

# Reduction of the risk of rhabdomyolysis after bariatric surgery with lower fluid administration in the perioperative period: a cohort study

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## KEY WORDS

fluid management,  
metabolic surgery  
complications,  
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## ABSTRACT

**INTRODUCTION** Obesity is a growing worldwide problem. One of the most effective treatments is a bariatric procedure; however, surgery is associated with the risk of complications, such as staple line leakage, suture line bleeding, and rhabdomyolysis (RML).

**OBJECTIVES** The objective of our study was to assess the risk of RML after bariatric surgery related to intravenous fluid administration in the perioperative period.

**PATIENTS AND METHODS** The study involved 194 patients who underwent a bariatric surgery (laparoscopic sleeve gastrectomy or laparoscopic gastric bypass). We studied an association between the development of RML and sex, age, weight, duration of surgery, type of surgery, and the volume of intravenously administered fluids during the perioperative period.

**RESULTS** The median duration of surgery was 132.5 minutes. The median volume of administered fluids was 3150 ml from the introduction of anesthesia to 24 hours after surgery. Biochemical RML (creatinine phosphokinase >1000 U/l) was observed in 30 patients (15.46%). RML with clinical manifestations developed in 6 patients. Multivariate logistic regression revealed an increase in the odds ratio of biochemical RML with an increase of weight on the day of surgery, operative time, and volume of intravenous fluids. A multiple regression model showed that every 500 ml of transfused fluid over the median volume increases creatine phosphokinase concentrations in the first postoperative day by 241.77 U/l over the median level, with the operative time and patient's weight remaining at median values.

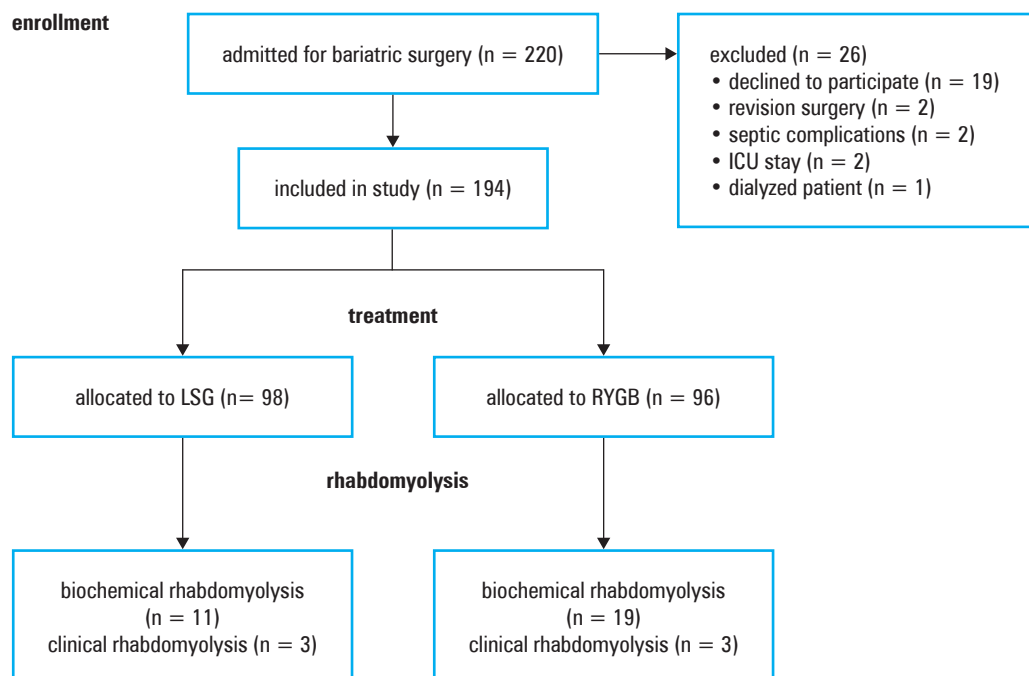
**CONCLUSIONS** We observed an association between the administration of lower fluid volumes and a lower risk of RML. We postulate that decreasing intravenous fluid administration may reduce the risk of RML after bariatric surgery.

