

Impact of Preoperative Hypoalbuminemia on Postoperative Outcomes in Major Gastrointestinal Surgeries: A Retrospective Cohort Study

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Abstract

Background:

Preoperative hypoalbuminemia is a well recognised modifiable risk factor that can be altered to predict poor surgical outcomes. This study aimed to assess whether preoperative serum albumin levels influenced postoperative morbidity and mortality in patients undergoing major gastrointestinal (GI) surgeries.

Methods:

The retrospective cohort study involved the analysis of medical records of patients who underwent elective major GI surgeries within a 12-month period (January 2024- December 2024) in a tertiary care facility. Thirty patients who met the inclusion criteria were identified. Two categories of patients (normal albumin (≥ 3.5 g/dL; n=19) and hypoalbuminemia (less than 3.5 g/dL; n=11)) were formed according to the level of serum albumin before surgery. The groups were compared in terms of postoperative outcomes such as surgical site infection (SSI), anastomotic leak, pneumonia, sepsis, length of stay, ICU hospitalization, re-operation, and 30-day mortality.

Results:

Hypoalbuminemic patients had increased SSI rates (36.4% vs. 10.5%; p=0.152), pneumonia (27.3% vs. 5.3%; p=0.126), wound dehiscence (27.3% vs. 5.3%; p=0.126) and ICU admission (36.4% vs. 10.5%; p=0.152). Overall morbidity was higher in the hypoalbuminemia group (63.6% vs. 26.3%; p=0.062). The length of hospital stay was significantly longer in the hypoalbuminemia group (13.8 ± 6.2 vs. 8.2 ± 3.4 days; p=0.003). Univariate analysis showed that hypoalbuminemia was associated with an almost fivefold rise in total morbidity (crude OR 4.90; 95% CI 1.01-23.82). Nevertheless, most comparisons failed to obtain conventional statistical significance as a result of the small sample size.

Conclusion:

The retrospective study demonstrates that preoperative hypoalbuminemia is associated with the development of additional postoperative complications and increased hospitalization in major GI surgery. The findings endorse the importance of preoperative serum albumin assessment as a risk factor during surgery and insist on bigger multicenter studies to confirm these findings and examine the significance of preoperative nutritional enhancement.

Keywords: Hypoalbuminemia, serum albumin, gastrointestinal surgery, postoperative complications, surgical outcomes, nutritional status, retrospective study

How to cite this article: Prabhu V, Balaji A, Ajmal IT, Annamalai A. Impact of Preoperative Hypoalbuminemia on Postoperative Outcomes in Major Gastrointestinal Surgeries: A Retrospective Cohort Study. Int J Drug Deliv Technol. 2026;16(18s): 741-749. DOI: 10.25258/ijddt.16.18s.80

1. Introduction

Major gastrointestinal (GI) surgeries result in postoperative complications in patients, which are a major clinical issue, causing significant patient morbidity, length of stay, escalated medical expenses, and mortality [1]. Although modern surgery techniques and improved perioperative care and recovery plans have

resulted in a reduction in the incidence of complications during major GI surgery procedures, the incidence of postoperative complications remains 20-50% irrespective of the type and complexity of operation [2,3]. Identifying modifiable risk factors that predispose patients to adverse outcomes is therefore of paramount importance in contemporary surgical practice.

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Nutritional status is a well-established determinant of surgical outcomes [4]. Serum albumin is the most commonly evaluated biochemical indicator of nutritional assessment and is the most studied one of the many existing markers of nutritional assessment [5]. Albumin is a protein produced by the liver with a half-life of 20 days, which represents a predictable surrogate of chronic nutritional condition as well as an indicator of systemic inflammation and hepatic synthetic function [6]. Hypoalbuminemia, which is commonly described as serum albumin below 3.5 g/dL, is an indicator of protein-energy malnutrition and it is often found in patients who have GI malignancies, chronic inflammatory diseases, hepatobiliary diseases and other systemic illnesses. [7,8]. Multiple large-scale trials, such as those by the National Surgical Quality Improvement Program (NSQIP) database have consistently shown preoperative hypoalbuminemia to be the most predictive factor of postoperative morbidity and mortality regardless of the type of surgery conducted in the patient [9,10]. In their seminal study of over 54,000 surgical patients, Gibbs et al. have found that preoperative hypoalbuminemia significantly predicts postoperative morbidity and mortality irrespective of the type of surgery the patient is under [11]. On the same lines, Hennessey and his coauthors showed that even mild hypoalbuminemia is a significant risk factor that leads to the development of major complications during colorectal surgery [12].

