Perioperative serum albumin a predictor of adverse outcomes in major abdominal surgery: Prospective Cohort hospital based study.

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Abstract

Background

Albumin is an important protein that transports hormones, fatty acids, and exogenous drugs; it also maintains plasma oncotic pressure. Albumin is considered a negative active phase protein because it decreases during injuries and sepsis. In spite of other factors predicting surgical outcomes, the effect of pre and postoperative serum albumin to surgical complications could be assessed by calculating percentage decrease in albumin (Delta albumin). This study aimed to explore perioperative serum albumin as a predictor of adverse outcomes in major abdominal surgeries.

Methodology:

All adults' eligible participants from Kilimanjaro Christian Medical Centre Surgical Department were enrolled conveniently. Data were collected using study questionnaire. Full Blood Count (FBP), serum albumin levels preoperatively and on postoperative day 1 was measured abiding to Laboratory Standard Operating Procedures (SOP). Data was entered and analyzed using STATA version 14. Association and extent of decrease in albumin levels as a predictor of surgical site infection (SSI), delayed wound healing and death within 30days of surgery was determined using ordinal logistic regression model. In determining the diagnostic accuracy, a Non-parametric Receiver Operating Curve (ROC) model was used. We adjusted for ASA classification which had negative confounding effect on the predictive power of percent drop in albumin to adverse outcomes.

Results

61 participants were studied; the mean age was 51.6 (SD16.3), majorities were males 40 (65.6%) and post-operative adverse outcome happened to 28 (45.9%) participants. In preoperative serum albumin values, 40 (67.8%) had lower than 3.4 g/l while 51 (91%) had postoperative albumin values lower than 3.4 g/l. Only 15 (27.3%) had high delta albumin with the median percentage value of 14.77%. Delta albumin was an independent significant factor associated with adverse outcome (OR: 6.68; 95% CI: 1.59, 28.09); with a good predictive power and area under ROC curve (AUC) of 0.72 (95% CI 0.55 0.89). The best cutoff value was 11.61% with the sensitivity of 76.92% and specificity of 51.72%.

Conclusion

Early perioperative decrease in serum albumin level may be a good, simple and cost effective tool to predict adverse outcomes in major abdominal surgeries.

Introduction

Abdominal surgery is a common procedure in surgical field. It is performed as either elective or on emergency basis. Underlying diseases may pose stress to the body tissues and surgical trauma adds to more stress that triggers body response to rectify the situation(1).

Albumin is the major protein of human plasma. It makes approximately 60% of the total plasma protein and its normal serum concentration is 3.5–5.0 g/dl. Plasma albumin has mainly three functions; osmotic, transportation and nutritional function and it accounts for more than 75–80% of total plasma osmotic pressure (25 mm Hg). Decrease in serum albumin level causes a fall in oncotic pressure which in turn leads to interstitial oedema. Studies also showed that hypoalbuminemia contributes in process of wound healing, fracture union and severity of disease(2).

Other multiple factors have been studied in relation to albumin levels. Decreased level of albumin was significant to male and middle aged patients compared to younger patients. The longer the time of surgery and the type of surgery such as colonic resection and stoma creations were associated with progressive decrease in serum albumin. Also patients with ASA classification of > 3 had postoperative lower albumin compared to more stable patients (3).

Hypoalbuminemia is a risk factor for mortality and postoperative complications such as SSI and reoperations together with longer hospital stay (8, 9). Additionally one study reported that early decrease of serum albumin level of ≥ 10 g/dl in postoperative day one has three folds increased risk in postoperative adverse complications in major abdominal surgeries; while in another study a decrease of albumin of > 15% from the mean value of 3.94 g/dl was associated with longer hospital stay, surgical site infections and higher risk of reoperation. In oesophagestomy study due to malignancy, patient with postoperative low albumin had higher chances of anastomotic leak and mortality within 7days of surgery (4).

