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Preoperative Serum Albumin as Predictor of Outcomes After Thyroidectomy

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Abstract

Objective. Albumin is considered to be a surrogate marker for inflammation and nutritional status. Levels usually decrease after surgery but little is known about the predictive value of preoperative albumin levels in patients undergoing thyroidectomy. This study aimed to investigate the 30-day incidence of postoperative outcomes in thyroidectomy patients with and without preoperative hypoalbuminemia.

Study Design. Retrospective cohort study.

Setting. TriNetX Database.

Methods. TriNetX, a federated deidentified database, was retrospectively queried to identify patients who underwent thyroidectomy. Postoperative outcomes within 30 days of thyroidectomy, based on International Classification of Disease, 10th Revision and Current Procedural Terminology codes, in patients with preoperative hypoalbuminemia (≤3.4 g/dL) (cohort 1) were analyzed and compared to patients without hypoalbuminemia (cohort 2).

Results. After propensity score matching, 2398 patients were identified in each cohort. Hypoalbuminemia patients were more likely to have postoperative pneumonia (odds ratio, OR: 3.472, 95% confidence interval, CI [2.016-5.978]), acute renal failure (OR: 3.872, 95% CI [2.412-6.217]), venous thromboembolism (OR: 1.766, 95% CI [1.016-2.819]), and surgical site infection (OR: 2.353, 95% CI [1.282-4.32]). Rates of recurrent laryngeal nerve injury were comparable between cohorts.

Conclusion. Patients undergoing thyroidectomy with preoperative hypoalbuminemia have a higher prevalence of postoperative complications compared to patients without preoperative hypoalbuminemia. While not routinely assessed, preoperative evaluation of serum albumin levels may help guide expectations and optimal management of thyroidectomy patients.

Keywords

albumin, hypoalbuminemia, postoperative outcomes, thyroid, thyroidectomy

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Thyroidectomy is one of the most common endocrine surgeries performed with very low mortality rates, but postoperative complications can significantly affect morbidity.[1] Indications for thyroidectomy include thyroid malignancy, goiter, toxic adenomas, and hyperthyroidism.[2] Complications of thyroidectomy have been reported to be associated with the extent of resection, surgeon expertise, institution case volume, advanced patient age, and comorbidities such as hypertension, diabetes, and chronic kidney disease.[3-5] Previous studies have also suggested malnutrition, as measured by serum albumin, as a predictor of poor surgical outcomes in neurosurgical, plastic and reconstructive, cardiac, and gastrointestinal surgeries.[6-9] Several studies have also investigated the effect of body mass index, but there are mixed findings on its significance as a predictor of adverse postoperative outcomes.[10,11] Albumin is considered a negative active-phase protein that typically decreases during injury and inflammatory conditions and has been shown to be an independent risk factor for mortality in the elderly.[12] However, little is known about the significance of early preoperative hypoalbuminemia as a predictor of postoperative outcomes following thyroidectomy. This study aims to leverage a national database to determine

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the association of 30-day outcomes associated with preoperative hypoalbuminemia in patients who underwent thyroidectomy.

Methods

A multi-institutional, deidentified database, TriNetX, was retrospectively queried via International Classification of Disease, 10th Revision (ICD-10) and Common Procedural Terminology (CPT) codes to evaluate postoperative outcomes. Codes used to identify patients who underwent thyroidectomy can be found in Supplemental 1, available online. The study population consisted of 2 cohorts, those with (cohort 1) and those without hypoalbuminemia (cohort 2). Patients were included if they were ≥18 years of age and if they underwent thyroidectomy. The codes used for thyroidectomy can be found in Supplemental 1, available online. For cohort 1, patients were included if their albumin levels were ≤3.4 g/dL 0 to 7 days before thyroidectomy. Patients were excluded if they had an albumin level ≥3.5 g/dL. For cohort 2, patients were included if their albumin levels were ≥3.5 g/dL 0 to 7 days prior to thyroidectomy. Patients were excluded if they had an albumin level ≤3.4 g/dL. (**Figure 1**). To assess for potential confounders, analysis was performed using propensity score matching based on age at index, demographics, and significant comorbidities. Statistical significance was defined as $P \leq 0.05$. Postoperative outcomes were evaluated within 1 month of the index event which was set at the time of thyroidectomy. Corresponding CPT and ICD-10 codes can be found in **Table 1**.

