38	**0.032**
Re-operation	0.92	0.34, 2.09	0.9
Discharge not home	1.89	0.78, 4.10	0.13

Note: Bold values are statistically significant ($p < 0.05$).
[a]OR = odds ratio, CI = confidence interval.

which found HA to be associated with non-home discharge [21, 48]. Of note, our selection criteria for outpatient, elective cases may have contributed to a selection bias accounting for our observed lack of association between HA and non-home discharge. In addition, MSG resection is a generally safe procedure with a high proportion of patients having same-day discharge, overnight observation, or short hospitalization. Studies of HA in several other otolaryngology procedures did not analyze non-home discharge, limiting our ability to draw additional comparisons.

Our results indicate that patients with HA were more likely to experience prolonged LOS (OR 1.58, 95% CI 0.43–2.38)

TABLE 6 | Rates of any medical or surgical complication by age and comorbidity status, *n* (%).

Characteristic	*N*	Overall	Hypoalbuminemia	Normoalbuminemia	*p*[a]
Age					
< 50	1205	42 (3.5%)	4 (9.5%)	38 (3.3%)	0.055
50–59	1296	53 (4.1%)	4 (6.8%)	49 (4.0%)	0.3
60–69	1628	57 (3.5%)	7 (7.9%)	50 (3.2%)	**0.033**
70–79	1135	70 (6.2%)	9 (12%)	61 (5.8%)	**0.043**
≥ 80	510	60 (12%)	8 (14%)	52 (11%)	0.5
Concurrent neck dissection	707	96 (14%)	5 (9.3%)	91 (14%)	0.3
Comorbidities	687	47 (6.8%)	7 (17%)	40 (6.2%)	**0.019**
Obesity	2511	118 (4.7%)	14 (9.8%)	104 (4.4%)	**0.003**
Hypertension medication use	2372	137 (5.8%)	19 (13%)	118 (5.3%)	**< 0.001**
Cigarettes	1431	76 (5.3%)	13 (15%)	63 (4.7%)	**< 0.001**
Diabetes mellitus	1150	77 (6.7%)	9 (10%)	68 (6.4%)	0.2
Primary MSG cancer	423	423 (7.3%)	28 (8.7%)	395 (7.2%)	0.3
Dyspnea	361	34 (9.4%)	6 (14%)	28 (8.8%)	0.3
Chronic obstructive pulmonary disease	322	28 (8.7%)	6 (16%)	22 (7.7%)	0.11
Steroid use	254	23 (9.1%)	5 (22%)	18 (7.8%)	**0.043**
Disseminated cancer	172	20 (12%)	3 (15%)	17 (11%)	0.7
Bleeding disorder	166	23 (14%)	1 (7.1%)	22 (14%)	0.7
Contaminated wound	120	18 (15%)	0 (0%)	18 (17%)	0.2
Poor functional status	72	15 (20%)	3 (18%)	12 (21%)	> 0.9
Wound infection	47	15 (32%)	0 (0%)	15 (39%)	**0.041**
Weight loss	33	4 (12%)	0 (0%)	4 (15%)	0.6
Dialysis	29	5 (17%)	5 (38%)	0 (0%)	**0.011**
Congestive heart failure	25	4 (16%)	0 (0%)	4 (18%)	> 0.9
Previous cardiac surgery	23	1 (4.3%)	0 (0%)	1 (5.3%)	> 0.9
Previous percutaneous coronary intervention	21	2 (9.5%)	0 (0%)	2 (11%)	> 0.9

Note: Bold values are statistically significant ($p < 0.05$).
[a]Fisher's exact test; Pearson's Chi-squared test.

compared with non-HA patients following MSG resection. This finding is similar to that of a study from Khawaja et al. which identified that patients with HA were nearly five times as likely to experience prolonged LOS than non-HA patients following parathyroidectomy for primary hyperparathyroidism [19]. Moghadamyeghaneh et al. reported a two-fold increase in prolonged hospitalization following colorectal surgery in patients with HA [49]. Extended hospital care was more likely in patients with HA undergoing open repair of the rotator cuff per Quan et al. [50] Low serum albumin was also associated with increased LOS in the management of acute surgical site infection following spinal surgery [51]. As suggested by previous studies, low serum albumin can serve as a surrogate marker for malnutrition, which has been linked to increased frailty, susceptibility to illness, and impaired healing [52, 53]. This could be an underlying mechanism potentially driving the observed relationship between HA and prolonged LOS.

The findings of this study should be considered in light of several limitations. ACS-NSQIP collects data from numerous institutions, which may affect the accuracy and consistency of data. Although surgical outcomes were assessed while adjusting for significant demographics and comorbidities when assessing surgical outcomes, other relevant factors such as disease severity and tumor characteristics were not reported in ACS-NSQIP. Given their relative infrequency, complications were also grouped into broader categories (i.e., medical or surgical) as validated by previous studies using the ACS-NSQIP database. Complications were also addressed as binary outcomes, and multiple hypothesis testing was not implemented as comparisons were not made between more than two cohorts. Moreover, there may be an inherent selection bias for patients requiring preoperative nutritional screening in our study due to the exclusion of patients without known preoperative albumin. This limits the generalizability of our study to patients who were specifically indicated for nutritional screening, who evidently had greater rates of comorbidities and postsurgical complications compared to those with undocumented albumin levels. Likewise, there is a lack of data on postoperative nutritional management in ACS-NSQIP, thus we were unable to assess potential therapeutic value of managing preoperative HA. The retrospective design of our study limits any interpretation to correlation, not causation. Although the exclusion of comorbidities with incidence <15 streamlined our patient sample and analysis, these may still be present in a real patient population. ACS-NSQIP is limited to 30-day postoperative outcomes, limiting the scope of this study to this short time frame and not long-term outcomes.

5 | Conclusion

The minority of patients undergoing MSG resection had HA. Preoperative HA is a poor prognostic factor associated with an increased risk of surgical complications and prolonged LOS among patients undergoing MSG resection. The adverse outcomes in patients with HA are consistent with existing literature identifying HA as a risk factor for poor postoperative outcomes across several surgical specialties. Our findings suggest a potential benefit of optimizing albumin levels and nutritional status prior to pursuing outpatient, elective MSG resection.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.