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C-Reactive protein as a predictor of post-operative complications in bariatric surgery patients

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Abstract

Background The primary objective of this study was to evaluate the utility of CRP in early identification of post-operative complications after bariatric surgery. The ability of this marker to acutely predict post-operative complications in bariatric surgery patients has not been determined.

Methods A retrospective chart review was conducted of adult patients who underwent a primary and revisional laparoscopic Roux-en-Y gastric bypass (LRYGB) or sleeve gastrectomy (LSG) between 2013 and 2017 at a single institution. Patients were identified using the prospective Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program database. CRP levels were drawn on post-operative day one per standard protocol. Univariate analyses were performed to determine the predictive impact of CRP levels on post-operative complications, readmissions, and reoperations.

Results There were 275 patients who underwent bariatric surgery, 222 primary and 53 revisional. Of the 275 patients, 36 (13.1%) had a complication. Bariatric surgery patients with a post-operative complication had higher CRP levels compared to those who did not (4.8 ± 4.6 vs. 2.9 ± 2.0; $p = 0.02$). A CRP ≥ 5 mg/dL had a sensitivity for a complication of 27% and a specificity of 88%. There was no difference in CRP levels for patients with a 30-day reoperation or readmission. There were no mortalities.

Conclusions Bariatric surgery patients with elevated post-operative CRP levels are at increased risk for 30-day complications. The low sensitivity of a CRP ≥ 5 mg/dL suggests that a normal CRP level alone does not rule out the possibility of a post-operative complication. However, with its high specificity, there should be an elevated clinical suspicion of a post-operative complication in patients with a CRP ≥ 5 mg/dL.

Keywords C-Reactive protein · Roux-en-Y gastric bypass · Sleeve gastrectomy · Post-operative complications · Bariatric surgery

Obesity and its associated comorbidities are an ongoing health-care crisis. Bariatric surgery is effective for long-term weight loss and resolution of obesity-related comorbidities in morbidly obese patients. White blood cells, neutrophils, and C-reactive protein (CRP) are commonly used systemic markers of inflammation and found to be elevated at baseline in obese patients [1]. CRP has been identified as a potential predictive marker of post-operative complications in bariatric surgery patients. CRP levels have been shown to detect leak or abscess after laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass with higher sensitivity and specificity than other markers (i.e., white blood cells and/or neutrophils) [2, 3]. Although white blood cells and neutrophils correlated with leak and abscess on select post-operative days, elevated CRP consistently correlated with these complications regardless of post-operative day. This suggests that CRP is a more accurate inflammatory marker for the early detection of post-operative complications in bariatric surgery patients.

Given the importance of detecting and treating post-operative complications in this high-risk patient population, any

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opportunity for early detection improves quality outcomes and patient care. There have been limited research studies on CRP and its association with post-operative complications in bariatric surgery patients. Those studies have primarily focused on the predictive impact of CRP on post-operative day two and beyond. However, the aim of this study was to determine the utility of CRP in early identification, on post-operative day one, of complications after bariatric surgery.

Materials and methods

The Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) database was used to identify patients in our institution who underwent a primary or revisional laparoscopic Roux-en-Y gastric bypass (LRYGB) or sleeve gastrectomy (LSG) between 2013 and 2017. The electronic medical record system at our institution was used to conduct a retrospective chart review of these patients. Inclusion criteria included adolescent and adult bariatric surgery patients who underwent a primary or revisional minimally invasive bariatric surgery, and had a CRP level drawn on post-operative day one. In our institution, post-operative CRP levels were routinely obtained based on surgeon preference; two of the four surgeons were not selective in checking a post-operative CRP level, and checked this lab routinely in all their bariatric surgery patients. CRP levels were drawn in addition to a complete blood count (CBC), which was drawn on post-operative day one in every patient. A cut-off of CRP $\geq$ 5 mg/dL was chosen as a categorical variable. The mean primary and revisional CRP levels in patients who experienced any complication was 5.0 ± 4.7 mg/dL. References ranges from the literature were unable to be used given the overall lower values of CRP in our patient population compared to the literature.

