

Clinical evaluation of C-reactive protein and procalcitonin for the early detection of postoperative complications after laparoscopic sleeve gastrectomy

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Abstract

Introduction: Among the most common early complications after bariatric surgery are anastomosis leak and bleeding. In order to react quickly and perform accurate treatment before the clinical signs appear, early predictors should be found. In the study C-reactive protein (CRP) and procalcitonin (PCT) levels were investigated. Characterized by a relatively short half-life, they can predict surgical complications.

Aim: To develop and implement certain standards for early detection of complications.

Material and methods: The study involved 319 adults who underwent laparoscopic sleeve gastrectomy (LSG) as a surgical intervention for morbid obesity at the Department of General Surgery of Ceynowa Hospital in Wejherowo. Every patient had CRP and PCT levels measured before the surgery and on the 1st and 2nd postoperative day (POD).

Results: Early postoperative complications occurred in 19 (5.96%) patients. Septic and non-septic complications occurred in 3 and 16 patients respectively. Among the patients with septic postoperative complications CRP level increased significantly on the 2nd POD compared to the remainder ($p = 0.0221$). Among the patients with non-septic postoperative complications CRP level increased significantly on the 1st and 2nd POD compared to the remainder. Among the patients with septic and non-septic postoperative complications PCT level increased significantly on the 2nd POD compared to the remainder.

Conclusions: The CRP and PCT level are supposed to be relevant diagnostic markers to predict non-septic and septic complications after LSG.

Key words: C-reactive protein, procalcitonin, bariatric surgery, complications, laparoscopic sleeve gastrectomy.

Introduction

Obesity, according to the World Health Organization, affects 13% of the population, which means that 600 million people have body mass index (BMI) over 30 kg/m² [1]. It is estimated that in Europe the range of obesity is from 10% to 30%, and it is still growing [2]. Obesity is not only excess weight but also it is associated with a high risk of comorbid-

ities. The strongest relation with gain of weight is with diabetes mellitus, hypertension or obstructive sleep apnoea. These diseases lead to functional impairment and to premature death. To avoid the consequences the obese should undertake actions leading to a quick but lasting and healthy reduction in weight as well as complications. Bariatric surgery is nowadays recommended as the first choice of

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treatment for obese with metabolic syndrome. It leads to significantly greater weight loss and improvement in comorbidities compared to non-surgical treatment [3].

Among the types of surgery the most common procedure performed in Poland and the 2nd worldwide gaining the biggest rise in popularity is laparoscopic sleeve gastrectomy [4, 5]. Although the literature indicates that the range of complications is lower than in other forms of bariatric surgery, the problem of adverse events still exists and complications still occur in less than 10% [6–10]. Among the early ones the most common are anastomosis leak and bleeding [6, 10]. In order to react quickly and provide accurate treatment before the clinical signs appear, early predictors should be found.

In the study C-reactive protein (CRP) and procalcitonin (PCT) levels were investigated. The CRP is synthesized by hepatocytes as a response of inflammation stimulated by interleukin 6 [11]. Increase in CRP levels is observed about 2 days after the initiation of inflammation and due to its short half-life time it is determined as a valuable marker to detect postoperative complications [11]. The PCT is a protein produced by C-cells of the thyroid gland, which increase in patients with severe bacterial infections and sepsis [12]. Characterized by a relatively short half-life, it can predict surgical complications such as infections or anastomosis leak.

Aim

The aim of this study was to develop and implement certain standards for early detection of complications. Such standards would enable identification of patients who should be taken under special supervision and offered extended diagnostics at an early stage.

Material and methods

The study involved 319 adults who underwent laparoscopic sleeve gastrectomy as a surgical intervention for morbid obesity at the Department of General Surgery of Ceynowa Hospital in Wejherowo, Poland, from January to June 2013. Patients were selected for the procedure according to WHO obesity guidelines. They underwent LSG using a standardized technique. The study involved patients after previous bariatric procedures, which ended with failure (lack of reduction of excess weight loss, regain weight af-

ter primary lost) as well. Patients were evaluated for comorbidity, i.e. diabetes, hypertension.

Every patient had the CRP level measured before the surgery, on the 1st and 2nd postoperative day (POD) as well as PCT level on the 1st and 2nd POD. On 2nd POD an upper gastroesophageal imaging study followed by drinking 100 ml of uropline was performed in all patients to control the tightness of the staple line and exclude anastomosis leak. Furthermore, levels of CRP and PCT were analysed in correlation with occurrence of early clinical symptoms of postoperative complications. The complications were codified as septic and non-septic.

