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Research Article

Effects of Liberal Versus Restrictive Fluid Therapy on Renal Function Indices in Laparoscopic Bariatric Surgery

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Abstract

Background: Earlier studies have suggested the liberal administration of fluids in favor of reducing the risk of rhabdomyolysis in obese patients, but the results are conflicting.
Objectives: The present study aimed at comparing the effects of liberal and restrictive fluid therapy on renal indices in laparoscopic gastric bypass surgery.
Methods: In a double-blinded randomized clinical trial, 72 candidates of bariatric surgery were randomly assigned into two groups of restrictive and liberal fluid therapy. Indices, including BUN, creatinine, creatine kinase, GFR, and urine output were measured before and 24 hours after the surgery. The clinical trial was registered at IRCT.ir under code IRCT20170109031852N3.
Results: There was no significant difference in BUN, creatinine, creatinine kinase, and GFR indices between the two groups of liberal and restrictive fluid therapy both before and 24 hours after surgery ($P > 0.05$). Intragroup comparisons before and after surgery revealed that BUN decreased in both groups after the surgery ($P < 0.05$). Also, creatinine and GFR values improved in patients who received a liberal fluid regimen, whereas these indices remained statistically unchanged in the restrictive group before and 24 hours after the surgery ($P > 0.05$).
Conclusions: Two methods of liberal and restrictive fluid therapy have comparable effects on traditional renal functional indices in laparoscopic bariatric surgery. The clinical significance of observed differences in outcomes should be investigated in further studies. The use of early biomarkers of acute kidney injury is warranted.

Keywords: Fluid Therapy, Surgery, Gastric Bypass, Renal Function, Creatinine

1. Background

Liberal infusion of intravenous (IV) fluids, whether in the form of a crystalloid solution or colloid-crystalloid combination, is usually taken into consideration in major surgeries (1). Nonetheless, studies on the effects of IV fluid infusion are limited to complications after the surgery, in which the protocols have challenged the prescription of liberal IV fluids and led to the design and implementation of various studies on the superiority of prescribing a restrictive volume of fluids over liberal fluids (2, 3). An earlier review study suggested that high volumes of fluids are accompanied by an increased risk of postoperative complications such as respiratory, cardiac, and even renal failures (4). It seems that the restriction of fluids reduces cell damage processes such as oxidative stress, by modulating the level of cell oxygenation (5, 6).

The level of tissue oxygenation is directly affected by the cardiac output and the volume of circulating fluid, keeping in mind that the excessive increase of fluid in circulation will apply extra cardiac loads (7, 8). In general, the strategy of substituting the restrictive volume of fluids is acceptable for certain surgeries (9, 10). Monitoring the renal function while maintaining the cardiac output will help find the optimum strategy of intraoperative fluid therapy.

2. Objectives

This study was conducted to evaluate the effects of restrictive versus liberal fluid administration on the renal function of patients in laparoscopic gastric bypass surgery.

3. Methods

In a double-blinded randomized clinical trial, 72 adult candidates of laparoscopic bariatric surgery (Roux-en-Y Gastric Bypass (RYGB) or Sleeve gastrectomy (SG)) with a BMI of more than 40 were recruited. The exclusion criteria included a history of renal disease, a history of cardiopulmonary disease, and the use of diuretics. The participants were randomly assigned into two groups of restrictive or liberal fluid therapy. Block randomization was used to assign an equal number of patients to each group. Both patients and the outcome assessor were blinded to the assignments. The local ethics committee approved the study protocol, and informed consent was obtained from all patients. The clinical trial was registered under the code of IRCT20170109031852N3.

Standard monitoring was implemented. In the restrictive group, half of the fluid deficit up to 500 ml was infused at preinduction, and total maintenance fluid according to the 1-2-4 formula was infused hourly, without substitution of third space. Blood loss was replaced with crystalloids in a 3:1 ratio up to the allowable blood loss (ABL). In the liberal group, 5 mL/kg of crystalloids were infused for volume expansion before anesthesia induction. Half of the estimated volume deficit was delivered in the first hour and the rest in the second and third hours of the surgery according to the 1-2-4 formula. The third-space losses were replaced by 3 mL/kg and blood loss with three times of crystalloids up to the ABL. All patients in both groups received Ringer's lactate and normal saline solutions sequentially with a 1:1 ratio.