Exclusion criteria included all open procedures and patients who did not have a CRP level drawn. All 30-day perioperative complications listed in the MBSAQIP dataset were identified. Additional outcomes analyzed included reoperation, readmission, and mortality. Institutional IRB approval was obtained for this study. Statistical analysis was performed using SPSS, version 21 (IBM Corp.). Categorical data were analyzed using Chi-square tests and continuous data were analyzed using independent samples *t* test (parametric) and Mann–Whitney *U* tests (non-parametric). A logistic regression was performed of perioperative demographic variables to determine risk factors contributing to any complication. Data were expressed as mean ± standard deviation (SD). A *p* value of $\leq$ 0.05 was considered statistically significant for all analyses.

Results

Of the 641 bariatric surgery patients, there were 275 patients who had a CRP level on post-operative day one. Of these 275, there were 222 primary and 53 revisional surgeries. The mean CRP level in primary patients was 3.0 ± 2.4 mg/dL and in revisional patients was 4.2 ± 3.0 mg/dL. The mean CRP level in primary LSG patients was 2.1 ± 1.2 mg/dL and 4.5 ± 3.2 mg/dL in primary LRYGB patients. The mean body mass index (BMI) for patients who underwent primary bariatric surgery was 48.7 ± 9.6 kg/m^2, with a mean age of 44.4 ± 13.2 years. The mean BMI of revisional bariatric surgery patients was 44.1 ± 8.2 kg/m^2, with a mean age of 46.9 ± 11.3 years. There were 167 females (75.2%) in the primary cohort and 52 (98.1%) females in the revisional cohort.

Overall, 36 (13.1%) patients experienced a complication. Patients with a 30-day post-operative complication had statistically higher CRP levels compared to those who did not (4.8 ± 4.6 vs. 2.9 ± 2.0 mg/dL; $p = 0.02$) (Table 1). Within this overall group of complications, there were 22 (9.9%) primary and 14 (26.4%) revisional patients who had a complication ($p = 0.001$). There was no statistically significant difference in CRP levels for patients who were readmitted or had a reoperation within 30 days post-operatively. A CRP $\geq$ 5 mg/dL had a sensitivity for a complication of 27% and a specificity of 88%. Of the complications, there was one anastomotic leak following a primary LRYGB, with a normal CRP level (0.8 mg/dL). There were no leaks in the revisional bariatric surgery cohort. Table 2 identifies the CRP levels for each type of complication in both primary and revisional bariatric surgery patients. When divided by type of complication, mean CRP levels for venous thromboembolism (6.88 ± 8.70 mg/dL) and blood transfusion

Table 1 Univariate analysis of CRP levels (mg/dL) and 30-day post-operative outcomes

Variable	CRP patients *n* (%)	Yes	No	*p* value	Non-CRP patients *n* (%)	*p* value
Any complication	36 (13.1)	4.8 ± 4.6	2.9 ± 2.0	0.02*	46 (10.8)	0.351
Primary	22 (9.9)	4.6 ± 4.9	2.8 ± 1.9	0.06	N/A	N/A
Revisional	14 (26.4)	5.4 ± 4.5	3.8 ± 2.2	0.32	N/A	N/A
Reoperation	9 (3.3)	4.3 ± 4.0	3.1 ± 2.5	0.22	12 (2.8)	0.730
Readmission	11 (4.0)	7.2 ± 7.4	3.0 ± 2.0	0.12	23 (5.4)	0.404

Table 2 CRP levels in both primary and revisional bariatric surgery patients, classified by complication type

Type of complication	*n* (%)	Mean CRP (mg/dL) ± SD
Urinary tract infection	13 (36.1)	3.94 ± 3.54
Venous thromboembolism	5 (15.2)	6.88 ± 8.70
Surgical site infection	8 (22.2)	4.90 ± 3.60
Blood transfusion	3 (9.1)	6.47 ± 6.35
Clostridium difficile infection	1 (3.0)	2.70 (no SD)
Anastomotic leak	1 (3.0)	0.80 (no SD)
Other	5 (13.9)	4.23 ± 1.82