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**INTRODUCTION** The prevalence of obesity and its health care burden have been increasing rapidly. Given the absence of effective methods for conservative treatment of obesity, the number of bariatric surgery operations performed in Poland and Europe is growing every year. Every surgical intervention unavoidably entails the risk of complications in the perioperative period. The most

common complications of bariatric surgery include staple line leakage, suture line bleeding, episodes of pulmonary embolism, and infection of the surgical site. Another potentially life-threatening complication of bariatric surgery is rhabdomyolysis (RML).<sup>1</sup> In most cases, RML proceeds subclinically and is identified on the basis of increased blood levels of myoglobin and enzymes

**FIGURE 1** Flowchart of study patients  
Abbreviations: ICU, intensive care unit; LSG, laparoscopic sleeve gastrectomy; RYGB, Roux-en-Y gastric bypass



**TABLE 1** Characteristics of the patients

| Parameter                                        | Value               |
|--------------------------------------------------|---------------------|
| age, mean $\pm$ SD                               | 42.32 $\pm$ 11.30   |
| sex, n (%)                                       |                     |
| female                                           | 122 (63)            |
| male                                             | 72 (37)             |
| height, cm                                       | 169 (165–176)       |
| max body weight, kg                              | 136 (122–155)       |
| max BMI, kg/m <sup>2</sup>                       | 46.61 (43.03–52.42) |
| preoperative BMI, kg/m <sup>2</sup>              | 45.27 (41.53–50.31) |
| preoperative body weight loss, kg/m <sup>2</sup> | 4 (0–8)             |
| preoperative body weight, kg                     | 130 (115–150)       |

Data are presented as median (interquartile range) unless otherwise stated.

Abbreviations: BMI, body mass index

released by the injured muscles. Spilled myocyte damage manifests with weakening and pain of the affected muscles and occasionally also with their swelling. In severe cases, hypovolemia may occur due to sequestration of water in the injured muscles. Without proper treatment, RML can lead to acute renal failure, respiratory failure, and disseminated intravascular coagulation. Given the presence of a number of perioperative risks in bariatric patients (long surgery duration, obesity, type 2 diabetes, hypertension, drugs used during anesthesia), RML may be an important clinical problem in this particular group.

We studied the development of RML, diagnosed defined as serum creatine phosphokinase (CPK) levels exceeded 1000 U/l, among patients undergoing bariatric surgery. We also examined the association of RML with several factors including sex, age, weight, surgery duration, type of surgery, occurrence of sleep apnea, and volume

of intravenously administered fluids during the perioperative period (from the introduction of anesthesia to 24 hours after surgery).

**PATIENTS AND METHODS** It was a prospective cohort study. Participants were recruited among patients operated for morbid obesity at the 2nd Department of General Surgery, Jagiellonian University Medical College in Kraków, Poland. The inclusion criteria were as follows: age, 18–65 years; body mass index (BMI), >40 kg/m<sup>2</sup> or >35 kg/m<sup>2</sup> if obesity-related comorbidities were present (such as type 2 diabetes mellitus, arterial hypertension, dyslipidemia, obstructive sleep apnea); and a scheduled laparoscopic sleeve gastrectomy (LSG) or laparoscopic Roux-en-Y gastric bypass (RYGB) surgery. We excluded patients who had revision surgery, were on dialysis, required treatment at the intensive care unit, developed septic complications, or were diagnosed with mental illness or with drug or alcohol addiction. Patients' flow through the study is illustrated in **FIGURE 1**.

The study included 194 consecutive patients (122 women, 72 men) operated between January 2010 and August 2014. Detailed demographic characteristics of the group are presented in **TABLE 1**. We performed 98 LSG (50.52%) and 96 laparoscopic RYGB (49.48%).

The most frequent comorbidities were respiratory disorders, present in 44 of the 194 operated patients (22.34%). Among them, the most common were sleep apnea (25 patients), chronic obstructive pulmonary disease (5 patients), asthma (3 patients), and other conditions (11 patients).