The anesthesia protocol in both groups was identical with midazolam 2 mg, fentanyl 2 μg/kg, and lidocaine 1 mg/kg as premedication, and propofol 2 mg/kg and atracurium 0.5 mg/kg for induction. Anesthesia was maintained with isoflurane 0.8 - 1.5%, fentanyl, and atracurium with BIS values in the range of 40 - 60. Drops in blood pressure were treated with the least effective doses of ephedrine. High blood pressures were controlled with incremental doses of labetalol. Blood samples were taken one hour before and 24 hours after the surgery, and renal function indices, including BUN, creatinine, creatine kinase, and GFR, were evaluated. Urinary catheterization with single-use Nelaton was performed for patients before awakening at the end of surgery, and urine volume was measured.

The sample size was calculated based on the standard formula to estimate the difference in means between two independent populations, where α = 0.05, β = 0.2, and the s1 and s2 were considered to be 0.1 and 0.2, respectively, for creatinine values. The estimated required sample size in each group was 36 participants. The normality of quantitative variables was assessed with the Kolmogorov-Smirnov test. The Student *t* test was used to compare quantitative variables and the chi-square test to compare nominal variables between the two groups. A paired *t* test was used for within-group analyses of quantitative variables. All comparisons were two-tailed. The P-values of < 0.05 were considered statistically significant. Statistical analyses were performed with SPSS version 22.0 software (SPSS, Inc., Chicago, IL, USA).

4. Results

The demographic variables, type, and duration of surgery were comparable between the two groups (Table 1). Inter-group comparisons showed no significant difference in BUN, creatinine, creatine kinase, and GFR both before and after the surgery ($P > 0.05$). However, intragroup comparisons showed significant differences before and after the surgery in both groups (Table 2). BUN, creatinine, and GFR in the liberal fluid group showed significant differences before and after the surgery ($P < 0.05$). Similarly, BUN decreased after the surgery in patients who received restrictive fluid ($P < 0.05$). The volume of crystalloid infusion was 1824 $\pm$ 310 ml in the liberal group and 746 $\pm$ 127 ml in the restrictive group. The intraoperative urine volume was 305 $\pm$ 39 mL in the liberal fluid group and 116 $\pm$ 42 ml in the restrictive fluid group ($P = 0.25$).

5. Discussion

The two groups were comparable in terms of age, gender, height, and BMI, and these confounding factors were unlikely to affect the results. In inter-group comparisons, there was no significant difference in BUN, creatinine, creatine kinase, and GFR between patients receiving restrictive or liberal fluid before and after the surgery. In addition, only BUN decreased after the surgery in both groups, which could be a dilutional effect, and lower indices of BUN and creatinine and a higher GFR index in the liberal fluid therapy group than in the restrictive group could be due to the difference in the volume loading of patients. Therefore, it seems that the two methods of liberal and restrictive fluid therapy have comparable effects on traditional kidney function indices in laparoscopic bariatric surgery, keeping in mind that this study could not investigate the clinical significance of the modest observed statistical differences.

The safety of limited volume treatment fluid has been challenging for physicians over the last years. Their main concern is the potential of hypovolemia and organ dysfunction after the surgery, such that acute renal injury is

Table 1. Demographic and Baseline Variables in Two Groups[a]

Variable	Fluid Regimen		P Value
	Liberal (N = 36)	Restrictive (N = 36)	
Age (years)	38 ± 10	38 ± 9	0. 92
Male Sex, No. (%)	13 (36.1)	12 (33.3)	0.97
Height (cm)	182 ± 24	175 ± 15	0.28
BMI (kg/m²)	40.1 ± 3.3	40.9 ± 2.3	0.29
Type of surgery			0.87
Roux-en-Y Gastric Bypass	24 (66.6)	22 (61.1)	
Sleeve gastrectomy	12 (33.3)	14 (38.8)	
Duration of surgery (min)	114 (28)	108 (19)	0.46

[a] Data are presented as mean (SD).

Table 2. Renal Function Indices in Two Groups Before and After Surgery

Variable/Time	Fluid Regimen		P Value[a]
	Liberal (N = 36)	Restrictive (N = 36)	
BUN			
Before surgery	28.3 ± 9.8	27.6 ± 9.5	0.07
After surgery	24.8 ± 9.4	24.3 ± 6.2	0.8
P value[b]	0.01	0.045	
Creatinine			
Before surgery	0.95 ± 0.24	0.91 ± 0.17	0. 24
After surgery	0.88 ± 0.16	0.9 ± 0.12	0.29
P value	0.001	0.88	
Creatine kinase			
Before surgery	185 ± 108	186 ± 107	0. 98
After surgery	165 ± 86	191 ± 114	0.47
P value	0.18	0.39	
GFR			
Before surgery	179 ± 64	179 ± 39	0. 54
After surgery	192 ± 63	178 ± 43	0.23
P value	0.01	0.58	

[a] P value: intergroup comparisons.
[b] P value: intragroup comparisons before and after surgery.