Different cutoff points of percentage decrease of perioperative albumin (delta albumin) has been proposed, some with 15% and others with 24.77%; however generally the higher percentage the higher odds of postoperative adverse complications with good predictive value(1, 3, 5).

Serum albumin is simple and easily interpreted biomarker with valuable impact in perioperative period; however in our setting it is not a routine investigation for preoperative assessment. Understanding the correlation and the strength of association of decrease serum albumin and surgical adverse complications will also improve management protocol at the department of surgery and help to reduce burden of healthcare expenditure by improvement of patient care and proper management of surgical resources.

Methods

Study Design And Setting

This was a prospective cohort study conducted from October 2018 to March 2019 at Department of General Surgery at KCMC which is at Moshi in Kilimanjaro region. KCMC is a Northern Zone Consultant Hospital in Tanzania. The hospital receives referred patients from northern and central regions namely Arusha, Manyara, Tanga, Dodoma, Singida and districts from Kilimanjaro region. The population served is more than 15 million people

Study Population

The study population was all patients aged 18 years and above, admitted for either elective or emergency reasons and indicated for major abdominal surgery; and had consented for the study.

Sample Size And Sampling Procedure

All patients eligible were included in final sample. A total of 144 patients were expected to be operated; an average of 6 patients per week in 6 months, however basing on eligibility criteria, a total of 61patients were included in the final sample. We conveniently enroll participants after completing the process of informed consent.

Definitions Of Outcome Measures

The outcomes of interest were Surgical Site Infection (SSIs), delayed wound healing and death within 30 days post operation. Surgical Site Infection (SSIs) was measured as wound infection within 3days post-surgery, delayed wound healing was counted as prolongation of healing for more than 7 days due to interruption of normal process of wound healing and death within 30 days post operation. When a participant encountered one of the named outcomes of interest, it was measured as an adverse outcome.

Clinical Characteristics

Laboratory parameters were serum albumin level on preoperative day and postoperative day 1; and full blood count (FBC).

Data collection methods, tools and study procedures

We use questionnaire to collect patient's demographics information, including age, sex, level of education. Laboratory parameters were processed abiding Standard Operating Procedures. Blood sample minimal of 2mls was collected from participants. Samples were stored at the temperature range 20–25˚C and serum was separated immediately from the clot and analysis of specimen was done promptly. COBAS Integra 400 Plus was used for specimen analysis with an interpretation of; expected normal adult serum albumin was 3.4–4.8 g/dl. Preoperative serum albumin was collected then followed by

postoperative serum albumin for day 1. The percentage change of albumin values (Delta Albumin) was calculated using formula ({POD-POD1}/POD × 100). The reference percentage change observed was approximately 14.77% as adopted from study done in China above which was associated with adverse outcome. Intraoperative data from patient case notes was followed up. Participants were followed up after 24 hours to 30 days postoperative to evaluate for adverse surgical outcome such as death, SSI, delayed wound healing and length of hospital stay; this was done at general surgery wards before discharge. After discharge, on day 7, 14, 21 and day 30 at Surgical Outpatient Department (SOPD) appointment was made through phone calls. Variables for the study were obtained from patient data and case note as in data sheet.

Data management and analysis plan

Data were entered, cleaned and analyzed by using STATA version 14. Descriptive statistics for patient's characteristics was summarized using frequencies and proportions for categorical variables while measure of central tendency and their respective measure of dispersion were used to summarize continuous variables depending on their distribution. Logistic regression was used to check association between different levels of decrease in serum albumin and adverse surgical outcomes. Significance was considered at 95% confidence interval and p-vale < 0.05. In determining the diagnostic accuracy, a Non-parametric Receiver operating curve (ROC) model was used. We adjusted for ASA classification which had negative confounding effect on the predictive power of percent drop in albumin to adverse outcomes

Results

Socio-demographic And Clinical Characteristics

Among all (61) studied participants, the mean age was 51.6 ± 16.3 with the majority 34 (55.7%) being aged 50 years and above. Males were 40 (65.6%) and majority 42 (68.9%) had attained primary education. Forty (65.6%) participants had emergency surgical indication and 28 (45.9%) had post-operative adverse outcome (Table 1.).