TriNetX is a global federated health research network providing access to electronic medical records (diagnoses, procedures, medications, laboratory values, genomic information) from large health care organizations (HCOs). The TriNetX platform only uses aggregated counts and statistical summaries of deidentified information. No Protected Health Information or Personal Data is made available to the users of the platform. Any data displayed on the TriNetX platform in aggregate form or any patient-level data provided in a data set generated by the TriNetX platform are deidentified per the deidentification standard defined in section 164.514(a) of the HIPAA privacy rule. This study was exempted from the Penn State Institutional Review Board review (STUDY00018629). To protect patient confidentiality, for outcomes experienced by ≤10 patients, TriNetX reports the number to 10. The use of this federated database and its validity were informed by previous literature, and exact details of the network have been

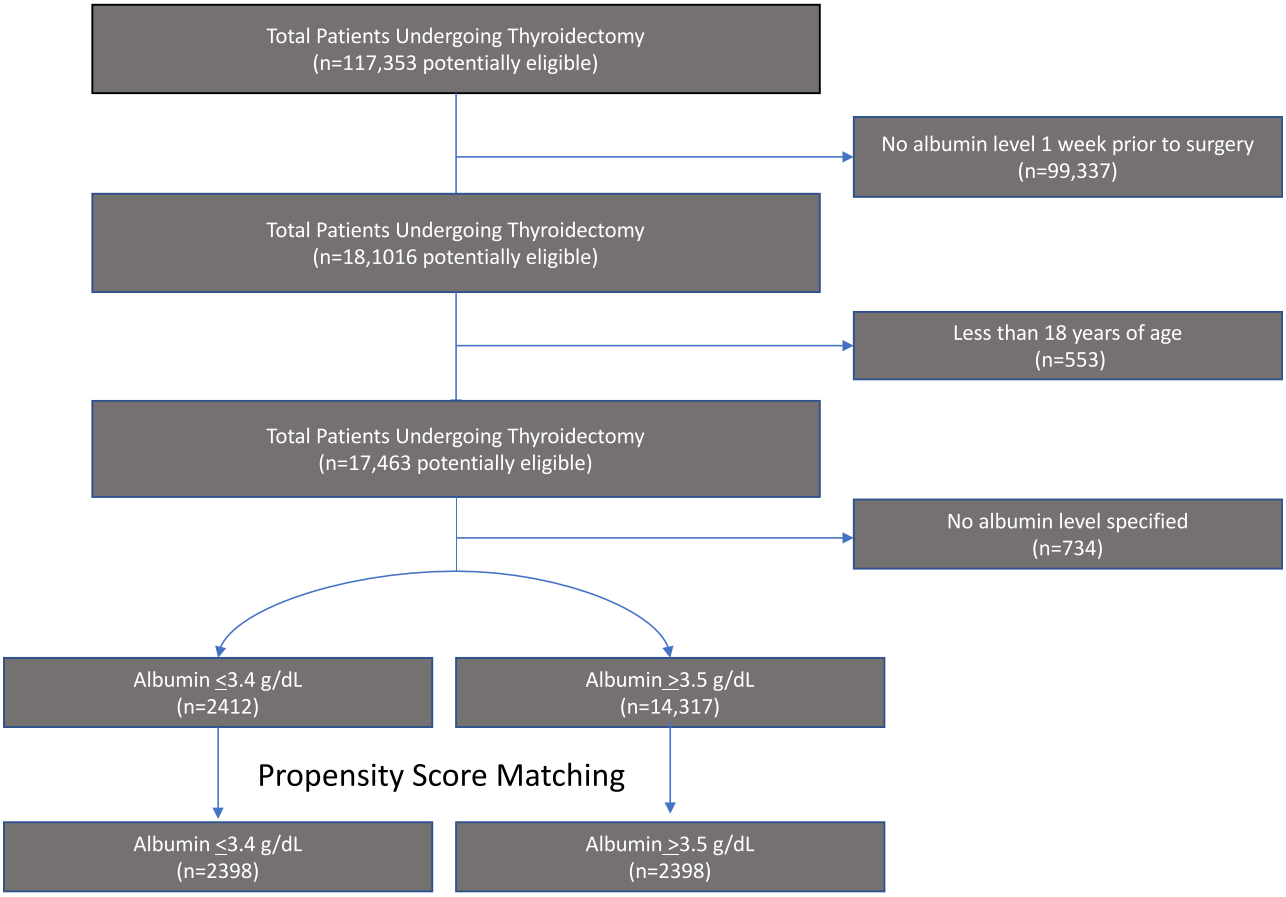

Figure 1. Participant flowchart.

