Should creatine kinase be routinely measured after bariatric surgery?

Original Article

Mohammed Elshwadfy Nageeb Abdelazez, George Abdelfady Nashed, Amr Anwar, Hany Armia Barsoum, Mohammed Nasr Shazly, Ahmed Maher Hassan

Department of General Surgery, Faculty of Medicine, Cairo University, Cairo, Egypt.

ABSTRACT

Background: Rhabdomyolysis (RML) is a postbariatric surgical complication that can lead to fatal outcomes, including acute kidney injury, so it needs an early diagnosis.

Aim: To determine whether creatinine kinase (CK) assessment should be routinely measured in high-risk patients after bariatric surgery.

Patients and Methods: This study was a single-center, prospective, observational study from January to June 2021.

All consecutive patients aged 18 years and above who were candidates for bariatric surgery were recruited and assessed for eligibility. With excluding patients who had previous bariatric surgery, significant long-standing heart/lung disease, or alcohol abuse.

Preoperatively, full clinical assessments were done, laboratory tests were done, and on day 1, postoperatively, including creatinine, CK, alanine aminotransferase, aspartate aminotransferase, sodium, potassium, and operative data. The primary outcome was the occurrence of RML, depending mainly on CK level on day 1 postoperative.

Results: Postoperative RML was diagnosed in eight (25%) patients with a mean BMI level of 60±4.5, operative duration of 5±1 h, and Creatine phosphokinase (CPK) mean level of 3965±2328.

Conclusion: As bariatric surgery volumes rise, clinicians should be ready to quickly identify and treat RML, which occurs in 25% of our patients. CK levels may increase 24 h after bariatric surgery. Higher BMI, diabetes, arterial hypertension, and postoperative CPK levels are risk factors for RML. In our series, aggressive fluid therapy and diuretics prevented acute kidney injury when elevated CK values were detected. We recommend routine CPK monitoring after bariatric surgery.

Key Words: Bariatric surgery, creatinine kinase, obesity, rhabdomyolysis.

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Corresponding Author: Mohammed Elshwadfy Nageeb, MD, Department of General Surgery, Faculty of Medicine, Cairo University, Cairo, Egypt. **Tel.:** +20 102 552 4630, **E-mail:** mohammedelshwadfy@kasralainy.edu.eg

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INTRODUCTION

Obesity is a developing epidemiologic issue that contributes to the development of significant diseases and complications. Several bariatric procedures have been invented to reduce this morbidity.

Rhabdomyolysis (RML), the disintegration of skeletal muscle, is uncommon but potentially fatal. Due to muscle sarcolemma necrosis, RML is a biochemical and clinical syndrome. This damage releases myoglobin into the circulation, which in 30% of RML patients can cause acute kidney injury (AKI) and a 20% mortality rate[1,2].

AKI is predominantly caused by tubular obstruction, direct ischemic tubule damage, or intrarenal vasoconstriction. While a specific threshold value for serum creatine kinase (CK) beyond which the risk of AKI substantially escalates remains undefined, the likelihood is minimal when levels reach 15 000 U/l[3]. However, RML must be diagnosed rapidly to prevent renal failure.

RML may occur without apparent symptoms, so it needs a high index of suspicion. Measuring CK level is a simple and rapid test that can predict RML early. So, our study aimed to determine whether CK assessment should be routinely measured in high-risk patients after bariatric surgery.

PATIENTS AND METHODS:

Study design

This study was a single-center, prospective, observational study in the Department of General Surgery from January 2021 to June 2021. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional

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research committee (Approval of ethics committee number Ms 116-2021) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Patient enrolment

All consecutive patients aged 18 years and above who were candidates for bariatric surgery were recruited and assessed for eligibility.

Patient exclusions from the study were as follows:

(1) Previous bariatric surgery.

(2) Significant long-standing heart/lung disease or other severe systemic illness, active substance, or alcohol abusComplete history and clinical assessment were done preoperatively.

Laboratory tests done preoperatively and on day 1 postoperatively:

Creatinine, CK, alanine aminotransferase, aspartate aminotransferase, sodium, and potassium.

Age, gender, BMI, associated comorbidities, any intraoperative/postoperative complications, and operative time will be documented. Insufflation pressure will be standardized and documented for all operations.