As summarized in Table 2 below, participants were tested for preoperative, postoperative serum albumin levels. The percentage change of their albumin value was calculated using formula ({POD-POD1}/POD × 100). Among 59 participants with preoperative serum albumin values, 40 (67.8%) had lower than 3.4 g/l while out of 56 participants 51 (91%) had postoperative albumin values lower than 3.4 g/l. Out of 55 participants 28 (50.9%) had high change in percentage difference between pre and postoperative (Delta albumin) with the median percentage value of 14.77% (…). About 24 participants had normal hematocrit amount and only one participant had low white blood cell count.

Distribution of adverse outcomes associated with low and high Delta albumin Participants

Participants with high percentage change in perioperative albumin were in higher chance of delayed wound healing, death with 30 days and significant chance of developing surgical site infection, as

illustrated in Fig. 1.

Factors Associated With Post-operative Adverse Outcomes

Among 61 studied participants, the prevalence of post-operative adverse outcome was 45.9%. Also 61% of those with postoperative adverse outcome had high Delta albumin. When adjusted for other factors participants' aged 25–49 years had almost 9.6 times higher odds of adverse outcome compared to those aged 18–24 years (OR: 9.62; 95% CI: 0.52, 177.36) while being female was 67% protective in getting adverse outcome compared to their male counterparts (OR: 0.33; 95% CI: 0.05, 1.37). Those participants with more than two hours of operative time had 73% higher chances of getting surgical adverse outcome compared to those with less operative time. (OR: 1.73; 95% CI: 0.35 8.45); however participants with higher percentage change in pre and post-operative albumin level (delta albumin) had significant chance of developing adverse compared to those with low delta albumin (OR: 6.68; 95% CI: 1.59, 28.09) with the *p*-value 0.01(Table 3).

Predictive Accuracy Of Delta Albumin To Adverse Surgical Outcome

The area under receiver operating characteristic curve (AUC) of 0.72 (95% CI 0.55, 0.89) was obtained, which signifies a good predictive power of delta albumin to adverse surgical outcome. The best cutoff value was 11.61% with the sensitivity of 76.92% and specificity of 51.72% (Fig. 2).

Table 1
Socio-demographic and clinical characteristics of participants (N = 61)

Characteristics	N	%
Age (years)		
18–24	5	8.2
25–49	22	36.1
50+	34	55.7
Mean ± SD (51.6 ± 16.3)		
Sex		
Male	40	65.6
Female	21	34.4
Education level		
Non formal	4	6.5
Primary level	42	68.9
Secondary and above	15	24.6
Surgical indication		
Emergency	40	65.6
Elective	21	34.4
American Society of Anesthesia classification (n = 52)		
1	21	40.4
2	31	59.6
Length of surgery (minutes) (n = 61)		
0–120	15	24.6
121 & above	46	75.4
Postoperative adverse outcome		
No	33	54.1
Yes	28	45.9

Table 2
Laboratory tests of the participants (N = 61) Clinical characteristics of study participants

Characteristics	N	%
Pre- operative albumin level (g/L) (n = 59)		
< 3.4	40	67.8
3.4–5.0	19	32.2
Mean ± SD (2.9 ± 9.8)		
Post- operative albumin level (g/L) (n = 56)		
< 3.4	51	91.1
3.4–5.0	5	8.9
Mean ± SD (2.5 ± 7.1)		
Delta albumin (%) (n = 55)		
<14.77	27	49.1
14.77 and above	28	50.9
Hematocrit count (n = 60)		
Low	22	36.7
Normal	24	40.0
High	14	23.3
WBC count (n = 60)		
Below normal range	1	1.6
Normal & above	60	98.4