previously described.[13-15] Analysis was performed through the TriNetX database using propensity score-matched cohorts, with the greedy-nearest neighbor algorithm with a caliper of 0.1 pooled standard deviations. Odds ratios were calculated using R's survival package v3.2-3 and validated, comparing the output to SAS version 9.4. χ^2 analysis and logistic regression were performed on categorical variables.

Results

After propensity score matching, a total of 2398 patients were identified in each cohort. The mean ages at index were 55.7 ± 15.6 and 55.6 ± 15 years in cohorts 1 and 2, respectively. Cohort 1 consisted of 70.18% females and cohort 2 consisted of 71.27% females. Baseline demographics and characteristics are shown in **Tables 2** and **3**.

Table **4** shows the rates of postoperative outcomes in thyroidectomy patients.

Patients with hypoalbuminemia had a greater than 3-fold increase in the rates of pneumonia (2.419% vs 0.709%; $P < 0.0001$) and acute renal failure (AKI) (3.461% vs 0.917%; $P < 0.0001$) compared to those without hypoalbuminemia. Less common postthyroidectomy complications such as venous thromboembolism (VTE) (2.043% vs 1.168%; $P = 0.0158$) were also found to be greater in patients with hypoalbuminemia. Rates of recurrent laryngeal nerve (RLN) injury were comparable between cohorts (2.919% vs 3.086%; $P = 0.7350$). Analyses of sepsis, tracheostomy, and respiratory dependence rates resulted in 10 or fewer patients, so differences between cohorts could not be compared. Similarly, analysis of mortality resulted in 10 or fewer patients (n = 43, 1.793% vs n ≤ 10, 0.417%; hazard ratio: 10.889 [3.909-30.335]) between patients with and without hypoalbuminemia respectively.

Table 1. Diagnosis and Procedure Codes

Outcome	Diagnosis and procedure codes
Deceased	
Pneumonia	J12, J13, J14, J15, J16, J17, J18
Acute renal failure	N17
Venous thromboembolism	I62, I82.4, I82.6
Sepsis	A40, A41, R65.2, T81.44
Surgical site infection	G9312, T81.4
Respiratory dependence	Z99.1
Tracheostomy	1014613, 31600
Recurrent laryngeal nerve injury	J38.0

Discussion

Albumin has traditionally been used as a marker for nutritional status and systemic inflammation. Mean albumin levels decrease with increasing age irrespective of comorbidities and in surgical cases, may reflect a postoperative metabolic immune response.[16] Studies have examined different indicators of nutritional status including serum albumin levels on postoperative outcomes of head and neck cancer surgeries, but many of them consist of smaller cohorts.[17,18]

Prior studies have suggested albumin as solely an inflammatory marker, but a meta-analysis by Vincent et al included studies that considered other markers such as C-reactive protein, lymphocyte count, neutrophil count, and transferrin levels and found that even with these factors considered, hypoalbuminemia remained an independent risk factor for poor clinical outcomes.[19] Our study identified an association between preoperative hypoalbuminemia and adverse surgical outcomes in patients who underwent thyroidectomy compared to those without hypoalbuminemia.