Outcome measures

Primary outcomes

Occurrence of RML following bariatric surgeries depending mainly on CK level on day 1 postoperative, which is the average level is up to 190 U/l, and in RML, the normal level increases five times (the cutoff limit).

Sample size

Using EPI INFO sample size calculator for survey study with 0.05 alpha error, confidence interval of 0.95, and power of the study 0.80.

The population of the study is the patients presenting undergoing bariatric surgery between January 2021 and June 2021, estimated to be 40 patients.

The actual incidence of RML after bariatric surgery has not been identified, having been estimated from 1.4 to 75% (cite second paper).

The minimum sample size calculated is 32 patients undergoing bariatric surgery.

Sampling technique:

A convenient sample of patients with bariatric surgery admitted to the General Surgery Department with the inclusion and exclusion criteria will be assigned for the study till the total sample size is calculated[4].

Data collection and statistical analysis

Data were collected on a specified Excel sheet prepared by the investigators. Various demographic variables, clinicopathological variables, laboratory tests, comorbidities and intraoperative variables, and details of the operative procedure.

Statistical data analysis

Microsoft Excel 2016 for Windows, included in the Microsoft Office bundle 2016, was utilized to compile, code, and enter the compiled data into a spreadsheet on behalf of Microsoft Corporation, USA. The data were analyzed using IBM Statistical Package for the Social Sciences (SPSS) software, specifically version 26.0 (IBM SPSS Statistics for Windows; IBM Corp., Armonk, New York, Redmond, Washington, United States USA). Utilizing the Kolmogorov–Smirnov test, the distribution's normality was confirmed. In contrast to continuous data, represented as means and SDs, medians, and interquartile ranges, categorical data were denoted by numbers and percentages. A significance level of 0.05 was applied to statistical values.

RESULTS:

Thirty-two consecutive morbidly obese patients underwent bariatric surgery during the study period. A total of 16 patients underwent laparoscopic Roux-en-Y gastric bypass (RYGBP) and 16 patients underwent laparoscopic sleeve gastrectomy (LSG).

The study comprised 24 females (75%, *n*=24) and eight males (25%, *n*=8), with an average age of 38±9 years (ranging from 19 to 64 years), a mean BMI of 43±6.8 kg/m^2 (ranging from 35 to 65 kg/m^2), a mean operation duration of 176 min, and a preoperative CPK level of 132 IU/l (Table 1).

Table 2 shows that postoperative RML was diagnosed in eight (25%) patients with a mean BMI level of 60±4.5, operative duration of 5±1 h, and CPK mean level of 3965±2328.

Table 3 compares patients who developed RML postoperatively and those who did not develop RML. A total of eight (25%) patients were identified as having postoperative RML: five (70%) in the RYGBP group and three (30%) in the LSG group. Significant disparities were observed between the two cohorts; specifically, individuals who developed RML exhibited a greater BMI (60±4.5 versus 48±7 kg/m^2), a greater prevalence of diabetes mellitus (67 vs. 43%), and an increased incidence of arterial hypertension (100 vs. 58%) in comparison to

those who did not develop RML. In addition, the duration of the operation was significantly longer in the RML group (5±1 h) than in the no-RML group (3±1 h). During the preoperative period, the average CPK level was 140±16 IU/l, with a range of 35–165 IU/l. The CPK level peaked on the initial day following the procedure, measuring 3965±2328 IU/l. Nobody among the patients developed acute renal failure; all survived.

The diagnostic accuracy of CPK was evaluated for the overall series using receiver operating characteristic curve analysis. CPK seems to have an excellent predictive value in RML groups, with the best cutoff value on CPK of more than 1075. This cutoff value has 100% sensitivity and 91% specificity, 91.7% with a positive predictive value, and 98.6% with a negative predictive value (Table 4).

Table 1: Perioperative data of overall 32 patients

Patients	Mean (range)	SD	95% CI (LL–UL)
Age (years)	38.5 (19–64)	10.93	35.4–41.6
BMI (kg/m^2)	43 (35–65.8)	5.23	42–44.5
Weight (kg)	118 (88–197)	20.6	112–123.2
Height (m)	1.64 (1.4–1.8)	0.18	1.6–1.6
Excess weight (kg)	57 (35–131)	17.6	53.4–62
Ideal weight (kg)	60 (44–76)	6.47	58.7–61.7
Operative time (min)	176 (75–375)	45.45	165–188
Preoperative creatinine (mg/dl)	0.79 (0.4–1.4)	0.17	0.75–0.8
Preoperative CPK (IU/l)	132±92	488	274–53
Hospital stay (days)	2.7 (1–8)	1.1	2.41–3

Intervals of confidence of 95% were computed.
CI, confidence interval; LL, lower limit; UL, upper limit.

