



# Hypoalbuminemia Predicts Serious Complications Following Elective Bariatric Surgery

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## Abstract

**Purpose** The aims of this study were to (1) characterize the prevalence of hypoalbuminemia (HA), (2) compare complication rates among HA and non-HA patients, and (3) determine the influence of HA on postoperative complications and 30-day mortality among bariatric surgery patients.

**Materials and Methods** Data was extracted from the MBSAQIP registry from 2015 to 2018. A presurgical serum albumin level of  $\leq 3.5$  g/dL was used to organize the patient population into HA and non-HA cohorts. Bivariate analysis and multi-variable logistic regression modeling were used.

**Results** Of 590,971 patients, 42,618 (7.2%) were identified as having serum albumin levels  $\leq 3.5$  g/dL. HA patients were younger ( $44.0 \pm 11.9$  vs.  $44.5 \pm 12.0$  years;  $p < 0.0001$ ), were of increased BMI ( $48.5 \pm 9.0$  kg/m<sup>2</sup> vs.  $45.1 \pm 7.7$  kg/m<sup>2</sup>;  $p < 0.0001$ ), and had a lower baseline functional status (1.6% vs. 1.0% dependent or partially dependent;  $p < 0.0001$ ). HA patients had more anastomotic leaks (0.46% vs. 0.38%;  $p = 0.02$ ), deep surgical site infections (0.37% vs. 0.24%;  $p < 0.0001$ ), and composite serious complications (4.4% vs. 3.3%;  $p < 0.0001$ ). At 30-day post-operation, complications including need for reintervention (1.6% vs. 1.2%;  $p < 0.0001$ ), readmission (4.8% vs. 3.7%;  $p < 0.0001$ ), and mortality (0.14% vs. 0.086%;  $p = 0.001$ ) were all more prevalent among HA patients. After functional status, HA was the strongest modifiable predictor of serious complications but was not predictive of 30-day mortality.

**Conclusion** We identified HA as one of the greatest modifiable factors predictive of serious complications. Adoption of strategies to identify and improve preoperative serum albumin levels may reduce overall serious complications among elective bariatric surgery patients.

**Keywords** Hypoalbuminemia · Sarcopenic obesity · Malnutrition · Bariatric surgery

## Key Points

1. Bariatric hypoalbuminemia is not a rare clinical entity and occurs in over 7% of all patients.
2. Hypoalbuminemia is associated with increased anastomotic leaks and serious complications.
3. Adverse 30-day outcomes are more common among hypoalbuminemic patients.
4. Hypoalbuminemia is a modifiable factor predictive of serious complications.

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## Introduction

Over the past three decades, the prevalence of obesity has dramatically increased throughout the world [1], and at present over one third of the US population is diagnosed with obesity [2]. Bariatric surgery remains the most effective long-term treatment for severe obesity and its metabolic comorbidities [3]. Yet, while bariatric procedures are generally regarded as safe, postoperative complications remain as high as 26% [4] despite ongoing advancements in perioperative care and surgical techniques, posing a substantial burden on patient morbidity and mortality [5, 6]. Recent literature has drawn growing attention to the importance of preoperative markers of nutritional status as potential predictors of surgical complications [7, 8]; however, the role of

these nutritional markers on bariatric outcomes is currently poorly understood.

Serum albumin has been identified as an indicator of malnutrition as well as an independent serological marker for adverse surgical outcomes [9]. Albumin is the most abundant protein in human plasma, and hypoalbuminemia (HA) is generally defined as serum albumin concentration  $\leq 3\text{--}4$  g/dL [10, 11]. HA has been associated with systemic inflammation, decreased collagen synthesis, excessive tissue edema, and ultimately poor tissue healing resulting in anastomotic leak as well as other serious postoperative complications [12–17]. Paradoxically, patients with severe obesity have decreased serum albumin levels and demonstrate a physiologic malnutrition and decreased muscle mass which may predispose to increased postoperative complications through a phenomenon termed sarcopenic obesity (SO) [7, 18]. The degree of HA and the impact of this phenomenon on patients undergoing elective bariatric surgery are not currently known.

We hypothesized that HA in patients undergoing elective bariatric surgery is not a rare clinical entity and is associated with adverse surgical outcomes. The aim of the present study was therefore to (1) characterize the prevalence and clinical characteristics of HA in bariatric surgery patients, (2) compare complication rates among bariatric surgery patients with low and normal presurgery serum albumin levels, and (3) determine if HA is an independent predictor of 30-day serious complications and 30-day mortality among bariatric surgery patients using multivariable logistic regression analysis.