Table 3
Factors associated with postoperative adverse outcome

Factors	Post-OP Adverse Outcome %	COR	(95% CI)	*P*-value	AOR	(95% CI)	*P*-value
Age (years)							
18–24	20.0	1			1		
25–49	59.1	5.77	(0.55, 60.60)	0.144	9.62	(0.52, 177.36)	0.128
50+	41.2	2.80	(0.28, 27.79)	0.379	5.95	(0.34, 104.06)	0.222
Sex							
Male	55.0	1			1		
Female	28.6	0.33	(0.11, 1.01)	0.053	0.26	(0.05, 1.37)	0.112
Delta albumin (%)							
<14.77	33.3	1			1		
14.77 and above	60.7	3.09	(1.03, 9.31)	0.45	6.68	(1.59, 28.09)	0.010
Surgical indication							
Emergency	50.0	1			1		
Elective	38.1	0.62	(0.21, 1.81)	0.377	1.28	(0.27, 6.11)	0.759
ASA							
1	47.6	1			1		
2	38.7	0.69	(0.23, 2.13)	0.524	0.44	(0.10, 2.12)	0.289
Length of surgery (min)							
0–120	38.9	1			1		
120 and above	48.8	1.50	(0.49, 4.60)	0.478	1.73	(0.35 8.45)	0.500

*Note: *COR - Crude odds ratio, AOR – Adjusted odds ratio*

Discussion

In this study majority of participants underwent major abdominal surgery, had lower preoperative and postoperative serum albumin level than the standard lower limit. The mean postoperative albumin was even lower than mean preoperative value. This observation explains the theory of decrease in albumin level due to inflammation and surgical trauma (6); similarly a reduction in albumin levels after surgical trauma is related to generalized inflammation, called systemic inflammatory response syndrome, which is characterized by increased capillary leakage of albumin. Also, in the study of early decrease in postoperative albumin as predictor of complications, there was significant decrease in postoperative albumin levels however the final analysis did not suggest its predictive role.

In contrast to this study were preoperative serum albumin level was not an independent factor for adverse outcome; in other study preoperative low albumin was an independent and significant risk factor for adverse surgical outcome (6). This may be associated with the involvement of only colorectal cancer patients in the study. These patients were at higher risk of malnutrition due to cancer-induced metabolism, lower dietary intake and effect of tumor necrosis factor-alpha on alteration of liver protein production.

Percentage decrease of serum albumin (delta albumin) after surgery was higher in participant with even lower postoperative albumin levels. In this study delta albumin was associated with adverse postoperative surgical site infection, delayed wound healing and death within 30 days. These findings correlate with a study done in Australia to evaluate the value of delta albumin to surgical complications in patients who underwent bowel resection due to Crohn's disease. Higher delta albumin levels were significantly associated with postoperative complications namely intra-abdominal abscess, anastomotic leak, reoperation and death. Neither preoperative nor postoperative serum albumin was an independent risk factor for surgical complications (7). Despite difference in ethnicity between the Australian participants and our participants; there were similar methods in calculating the percentage difference of albumin levels and correlating them with postoperative outcomes.

The delta albumin (ΔAlb) was an independent risk factor for severe complications in CRC patients after curative laparoscopic surgery(8). The study done in Thailand also revealed similar findings that hypoalbuminemia is a potential predictor of delayed recovery of bowel function postoperatively and significantly associated with postoperative complications(9). In both cohorts, there were similar risk of hypoalbuminemia due to malignancy hence depicted the similar outcome pattern.

In this cohort postoperative adverse outcome were evident to approximately 46%, these include surgical site infection, delayed wound healing and death with 30 days post operatively. However other factors were associated to surgical outcome; longer operation time of more than two hours was 73% suggestive of poor outcome than the shorter surgeries. This may be due to longer surgical trauma, longer inflammatory phase post-surgery and higher risk of delay recovery time.