The effects of hypoalbuminemia are especially pertinent to gastrointestinal tract in the specific context of GI surgery which often predisposes patients to malnutrition through a decrease in oral intake, malabsorption, underlying disease, or malignant progression present during surgery [13,14]. The gastrointestinal tract is a significant site of albumin metabolism, and further impairs protein homeostasis in the preoperative period. Though this pathophysiological explanation and accumulating body of evidence demonstrates this, regular preoperative albumin testing has continued to be variably implemented in much of the surgical units and targeted nutritional prehabilitation is underutilized [16,17].

The current research was aimed at retrospectively assessing the effect of the preoperative levels of serum albumin on the postoperative outcomes in patients undergoing major GI surgeries in a tertiary care center. The main aim was to find out whether preoperative hypoalbuminemia was linked with a high risk of

postoperative complications, longer hospital stays, and death.

2. Materials and Methods

2.1 Study Design and Setting

This was a retrospective cohort study that was carried out in the Department of General Surgery, in Chettinad Hospital and Research Institute (CHRI), Kelambakkam. Patients who underwent elective major GI surgeries were included in the review of medical records of 12 months, i.e., between January 2024 and December 2024. This was carried out under the protocol of the study that was approved by the Institutional Ethics Committee (IEC) and in line with the requirements of Declaration of Helsinki and Good Clinical Practice guidelines.[18]. Since the study was retrospective in nature, the ethics committee waived the individual informed consent requirement but ensured patient confidentiality and de-identified all data before analyzing them.

2.2 Study Population

Medical records of each patient of age 18 years and older that had undergone elective major GI surgeries during the study period were screened. The number of patients identified by meeting the inclusion criteria was 30. Major GI surgeries were considered surgeries that involved resection and/or reconstruction of esophagus, stomach, small intestine, colon, rectum, liver, pancreas or biliary system where the surgeon reported an operative time greater than 2 hours [19]. Exclusion criteria were emergency cases, chronic liver disease (Child-Pugh B or C), nephrotic syndrome, pregnancy, patients who were fed parenterally within 2 weeks before surgery, and incomplete laboratory or follow-up data.

2.3 Data Collection and Definitions

The clinical and perioperative data collection involved gathering of the hospital case files, operative reports, laboratory data systems and discharge records. Serum albumin levels measured preoperatively within 48 hours of surgery were incorporated into the examination; the levels had been measured using bromocresol green method. The samples were then categorized in terms of albumin concentration into two groups, namely, normal albumin group (3.5 g/dL or above) and hypoalbuminemia group (3.5 g/dL or less), based on cut-offs reported in the ACS NSQIP standards and earlier studies on surgical outcomes. Age, sex and body mass index were collected together with comorbid conditions such as diabetes mellitus, hypertension, and chronic obstructive pulmonary disease. There were also operative variables

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(type of procedure, estimated blood loss, the estimated duration of the procedure) and diagnostic categorization (benign versus malignant pathology).

2.4 Outcome Measures

The main primary outcome measures were 30-day postoperative morbidity and 30-day mortality. Among its secondary outcomes were individual postoperative complications such as surgical site infection (SSI) according to the Centers for Disease Control and Prevention criteria,[21] anastomotic leak as identified by clinical features and radiographic or operative evidence as recorded in the records, postoperative pneumonia according to clinical and radiographic criteria, sepsis according to the Sepsis-3 consensus,[22] wound dehiscence, required reoperation, unplanned ICU stay, and total length of hospital stay. The severity of postoperative complications was graded according to the system of Clavien-Dindo classification system[23].