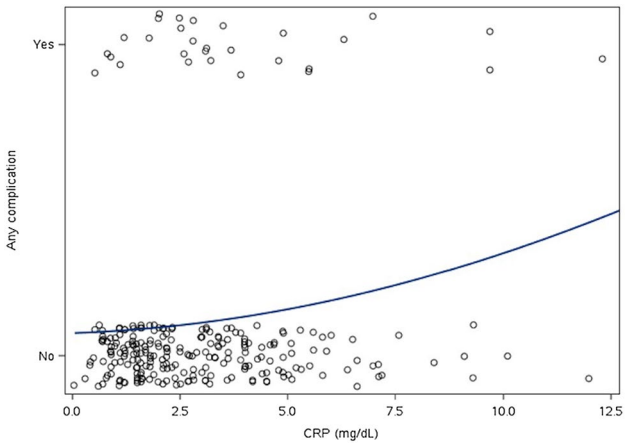

Fig. 1 Scatter plot for any complication and CRP with a spline showing the trend

(6.47 ± 6.35 mg/dL) were ≥ 5 mg/dL. There were no mortalities. Figure 1 represents the trend of CRP in patients with and without any complication.

Values listed as mean ± standard deviation

*statistical significance ($p \leq 0.05$)

When comparing the above outcomes in patients who had a CRP level, primary and revisional bariatric surgery patients in the study cohort who did not have a CRP performed were also analyzed. Of the 472 patients, there were 46 patients (10.8%) with any complication, 12 patients (2.8%) with a reoperation, and 23 (5.4%) with a readmission. There was no statistically significant difference between these outcomes for CRP and non-CRP bariatric surgery patients. This comparison with the CRP patients is provided in Table 1.

Table 3 compares the demographics of patients with and without a post-operative complication. Patients with diabetes had a decreased incidence of a post-operative complication, whereas this was increased in those with gastroesophageal reflux disease. Additionally, patients with any complication had a longer length of stay at 4.1 ± 3.1 days compared to patients without a complication of 1.8 ± 1.0 days ($p < 0.001$). Table 4 reflects a logistic regression performed of perioperative variables influencing post-operative complications. This analysis was performed dependently, with all variables adjusted for one another. Of the variables in this regression model, CRP and gastroesophageal reflux disease had statistically significant adjusted odds ratio of 1.19 and 2.53, respectively.

Table 5 and Fig. 2 characterize the sensitivities and specificities of CRP levels in relation to any complication. Based on the ROC curve, the Area Under the Curve (AUC)

Table 3 Patient demographics and risk factors based on any complication

Variable	Any complication $n = 36$	No complication $n = 239$	*p* Value
Body Mass Index (kg/m^2)	48.6 ± 10.9	47.7 ± 9.3	0.61
Age (years)	45.2 ± 11.4	44.9 ± 13.1	0.90
Sex—Female	31 (86.1%)	188 (78.7%)	0.30
Race—White	17 (73.9%)	139 (69.5%)	0.883
Diabetes	15 (41.7%)	154 (64.4%)	0.009*
Smoker	4 (11.1%)	18 (7.5%)	0.46
OSA	12 (33.3%)	86 (36.0%)	0.76
GERD	23 (63.9%)	85 (35.6%)	0.001*
Hypertension	23 (62.2%)	121 (50.8%)	0.20
Hyperlipidemia	10 (27.0%)	74 (31.1%)	0.62
ASA class			0.87
ASA class I/II	3 (8.3%)	22 (9.2%)	
ASA class III/IV	33 (91.7%)	217 (90.8%)	
Length of stay	4.1 ± 3.1	1.8 ± 1.0	< 0.001*

GERD gastroesophageal reflux disease, *OSA* obstructive sleep apnea, *ASA* American Association of Anesthesiologists

*Statistical significance ($p \leq 0.05$)

Table 4 Logistic regression for any complication, adjusted for all variables

Variable	Odds ratio (95% CI)	*p* Value
CRP (mg/dL)	1.19 (1.03, 1.37)	0.020*
ASA class (III/IV vs. I/II)	0.86 (0.17, 4.27)	0.85
Body Mass Index (kg/m^2)	1.02 (0.98, 1.06)	0.39
Diabetes (yes vs. no)	0.57 (0.25, 1.29)	0.17
GERD (yes vs. no)	2.53 (1.08, 5.94)	0.03*
OSA (yes vs. no)	0.61 (0.24, 1.52)	0.29
Smoker (yes vs. no)	2.20 (0.65, 7.40)	0.20