Also patients who underwent elective operations had protective effect of 40% compared to emergency cases. Elective patients were clinically more stable with fair nutritional status. This observation may be attributed to less morbid condition of elective patients. In rectal surgery hypoalbuminemia combined with

higher ASA classification was significant associated with wound infection, remote infections such as pneumonia, and anastomotic leakage, other complication included reoperation and death(10). This may be attributed other comorbid situation like hypertensive heart disease and diabetic mellitus together with operative stress.

In the view of how accurate the decrease in albumin level would predict the adverse outcome; delta albumin showed association with surgical site infection. An area under receiver operating characteristic curve (AUC) of 0.72 (95% CI 0.55 0.89) was obtained which is a good predictive power. The best cutoff value was 11.61% with the sensitivity of 76.92% and specificity of 51.72%.This explains how good perioperative decrease in serum albumin is a predictor for potential surgical complications with 30 days of surgery. The findings were consistent with other studies which delta albumin of more than 15% was a cutoff point with higher sensitivity and specificity (8). Also in studies done in China, Thailand and Australia, the cutoff point of 15.0%, 13.2%, and 24.27% were associated with larger AUC and high sensitivity and specificity. These similar findings render the predictive accuracy of decrease of serum albumin as a predictor of adverse surgical outcome (1, 7, 8).

We conducted a prospective study where individual follow-up of each study participants both preoperatively and postoperatively was done, this maximized reliability of collected information as there was less recording and recall biases. However the study was conducted in a single institution; this may affect a true sample representation of developing world. The recruitment time for participants was as short as six months; the number of participants was small, this may affect the power of this study. This study did not take the impacts of liver function and body fluid volume on serum albumin concentrations into consideration. An adequate function of the hepatocytes is a prerequisite of production of normal serum albumin levels, therefore preoperative assessment of liver functions tests would exclude confounding liver diseases as well as explaining a low preoperative albumin. Therefore abnormal liver function tests would provide important exclusion criteria for the studied patients.

Conclusion

This study showed that an early perioperative decrease in serum albumin level predicts postoperative adverse outcomes in patients undergoing major abdominal surgeries. Surgical care team is recommended to be aware of percentage decrease of serum albumin in the early postoperative period, even for patients with normal preoperative serum albumin levels. Therefore serum albumin may be used as a simple and low-cost prognostic tool to predict the risk of adverse surgical outcomes. Nevertheless multiple limitations open opportunity for better precise studies to cement the revealed association.

Abbreviations

ASA America Society of Anaethesia

AUROCC Area Under Receiver Characteristic Curve

CRC Colorectal Cancer

CRC Colorectal Cancer

CRP C-reactive Protein

FBC Full Blood Count

HCT Hematocrit

KCMC Kilimanjaro Christian Medical Centre

KCMUCo Kilimanjaro Christian Medical University College

kDa Kilo Dalton

POD Postoperative Day

SSI Surgical Site Infection

WBC White Blood Count

ΔAlb Reduction in Serum Albumin

Declarations

Ethical Approval and Consent to participants

Ethical approval number 2336 was sought from Tumaini University Makumira KCMUCo Research and Ethical Committee. The study observed confidentiality and privacy of the subjects. No participant's name was used instead unique identifiers was used. Also no participant was entitled to incur laboratory investigations cost.

Written informed consent was sort preoperatively to every eligible participant. The document was prepared in Swahili for conveniences.

Consent for publication

Not applicable

Availability of Data and Materials

All data and materials concerning this research article are available for sharing if needed.

Competing interests

There are no conflicts of interest regarding this paper to be disclosed.

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No fund was received to facilitate publication of this work.

Authors' Contribution

CEI designed the study, wrote the manuscript and participated in data collection. DM, KC, AY, ES, and SC participated in reviewing the manuscript for intellectual content. FS and EN collected samples from patients and other data from case notes. JP participated in laboratory samples analysis and result authorization; HM, EM, LS, BJ and SA compiled and analyzed final data. All authors read and approved the final manuscript.