Statistical analysis

The data were analysed retrospectively. All the statistical calculations were performed using StatSoft Inc. (2011) statistical package Statistica, version 10.0. www.statsoft.com and the Excel spreadsheet. Quantitative variables were characterized by arithmetic mean, standard deviation, median, minimum and maximum value (range) and confidence interval (95% CI), whereas qualitative variables were presented using numerical amounts and percentages.

Significance of differences between two groups was verified with significance of differences tests: Student's *t*-test or Mann-Whitney *U* test if conditions of Student's *t*-test applicability were not met or in the case of variables measured on an ordinal scale. Significance of differences between more than two groups was verified with the F-test (ANOVA).

In order to determine the relationship, strength and direction between the variables, correlation analysis was applied by calculating Spearman's correlation coefficient. In all the calculations *p*-values < 0.05 were considered significant.

Results

In the study there were 233 (73.0%) women and 88 (26.0%) men. The average age was 38.4 ± 10.3 years. One hundred and sixty-seven (52.4%) patients declared comorbidities – 21.3% diabetes mellitus type 2, 44.8% hypertension, 35.1% other, i.e. heart failure, heart arrhythmia, osteoarthritis, obstructive sleep apnoea, asthma, hyperlipidaemia, hypothyroidism, depression.

Early postoperative complications occurred in 19 (5.96%) patients. Septic and non-septic compli-

Table I. Frequency of complications

Complications		Result, n (%)
Septic	Anastomosis leak	3 (0.94)
Non-septic	Bleeding	12 (3.76)
	Respiratory failure requiring life support	2 (0.63)
	Subdermal hematoma	2 (0.63)

cations occurred respectively in 3 and 16 patients (Table I). Two (0.6%) patients with anastomosis leak, confirmed by contrast examination, presented tachycardia > 100 HR/min and moderate shortness of breath required reoperation on the 2nd POD. One patient was re-hospitalised and reoperated on the 6th POD with anastomosis leak as a consequence of strangulated umbilical hernia.

C-reactive protein level

Mean preoperative CRP level was 9.1 ±6.9 mg/l, on the 1st POD 30.7 ±23.4 mg/l, the 2nd POD 55.7 ±46.5 mg/l (Figure 1). The CRP level increased statistically significantly during the observation time (*p* < 0.05). Among the patients with septic postoperative complications CRP level increased significantly on the 2nd POD compared to the remainder (*p* = 0.0221). Among the patients with non-septic postoperative complications the CRP level increased

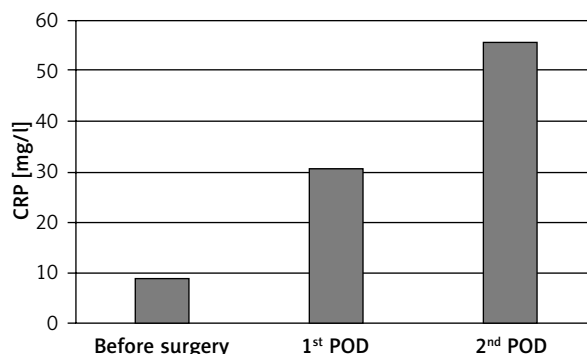


Figure 1. C-reactive protein (CRP) at three observation times

significantly on the 1st and 2nd POD compared to the remainder (respectively *p* = 0.0357, *p* = 0.0001) (Table II). The CRP level on the 2nd POD in patients with septic complications was 2 times higher than in patients with non-septic complications (*p* = 0.0355) (Table III).

Procalcitonin level

Among the patients with septic and non-septic postoperative complications the PCT level increased significantly on the 2nd POD compared to the remainder (respectively *p* = 0.0204, *p* = 0.0263) (Table IV). The PCT level on the 2nd POD in patients with septic complications was more than 6 times higher than in

Table II. Dependence of C-reactive protein levels in patients with septic and non-septic complications compared to the remainder at three observation times

Observation time	Septic complications N = 3	Remainder N = 316	P-value	Non-septic complications N = 16	Remainder N = 316	P-value
Before surgery, mean ± SD	3.5 ±2.1	9.2 ±6.9	0.0720	8.2 ±4.2	9.2 ±7.0	0.9071
1 st POD, mean ± SD	30.6 ±20.8	30.7 ±23.5	0.9770	47.4 ±42.0	29.9 ±22.1	0.0357
2 nd POD, mean ± SD	226.6 ±155.4	54.1 ±41.8	0.0221	105.0 ±70.0	51.3 ±37.9	0.0001

SD – standard deviation, POD – postoperative day.