All procedures involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by an institutional

**TABLE 2** Univariate logistic regression analyses of parameters with a possible effect on the odds ratio of rhabdomyolysis

| Parameter                                                          |        | RML                 | No RML              | OR   | CI        | P value |
|--------------------------------------------------------------------|--------|---------------------|---------------------|------|-----------|---------|
| sex, n (%)                                                         | male   | 16 (53.33)          | 56 (34.15)          | 0.45 | 0.16–1.31 | 0.142   |
|                                                                    | female | 14 (46.67)          | 108 (65.85)         |      |           |         |
| sleep apnea syndrome, n (%)                                        | yes    | 11 (36.67)          | 14 (8.54)           | 0.99 | 0.11–8.83 | 0.687   |
|                                                                    | no     | 19 (63.33)          | 153 (91.46)         |      |           |         |
| type of surgery, n (%)                                             | RYGB   | 19 (63.33)          | 77 (46.95)          | 0.51 | 0.19–1.36 | 0.179   |
|                                                                    | LSG    | 11 (36.67)          | 87 (53.05)          |      |           |         |
| age, y, mean $\pm$ SD                                              |        | 46.40 $\pm$ 10.00   | 41.57 $\pm$ 11.40   | 1.04 | 1.00–1.08 | 0.035   |
| maximum weight, kg                                                 |        | 150.5 (130–163)     | 134.0 (120–153)     | 1.02 | 1.00–1.04 | 0.011   |
| maximum BMI, kg/m <sup>2</sup>                                     |        | 48.31 (44.57–54.08) | 46.41 (42.87–51.90) | 1.03 | 0.98–1.09 | 0.252   |
| preoperative weight loss, kg                                       |        | 3.25 (0–7)          | 4 (0–8)             | 0.98 | 0.93–1.04 | 0.59    |
| BMI on the day of surgery, kg/m <sup>2</sup>                       |        | 48.17 (43.36–53.41) | 45.18 (41.45–50.12) | 1.05 | 0.99–1.12 | 0.11    |
| weight on the day of surgery, kg                                   |        | 146 (127–158)       | 128 (114–147)       | 1.02 | 1.01–1.04 | 0.005   |
| procedure time, min                                                |        | 180 (150–220)       | 120 (100–160)       | 1.02 | 1.01–1.03 | <0.001  |
| volume of fluids administered intravenously, No. of 500 ml bottles |        | 7.5 (5–10)          | 6 (4–8)             | 1.14 | 1.01–1.30 | 0.03    |

P value of less than 0.05 is considered statistically significant.

Data are presented as median (interquartile range) unless otherwise stated.

Abbreviations: CI, coincidence interval; OR, odds ratio; RML, rhabdomyolysis; others: see [TABLE 1](#) and [FIGURE 1](#)

review board of Jagiellonian University, and all patients were informed about the objectives and aims of the study and gave written consent to participate in the study.

**Surgical procedures** The LSG was performed in a routine way with Echelon Flex® staplers (Ethicon Company, Cornelia, Georgia, United States). The entire length of the staple line was additionally secured with 2 Ethicon PDS® 3.0 continuous monofilament sutures on the serous membrane.

The laparoscopic RYGB was performed in a routine way. Anastomosis of the gastric pouch with the Roux limb was performed with a ligating and dividing linear stapler (Ethicon 45-mm Echelon-Flex® stapler, using a 1.5-mm cartridge), closing the site of its introduction with an Ethicon continuous Vicryl® 3–0 suture on a 26 needle.

The duration of surgery was measured from the time of skin incision in the first trocar site until the last suture.

**Anesthesia** Two hours prior to the start of anesthesia, patients were given orally 400 ml of high carbohydrate content fluid (PreOp® Nutricia; Nutricia Polska, Warsaw, Poland).

As prophylaxis for venous thromboembolism, enoxaparin was administered subcutaneously 2 hours before surgery at the recommended dose of 40 mg. At the time of induction of anesthesia, patients were given a prophylactic dose of antibiotic (ceftriaxone, 2 g IV) and 40 mg of pantoprazole.