2.5 Statistical Analysis

The SPSS version 26.0 (IBM Corp., Armonk, NY) was used to carry out the statistical analysis. Continuous variables were presented as mean \pm standard deviation and the independent samples t-test or Mann-Whitney U test were used when comparing the variables. The variables of the categories were displayed in frequencies and percentages and were compared with the help of Fisher exact test due to the small sample size. Categorical outcomes were analyzed to give crude odds ratios (OR) with 95% confidence intervals (CI). Multivariate logistic regression model was used to determine the possible independent predictors of postoperative morbidity, which adjusted for age, ASA grade, and diagnosis but the small sample size limits the amount of covariates that can be statistically included. The p-value was set to be lower than 0.05. Clinically meaningful observations with trends that were approaching significance ($p < 0.10$) were also reported to be investigated further[24].

3. Results

3.1 Patient Demographics and Baseline Characteristics

Nineteen out of 30 patients exhibited normal preoperative serum albumin levels (≥ 3.5 g/dL) (19/30) and 11 (36.7%) had hypoalbuminemia (< 3.5 g/dL). Serum albumin normal mean was 4.0 ± 0.4 g/dL and in the hypoalbuminemia, group was 2.9 ± 0.4 g/dL. Table 1 shows the demographic and baseline clinical characteristics of the two groups.

Table 1: Baseline Demographics and Clinical Characteristics (n=30)

Variable	Normal Albumin (n=19)	Hypoalbuminemia (n=11)	p-value	Test
Age (years, mean \pm SD)	51.8 \pm 14.2	59.4 \pm 13.6	0.146	t-test
Male, n (%)	12 (63.2%)	7 (63.6%)	1.000	Fisher's
BMI (kg/m ² , mean \pm SD)	24.3 \pm 3.4	21.6 \pm 4.2	0.062	t-test
Diabetes mellitus, n (%)	4 (21.1%)	3 (27.3%)	1.000	Fisher's
Hypertension, n (%)	5 (26.3%)	4 (36.4%)	0.694	Fisher's
ASA Grade \geq III, n (%)	4 (21.1%)	5 (45.5%)	0.222	Fisher's
Malignancy, n (%)	10 (52.6%)	8 (72.7%)	0.449	Fisher's

SD = Standard Deviation; BMI = Body Mass Index; ASA = American Society of Anesthesiologists. Fisher's exact test used for all categorical comparisons.

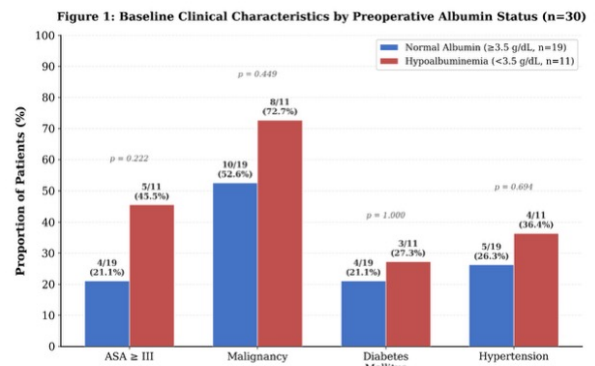


Figure 1: Bar chart comparing baseline characteristics (ASA \geq III, Malignancy, Diabetes, Hypertension) between Normal Albumin and Hypoalbuminemia groups

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The hypoalbuminemia group was more likely to be older, (59.4 ±13.6 vs. 51.81±4.2 years; p = 0.146), have a lower BMI (21.6±4.2 vs. 24.3±3.4 kg/m²; p = 0.062), more likely to have a higher ASA grade (ASA ≥ III : 45.5 vs. 21.1; p = 0.222). Nonetheless, all these differences were not statistically significant. Sex distribution was not different between the groups.

3.2 Surgical Procedures

Colorectal resections (10 patients, 33.3%), gastrectomy (6 patients, 20.0%), pancreaticoduodenectomy (4 patients, 13.3%), hepatic resections (3 patients, 10.0%), esophagectomy (2 patients, 6.7%), small bowel resections (3 patients, 10.0%), and biliary reconstructive procedures (2 patients, 6.7%) were the most frequently used procedures. The allocation of surgery procedures was similar in the two groups (p = 0.518, Fisher exact test). The average operating time among the hypoalbuminemia group was 208.4 and that of the normal albumin was 186.5 which does not differ significantly (p = 0.326).