the main concern. Systematic reviews suggest that the liberal fluid regimen may result in extra-vascular losses and end-organ damages, namely kidney injuries. Thus, the restrictive fluid regimen, together with individualized goal-directed colloid administration to maintain a maximal stroke volume, could be the optimal strategy (3). However, there are limited studies so far on the comparison of the effects of liberal and restrictive fluid on renal function indices in laparoscopic gastric bypass surgery. An earlier study reported no difference in the creatinine level of patients suffering from early respiratory and renal failures during major abdominal surgeries between the two groups of limited (5 mL/kg/h) and free (10 mL/kg/h) volumes of fluid therapy (7). In a more recent study, the rate of acute kidney injury (AKI) was higher after the surgery in patients undergoing major abdominal surgeries who had received limited volumes of fluid than in those who were on a more liberal fluid regimen. This inconsistency might be due to the prescription method of the treatment fluid and the surgical method applied to patients in the two studies (11). Neutral findings in renal complications after abdominal surgeries between patients receiving liberal and restrictive regimens have been reported in meta-analysis and clinical trials, as well (10, 12-14).

Renal blood flow, GFR, and urine output will decrease in laparoscopic surgeries due to increased intra-abdominal pressure. Therefore, the monitoring of urine output for the adequacy of hydration could be misleading. Obesity makes this index more challenging. Serial serum creatinine measurements are most often used to detect acute kidney injury. However, there is a delay between the onset of kidney injury and the rise in serum creatinine levels. Several novel markers for the early detection of AKI have been introduced. Of those, cystatin C, β-trace protein, and β-2 microglobulin are used to detect filtration-based renal dysfunction (15-17). As a limitation of this study, the early markers of AKI were not available, and we did not measure serum and plasma osmolality as a marker of hydration status.

Finally, it seems that the two regimens of liberal and restrictive fluid therapy have comparable effects on traditional renal function indices, including BUN, creatinine, creatine kinase, and GFR in laparoscopic bariatric surgery. The clinical significance of observed differences in the outcome should be investigated in further studies. Avoidance of excessive crystalloids and goal-directed fluid therapy may decrease the cardiac load and reasonably reduce the damage to end-organs, such as the renal system (18-20). Further studies with the early biomarkers of AKI are warranted.

Footnotes

Authors' Contribution: Study concept and design: Alimian, Mahzad and Mohseni, Masood; Analysis and interpretation of data: Omid Moradi Moghadam and Seyed Alireza Seyed Siamdoust; Drafting of the manuscript: Moazzami, Javad.

Clinical Trial Registration Code: IRCT20170109031852N3.