During surgery, patients received general anesthesia with sevoflurane inhalation in a controlled variable flow in a closed anesthetic system at low and very low flow rates. The sedative drugs used during anesthesia were short-acting

benzodiazepines (midazolam). A nondepolarizing drug, cisatracurium, was used for muscle relaxation. During anesthesia, the heart rate was monitored by means of electrocardiography; oxygen saturation, by pulse oximetry; blood pressure, using noninvasive periodic measurements; the concentration of anesthetic gases and carbon dioxide in the closed system, using biochemical analyzers and a capnograph; and the depth of relaxation, by means of an objective system used for quantitative monitoring of neuromuscular transmission. At the end of the surgery, a transverse abdominis plane block was performed.

**Laboratory measurements** Twenty-four hours after the surgery, blood samples were collected from patients for laboratory testing. CPK levels were measured using the kinetic method (creatinine phosphate/ADP – NAC accelerator). The reference value was 165 U/l. All laboratory measurements were performed at the Department of Laboratory Diagnostics of the University Hospital in Kraków.

**Statistical analysis** A statistical analysis was performed using the Statsoft Statistica 10.0 PL software (StatSoft Inc., Tulsa, Oklahoma, United States). The results were presented as medians with interquartile ranges unless otherwise stated. Qualitative and quantitative variables were analyzed in univariate and multivariate logistic regression analyses. For the analysis of quantitative variables, we used the Spearman's rank correlation coefficient, linear regression model, and multiple regression analysis. The level of statistical significance was set at a P value of less than 0.05.

**RESULTS** The median duration of surgery was 132.5 minutes (range, 100–170 minutes). The

**TABLE 3** Multivariate logistic regression analysis of parameters affecting the odds ratio of rhabdomyolysis

| Parameter                                   | OR   | CI        | P value |
|---------------------------------------------|------|-----------|---------|
| age                                         | 1.03 | 0.99–1.08 | 0.125   |
| weight on the day of surgery                | 1.03 | 1.01–1.05 | 0.003   |
| procedure time                              | 1.02 | 1.01–1.03 | <0.001  |
| volume of fluids administered intravenously | 1.11 | 1.00–1.29 | 0.012   |

P value of less than 0.05 is considered statistically significant.

Abbreviations: see [TABLE 2](#)

**TABLE 4** Factors increasing creatine phosphokinase (CPK) levels: multiple regression model

| Factor                                                 | Volume of fluids administered intravenously | Weight on the day of the surgery | Procedure time |
|--------------------------------------------------------|---------------------------------------------|----------------------------------|----------------|
| median                                                 | 3150 ml                                     | 130 kg                           | 132.5 min      |
| factor value increased by                              | +500 ml                                     | +10 kg                           | +10 min        |
| predicted increase in CPK levels over the median level | 241.77 U/l                                  | 249.07 U/l                       | 144.16 U/l     |

median volume of fluids administered during the period from the time of anesthesia induction until the end of the first postoperative day was 3150 ml (range, 2150–4000 ml). The median time for starting full oral fluid intake after surgery was 23 hours after surgery (range, 16–38 hours).

Biochemical RML, defined as CPK levels exceeding 1000 U/l, was diagnosed in 30 of 194 patients (15.46%), of whom 11 underwent LSG (36.67%) and 19 underwent RYGB (63.33%). RML with clinical manifestations of musculoskeletal pain developed in 6 of 194 patients (3.09%), of whom 3 underwent LSG and 3 underwent RYGB. All patients maintained proper diuresis on the day of surgery.

The median length of the hospitalization was 3 days for patients without biochemical characteristics of RML, 4 days for patients with biochemical RML, and 6 days for those with clinical RML.