CRP C-reactive protein, *ASA* American Society of Anesthesiologists, *GERD* gastroesophageal reflux disease, *OSA* obstructive sleep apnea

*Statistical significance ($p < 0.05$)

Table 5 Sensitivity and specificity for each value of CRP and area under the curve (AUC)

CRP (mg/dL)	Sensitivity	Specificity	AUC (95% CI)
1	0.90 (28/31)	0.11 (25/225)	0.63 (0.52, 0.74)
2	0.81 (25/31)	0.41 (93/225)	
3	0.55 (17/31)	0.59 (132/225)	
4	0.35 (11/31)	0.74 (166/225)	
5	0.29 (9/31)	0.87 (196/225)	
6	0.23 (7/31)	0.93 (209/225)	
7	0.19 (6/31)	0.95 (214/225)	
8	0.16 (5/31)	0.97 (219/225)	
9	0.16 (5/31)	0.98 (220/225)	
10	0.10 (3/31)	0.99 (223/225)	

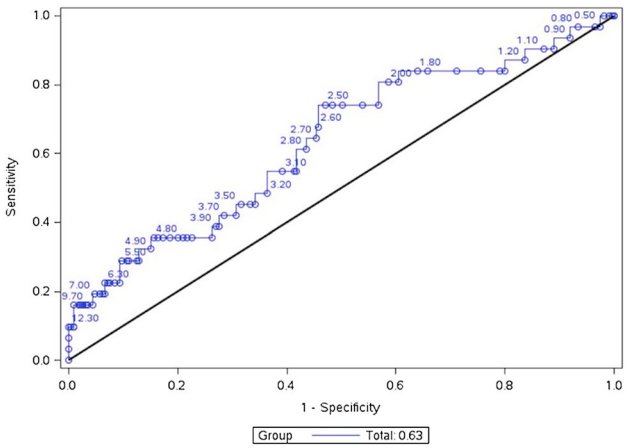

Fig. 2 ROC curve for CRP and any complication

was 0.63. Therefore, CRP should be considered an adjunct predictor of any complication. It is associated with post-operative complications, but it is not a strong predictor of a complication by itself.

Discussion

Post-operative complications following bariatric surgery are a significant quality metric, influencing overall morbidity as well as mortality [4–7]. Particularly in this high-risk patient population, it is important to identify tools that can detect complications as early as possible. However, early diagnosis of post-operative complications continues to pose a challenge to bariatric surgeons. The use of a serum marker, such as CRP, that can determine patients at high risk for complications is crucial to optimizing patient health outcomes. This retrospective study assessed the utility of CRP in early identification of post-operative complications following primary and revisional LRYGB and LSG. Of the 275 patients in this study, 36 (13.1%) had a complication, the majority of which were urinary tract infections and venous thromboembolism.

A CRP $\geq$ 5 mg/dL had a sensitivity for a complication of 27% and a specificity of 88%. Therefore, there should be an elevated clinical suspicion of a post-operative complication in patients with a CRP $\geq$ 5 mg/dL. This value was chosen as a categorical variable as it was the mean of the primary and revisional bariatric surgery patients who had CRP levels drawn post-operatively. Other studies in the literature that analyze CRP and post-operative outcomes in bariatric surgery patients had higher CRP levels than our patient population, and therefore we could not use their data as a reference [3, 8].

In this study, patients with a 30-day post-operative complication had higher CRP levels compared to those who did not (4.8 $\pm$ 4.6 mg/dL vs. 2.9 $\pm$ 2.0 mg/dL; $p = 0.02$). Munoz et al. [8] reported similar findings and demonstrated the influence of CRP levels in predicting post-operative outcomes. Elevated CRP levels on the first post-operative days demonstrated correlation with septic complications, such as anastomotic leaks, following laparoscopic sleeve gastrectomy. The data showed that a CRP of $\geq$ 9 mg/dL on post-operative day one for predicting staple line leak achieved 85% sensitivity and 90% specificity. CRP levels were also found to be significantly elevated in septic complications, before the onset of other clinical symptoms, such as fever, tachycardia, and abdominal pain. This similarity suggests that CRP can potentially be utilized as an early indicator of post-operative complications in sleeve gastrectomy patients.