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Figures

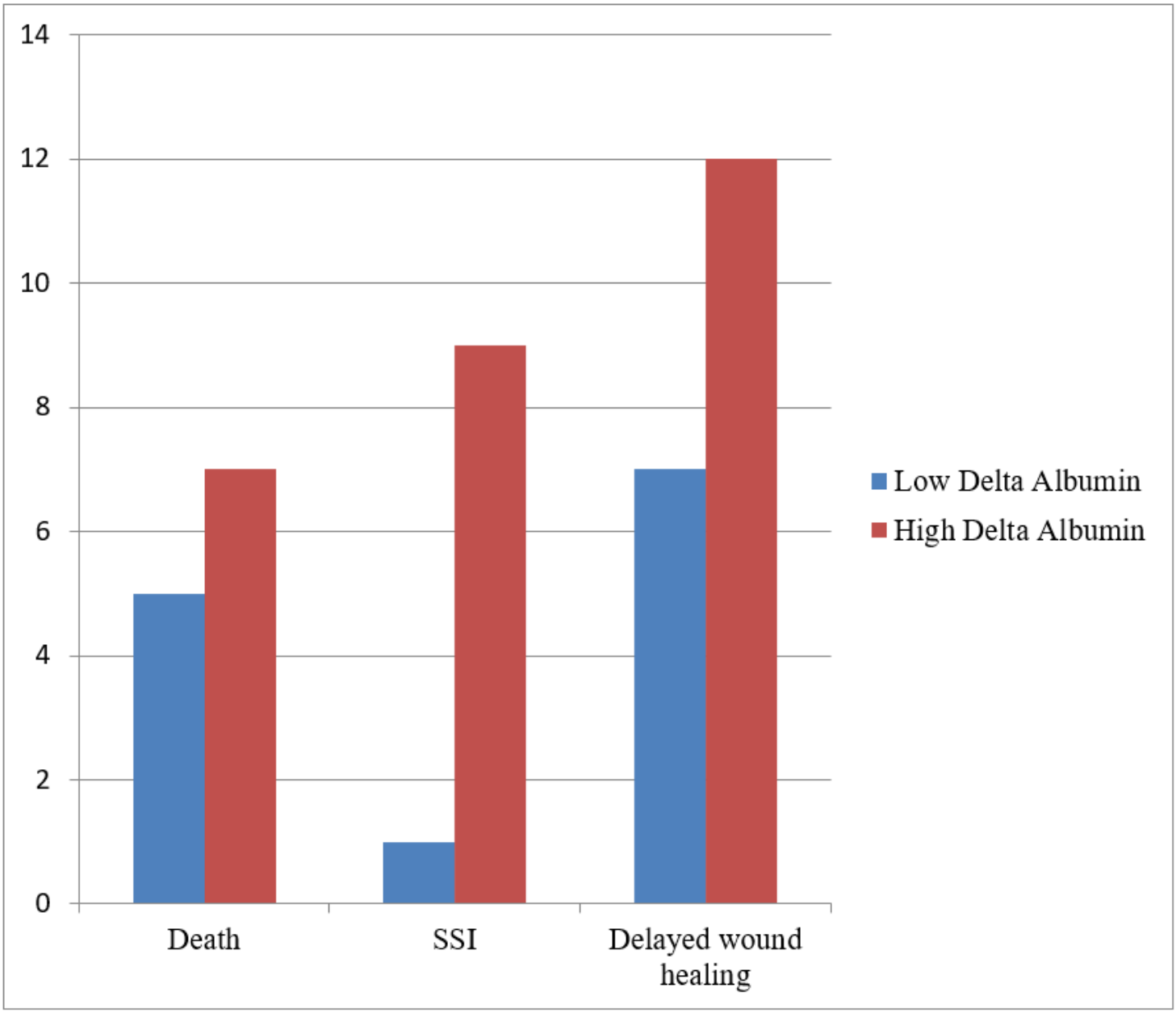

Figure 1

Distribution of adverse surgical outcomes by delta albumin

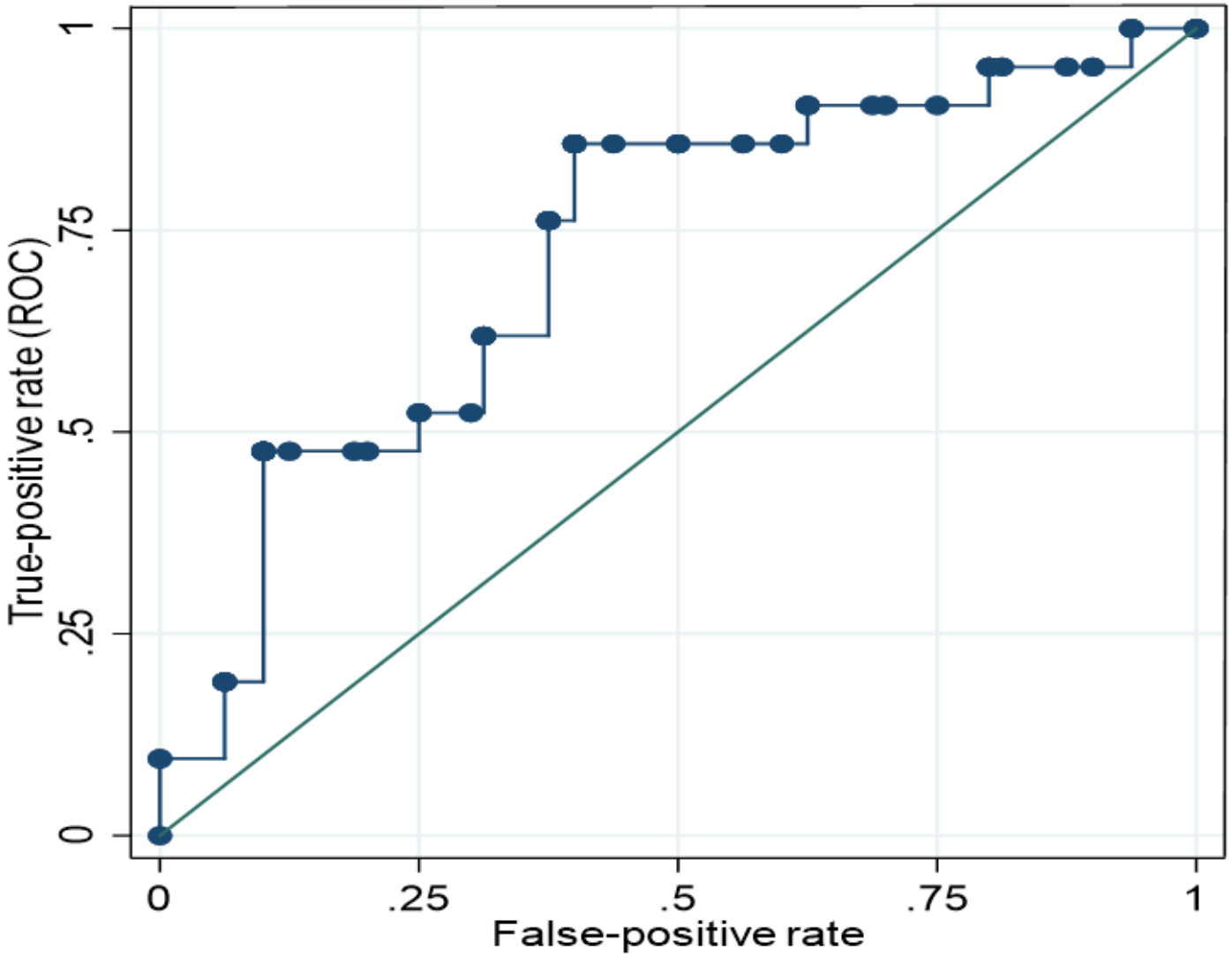

Figure 2

Area under receiver operating characteristics curve for predicting adverse outcomes using delta albumin while adjusting for ASA classification of participants from October 2018 to March 2019