Table 2. Baseline Demographics of Thyroidectomy Patients After Propensity Score Matching (n = 2398)

Characteristics	Hypoalbuminemia (cohort 1), n (%)	Nonhypoalbuminemia (cohort 2), n (%)	*P* value	Standard mean difference
Age at index	55.7 ± 15.6 y	55.6 ± 15 y		
Female	1683 (70.18%)	1709 (71.27%)	0.409	0.024
White	1534 (63.97%)	1536 (64.05%)	0.952	0.002
Black or African American	511 (21.31%)	539 (22.48%)	0.328	0.028
Asian	66 (2.75%)	45 (1.88%)	0.044	0.058
Other race	47 (1.96%)	56 (2.34%)	0.370	0.026
American Indian or Alaska Native	13 (0.54%)	10 (0.42%)	0.531	0.018
Native Hawaiian or other Pacific Islander	0 (0%)	0 (0%)	0.707	0.011
Not Hispanic or Latino	1707 (71.18%)	1730 (72.14%)	0.461	0.021
Hispanic or Latino	346 (14.43%)	326 (13.60%)	0.405	0.024
Unknown ethnicity	345 (14.39%)	342 (14.26%)	0.902	0.004

Table 3. Propensity Score Matching Results for Common Comorbidities of Thyroidectomy Patients (n = 2398)

ICD-10 code	Diagnoses	Hypoalbuminemia (cohort 1), n (%)	Nonhypoalbuminemia (cohort 2), n (%)	*P* value	Standard mean difference
I10-I16	Hypertensive diseases	1256 (52.38%)	1264 (52.71%)	0.817	0.007
E78	Disorders of lipoprotein metabolism and other lipidemias	789 (32.90%)	800 (33.36%)	0.736	0.010
C73	Malignant neoplasm of the thyroid gland	677 (28.23%)	677 (28.23%)	1.000	0.000
E65-E68	Overweight, obesity, and other hyperalimentation	660 (27.52%)	667 (27.82%)	0.821	0.007
E08-E13	Diabetes mellitus	602 (25.10%)	608 (25.35%)	0.842	0.006
J40-J47	Chronic lower respiratory diseases	565 (23.56%)	561 (23.39%)	0.892	0.004
E05	Thyrotoxicosis (hyperthyroidism)	543 (22.64%)	568 (23.69%)	0.392	0.025
R13	Aphagia and dysphagia	542 (22.60%)	547 (22.81%)	0.863	0.005
E03	Other hypothyroidism	507 (21.14%)	495 (20.64%)	0.670	0.012
F17	Nicotine dependence	406 (16.93%)	398 (16.60%)	0.757	0.009
I20-I25	Ischemic heart diseases	405 (16.89%)	411 (17.14%)	0.818	0.007
N18	Chronic kidney disease	301 (12.55%)	299 (12.47%)	0.930	0.003
I50	Heart failure	264 (11.01%)	263 (10.97%)	0.963	0.001
I48	Atrial fibrillation and flutter	254 (10.59%)	248 (10.34%)	0.777	0.008
K70-K77	Diseases of liver	249 (10.38%)	253 (10.55%)	0.850	0.005
E06	Thyroiditis	152 (6.34%)	145 (6.05%)	0.675	0.012
I82	Other venous embolism and thrombosis	127 (5.30%)	127 (5.30%)	1.000	0.000
D34	Benign neoplasm of the thyroid gland	87 (3.63%)	93 (3.88%)	0.648	0.013
F10.1	Alcohol abuse	77 (3.21%)	83 (3.46%)	0.629	0.014
M32	Systemic lupus erythematosus	30 (1.25%)	37 (1.54%)	0.389	0.025
N04	Nephrotic syndrome	12 (0.50%)	10 (0.42%)	0.669	0.012
F50.0	Anorexia nervosa	10 (0.42%)	0 (0%)	0.002	0.092

Abbreviation: ICD-10, International Classification of Diseases 10th Revision.

Table 4. 30-Day Postoperative Outcomes in Thyroidectomy Patients With and Without Hypoalbuminemia (n = 2398)

Outcome	Hypoalbuminemia (cohort 1), n (%)	Nonhypoalbuminemia (cohort 2), n (%)	Odds ratio (95% CI)	*P* value
Pneumonia	58 (2.419%)	17 (0.709%)	3.472 (2.016-5.978)	**<0.0001**
Acute renal failure	83 (3.461%)	22 (0.917%)	3.872 (2.412-6.217)	**<0.0001**
Venous thromboembolism	49 (2.043%)	28 (1.168%)	1.766 (1.016-2.819)	**0.0158**
Surgical site infection	35 (1.46%)	15 (0.626%)	2.353 (1.282-4.32)	**0.0045**
Recurrent laryngeal nerve injury	70 (2.919%)	74 (3.086%)	0.944 (0.678-1.316)	0.7350
Sepsis	35 (1.46%)	≤10 (0.417%)	3.537 (1.748-7.159)	0.0002*
Tracheostomy	14 (0.584%)	≤10 (0.417%)	1.402 (0.622-3.163)	0.4130*
Respiratory dependence	23 (0.959%)	≤10 (0.417%)	2.313 (1.098-4.869)	0.0232*

Bolded values are significant.
*n value of n ≤ 10.