## Methods

### Data Source

All data was extracted from the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) database from 2015 to 2018 inclusive. The MBSAQIP is the largest clinical data registry that captures the majority of bariatric procedures performed in over 800 accredited North American bariatric centers. Contributing centers are subject to careful and frequent review of practice and data integrity. Prospective data collection is performed by trained clinical reviewers and encompasses a standardized set of pre-, intra-, and postoperative variables.

### Study Design, Variable Definitions, and Population

All patients who underwent sleeve gastrectomy (SG) or Roux-en-Y gastric bypass (RYGB) between 2015 and 2018 were included in this retrospective cohort study. Patients who underwent prior bariatric surgery, emergency

surgery, conversion procedures, or revision procedures were excluded. For this work, we defined HA as a presurgery serum albumin level of  $\leq 3.5$  g/dL [19], as identified on standard preoperative blood work. We then organized our results into two cohorts represented by low (HA) and normal (non-HA) serum albumin. To minimize coding errors, patients with albumin values  $< 1$  g/dL or  $> 6$  g/dl were excluded.

Our primary objectives were to first to characterize the prevalence of and clinical characteristics of bariatric surgery patients with HA and second, to compare complication rates among bariatric surgery patients with HA and those with normal presurgery serum albumin levels. As a secondary objective, we sought to determine the influence of HA on serious postoperative complications and 30-day mortality among bariatric surgery patients.

Clinical characteristics of patients with low and normal presurgery serum albumin levels included a comprehensive list of pre-, intra-, and postoperative factors. Patient factors included age, sex, body mass index (BMI), functional status (independent, partially dependent, and dependent prior to surgery), smoking status, and the American Society of Anesthesiologists (ASA) physical status classifications. Comorbidities investigated included diabetes (non-diabetic and diet controlled, non-insulin dependent, and insulin dependent), hypertension, dyslipidemia, gastroesophageal reflux disease (GERD), chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA), history of venous thromboembolism (VTE), prior myocardial infarction (MI), and renal insufficiency. Additional comorbid factors included oxygen dependence, chronic steroid use, anticoagulation status, prior cardiac surgery, prior percutaneous coronary intervention (PCI), and dialysis dependence. Surgical factors assessed included type of procedure and operative length.

Specific postoperative complications that were investigated included leak, bleed, cardiac complications, pneumonia, acute kidney injury (AKI), deep and superficial surgical site infections (SSI), wound disruption, sepsis, unplanned intubation, *Clostridioides difficile* infection (*C. diff*), and a composite variable of overall serious complications. Additionally, 30-day reoperation, intervention, readmission, and mortality rates were assessed.

### Statistical Analysis

Categorical variables were expressed as absolute values and percentages, and bivariate analysis was performed using chi-squared tests. Continuous variables were expressed as means  $\pm$  standard deviations (SD), and analysis was performed using ANOVA. To determine the influence of HA on postoperative complications and 30-day mortality, a non-parsimonious multivariable logistic regression model was developed using a hypothesis-driven purposeful selection methodology. Bivariate

analysis of variables with a  $p$ -value  $< 0.1$  or from variables previously deemed clinically relevant to our primary outcome was used to generate a preliminary main effects model. Significant variables in the multivariable model were then identified (Wald test  $p < 0.05$ ) and linear assumption of continuous variables and multi-collinearity were checked using the variance inflation factor (VIF). Variables with a VIF greater than 10 were further explored using collinearity diagnostic tests and excluded from the final model if deemed collinear. The Brier Score (BS) and the receiver operating characteristic (ROC) curve were used to assess goodness of fit. All statistical analysis was performed using Stata 15 (STATA Corp LP, College Station, TX).