The results of the univariate logistic regression analyses are presented in [TABLE 2](#). Age (odds ratio [OR], 1.04; confidence interval [CI], 1.00–1.08), maximum preoperative weight (OR, 1.02; CI, 1.00–1.04), weight on the day of surgery (OR, 1.02; CI, 1.01–1.04), procedure time (OR, 1.02; CI, 1.01–1.03), and the volume of fluids administered intravenously during the surgery and 1 day after the surgery (OR, 1.14; CI, 1.01–1.30) showed a significant association with an increase in the OR of RML in the perioperative period. To enable the analysis of fluid volume, this parameter was converted to the number of 500-ml bottles. Patients' sex, concomitant obstructive sleep apnea syndrome, type of surgery (RYGB vs LSG), preoperative weight loss, as well as the maximum preoperative BMI and a BMI on the day of surgery were not significant factors in the univariate logistic regression model.

Afterwards, parameters found to be significant in univariate analyses were included in the multivariate logistic regression analysis ([TABLE 3](#)). Weight on the day of surgery (OR, 1.03; CI, 1.01–1.05), procedure time (OR, 1.02; CI, 1.01–1.03), and volume of fluids administered intravenously (OR, 1.11; CI, 1.00–1.29) were independent factors increasing the OR of RML. The maximum preoperative weight contributed significantly to an increase in the OR of RML, but it was strongly associated with the weight on the day of surgery and contributed to a lesser extent in the multivariate regression analysis. Finally, the maximum preoperative weight was excluded from the multivariate analysis. Age, considered as a significant factor in the univariate analysis, was found not to be significant in the multivariate logistic regression analysis.

Next, we conducted a linear regression analysis to determine correlations between quantitative parameters and CPK levels. The analysis revealed significant correlations of height, weight, maximum preoperative BMI, and BMI on the day of surgery with CPK levels. The Spearman's rank correlation coefficients revealed interrelations between height, the maximum preoperative BMI, and BMI on the day of surgery. Neither the duration of the procedure nor the volume of fluids administered intravenously was correlated with height, maximal preoperative weight, weight on the day of surgery, maximal preoperative BMI, and BMI on the day of surgery.

Using a multiple regression model (adjusted R<sup>2</sup>, 22.12%; P < 0.001), we determined a significant prognostic influence of the weight on the day of surgery, duration of surgery, and fluids administered intravenously on an increase in CPK levels (used here as a marker of the development of RML). As presented in [TABLE 4](#), we predicted that every 500 ml of transfused fluid over the median fluid volume resulted in an increase in CPK levels in the first postoperative day by 241.77 U/l over median CPK levels, while maintaining the 2 other factors at median values. Considering the effect of weight on the day of surgery, any 10 kg more over the median weight resulted in an increase in CPK levels by 249.07 U/l over the median CPK level, while maintaining the 2 other factors at median values. The extension of surgery duration by 10 minutes over the median surgery time resulted in an increase in CPK levels in the first postoperative day by 144.16 U/l over the median CPK levels.

**DISCUSSION** Although there have been several reports describing RML as a complication of bariatric procedures, most of them are old and include patients in whom gastric bypass procedures were performed with a classic open surgery. We identified only 6 papers on RML as a complication of LSG, of which 4 were case studies.<sup>2-7</sup> For patients who underwent LSG, this complication received even less attention from bariatric surgeons—we identified only 2 case reports on this

topic.<sup>8-9</sup> As a result, our prospective cohort study includes one of the largest group of such patients: 98 patients who underwent LSG and 96 patients who underwent RYGB.

RML develops more frequently in patients with a higher body weight and BMI, as documented by numerous studies.<sup>5,10,11</sup> We also observed that weight on the day of surgery contributes to an increase in the OR of RML by 3% with every kilogram over the median value and is an independent factor increasing CPK levels.