Mortality rates were found to be increased in patients with hypoalbuminemia, but this was not statistically significant between cohorts. However, this finding is expected as thyroidectomy is considered a generally safe procedure, and middle-aged patients, as reflected in our study, rather than elderly patients, make up the average cohort of patients who undergo this surgery.[20] While our study did not specify the indications for thyroidectomy, the presence of thyroid malignancy, hyperthyroidism, and hypothyroidism were included in propensity score matching. Our results are also similar to a study by Khawaja et al that reported comparable 30-day mortality rates in patients, who are of a similar mean age, with and without hypoalbuminemia who underwent parathyroidectomy.[21]

Postoperative outcomes that were significantly increased in those with hypoalbuminemia include pneumonia, AKI, VTE, and SSI. Pneumonia is the third most common surgical complication and the overall complication rate

after thyroidectomy is low, but pneumonia has been found to make up half of the reported complications.[22] Early patient reported dysphagia is common and often self-limiting, but can increase the risk of aspiration.[23] Additionally, RLN injury is a rare complication and is typically unilateral, but may also contribute to an increased risk of pneumonia.[1] One study further stratified the severity of admission serum albumin levels and reported an independent association with an increased risk of pneumonia.[24]

Our study's finding of a greater than 3-fold increase in the rate of acute kidney failure is also similar to prior studies. Abnormal albumin levels can cause fluid shifts due to its oncotic properties. Joo et al analyzed pre-operative values and observed that thyroidectomy patients who had low serum albumin levels had an increased risk of AKI.[25] Other studies also report low serum albumin as an independent predictor of AKI and death following AKI for patients in multiple hospital environments including cardiac, transplant, and orthopedic surgeries.[26-28]

Our study also found a higher rate of VTE in the hypoalbuminemia cohort, which was also seen in hypoalbuminemia patients undergoing parathyroidectomy and colorectal surgery.[21,29] The risk of developing VTE is lower compared to the risk of postoperative hemorrhage so prophylaxis is not routinely indicated.[30] Liver and kidney diseases, which can alter albumin levels, were considered in propensity score matching, but information on disease severity is not known.[31] The percentage of thyroidectomies that included a neck dissection, which prolongs operative duration and may increase hypercoagulability, was not known but various indications for thyroidectomy were also included in propensity score matching. Our study's higher rate of postoperative AKI may also be partly responsible for the increased risk of VTE.

Our study's finding of a higher rate of surgical site infections in patients with hypoalbuminemia is supported by prior studies. A study of wound infections after surgery for oral cavity cancer reported a significantly increased rate of wound infections in patients with hypoalbuminemia. However, this relation was noted in postoperative albumin values so it could be that hypoalbuminemia was a result of the infection rather than a cause of infection. The study considered hypoalbuminemia levels to be ≤2.8 g/dL indicating more severe hypoalbuminemia.[32] In contrast, a database study found similar rates of hypoalbuminemia in patients with and without SSI, but there were higher rates of tobacco use in patients with SSI, and the cutoff value for hypoalbuminemia was not reported.[33]

Rates of RLN injury were comparable between cohorts. This finding was not unexpected since if it occurs, it is likely almost entirely related to iatrogenic factors or tumor factors.[34] Operative techniques, such as the use of neuromonitoring, could be a potential confounder, which is not known in the database.[35] Rates of mortality, sepsis, tracheostomy, and respiratory dependence were higher in patients with hypoalbuminemia, but could not be compared because of 1 cohort having a $n \leq 10$. An increased risk of sepsis has been observed in hypoalbuminemia patients who underwent parathyroidectomy.[21] On the other hand, the benefit of albumin administration for patients with sepsis is not clear as 1 study did not find improved rates of mortality in severely septic patients who received albumin in addition to normal fluids.[36]