3.3 Postoperative Outcomes

Table 2 shows postoperative complications and outcome based on preoperative albumin status. The overall consistency in higher rates in patients with hypoalbuminemia was shown in all of the adverse outcomes measured although most one-on-one comparisons were not statistically significant because of the small sample size.

Table 2: Postoperative Outcomes by Preoperative Albumin Status (n=30)

Outcome	Normal Albumin (n=19)	Hypoalbuminemia (n=11)	P-value	OR (95% CI)
Surgical site infection, n (%)	2 (10.5%)	4 (36.4%)	0.152	4.86 (0.72 – 32.76)
Anastomotic leak, n (%)	1 (5.3%)	2 (18.2%)	0.537	4.00 (0.32 – 50.20)

Pneumonia, n (%)	1 (5.3%)	3 (27.3%)	0.126	6.75 (0.59 – 76.82)
Sepsis, n (%)	1 (5.3%)	2 (18.2%)	0.537	4.00 (0.32 – 50.20)
Wound dehiscence, n (%)	1 (5.3%)	3 (27.3%)	0.126	6.75 (0.59 – 76.82)
30-day mortality, n (%)	0 (0%)	1 (9.1%)	0.367	—
ICU admission, n (%)	2 (10.5%)	4 (36.4%)	0.152	4.86 (0.72 – 32.76)
Hospital stay (days, mean±SD)	8.2 ± 3.4	13.8 ± 6.2	0.003	—
Reoperation, n (%)	1 (5.3%)	2 (18.2%)	0.537	4.00 (0.32 – 50.20)
Overall morbidity, n (%)	5 (26.3%)	7 (63.6%)	0.062	4.90 (1.01 – 23.82)

OR = Odds Ratio; CI = Confidence Interval; SSI = Surgical Site Infection; ICU = Intensive Care Unit. Fisher's exact test used for all categorical comparisons. OR not calculable for 30-day mortality due to zero events in one group.

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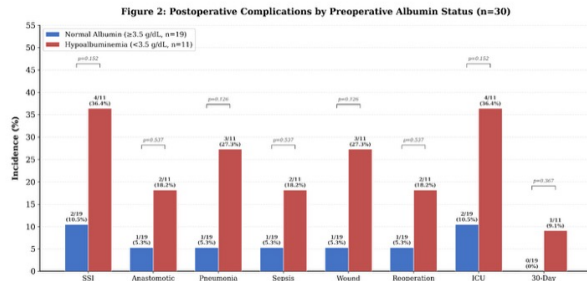


Figure 2: Grouped bar chart comparing rates of individual postoperative complications between the two groups

The total postoperative morbidity rate was 63.6% (7/11) in the hypoalbuminemia group versus 26.3% (5/19) in the normal albumin group ($p = 0.062$) which is close to the statistical significance level. The higher-grade complications (Clavien-Dindo Grade III or more) were detected in 3 of 11 (27.3%) hypoalbuminemic patients compared to 1 of 19 (5.3) in the normal albumin group ($p = 0.126$). The only result that reached the conventional statistical significance was length of stay, which was significantly longer in the hypoalbuminemia group (13.8 ± 6.2 vs. 8.2 ± 3.4 days; $p = 0.003$). The mortality rate (9.1%) in the hypoalbuminemia group was as compared to zero in the normal albumin group.

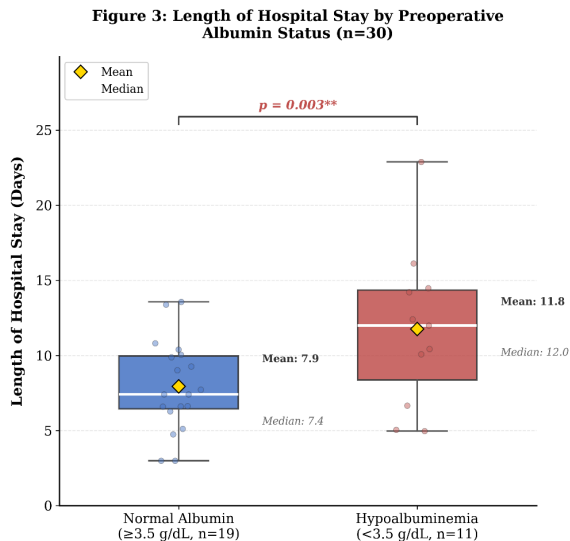


Figure 3: Box-and-whisker plot comparing length of hospital stay (days) between Normal Albumin and Hypoalbuminemia groups