The duration of the surgical procedure is another independent risk factor for the development of RML, and one that can be directly affected by the surgical environment. Virtually every publication on the risk of developing RML has shown that an increase in the duration of the procedure increases the risk of developing the complication. In this respect, our results are not surprising.<sup>4,7,12</sup>

A particularly interesting aspect of research on RML is focused on the association between the volume of fluid administered to patients and the risk of developing the condition. Since RML was first described during the Second World War, high fluid intake was seen as a way to treat patients with the condition. Numerous surgeons also came to believe that large intravenous fluid intake could protect against the development of RML. So far, only Wool et al,<sup>2</sup> in a study on perioperative intravenous fluid treatment, argued that increasing the volume of perioperative intravenous fluids did not reduce the risk of RML. The analysis of the volume of fluids administered intravenously from the induction of anesthesia, through surgery, perioperative period, to 24 hours after surgery showed that in the group of patients who developed RML, the median administered fluid volume was 3750 ml, compared with 3000 ml for the group who did not develop the condition. Every 500 ml above the median resulted in an increase in the OR of RML by 11%. Moreover, using the multiple regression analysis, we estimated that every 500 ml of fluid administered over the median fluid volume, when procedure time and weight remained at median levels in the model, resulted in an increase in CPK levels by 241.77 U/l over median CPK levels on the first postoperative day. However, due to the lack of similar analyses performed by other researchers, we cannot confirm this finding.

We did not observe significant differences in the development of RML between patients who underwent LSG and those who underwent laparoscopic RYGB. However, again we are unable to compare these results to those made by other researchers because, to the best of our knowledge, no such comparisons have been reported in the literature.

**Contribution statement** MM was responsible for study design and data interpretation. P. Major, LH, MN, and MP were responsible for data collection and interpretation. P. Malczak was responsible for data collection, data analysis, and final

revision of the manuscript. MW was responsible for statistical analysis. KK was responsible for study design and final revision of the manuscript. AB was responsible for drafting and critical revision of the manuscript.

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# Zmniejszenie ryzyka rhabdomyolizy po zabiegu bariatrycznym przy mniejszej podaży płynów w okresie okołoperacyjnym – badanie kohortowe

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## SŁOWA KLUCZOWE

płynoterapia,  
powikłania chirurgii  
metabolicznej,  
rhabdomyoliza

## STRESZCZENIE

**WPROWADZENIE** Otyłość jest rosnącym problemem na światową skalę. Jedną z najskuteczniejszych metod leczenia jest zabieg bariatryczny, z operacją związane jest jednak ryzyko powikłań takich jak przeciek z linii cięcia staplerem, krwawienie z linii szycia oraz rhabdomyoliza (RML).

**CELE** Celem naszej pracy była ocena ryzyka RML po zabiegach bariatrycznych w powiązaniu z podażą płynów w okresie okołoperacyjnym.

**PACJENCI I METODY** W badaniu wzięło udział 194 pacjentów, u których wykonano operację bariatryczną (laparoskopową rękawową resekcję żołądka lub laparoskopowe wyłączenie żołądkowe). Zbadaliśmy powiązanie rozwoju RML z płcią, wiekiem, wagą, długością operacji, typem zabiegu oraz objętością płynów podanych dożylnie w okresie okołoperacyjnym.

**WYNIKI** Mediana długości zabiegu wynosiła 132,5 minut. Mediana objętości podanych płynów wynosiła 3150 ml w okresie od znieczulenia pacjenta do 24 godzin po zabiegu. RML biochemiczna (poziom fosfatazy kreatynowej > 1000 U/l) wystąpiła u 30 pacjentów (15,46%). RML z objawami klinicznymi wystąpiła u 6 pacjentów. Wieloczynnikowa regresja logistyczna wykazała wzrost ilorazu szans RML biochemicznej wraz ze wzrostem wagi w dniu zabiegu, długości zabiegu oraz objętości płynów podanych dożylnie. Model regresji wielorakiej wykazał, że każde 500 ml płynów podanych powyżej poziomu mediany płynów zwiększa stężenie fosfatazy kreatynowej w 1. dniu po zabiegu o 241,77 U/l powyżej przeciętnego poziomu, przy wartościach czasu zabiegu i wagi pacjenta na poziomie median.

**WNIOSKI** Zaobserwowaliśmy związek między niższą podażą płynów a mniejszym ryzykiem wystąpienia RML. Postulujemy, że obniżenie dożylnej podaży płynów zmniejsza ryzyko RML po zabiegu bariatrycznym.

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