To our knowledge, this is the largest retrospective study of thyroidectomy patients which increases the generalizability of the results. The major limitation of this study was that it was retrospective. Furthermore, due to the nature of the database, patient-level data such as the severity of specific outcomes could not be collected. Pathologic and radiologic information was unavailable, but these limitations were addressed by including different indications for thyroidectomy such as malignancy in propensity score matching. In our study, cases of partial thyroidectomy/lobectomy were not separated from patients who underwent total thyroidectomy which has a longer operative time. Most of the complication rates reported were between 1% and 2% so it was not entirely surprising that there was an insufficient number of cases of partial or unilateral thyroidectomy/lobectomy for a separate analysis (outcomes $n \leq 10$). It may be possible that this longer duration could play a role in outcomes. The data collected was from the electronic health record and therefore was for billing purposes, not necessarily for clinical use, and thus much clinical information is missing. Outcomes were analyzed by billing codes, so all postoperative outcomes may not be fully encompassed under the codes used, but TriNetX collects information from multiple HCOs including both inpatient and outpatient facilities. Lastly, analysis in database studies is limited by the accuracy of data entry so misidentification is inevitable.

Preoperative interventions to optimize albumin levels in patients may limit adverse postoperative outcomes. Some studies have begun to investigate the therapeutic benefit of perioperative albumin supplementation, but there are no definitive guidelines that recommend its use.[37] Future studies should examine the effect of preoperative hypoalbuminemia on the length of hospital stay and risk of reoperation. The findings in our study are likely not specific to thyroidectomy, but further studies are necessary to investigate the effect of the change in albumin levels on postoperative outcomes in head and neck surgeries. Risk factors such as tobacco and alcohol use and pathologies that affect the head and neck area may also impair mastication or be associated with malnutrition.

Conclusion

Our study found that hypoalbuminemia patients were more likely to experience adverse postthyroidectomy

complications compared to those without hypoalbuminemia. Overall rates of complications are low, but these complications can significantly impact morbidity. These findings may not be specific to thyroidectomy, but an understanding of the impact of preoperative hypoalbuminemia as a surrogate marker for surgical complications may help guide expectations and optimal management of thyroidectomy patients. While not routinely assessed, preoperative albumin levels could be used as prognostic indicators of malnutrition and risk of adverse postoperative outcomes and be a target of preoperative intervention.

Author Contributions

Bao Yue Sciscent, concept design, acquisition, analysis, or interpretation of data, writing the manuscript, presentation; **Hanel Watkins Eberly**, acquisition, analysis, or interpretation of data, critical editing of the manuscript; **F. Jeffrey Lorenz**, acquisition, analysis, or interpretation of data, critical editing of the manuscript; **Nguyen Truong**, interpretation of data, critical editing of the manuscript; **David Goldenberg**, concept design, reviewing data analysis, critical editing of the manuscript; **Neerav Goyal**, concept design, reviewing data analysis, critical editing of the manuscript, final approval.

Disclosures

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Supplemental Material

Additional supporting information is available in the online version of the article.