Table III. Dependence of C-reactive protein (CRP) and procalcitonin (PCT) levels in patients with septic complications compared to non-septic complications on 2nd postoperative day

CRP			PCT		
Septic complications N = 3	Non-septic complications N = 316	P-value	Septic complications N = 3	Non-septic complications N = 316	P-value
105.0 ±70.0	226.6 ±155.4	0.0355	2.0 ±1.9	0.3 ±0.5	0.0037

Results presented in mean ± standard deviation.

Table IV. Dependence of procalcitonin levels in patients with septic and non-septic complications compared to the remainder at three observation times

Observation time	Septic complications N = 3	Remainder N = 316	P-value	Non-septic complications N = 16	Remainder N = 316	P-value
1 st POD, mean ± SD	0.4 ± 0.5	0.1 ± 0.2	0.1968	0.4 ± 1.0	0.1 ± 0.1	0.4236
2 nd POD, mean ± SD	2.0 ± 1.9	0.1 ± 0.1	0.0204	0.3 ± 0.5	0.1 ± 0.1	0.0263

SD – standard deviation, POD – postoperative day.

patients with non-septic complications ($p = 0.0037$) (Table III).

Correlation of C-reactive protein and procalcitonin

Within the increase in the level of CRP on the 1st POD the PCT level increased statistically significantly on the 1st POD and 2nd POD (Spearman correlation coefficient 0.31, $p = 0.0001$; 0.25, $p = 0.0001$, respectively) (Table V). Within the increase in CRP level on the 2nd POD the PCT level increased statistically significantly on the 1st POD and 2nd POD (Spearman correlation coefficient 0.27, $p = 0.0001$; 0.31, $p = 0.0001$, respectively) (Table V). The CRP and PCT levels in patients with and without complications on the 1st POD and 2nd POD are shown in Table VI.

All the patients, irrespective of complications development, had an upward trend in CRP level during

the observation time from the 1st and 2nd POD. Patients with a slight increase in CRP level did not develop complications, in contrast to the patients with a rapid increase in CRP level, who developed complications (ANOVA $F = 57.36$, $p = 0.0001$) (Figure 2).

Patients without an increase in PCT level during the observation time from the 1st to 2nd POD did not develop complications, in contrast to the patients with the increase in PCT level during this time, who developed complications (ANOVA $F = 13.18$, $p = 0.0003$) (Figure 3).

Discussion

In the study early postoperative complications occurred in 5.96% of patients, and 0.94% had anastomosis leak. It is comparable with the worldwide results from the observation time [5, 6, 8]. A review by Trastulli *et al.* reported rates of 0.9% for leak and 3.3% for bleeding [6].

Table V. Dependence of correlation of C-reactive protein (CRP) and procalcitonin (PCT) levels at three observation times

CRP	PCT 1 st POD		PCT 2 nd POD	
	R	P-value	R	P-value
Before surgery	-0.04	0.5282	-0.11	0.0748
1 st POD	0.31	0.0001	0.25	0.0001
2 nd POD	0.27	0.0001	0.31	0.0001

POD – postoperative day, R – correlation rate.

Table VI. C-reactive protein (CRP) and procalcitonin (PCT) levels in patients with and without complication at two observation times

Observation time	CRP		PCT	
	Without complications	With complications	Without complications	With complications
1 st POD, mean ± SD	29.9 ± 22.1	44.5 ± 39.1	0.1 ± 0.1	0.4 ± 0.9
2 nd POD, mean ± SD	51.3 ± 37.9	124.2 ± 94.0	0.1 ± 0.1	0.6 ± 1.1

SD – standard deviation, POD – postoperative day.