## Results

### Basic Demographics and Univariate Analysis of HA vs. Non-HA Cohorts

A total of 590,971 patients that underwent primary SG and RYGB were identified from 2015 to 2018 using the MBSAQIP data registry. Of these, 42,618 (7.2%) were identified as having presurgical serum albumin levels  $\leq 3.5$  g/dL and were therefore classified within the HA cohort. Overall, HA patients were younger ( $44.0 \pm 11.9$ ;  $p < 0.0001$  vs.  $44.5 \pm 12.0$  years), of increased BMI ( $48.5 \pm 9.0$  kg/m<sup>2</sup> vs.  $45.1 \pm 7.7$  kg/m<sup>2</sup>;  $p < 0.0001$ ), and more likely to be of female sex (85.8% vs. 78.7%;  $p < 0.0001$ ) (Table 1). HA patients were more likely to be smokers of cigarettes (9.9% vs. 8.4%;  $p < 0.0001$ ) and have a lower baseline functional status (1.6% vs. 1.0% dependent or partially dependent;  $p < 0.0001$ ) when compared to patients with normal presurgical serum albumin.

HA patients tended to have higher presurgical ASA classifications (6.0% vs. 3.4% ASA category 4–5;  $p < 0.0001$ ). Similarly, certain comorbidities were significantly associated with low presurgical serum albumin including medication-dependent diabetes mellitus (30.4% vs. 26.0%;  $p < 0.0001$ ), hypertension (50.1% vs. 47.8%;  $p < 0.0001$ ), GERD (30.8% vs. 30.4%;  $p = 0.02$ ), and COPD (2.2% vs. 1.6%;  $p < 0.0001$ ). Higher incidences of preoperative cardiac, renal, and hematologic comorbidities were similarly associated with HA (Table 1). Interestingly, OSA (38.3% vs. 36.2%;  $p < 0.0001$ ) and dyslipidemia (23.8% vs. 22.6%;  $p < 0.0001$ ) were more prevalent among patients with normal presurgical albumin levels.

### Bivariate Analysis of Postoperative Complications in HA vs. Non-HA Cohorts

To identify if HA was associated with development of postoperative complications, we compared complication rates between low and normal albumin cohorts (Table 2).

In comparison to the normal presurgical albumin cohort, HA patients had more anastomotic leaks (0.46% vs. 0.38%;  $p = 0.02$ ), deep surgical site infections (0.37% vs. 0.24%;  $p < 0.0001$ ), wound disruptions (0.07 vs. 0.05;  $p = 0.04$ ), postoperative sepsis (0.14% vs. 0.10%;  $p = 0.004$ ), and composite serious complications (4.4% vs. 3.3%;  $p < 0.0001$ ). Unplanned reintubation, postoperative pneumonia, acute kidney injury, and subsequent *C. diff* rates were also higher among the HA cohort. No significant difference was found between patients with low vs. normal presurgical serum albumin levels with regard to postoperative bleed and cardiac complications. At 30-day postoperation, complications including need for reoperation (1.4% vs. 1.2%;  $p = 0.002$ ), reintervention (1.6% vs. 1.2%;  $p < 0.0001$ ), readmission (4.8% vs. 3.7%;  $p < 0.0001$ ), and mortality (0.14% vs. 0.086%;  $p = 0.001$ ) were all increased in HA patients.

### Multivariable Logistic Regression Analysis for Predictors of Serious Complications and 30-Day Mortality

A multivariable logistic regression model was then developed to identify if HA was independently predictive of serious postoperative complications (Table 3) or mortality after adjusting for covariates (Table 4). ROC areas and BS for both serious complications (0.65; BS 0.03) and mortality (ROC 0.83; BS 0.009) models indicated an appropriate ability to predict our desired outcomes.

Our first model evaluated predictors of 30-day serious complications (Table 3). The following five variables were found to be independently predictive of this outcome from greatest to lowest effect, respectively: RYGB, renal insufficiency, MI, COPD, and poor functional status. Of modifiable preoperative patient factors, HA was one of the largest independent predictors of serious complications (OR 1.20; 95% CI 1.14–1.26;  $p < 0.0001$ ) after poor functional status.

The second model evaluating predictors of 30-day mortality (Table 4) identified a number of significant factors predictive of mortality including leak, bleed, COPD, MI, and renal insufficiency. Unlike the previous model, HA was not found to be a predictor of mortality after adjusting for comorbidities (OR 1.13; 95% CI 0.85–1.49;  $p = 0.4$ ). Female sex was found to be protective for improved 30-day mortality, while no variables was found to be protective for serious complications.