3.4 Logistic Regression Analysis

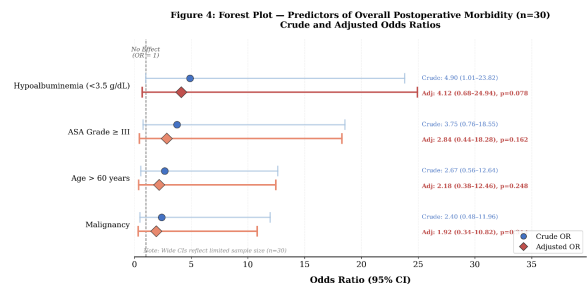
Preoperative hypoalbuminemia had a significant association with an almost five-fold increased overall

postoperative morbidity (crude OR 4.90; 95% CI 1.01-23.82; $p = 0.049$). The association did not, however, retain statistical significance when age, ASA grade and malignancy were added to the model on the multivariate logistic regression (adjusted OR 4.12; 95% CI 0.68-24.94, $p = 0.078$), probably due to the low statistical power of the small sample size (Table 3). The single event prevented the reliability of the multivariate analysis of 30-day mortality.

Table 3: Univariate and Multivariate Logistic Regression Analysis for Predictors of Overall Postoperative Morbidity (n=30)

Variable	Crude OR	95% CI	Adjusted OR	P-value	Outcome
Hypoalbuminemia (<3.5 g/dL)	4.90	1.01 – 23.82	4.12	0.078	Overall morbidity
ASA Grade \geq III	3.75	0.76 – 18.55	2.84	0.162	Overall morbidity
Age > 60 years	2.67	0.56 – 12.64	2.18	0.248	Overall morbidity
Malignancy	2.40	0.48 – 11.96	1.92	0.314	Overall morbidity

OR = Odds Ratio; CI = Confidence Interval. Multivariate model adjusted for age (>60 years), ASA grade (\geq III), and diagnosis (malignancy). Number of covariates limited due to small sample size (events per variable consideration).



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Figure 4: Forest plot displaying crude and adjusted odds ratios with 95% confidence intervals for predictors of overall postoperative morbidity

4. Discussion

The current retrospective analysis assessed the relationship between preoperative hypoalbuminemia and outcomes after major surgery in 30 patients who had undergone major GI surgeries. Although the sample size is small, the results suggest a trend towards increased postoperative complications in hypoalbuminemic patients, with the general morbidity rates of 63.6% and 26.3% respectively, in the control group of adult patients with normal albumin content. The length of stay in the hospital was the only variable that obtained conventional statistical significance and was significantly extended in the hypoalbuminemia group (13.8 vs. 8.2 days; $p = 0.003$). Such findings are in line with the current evidence base and provide the clinical significance of preoperative albumin measurements. [25,26].

The prevalence of preoperative hypoalbuminemia was 36.7% in the study cohort which is comparable with other larger studies that have been done among major GI surgical populations. According to Bohl et al, prevalence rates were 36.4% in patients undergoing colorectal surgery,[27] and Lohsiriwat et al. had a prevalence of 40.2 in patients undergoing abdominal surgery to treat malignancy.[28]. The representativeness of our population of study is supported by this similarity in prevalence.

The correlation between hypoalbuminemia and surgical site infections in our study is in line with the pathophysiological explanation (36.4% vs. 10.5%; crude OR 4.86). Albumin is important to the immune system, wound healing, and oncotic pressure maintenance in the body [29]. Low albumin levels impair neutrophil function, decreases the activation of complement, and represses the inflammatory response to promote wound healing. This difference was not statistically significant in our cohort ($p = 0.152$), but the effect size (almost five-fold) is of clinical significance and is consistent with larger studies. A study of more than 1,000 patients by Hu WH, Cajas-Monson LC, Eisenstein S, et al. noted that the risk of SSI increased three times in hypoalbuminemic patients undergoing gastrointestinal surgery [31].