Warschkow et al. [3] assessed CRP levels as a predictor of early post-operative complications, such as intestinal leaks, in patients undergoing LRYGB. This retrospective study found that of the 410 patients in the cohort, 49 (12.0%) developed post-operative complications, and leaks occurred in 17 patients (4.1%) at a median of 5 days after surgery. More specifically, elevated CRP levels on

post-operative day two provided the best diagnostic values for general complications as well as for intestinal leaks. For a CRP level > 22.9 mg/dL, there was a sensitivity of 53% and specificity of 91%. The sensitivity for intestinal leaks reached 100%. In comparison to these findings, our study demonstrated a similar overall sensitivity for a complication of 27% and a specificity of 88%. Additionally, our study found that CRP was predictive of complications on post-operative day one, which is important in the era of enhanced recovery after surgery.

In addition, our study observed that patients who had post-operative complications following a LRYGB had higher CRP levels compared to patients who underwent a LSG. This is a unique finding that has not been addressed thus far in the literature. Higher CRP levels following LRYGB could be due to the technical complexity of the operation, in comparison to a LSG. Additionally, time under general anesthesia is increased in LRYGB patients. Furthermore, LSG has been shown to have a decreased incidence of post-operative complications compared to LRYGB, such as a lower rate of perioperative blood transfusion, surgical site infections, and 30-day reoperation rates [9, 10]. In another study, Javanainen et al. investigated complications of LRYGB and LSG operations and found that significantly fewer late complications requiring operative intervention were identified in LSG compared to LRYGB patients [11]. This heightened inflammatory response in LRYGB could likely explain the overall increase in CRP levels.

The most common complication in this cohort of patients was a UTI at 36.1%. At our institution, the cost of obtaining a CRP level is $34.00, which is less expensive than a urinalysis, which costs $41.00 and a urine culture which costs between $29.00 and $78.00. Additionally, a 7-day course of oral ciprofloxacin for treatment of a UTI costs $61.00 Therefore, the cost of a CRP level at $34.00 is significantly less expensive than the cost of diagnosing and treating a UTI, which costs between $131.00 and $180.00.

This is the first study that analyzes an association between CRP and post-operative outcomes in primary and revisional bariatric surgery patients. Revisional bariatric surgery patients comprise about 13% of the national bariatric surgeries performed, and about 19% in our study population. When dividing the study cohort into primary and revisional patients, we found that CRP levels were no longer significantly different in primary bariatric surgery patients who had a post-operative complication compared to revisional patients. The cohort of revisional patients with a post-operative complication in this study was small ($n = 14$), compared to primary patients ($n = 22$), which could have contributed to the statistical variability. When grouped together, the overall power of the analyses increases, which may explain this finding. As there was no difference between the CRP levels of primary and revisional patients with a post-operative complication, this concludes that CRP can be a useful marker of post-operative complications in both groups of patients.

There are several limitations to this study. This is a retrospective review of prospectively collected data. In addition, our patient sample size was limited due to the fact that our research was conducted at a single institution. Furthermore, at our institution some providers routinely obtain CRP after bariatric surgery, while other providers do not. Therefore, perioperative complications and CRP levels could not be correlated for all of our bariatric surgery patients.

In conclusion, bariatric surgery patients with elevated post-operative CRP levels are at increased risk for 30-day complications. CRP levels can be used as an early indicator, in conjunction with other clinical markers, to identify patients at high risk for a post-operative complication.

Compliance with ethical standards

Disclosures Matthew Goldblatt is a speaker and consultant for WL Gore and Medtronic, a consultant for Allergan, and receives research funding from Bard and Merck. Jon Gould is a consultant for Torax Medical. Ashley Villard, Melissa Helm, Tammy L. Kindel, and Rana Higgins have no conflicts of interest or financial ties to disclose.

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