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References

1. Bhattacharyya N, Fried MP. Assessment of the morbidity and complications of total thyroidectomy. *Arch Otolaryngol Head Neck Surg*. 2002;128(4):389-392. doi:10.1001/archotol.128.4.389
2. Indications for thyroidectomy. *Lancet*. 1973;2(7820):82.
3. Abraham CR, Ata A, Carsello CB, Chan TL, Stain SC, Beyer TD. A NSQIP risk assessment for thyroid surgery based on comorbidities. *J Am Coll Surg*. 2014;218(6):1231-1237. doi:10.1016/j.jamcollsurg.2014.01.055
4. Lamadé W, Renz K, Willeke F, Klar E, Herfarth C. Effect of training on the incidence of nerve damage in thyroid surgery. *Br J Surg*. 1999;86(3):388-391. doi:10.1046/j.1365-2168.1999.01017.x
5. Al-Qurayshi Z, Robins R, Hauch A, Randolph GW, Kandil E. Association of surgeon volume with outcomes and cost savings following thyroidectomy: a national forecast. *JAMA Otolaryngol Head Neck Surg*. 2016;142(1):32-39. doi:10.1001/jamaoto.2015.2503
6. Dasenbrock HH, Liu KX, Chavakula V, et al. Body habitus, serum albumin, and the outcomes after craniotomy for tumor: a National Surgical Quality Improvement Program analysis. *J Neurosurg*. 2017;126(3):677-689. doi:10.3171/2016.2.jns152345
7. Berbel-Franco D, Lopez-Delgado JC, Putzu A, et al. The influence of postoperative albumin levels on the outcome of cardiac surgery. *J Cardiothorac Surg*. 2020;15(1):78. doi:10.1186/s13019-020-01133-y
8. Luchetti TJ, Chung A, Olmscheid N, Bohl DD, Hustedt JW. Hypoalbuminemia is associated with increased postoperative mortality and complications in hand surgery. *Hand*. 2020;15(4):547-555. doi:10.1177/1558944718820959
9. Joliat GR, Schoor A, Schäfer M, Demartines N, Hübner M, Labgaa I. Postoperative decrease of albumin (ΔAlb) as early predictor of complications after gastrointestinal surgery: a systematic review. *Perioper Med*. 2022;11(1):7. doi:10.1186/s13741-022-00238-3
10. Montazerghaem H, Safaie N, Samiei Nezhad V. Body mass index or serum albumin levels: which is further prognostic following cardiac surgery? *J Cardiovasc Thorac Res*. 2014;6(2):123-126. doi:10.5681/jcvtr.2014.026
11. Rind F, Zhao S, Haring C, et al. Body mass index (BMI) related morbidity with thyroid surgery. *Laryngoscope*. 2023;133:2823-2830. doi:10.1002/lary.30789
12. Corti MC. Serum albumin level and physical disability as predictors of mortality in older persons. *JAMA*. 1994;272(13):1036-1042.
13. Taquet M, Geddes JR, Husain M, Luciano S, Harrison PJ. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. *Lancet Psychiatry*. 2021;8(5):416-427. doi:10.1016/s2215-0366(21)00084-5
14. Taquet M, Husain M, Geddes JR, Luciano S, Harrison PJ. Cerebral venous thrombosis and portal vein thrombosis: a retrospective cohort study of 537,913 COVID-19 cases. *EClinicalMedicine*. 2021;39:101061. doi:10.1016/j.eclinm.2021.101061
15. Topaloglu U, Palchuk MB. Using a federated network of real-world data to optimize clinical trials operations. *JCO Clin Cancer Inform*. 2018;2:1-10. doi:10.1200/cci.17.00067
16. Salive ME, Cornoni-Huntley J, Phillips CL, et al. Serum albumin in older persons: relationship with age and health status. *J Clin Epidemiol*. 1992;45(3):213-221. doi:10.1016/0895-4356(92)90081-w
17. van Bokhorst-de van der Schueren MAE, van Leeuwen PAM, Sauerwein HP, Kuik DJ, Snow GB, Quak JJ. Assessment of malnutrition parameters in head and neck cancer and their relation to postoperative complications. *Head Neck*. 1997;19(5):419-425. doi:10.1002/(sici)1097-0347(199708)19:5<419::aid-hed9>3.0.co;2-2
18. Danan D, Shonka Jr. DC, Selman Y, Chow Z, Smolkin ME, Jameson MJ. Prognostic value of albumin in patients