Table 2: Characteristics of the patients with rhabdomyolysis – total of eight (25%) patients

The factors	Mean±SD
Age (years)	50±5
BMI (kg/m^2)	60±4.5
Operative time (h)	5±1
Highest CPK level (IU/l)	3965±2328

Intervals of confidence of 95% were computed.

Table 3: Patients without postoperative rhabdomyolysis are compared to those with postoperative rhabdomyolysis

Postoperative sample characteristics	Without RML (mean±SD or %)	With RML (mean±SD or %)
N	24 (75)	8 (25)
Age (years)	47±11	50±5
BMI (kg/m^2)	48±7	60±4.5
Diabetes mellitus	10 (43)	5 (67)
Arterial hypertension	14 (58)	8 (100)
Underwent LSG technique	17 (73)	3 (30)
Underwent RYGBP technique	7 (27)	5 (70)
Operative time (h)	3±1	5±1
Preoperative CPK (IU/l)	132±92	140±16
CPK 1st day after surgery (IU/l)	253±94	3965±2328
Creatinine 1st day after surgery (mg/dl)	0.68±0.22	0.9±0.33

To compare groups, the Mann–Whitney test was utilized for continuous variables, while Fisher's exact test and the $\chi 2$ test were applied to categorical variables.
LSG, laparoscopic sleeve gastrectomy; RML, rhabdomyolysis; RYGBP, Roux-en-Y gastric bypass.

Table 4: Sensitivity, specificity, and accuracy for CPK in the diagnosis of rhabdomyolysis

Cut off point	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
CPK	0.948	100	91	91.7	98.9	86

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value.

DISCUSSION

RML is an uncommon complication of obesity surgery that is potentially fatal[5].

RML is showing muscle necrosis resulting from injury to the muscle sarcolemma. When this occurs, myoglobin reaches the blood, which can cause AKI. AKI occurs in one-third of the patients with RML, with a 20% mortality rate[6].

Early diagnosis of RML is vital for prompt management to prevent renal failure. The precise prevalence of RML in bariatric surgery ranges from 1.4 to 75% and is undocumented; case reports and case series provide the only description[7].

RML may be more prevalent in bariatric surgery patients than in nonbariatric surgery due to the presence of multiple risk factors.

The study sample comprised 32 consecutive patients who were morbidly obese and had undergone bariatric surgery. Sixteen patients were randomized into two groups: those who received LSG and those who received laparoscopic RYGBP.

As regards demographic data, the study sample included eight males (25%, *n*=8) and 24 females (75%, *n*=24) with a mean age of 38±9 years (range, 19–64 years); mean BMI 43±6.8 kg/m^2 (range, 35–65 kg/m^2); mean duration of operation 176 min.

In our study, regarding the comparison between the preoperative and postoperative in both RYGBP and LSG groups. There were variables with statistically significant differences between the RYGBP and LSG groups, such as BMI, CPK peak, and excess weight ($P<0.05$), which were higher in the RYGB group.

Definite factors are associated with an increase in the risk of developing RML postbariatric surgeries, mainly in RYGB patients, and were associated mostly with increased BMI and CPK peak postoperatively[8].

The documented occurrence of RML exhibits considerable variability, with rates varying from 0 to 5% after laparoscopic renal surgery and peaking at a significantly higher 75% during bariatric surgery[6].

Our study showed that postoperative RML was diagnosed in eight (25%) patients. By analyzing their data, the mean BMI level was 60±4.5, operative duration was 5±1 h, and CPK mean level was 3965±2328.

Concerning comparing patients who did not have postoperative RML and those who did have postoperative RML. Diagnosis of postoperative RML was in eight (25%) patients: five (70%) patients in the RYGBP group and three (30%) patients in the LSG group. There were significant differences between both groups; patients who were complicated by RML had a higher BMI (60±4.5 vs. 48±7 kg/m^2), a higher diabetes mellitus incidence (67 vs. 43%), and a higher incidence of arterial hypertension (100 vs. 58%) compared to the no-RML group. Furthermore, operative time was higher in the RML group compared to the no-RML group (5±1 vs 3±1 h). In the preoperative period, the mean CPK level was 140±16 IU/l (range, 35–165 IU/l). The highest level of CPK was found on the first postoperative day (3965±2328 IU/l). All patients survived, and no one developed acute renal failure.