An anastomotic leak was found in 2 of 11 (18.2%) hypoalbuminemic patients and 1 of 19 (5.3%) in the normal group. The anastomotic site requires adequate perfusion of oxygen through tissues as well as protein

synthesis in tissue at the site of anastomosis [32]. The effects of hypoalbuminemia are a decrease in the colloid oncotic pressure resulting in tissue edema, impairment of microvascular perfusion, and slow collagen production [33]. In an expanded group of 1,200 patients, preoperative albumin was found to be the greatest modifiable item of anastomotic failure by Telem and colleagues [34].

The most statistically significant result in this research study was the considerably long hospital stay of hypoalbuminemia group (13.8 ± 6.2 vs. 8.2 ± 3.4 days; $p = 0.003$) probably due to the fact that length of stay is a continuous variable that provides more statistical power compared to dichotomous outcome of complications. This observation has significant implications on the use of healthcare resources. Oral nutritional supplements and immunonutrition during prehabilitation have proven to reduce the postoperative complications and hospital stay in a number of randomized controlled trials [35,36].

At the univariate level, hypoalbuminemia was linked to a near significant rise in total morbidity (crude OR 4.90; 95% CI 1.01-23.82; $p = 0.049$). The large confidence interval demonstrates the inaccuracy of the small sample. In multivariate analysis, the connection was not strong (adjusted OR 4.12; $p = 0.078$) and this fact is natural because the number of events per variable was less than the recommended value of 10 which does not allow the multivariate modeling to be very reliable. This is one of the weaknesses of the present study and explains why confirmatory research should be powered.

The development of the NSQIP by Gibbs et al. created preoperative albumin as the strongest single predictor of perioperative mortality in operated patients of a cohort of more than 54,000 cases [11]. A meta-analysis of more than 120,000 patients confirmed that every 1 g/dL fall in serum albumin corresponded with a 137 per cent rise in mortality odds ratio of the individual [38]. Although our analysis of one mortality event cannot assert its claim on mortality risk, the fact that the only death in the hypoalbuminemia group has occurred, is in line with this trend.

It is important to recognize that albumin is both a nutritional marker and an acute-phase reactant. Low albumin may therefore reflect not only poor nutritional reserve but also an underlying systemic inflammatory state, which itself is independently associated with adverse surgical outcomes [29]. The integration of

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albumin measurement with other nutritional and inflammatory markers, such as prealbumin, C-reactive protein, or the Prognostic Nutritional Index (PNI), may provide a more comprehensive risk assessment framework and should be considered in future studies [39].

There are a number of weaknesses of this study which should be noted. First, the retrospective design presents such inherent limitations as potential selection bias, information bias and the failure to determine causality. Data was based on the reliability and completeness of medical documentation and hence some variables which might affect the results like the management of perioperative fluids, compliance to enhanced recovery guidelines and the specific nutritional intake could not be reliably measured. Second, the sample size is 30 patients, which is not sufficient to identify significant differences in the rates of individual complication and limits the validity of multivariate analysis. Third, the single center design might not allow extrapolating the findings to other groups and practice environments. Fourth, the research failed to evaluate the effects of postoperative albumin trend or nutritional response intervention. Fifth, unmeasured confounders such as surgical technique and experience of surgeon might have affected results. Irrespective of these shortcomings, similar patterns in the trends of several outcomes offer supportive data to support the correlation between hypoalbuminemia and poor surgery outcome.

5. Conclusion

This retrospective study indicates that preoperative hypoalbuminemia is associated with postoperative morbidity and it significantly increases the length of hospital stay following major gastrointestinal surgeries in patients. Even though the individual complication rates did not reach the conventional statistical significance level since the sample size was very small, the overall pattern of worse results in hypoalbuminemic patients and almost five times higher morbidity rates overall attest to the clinical significance of preoperative albumin testing. Measuring the serum albumin should be listed among the elements of surgical risk assessment since it is done routinely before the operation. Large and multicentric, prospective studies should be conducted in the future to verify these results and also to determine validity of preoperative nutritional optimization measures in minimization of postoperative complications in major GI surgery.

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Society Recommendations: 2018. World J Surg.
2019;43(3):659-695.