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References

1. Banz VM, Jakob SM, Inderbitzin D. Review article: improving outcome after major surgery: pathophysiological considerations. *Anesth Analg*. 2011;**112**(5):1147–55. doi: 10.1213/ANE.0b013e3181ed114e. [PubMed: 20736438].
2. Kehlet H. [Principles of fast track surgery. Multimodal perioperative therapy programme]. *Chirurg*. 2009;**80**(8):687–9. doi: 10.1007/s00104-009-1675-2. [PubMed: 19669716].
3. Bundgaard-Nielsen M, Secher NH, Kehlet H. 'Liberal' vs. 'restrictive' perioperative fluid therapy–a critical assessment of the evidence. *Acta Anaesthesiol Scand*. 2009;**53**(7):843–51. doi: 10.1111/j.1399-6576.2009.02029.x. [PubMed: 19519723].
4. Holte K, Foss NB, Andersen J, Valentiner L, Lund C, Bie P, et al. Liberal or restrictive fluid administration in fast-track colonic surgery: a randomized, double-blind study. *Br J Anaesth*. 2007;**99**(4):500–8. doi: 10.1093/bja/aem211. [PubMed: 17681972].
5. Futier E, Constantin JM, Petit A, Chanques G, Kwiatkowski F, Flamein R, et al. Conservative vs restrictive individualized goal-directed fluid replacement strategy in major abdominal surgery: A prospective randomized trial. *Arch Surg*. 2010;**145**(12):1193–200. doi: 10.1001/archsurg.2010.275. [PubMed: 21173294].
6. Donati A, Loggi S, Preiser JC, Orsetti G, Munch C, Gabbanelli V, et al. Goal-directed intraoperative therapy reduces morbidity and length of hospital stay in high-risk surgical patients. *Chest*. 2007;**132**(6):1817–24. doi: 10.1378/chest.07-0621. [PubMed: 17925428].
7. Sahmeddini MA, Janatmakan F, Khosravi MB, Ghaffaripour S, Eghbal MH, Nickeghbalian S, et al. Restricted crystalloid fluid therapy during orthotopic liver transplant surgery and its effect on respiratory and renal insufficiency in the early post-operative period: A randomized clinical trial. *Int J Organ Transplant Med*. 2014;**5**(3):113–9. [PubMed: 25184031]. [PubMed Central: PMC4149738].
8. Schol PB, Terink IM, Lance MD, Scheepers HC. Liberal or restrictive fluid management during elective surgery: a systematic review and meta-analysis. *J Clin Anesth*. 2016;**35**:26–39. doi: 10.1016/j.jclinane.2016.07.010. [PubMed: 27871539].
9. Jia FJ, Yan QY, Sun Q, Tuxun T, Liu H, Shao L. Liberal versus restrictive fluid management in abdominal surgery: a meta-analysis. *Surg Today*. 2017;**47**(3):344–56. doi: 10.1007/s00595-016-1393-6. [PubMed: 27539606].
10. Pang Q, Liu H, Chen B, Jiang Y. Restrictive and liberal fluid administration in major abdominal surgery. *Saudi Med J*. 2017;**38**(2):123–31. doi: 10.15537/smj.2017.2.15077. [PubMed: 28133683]. [PubMed Central: PMC5329622].
11. Myles PS, Bellomo R, Corcoran T, Forbes A, Peyton P, Story D, et al. Restrictive versus liberal fluid therapy for major abdominal surgery. *N Engl J Med*. 2018;**378**(24):2263–74. doi: 10.1056/NEJMoa1801601. [PubMed: 29742967].
12. Mandee S, Butmangkun W, Aroonpruksakul N, Tantemsapya N, von Bormann B, Suraseranivongse S. Effects of a restrictive fluid regimen in pediatric patients undergoing major abdominal surgery. *Paediatr Anaesth*. 2015;**25**(5):530–7. doi: 10.1111/pan.12589. [PubMed: 25495505].
13. Lobo SM, Ronchi LS, Oliveira NE, Brandao PG, Froes A, Cunrath GS, et al. Restrictive strategy of intraoperative fluid maintenance during optimization of oxygen delivery decreases major complications after high-risk surgery. *Crit Care*. 2011;**15**(5):R226. doi: 10.1186/cc10466. [PubMed: 21943111]. [PubMed Central: PMC3334772].
14. Matot I, Paskaleva R, Eid L, Cohen K, Khalaileh A, Elazary R, et al. Effect of the volume of fluids administered on intraoperative oliguria in laparoscopic bariatric surgery: a randomized controlled trial. *Arch Surg*. 2012;**147**(3):228–34. doi: 10.1001/archsurg.2011.308. [PubMed: 22106246].
15. Adedeji AO, Pourmohamad T, Chen Y, Burkey J, Betts CJ, Bickerton SJ, et al. Investigating the value of urine volume, creatinine, and cystatin c for urinary biomarkers normalization for drug development studies. *Int J Toxicol*. 2019;**38**(1):12–22. doi: 10.1177/1091581818819791. [PubMed: 30673360].

16. Hoste E, Bihorac A, Al-Khafaji A, Ortega LM, Ostermann M, Haase M, et al. Identification and validation of biomarkers of persistent acute kidney injury: the RUBY study. *Intensive Care Med*. 2020;**46**(5):943–53. doi: 10.1007/s00134-019-05919-0. [PubMed: 32025755]. [PubMed Central: PMC7210248].
17. Luft FC. Biomarkers and predicting acute kidney injury. *Acta Physiol*. 2020. doi: 10.1111/apha.13479.
18. Soleimanpour H, Safari S, Sanaie S, Nazari M, Alavian SM. Anesthetic considerations in patients undergoing bariatric surgery: A review article. *Anesth Pain Med*. 2017;**7**(4). e57568. doi: 10.5812/aapm.57568. [PubMed: 29430407]. [PubMed Central: PMC5797674].
19. Hosseinzadeh Maleki M, Derakhshan P, Rahmanian Sharifabad A, Amouzeshi A. Comparing the effects of 5% albumin and 6% hydroxyethyl starch 130/0.4 (voluven) on renal function as priming solutions for cardiopulmonary bypass: A randomized double blind clinical trial. *Anesth Pain Med*. 2016;**6**(1). e30326. doi: 10.5812/aapm.30326. [PubMed: 27110527]. [PubMed Central: PMC4834664].
20. Imani F, Shirani Amniyeh F, Bastan Hagh E, Khajavi MR, Samimi S, Yousefshahi F. Comparison of arterial oxygenation following head-down and head-up laparoscopic surgery. *Anesth Pain Med*. 2017;**7**(6). e58366. doi: 10.5812/aapm.58366. [PubMed: 29696125]. [PubMed Central: PMC5903378].