## Discussion

There is a paucity of information surrounding the prevalence and implications of presurgical HA in patients undergoing elective bariatric surgery. Using the largest and most comprehensive bariatric database, our study highlights

**Table 1** Basic demographics of patients with low (HA) and normal (non-HA) serum albumin levels prior to bariatric surgery. Values represent raw numbers and percentages

|                                  | Non-HA (n = 548,353) | HA (n = 42,618) | p-value  |
|----------------------------------|----------------------|-----------------|----------|
| Age                              |                      |                 | < 0.0001 |
| < 18                             | 968 (0.18)           | 49 (0.11)       |          |
| 18–30                            | 64,730 (11.8)        | 4997 (11.7)     |          |
| 30–40                            | 140,041 (25.5)       | 11,866 (27.8)   |          |
| 40–50                            | 158,018 (28.8)       | 13,006 (30.5)   |          |
| 50–60                            | 122,120 (22.3)       | 7952 (18.7)     |          |
| > 60                             | 433,658 (79.1)       | 4748 (11.1)     |          |
| Female                           | 309,577 (78.7)       | 36,548 (85.8)   | < 0.0001 |
| BMI                              |                      |                 | < 0.0001 |
| < 35                             | 18,927 (3.5)         | 667 (1.6)       |          |
| 35–40                            | 126,662 (23.3)       | 5821 (13.7)     |          |
| 40–50                            | 170,443 (31.3)       | 10,733 (25.3)   |          |
| 50–60                            | 111,564 (20.5)       | 9538 (22.5)     |          |
| 60–70                            | 92,060 (16.9)        | 11,226 (26.5)   |          |
| > 70                             | 25,159 (4.6)         | 4391 (10.4)     |          |
| Functional status                |                      |                 | < 0.0001 |
| Independent                      | 543,039 (99.0)       | 41,961 (98.5)   |          |
| Partially dependent              | 3228 (0.59)          | 454 (1.1)       |          |
| Dependent                        | 2086 (0.38)          | 203 (0.48)      |          |
| Smoker                           | 45,986 (8.4)         | 4232 (9.9)      | < 0.0001 |
| ASA category                     |                      |                 | < 0.0001 |
| ASA 1–2                          | 124,732 (22.9)       | 7366 (17.3)     |          |
| ASA 3                            | 402,750 (74.8)       | 32,626 (76.7)   |          |
| ASA 4–5                          | 18,342 (3.4)         | 2545 (6.0)      |          |
| Diabetes                         |                      |                 | < 0.0001 |
| Non-diabetic and diet controlled | 406,250 (74.1)       | 29,445 (69.1)   |          |
| Non-insulin dependent            | 97,430 (17.8)        | 7591 (17.8)     |          |
| Insulin dependent                | 44,673 (8.2)         | 5582 (13.1)     |          |
| OSA                              | 209,833 (38.3)       | 15,418 (36.2)   | < 0.0001 |
| HTN                              | 262,178 (47.8)       | 21,330 (50.1)   | < 0.0001 |
| GERD                             | 166,741 (30.4)       | 13,145 (30.8)   | 0.02     |
| COPD                             | 8794 (1.6)           | 948 (2.2)       | < 0.0001 |
| DLD                              | 130,752 (23.8)       | 9631 (22.6)     | < 0.0001 |
| Chronic steroids                 | 9265 (1.7)           | 925 (2.2)       | < 0.0001 |
| Renal insufficiency              | 3089 (0.56)          | 666 (1.6)       | < 0.0001 |
| Dialysis                         | 1562 (0.28)          | 287 (0.67)      | < 0.0001 |
| Prior VTE                        | 12,383 (2.3)         | 1326 (3.1)      | < 0.0001 |
| Therapeutic anticoagulation      | 14,151 (2.6)         | 1580 (3.7)      | < 0.0001 |
| Oxygen dependent                 | 3594 (0.66)          | 499 (1.2)       | < 0.0001 |
| Prior MI                         | 6716 (1.2)           | 711 (1.7)       | < 0.0001 |
| Prior cardiac surgery            | 5780 (1.1)           | 554 (1.3)       | < 0.0001 |
| RYGB                             | 144,245 (26.3)       | 12,696 (29.8)   |          |
| Operative length (h)             |                      |                 | < 0.0001 |
| < 1                              | 183,895 (33.5)       | 13,574 (31.9)   |          |
| 1–2                              | 264,110 (48.2)       | 21,259 (49.9)   |          |
| 2–3                              | 77,495 (14.1)        | 5928 (13.9)     |          |
| > 3                              | 22,853 (4.2)         | 1857 (4.4)      |          |