with head and neck cancer. *Laryngoscope*. 2016;126(7): 1567-1571. doi:10.1002/lary.25877
19. Vincent JL, Dubois MJ, Navickis RJ, Wilkes MM. Hypoalbuminemia in acute illness: is there a rationale for intervention? A meta-analysis of cohort studies and controlled trials. *Ann Surg*. 2003;237(3):319-334. doi:10.1097/01.sla.0000055547.93484.87
20. Echanique KA, Govindan A, Mohamed OM, et al. Age-related trends of patients undergoing thyroidectomy: analysis of US inpatient data from 2005 to 2013. *Otolaryngol Head Neck Surg*. 2019;160(3):457-464. doi:10.1177/0194599818825455
21. Khawaja IM, Randhawa A, Randhawa K, et al. Effect of hypoalbuminemia in patients undergoing parathyroidectomy for primary hyperparathyroidism. *Laryngoscope*. 2023;133:2035-2039. doi:10.1002/lary.30691
22. Fassas S, Mamidi I, Lee R, et al. Postoperative complications after thyroidectomy: time course and incidence before discharge. *J Surg Res*. 2021;260:210-219. doi:10.1016/j.jss.2020.11.008
23. Krekeler BN, Wendt E, Macdonald C, et al. Patient-reported dysphagia after thyroidectomy: a qualitative study. *JAMA Otolaryngol Head Neck Surg*. 2018;144(4):342-348. doi:10.1001/jamaoto.2017.3378
24. Viasus D, Garcia-Vidal C, Simonetti A, et al. Prognostic value of serum albumin levels in hospitalized adults with community-acquired pneumonia. *J Infect*. 2013;66(5): 415-423. doi:10.1016/j.jinf.2012.12.007
25. Joo EY, Kim YJ, Go Y, Song JG. Relationship between perioperative thyroid function and acute kidney injury after thyroidectomy. *Sci Rep*. 2018;8(1):13539. doi:10.1038/s41598-018-31946-w
26. Wiedermann CJ, Wiedermann W, Joannidis M. Causal relationship between hypoalbuminemia and acute kidney injury. *World J Nephrol*. 2017;6(4):176-187. doi:10.5527/wjn.v6.i4.176
27. Nelson CL, Elkassabany NM, Kamath AF, Liu J. Low albumin levels, more than morbid obesity, are associated with complications after TKA. *Clin Orthopaed Relat Res*. 2015;473(10):3163-3172. doi:10.1007/s11999-015-4333-7
28. Kim HJ, Koh WU, Kim SG, et al. Early postoperative albumin level following total knee arthroplasty is associated with acute kidney injury: a retrospective analysis of 1309 consecutive patients based on kidney disease improving global outcomes criteria. *Medicine*. 2016;95(31):e4489. doi:10.1097/md.0000000000004489
29. Hu WH, Eisenstein S, Parry L, Ramamoorthy S. Preoperative malnutrition with mild hypoalbuminemia associated with postoperative mortality and morbidity of colorectal cancer: a propensity score matching study. *Nutr J*. 2019;18(1):33. doi:10.1186/s12937-019-0458-y
30. Limongelli P, Tolone S, Gubitosi A, et al. Relationship between postoperative venous thromboembolism and hemorrhage in patients undergoing total thyroidectomy without preoperative prophylaxis. *Int J Surg*. 2014;12(suppl 1): S198-S201. doi:10.1016/j.ijsu.2014.05.009
31. Matsushita K, van der Velde M, Astor BC, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet*. 2010;375(9731): 2073-2081. doi:10.1016/s0140-6736(10)60674-5
32. Liu SA, Wong YK, Poon CK, Wang CC, Wang CP, Tung KC. Risk factors for wound infection after surgery in primary oral cavity cancer patients. *Laryngoscope*. 2007;117(1): 166-171. doi:10.1097/01.mlg.0000249737.05840.29
33. Myssiorek D, Ahmed Y, Parsikia A, Castaldi M, McNelis J. Factors predictive of the development of surgical site infection in thyroidectomy—an analysis of NSQIP database. *Int J Surg*. 2018;60:273-278. doi:10.1016/j.ijsu.2018.11.013
34. Aygun N, Kostek M, Unlu MT, Isgor A, Uludag M. Clinical and anatomical factors affecting recurrent laryngeal nerve paralysis during thyroidectomy via intraoperative nerve monitorization. *Front Surg*. 2022;9:867948. doi:10.3389/fsurg.2022.867948
35. Duong W, Grigorian A, Farzaneh C, et al. Nerve monitoring decreases recurrent laryngeal nerve injury risk for neoplasm-related thyroidectomy. *Am J Surg*. 2022;223(5):918-922. doi:10.1016/j.amjsurg.2021.10.013
36. Caironi P, Tognoni G, Masson S, et al. Albumin replacement in patients with severe sepsis or septic shock. *N Engl J Med*. 2014;370(15):1412-1421. doi:10.1056/NEJMoa1305727
37. Xu H, Han Z, Ma W, Zhu X, Shi J, Lin D. Perioperative albumin supplementation is associated with decreased risk of complications following microvascular head and neck reconstruction. *J Oral Maxillofac Surg*. 2021;79(10): 2155-2161. doi:10.1016/j.joms.2021.04.030