Several studies have found that bariatric surgery is associated with high rates of postoperative morbidity, such as RML and AKI, which are most prevalent in patients with a high BMI (50 kg/m^2) and a lengthy operating time (>4 h)[6,9,10].

Additionally, BMI was cited as a potential risk factor in the onset of RML. Two recent articles examined the incidence of RML in obese patients who underwent bariatric surgery; intriguingly, a BMI of 45 kg/m^2 was found to be associated with an increased risk of RML[9]. A significant proportion of RML cases were observed in patients who had undergone biliopancreatic diversion and gastric bypass.

The significant results in our study are consistent with the results of Moulla *et al*.[11] study. They performed their cohort study to elucidate risk factors for developing RML after bariatric surgeries. Elevated serum myoglobin levels occurred 4 h after bariatric surgery (range, 25–22 064 ng/ml; median, 124 ng/ml). Age, BMI, the presence of diabetes mellitus type II, the duration of bariatric surgery, and preoperative serum myoglobin levels were all significant predictors of postoperatively elevated serum myoglobin levels, according to multivariable analysis. In addition, the patients were categorized based on the duration of their bariatric surgery and BMI. Individuals who had undergone surgery for 160 min (OP-time) and had a BMI of 60 kg/m^2 exhibited

the highest levels of postoperative serum myoglobin (32% with values ≥3000 ng/ml). The incidence of postoperative morbidity, such as compartment syndrome, RML, and AKI, was considerably elevated. The aforementioned data validates our findings.

In our study, RML was associated with longer operation time. This is documented in the previous study (Grammer R)[12], as they reported that RML has been associated with prolonged surgical operations but rarely reported in the maxillofacial surgery literature.

High CK levels were only associated with operative times over 7 h in normal-weight patients[13]. In 30 neurosurgical patients with elective craniotomies, logistic regression analysis found that only surgery length increased CPK[13]. In our study, eight consecutive overweight surgical patients had postoperative CK values above 2000 U/l, but none had an operative time over 7 h. If operation time was prolonged, bariatric patients may have a higher RML rate than normal-weight patients.

Our study regards the sensitivity, specificity, and accuracy of CPK in diagnosing of RML. The diagnostic accuracy of CPK was evaluated for the overall series using receiver operating characteristic curve analysis. CPK seems to have an excellent predictive value in RML groups, with the best cutoff value on CPK of more than 1075 IU/l. This cutoff value has 100% sensitivity and 92% specificity, 91.7% with a positive predictive value, and 98.6% with a negative predictive value. The sole significant independent predictive factor identified by logistic regression was CPK (*P<0.001*).

This level was lower than the study of Moulla *et al*.[11]. They considered the myoglobin level of 3000 ng/ml as a cutoff value for RML in their current study. A prospective study of Kasaoka *et al*.[14] defined a serum myoglobin level over 4000 ng/ml as an indicator for AKI in patients with RML. However, a cutoff value for bariatric patients has not been established yet. However, these results are consistent with our results as they concluded that CPK is an independent factor in predicting RML.

In the study of Ettinger *et al*.[15], they concluded that RML incidence was 7%. The factors associated with RML in the bivariate analysis were hepatic steatosis, high BMI, high weight, higher excess weight, and prolonged operative time. The risk factor for RML in the multivariate analysis was BMI more than or equal to 50 kg/m^2. When the operative time was below 2 h, the incidence of RML was 0, which was not significant in the multivariate analysis. The factors associated with a higher risk of CPK elevation (multivariate analysis) were hypertension and open technique.

Also, different bariatric techniques did not result in possible risk factors. We believe that higher RML incidence reported in gastric bypass can be explained by the fact that these two techniques usually need more time than a sleeve gastrectomy[5].

Given that obesity and bariatric surgery volumes are rising, clinicians should be ready to quickly identify and treat RML, which occurred in 25% of our patients. CK levels may increase 24 h after bariatric surgery. We found that higher BMI, diabetes, arterial hypertension, and CPK postoperatively are risk factors for RML. When elevated CK values were detected, aggressive fluid therapy and diuretics prevented AKI in our series.