*BMI*, body mass index; *ASA*, American Society of Anesthesiologists; *OSA*, obstructive sleep apnea; *HTN*, hypertension; *GERD*, gastroesophageal reflux disease; *COPD*, chronic obstructive pulmonary disease; *DLD*, dyslipidemia; *VTE*, venous thromboembolism; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *RYGB*, Roux-en-Y gastric bypass

**Table 2** Postoperative complications of patients with normal (non-HA) and low (HA) preoperative serum albumin levels following bariatric surgery. Values represent raw numbers and percentages

|                       | Non-HA (n = 548,353) | HA (n = 42,618) | p-value |
|-----------------------|----------------------|-----------------|---------|
| Leak                  | 2084 (0.38)          | 198 (0.46)      | 0.02    |
| Bleed                 | 5018 (0.92)          | 416 (0.98)      | 0.3     |
| Cardiac               | 351 (0.06)           | 36 (0.08)       | 0.1     |
| Pneumonia             | 985 (0.18)           | 115 (0.27)      | <0.0001 |
| AKI                   | 623 (0.11)           | 132 (0.31)      | <0.0001 |
| Deep SSI              | 1342 (0.24)          | 157 (0.37)      | <0.0001 |
| Wound disruption      | 256 (0.05)           | 29 (0.07)       | 0.04    |
| Sepsis                | 542 (0.10)           | 61 (0.14)       | 0.004   |
| Unplanned intubation  | 706 (0.13)           | 100 (0.23)      | <0.0001 |
| <i>C. diff</i>        | 494 (0.12)           | 66 (0.20)       | <0.0001 |
| Serious complications | 18,065 (3.3)         | 1860 (4.4)      | <0.0001 |
| 30-day reoperation    | 6456 (1.2)           | 587 (1.4)       | 0.002   |
| 30-day reintervention | 6552 (1.2)           | 690 (1.6)       | <0.0001 |
| 30-day readmission    | 20,008 (3.7)         | 2037 (4.8)      | <0.0001 |
| 30-day mortality      | 473 (0.086)          | 59 (0.14)       | 0.001   |

AKI, acute kidney injury; SSI, superficial site infection; *C. diff*, *Clostridioides difficile* infection

**Table 3** Predictors of serious complications of patients with normal and low preoperative serum albumin levels following bariatric surgery

| Predictors of serious complications                    | Odds ratio | 95% confidence interval | p-value |
|--|------------|-------------------------|---------|
| Hypoalbuminemia  | 1.20       | 1.14–1.26               | <0.0001 |
| Older age (per 10 years)                               | 1.04       | 1.03–1.06               | <0.0001 |
| Higher BMI (per 5 kg/m <sup>2</sup> )                  | 1.03       | 1.02–1.04               | <0.0001 |
| Female   | 0.99       | 0.96–1.03               | 0.7     |
| Race   |            |                         | <0.0001 |
| Black vs. White  | 1.30       | 1.26–1.35               |         |
| Other vs. White  | 0.90       | 0.86–0.95               |         |
| Functional status                                      |            |                         | <0.0001 |
| Partially dependent vs. independent                    | 1.54       | 1.35–1.75               |         |
| Dependent vs. independent                              | 1.59       | 1.32–1.92               |         |
| Diabetes   |            |                         |         |
| Non-insulin dependent vs. non-diabetic/diet controlled | 1.00       | 0.97–1.04               | 0.8     |
| Insulin dependent vs. non-diabetic/diet controlled     | 1.16       | 1.11–1.22               | <0.0001 |
| OSA  | 1.10       | 1.06–1.13               | <0.0001 |
| HTN  | 1.10       | 1.06–1.13               | <0.0001 |
| DLD  | 1.05       | 1.02–1.09               | 0.006   |
| GERD   | 1.28       | 1.24–1.32               | <0.0001 |
| COPD   | 1.57       | 1.44–1.70               | <0.0001 |
| Renal insufficiency                                    | 2.14       | 1.91–2.41               | <0.0001 |
| Prior MI   | 1.59       | 1.45–1.74               | <0.0001 |
| RYGB   | 2.37       | 2.30–2.44               | <0.0001 |

BMI, body mass index; OSA, obstructive sleep apnea; HTN, hypertension; DLD, dyslipidemia; GERD, gastroesophageal reflux disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; RYGB, Roux-en-Y gastric bypass

that bariatric HA is not a rare clinical entity and occurs in over 7% of all patients. Further, we demonstrate that HA is associated with increased anastomotic leaks, deep surgical site infections, wound disruptions, postoperative sepsis, and serious complications. Adverse 30-day outcomes

like reoperation, reintervention, readmission, and mortality were also more common among HA patients. Lastly, HA was found to be one of the greatest modifiable predictors of serious complications but was not found to be predictive of 30-day mortality.