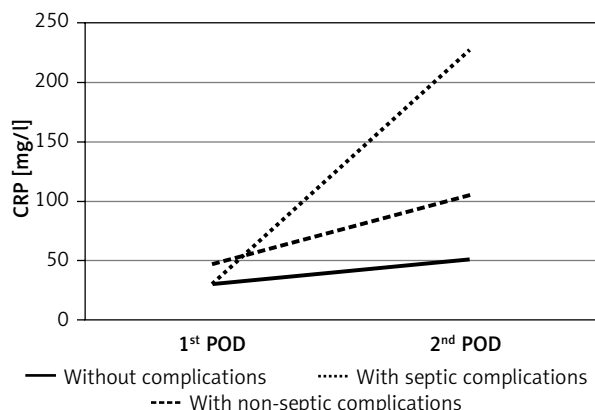


Figure 2. C-reactive protein (CRP) level at two observation times in patients with septic and non-septic complications and without any

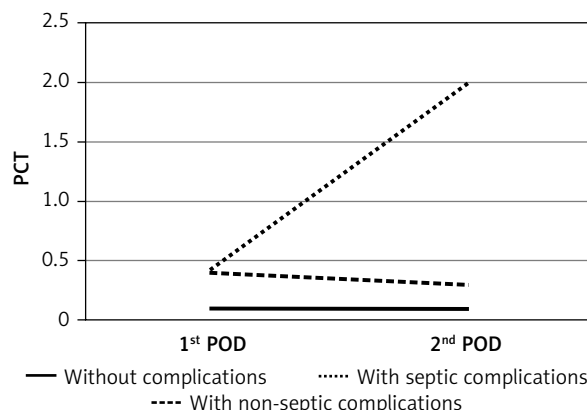


Figure 3. Procalcitonin (PCT) level at two observation times in patients with septic and non-septic complications and without any

The CRP and PCT levels were analysed in the study. Irrespective of development of complications the CRP level increases on the 1st and 2nd POD. It is said to be the organism’s response to trauma. According to the literature the CRP level increased in all patients within the first days after bariatric surgery, reaching the highest level on the 2nd, 3rd or 5th POD, and then decreases and normalizes within the first month after surgery [13–15]. In this study the CRP level on the 2nd POD was almost 2 times higher among patients with non-septic complications and 4 times higher among patients with septic complications, in contrast to the remainder (Figure 2). Albanopoulos *et al.* observed, based on an analysis of 177 patients undergoing LSG, that a highly increased CRP level on the 1st and 3rd POD may indicate early septic complications [13]. They determined the CRP cut-off as 150 mg/l on the 1st day with 83.2% sensitivity and 100% specificity; furthermore, on the 3rd POD the cut-off was 200 mg/l with 100% sensitivity and specificity. Similar conclusions were drawn by Warschkow *et al.* [16] and Williams *et al.* [17] analysing patients after laparoscopic Roux-en-Y gastric bypass surgery. Warschkow *et al.* determined the CRP cut-off as 229 mg/l on the 2nd POD with 53% sensitivity and 100% specificity, while Williams reported 127 mg/l with 93% sensitivity and 64% specificity, suggesting that further radiological investigation should be performed in patients who achieve this CRP level. According to researchers CRP on the 2nd POD has been shown to be a good predictor of complications after Roux-en-Y gastric bypass. Moreover, other researchers have noted the connection be-

tween higher CRP level after surgery and the necessity to extend the diagnostics in colorectal and oesophageal surgery if the persistent CRP level on the 3rd and 4th POD varies from 123 to 190 mg/l [18–26]. Based on our study, we cannot establish the CRP cut-off, due to the small number of septic complications.

Our study indicates that the PCT level should not increase after the surgery in patients without complications, although the level is almost 6 times higher among patients with non-septic complications and about 20 times higher among patients with septic complications, in contrast to the remainder (Figure 3). Similar observations were noted in colorectal surgery [27, 28]. In our study the patient who had signs on the 6th POD did not have a significantly elevated PCT level on the 1st and 2nd POD. The reason is that the anastomosis leak was induced by strangulation of the umbilical hernia, not by ischaemia.

Kassir *et al.* investigated both CRP and PCT levels in 97 patients after sleeve gastrectomy [29]. Mean postoperative CRP in patients with complications was about 2.5 times higher than in uncomplicated patients ($p = 0.02$). Mean postoperative PCT was almost 2 times higher in patients with complications versus those without them ($p = 0.0006$).

Conclusions

The CRP and PCT levels are considered to be relevant diagnostic markers to predict non-septic and septic complications after LSG. The CRP level increases in all patients undergoing LSG on the 1st and 2nd POD, although it increases 2-fold on the 2nd POD

among patients with non-septic complication and 4-fold in the case of septic complications. The PCT level should not increase in uncomplicated patients, while it increases 6-fold in patients with non-septic complications and about 20-fold in patients with septic complications. Thus growth in these inflammatory markers during the observation period should suggest the need to perform further diagnostics.

Conflict of interest

The authors declare no conflict of interest.

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