CONCLUSION

As obesity and bariatric surgery volumes rise, clinicians should be ready to quickly identify and treat RML, which occurred in 25% of our patients. CK levels may increase 24 h after bariatric surgery. Higher BMI and longer operative time are independent risk predictors of RML after bariatric surgery. RYGB is more susceptible to RML than sleeve gastrectomy. The comorbidities, including diabetes, arterial hypertension, and postoperative CPK levels, increase the risk for RML. In our series, aggressive fluid therapy and diuretics prevented AKI when elevated CK values were detected. We recommend routine CPK monitoring after bariatric surgery.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Bostanjian D, Anthone GJ, Hamoui N, Crookes PF. Rhabdomyolysis of gluteal muscles leading to renal failure: a potentially fatal complication of surgery in the morbidly obese. Obesity surgery. 2003 Apr;13(2):302-5.

2. HAMILTON RW, GARDNER LB, PENN AS, GOLDBERG M. Acute tubular necrosis caused by exercise-induced myoglobinuria. Annals of internal medicine. 1972 Jul 1;77(1):77-82.

3. Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. N Engl J Med 2009; 361:62–72.

4. Park YM, White AJ, Nichols HB, O'Brien KM, Weinberg CR, Sandler DP. The association between metabolic health, obesity phenotype and the risk of breast cancer. International journal of cancer. 2017 Jun 15;140(12):2657-66.

5. Tolone S, Pilone V, Musella M, Rossetti G, Milone M, Fei L, *et al*. Rhabdomyolysis after bariatric surgery: a multicenter, prospective study on incidence, risk factors, and therapeutic strategy in a cohort from South Italy. Surgery for Obesity and Related Diseases. 2016 Feb 1;12(2):384-90.

6. Chakravartty S, Sarma DR, Patel AG. Rhabdomyolysis in bariatric surgery: a systematic review. Obes Surg 2013; 23:1333–1340.

7. Forestieri P, Formato A, Pilone V, Romano A, Monda A, Tramontano S. Rhabdomyolysis after sleeve gastrectomy: increase in muscle enzymes does not predict fatal outcome. Obesity surgery. 2008 Mar;18:349-51.

8. Faintuch J, de Cleva R, Pajecki D, Garrido Jr AB, Cecconello I. Rhabdomyolysis after gastric bypass: severity and outcome patterns. Obesity surgery. 2006 Sep;16(9):1209-13.

9. Youssef T, Abd-Elaal I, Zakaria G, Hasheesh M. Bariatric surgery: rhabdomyolysis after open Roux-en-Y gastric bypass: a prospective study. International Journal of Surgery. 2010 Jan 1;8(6):484-8.

10. Oliveira LD, Diniz MT, Diniz MD, Savassi-Rocha AL, Camargos ST, Cardoso F. Rhabdomyolysis after bariatric surgery by Roux-en-Y gastric bypass: a prospective study. Obesity surgery. 2009 Aug; 19:1102-7.

11. Moulla Y, Lyros O, Adolf D, Kaiser T, Dietrich A. A nomogram based on clinical factors to predict the serum myoglobin levels following bariatric surgery. Obesity Surgery. 2018 Jun;28:1697-703.

12. Grammer R, Wang J, Lahey E. Rhabdomyolysis after prolonged surgery: report of 2 cases and review of literature. J Oral Maxillofac Surg 2018; 76:1424–1430.

13. Poli D, Gemma M, Cozzi S, Lugani D, Germagnoli L, Beretta L. Muscle enzyme elevation after elective neurosurgery. European journal of anaesthesiology. 2007 Jun;24(6):551-5.

14. Kasaoka S, Todani M, Kaneko T, Kawamura Y, Oda Y, Tsuruta R, Maekawa T. Peak value of blood myoglobin predicts acute renal failure induced by rhabdomyolysis. Journal of critical care. 2010 Dec 1;25(4):601-4.

15. Ettinger JE, Marcílio de Souza CA, Ázaro E, Mello CA, Santos-Filho PV, Orrico J, *et al*. Clinical features of rhabdomyolysis after open and laparoscopic roux-en-Y gastric bypass. Obesity surgery. 2008 Jun;18:635-43.