**Table 4** Predictors of 30-day mortality of patients with normal and low preoperative serum albumin levels following bariatric surgery

| Predictors of 30-day mortality                         | Odds ratio | 95% confidence interval | <i>p</i> -value |
|--|------------|-------------------------|-----------------|
| Hypoalbuminemia  | 1.13       | 0.85–1.49               | 0.4             |
| Older age (per 10 years)                               | 1.60       | 1.46–1.74               | <0.0001         |
| Higher BMI (per 5 kg/m <sup>2</sup> )                  | 1.33       | 1.28–1.38               | <0.0001         |
| Female   | 0.47       | 0.39–0.57               | <0.0001         |
| Race   |            |                         |                 |
| Black vs. White  | 1.73       | 1.41–2.13               | <0.0001         |
| Other vs. White  | 0.84       | 0.58–1.20               | 0.3             |
| Functional status                                      |            |                         |                 |
| Partially dependent vs. independent                    | 1.75       | 1.11–2.76               | 0.02            |
| Dependent vs. independent                              | 1.90       | 0.84–4.31               | 0.1             |
| Diabetes   |            |                         |                 |
| Non-insulin dependent vs. non-diabetic/diet controlled | 0.92       | 0.73–1.15               | 0.5             |
| Insulin dependent vs. non-diabetic/diet controlled     | 1.23       | 0.96–1.57               | 0.1             |
| OSA  | 0.99       | 0.82–1.19               | 0.9             |
| HTN  | 1.18       | 0.95–1.47               | 0.1             |
| DLD  | 1.18       | 0.96–1.45               | 0.1             |
| GERD   | 1.11       | 0.93–1.33               | 0.3             |
| COPD   | 2.32       | 1.69–3.18               | <0.0001         |
| Renal insufficiency                                    | 2.00       | 1.27–3.15               | 0.003           |
| Prior MI   | 1.98       | 1.37–2.86               | <0.0001         |
| RYGB   | 1.64       | 1.38–1.96               | <0.0001         |
| Complication   |            |                         |                 |
| Bleed  | 7.56       | 5.71–10.02              | <0.0001         |
| Leak   | 12.91      | 9.19–18.13              | <0.0001         |

*BMI*, body mass index; *OSA*, obstructive sleep apnea; *HTN*, hypertension; *DLD*, dyslipidemia; *GERD*, gastroesophageal reflux disease; *COPD*, chronic obstructive pulmonary disease; *MI*, myocardial infarction; *RYGB*, Roux-en-Y gastric bypass

Serum albumin is the most abundant protein in human plasma and has a number of functions which are directly implicated in postoperative healing [15, 16, 20]. Albumin has been shown to regulate capillary permeability by maintaining oncotic pressure, serving as an antioxidant by scavenging free radical metabolites, and modulating platelet aggregation to promote hemostasis [10]. Surgical procedures are well known to elicit a substantial inflammatory stress response, resulting in cytokine production and subsequent formation of deleterious free radicals [21]. This oxidative stress may then lead to damage of lipid, protein, and nucleic acid by-products which increase capillary permeability and disrupt endogenous host tissue repair [20, 21]. Intrinsic antioxidant properties of serum albumin are thought to neutralize these harmful metabolites and promote tissue healing. Albumin also has important anticoagulant and antithrombotic functions mediated by its capacity to bind nitric oxide (NO) forming S-nitrosothiols, thereby delaying the rapid inactivation of NO and inhibiting prolonged platelet aggregation [20]. Together, these biological mechanisms may, in part, contribute to the higher rate of serious complications seen in our HA patients.

In addition to mechanisms which directly mediate postoperative outcomes, serum albumin is also an important marker associated with sarcopenic obesity (SO)—a theoretical phenomenon that is currently underreported and a topic of growing clinical interest [18, 22–25]. SO is characterized by adipose tissue infiltration of skeletal muscle leading to reduced functional muscle mass and impaired functional status [26]. Clinically, SO is thought to be an important entity as it has been shown to strongly predict increased surgical morbidity and mortality [23]. While our study was not able to truly characterize SO due to a lack of required diagnostic gait speed or grip strength metrics, the significantly higher proportion of functional impairment observed in the HA patients strongly suggests a correlation with SO. Further work is needed to validate these associations; however, if established as a true marker of SO, albumin may provide a cost-effective screening method to identify at-risk bariatric patients benefiting from preoperative optimization.

Prior literature has demonstrated HA as an accurate preoperative prognostic indicator in a variety of surgical subspecialties including trauma [27], cardiac [28], and

colorectal surgery [17]. This was illustrated in a large-scale retrospective study of 54,215 patients from 44 tertiary care centers that looked at HA and surgical outcomes in noncardiac surgery patients [16]. Multivariate analysis revealed that albumin levels were the strongest predictor of both mortality (OR = 0.44; 95%CI: 0.41–0.48) and morbidity (OR = 0.58; 95%CI: 0.56–0.60) after major surgery and a decrease of 1.0 g/dL in albumin value was associated with more than a twofold increase in the odds of dying and almost a twofold increase in the odds of a complication. HA also appears to be a dose-dependent predictor of adverse outcomes. A broad meta-analysis of 90 cohort studies with 291,433 total patients found that HA was a potent, dose-dependent, and independent predictor of poor outcome in acutely ill patients [29]. Each 1.0-g/dL decline in serum albumin concentration significantly raised the odds of mortality by 137%, morbidity by 89%, prolonged intensive care unit stay by 28%, and total hospital stay by 71%. Together with our study's findings, this body of work suggests that strategies which optimize presurgical HA are of great promise in improving outcomes following bariatric surgery.

Our work has a number of novel implications. We show that, paradoxically, physiological malnutrition as evidence by HA occurs in 7% of all bariatric patients undergoing elective SG and RYGB. HA and functional impairments were found to be the greatest predictors of serious complications highlighting the likely impact of SO on bariatric outcomes and the need to address this phenomenon through aggressive multidisciplinary pre-habilitation. Given the importance of identifying SO in these patients, screening tools such as the strength, assistance with walking, rising from a chair, climbing stairs, and falls (SARC-F) questionnaire [18, 30] should be implemented at the time of entry to bariatric clinics. Positive screens should then undergo muscle strength assessments such as grip strength testing or the chair to stand test to confirm and further risk stratify SO. We advocate that patients with a high likelihood of SO undergo rigorous nutritional counseling to increase protein intake in addition to physiotherapist prescribed resistance training.

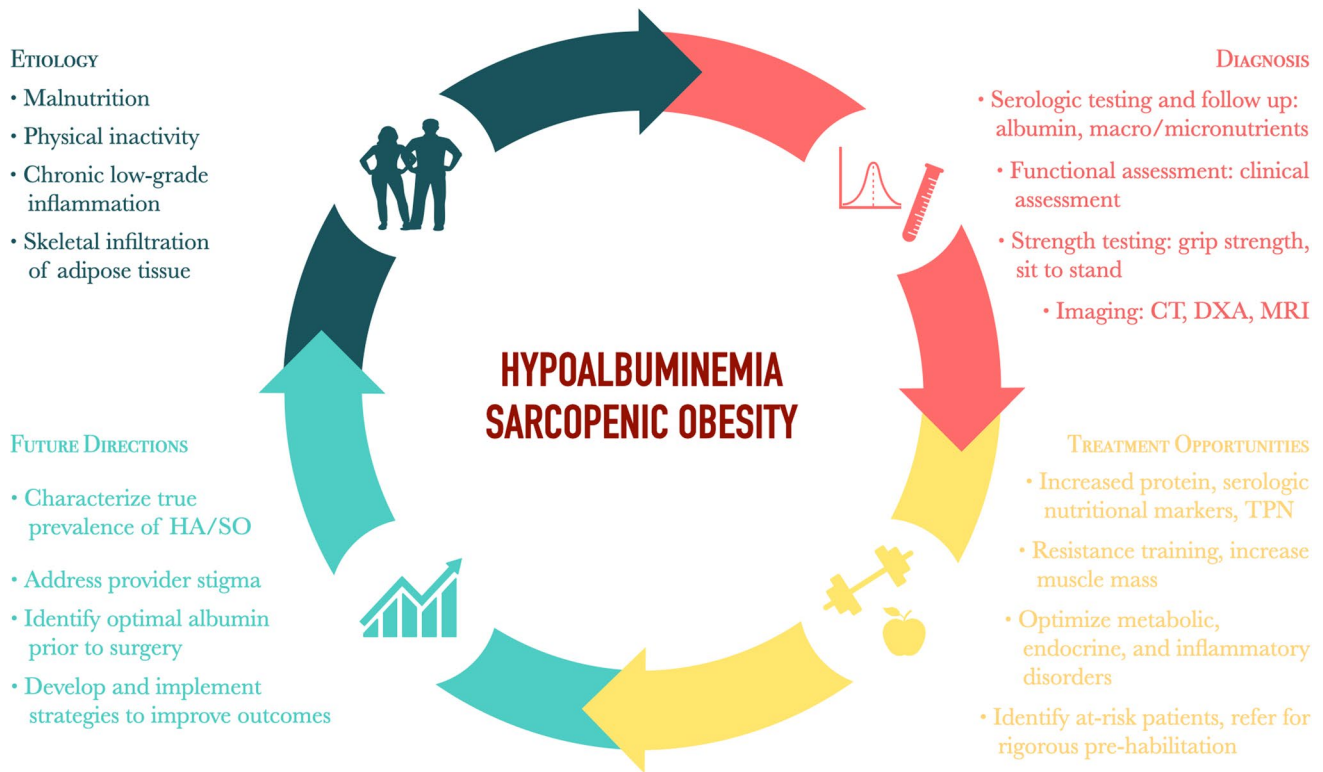
Questions, however, remain as to how best optimize HA prior to bariatric surgery while also achieving a 10% preoperative weight loss to decrease liver size allow for an easier operation. Presurgical total parenteral nutrition (TPN) has been found to be beneficial in malnourished patients receiving abdominal surgery [7], yet TPN is unfortunately also associated with increased risk of steatohepatitis in severe obesity which may increase liver size and technical difficulty. Alternatively, a presurgical enteral

nutrition protocol of greater than 3 weeks (the half-life of serum albumin), with defined energy and protein requirements estimated using 25–30 kcal/kg and 1.5 g/kg ideal body weight, as recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN) [31], may be beneficial. Moreover, pre-habilitation programs that focus on both nutritional optimization and increasing muscle mass and improving functional status may confer additional benefits on postoperative physical function, length of hospital stay, and mortality [32]. While the optimal albumin targets and methods with which to achieve them are not yet clear, it is evident that optimizing HA is a promising avenue in our quest to continue improving the safety of bariatric surgery. We argue that in no surgical discipline is preoperative nutritional optimization more important than for bariatric procedures which ultimately impart the highest risk of subsequent nutritional deficiencies.

Our study has a number of limitations in keeping with the retrospective nature of our study design. Unlike weight variables which are tracked several times by the MBSAQIP, only one albumin value is captured which limits our ability to evaluate the role of changes in albumin on postoperative outcomes. While HA has strong associations with SO, the MBSAQIP does not capture specific strength or functional data, limiting our ability to ascertain the true extent of SO in this population or to accurately evaluate its relationship to HA. Gold standard SO imaging modalities such as computed tomography, magnetic resonance imaging, or dual-energy X-ray absorptiometry could also not be correlated with either HA or SO and warrant further evaluation in the context of patients with severe obesity undergoing bariatric surgery. Similarly, liver function tests are not captured by the MBSAQIP, limiting overall interpretation of the data. Additionally, it is possible that a confounder exists which we were not able to account for that may have influenced the findings of our multivariable regression models.

## Conclusion

HA among elective bariatric surgery patients is prevalent and comprises over 7% of all elective MBSAQIP cases. After adjusting for comorbidities, we identified HA as one of the greatest modifiable factors predictive of serious complications. Adoption of strategies to identify and improve preoperative malnutrition, specifically focused on improving serum albumin levels, may reduce overall serious complications among elective bariatric surgery patients (Fig. 1).



**Fig. 1** Summary of key features underlying hypoalbuminemia (HA) and sarcopenic obesity (SO)

## Declarations

**Ethics Approval and Consent to Participate** As this was a retrospective study, formal consent is not required. All procedures performed that contributed to the data registry were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Conflict of Interest** The authors declare no competing interests.

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