Original Article

Effect of liberal versus restrictive fluid therapy on intraoperative lactate levels in robot- assisted colorectal surgery

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ABSTRACT

Background and Aims: Minimally invasive and robotic surgeries need lesser fluid replacement but the role of restricted fluids in robotic surgeries other than prostatic surgeries has not been clearly defined. Our primary aim was to evaluate the effects of a restrictive fluid regimen versus a liberal policy on intra-operative lactate in robotic colorectal surgery. Secondary outcomes were need for vasopressors, extubation on table, post-operative renal functions and length of ICU (LOICU) stay. **Methods:** American society of anaesthesiologists (ASA) physical status I–II patients scheduled for robot-assisted colorectal surgery were randomised into one of two groups, receiving either 2 mL/kg/h (Group R) or 4mL/kg/h, (group L). Fluid boluses of 250 ml were administered if mean arterial pressure (MAP) <65 mmHg or urine output <0.5 ml/kg/h. Norepinephrine was added for the blood pressure after 2 fluid boluses. Surgical field was assessed by modified Boezaart's scale and surgeon satisfaction by Likert scale. **Results:** Demographics and baseline renal functions were comparable. Adjusted intra-operative lactate at 2 h, 4 h, and 6 h and need for noradrenaline and post-operative creatinine were similar. One patient in the group L was ventilated due to hypothermia. The field was better at the 4 h in group R and comparable at other time points. The LOICU stay was longer in Group L. **Conclusion:** The use of restrictive fluid strategy of 2 mL/kg/h (group R) does not increase lactate levels or creatinine, improves surgical field at 4 h and shortens ICU stay in comparison to a liberal 4 mL/kg/h (group L) in robotic colorectal surgery.

Key words: Lactate, restrictive fluid therapy, robotic colorectal surgery

INTRODUCTION

Robotic surgery is increasingly replacing open surgery in several specialties by being minimally invasive, offering an increased range of hand motion and improved vision during surgery.[1] Fluid restrictive strategies have a role in robotic urological prostatic surgeries. There is insufficient evidence on the definition of and safety of a restrictive fluid strategy in robotic colorectal surgery, contrary to open surgery,[2] where reductions in complications have been observed.[3] In the absence of clear-cut guidelines on restrictive versus liberal fluids in robotic surgery, we considered 4 mL/kg/h as liberal and 2 mL/kg/h as restrictive in our study group. We proposed to evaluate the impact of a restrictive policy on tissue perfusion as measured by serum lactate levels and renal functions in robotic colorectal surgery.

Our primary outcome was the measurement of lactate at 2 h intervals during surgery. Secondary outcome measures included post-operative renal functions, extubation on table and length of ICU stay (LOICU).

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METHODS

Following Institutional ethics committee approval, fifty five consenting adult patients undergoing elective robotic colorectal surgery were enrolled and forty patients satisfying criteria analysed in a prospective randomised controlled registered trial. (CTRI/2017/10/010169). This study was conducted between October 2017 and November 2018.

Forty adult patients of American Society of Anaesthesiologists (ASA) physical status I and II, aged between 18 and 70 years undergoing elective surgery for primary colorectal malignancies were included [Figure 1]. Patients with ASA status 3 and above, pre operative renal dysfunction, (S. Creatinine >1.6 mg/dL), known hepatic or LV dysfunction (EF <40%) and uncontrolled hypertension (>180/110 mmHg) were excluded.

Pre-operative preparation included bowel preparation 16–20 h prior to the surgery and premedication with tablet alprazolam 0.25 mg and tablet pantoprazole the night prior to surgery. ACE inhibitors and angiotensin receptor blockers were withheld on the night before and on the morning of surgery. On arrival to the operating room (OR), an intravenous (IV) access was obtained and 400–500 mL of balanced salt solution (Kabilyte, FreseniusKabi) was administered as replacement.

Anaesthesia was induced by standard protocols with intravenous midazolam 1–2 mg, fentanyl 2 μg/kg and propofol titrated to loss of verbal response. Airway was secured with succinyl choline or atracurium and maintained with oxygen air mixture and isoflurane at 0.7–1.0 minimum alveolar concentration (MAC). Atracurium was the relaxant of choice. Patients were ventilated in the pressure controlled mode targeting a peak inspiratory pressure less than 35 cm H_20 and end tidal carbon dioxide ($EtCO_2$) between 35 and 40 mm Hg. The intra-abdominal pressure was kept below 14 mm Hg, and patients were placed at steep Trendelenburg with lateral tilt as needed. The choice of analgesia was fentanyl infusion or abdominal wall blocks (transverse abdominus plane and rectus sheath) as per port sites planned or local infiltration with peri-operative boluses of fentanyl as per the discretion of the anaesthesiologist. Central neuraxial blockade that could cause haemodynamic changes influencing fluid management was avoided.

Patients were randomised to one of two groups, computer-generated random number sequence that was placed in opaque envelopes. The liberal fluid group L received 4 mL/kg/h of balanced salt solution (Kabilyte, Fresenius Kabi). Group R the restrictive group received 2 mL/kg/h of the same solution. Rescue

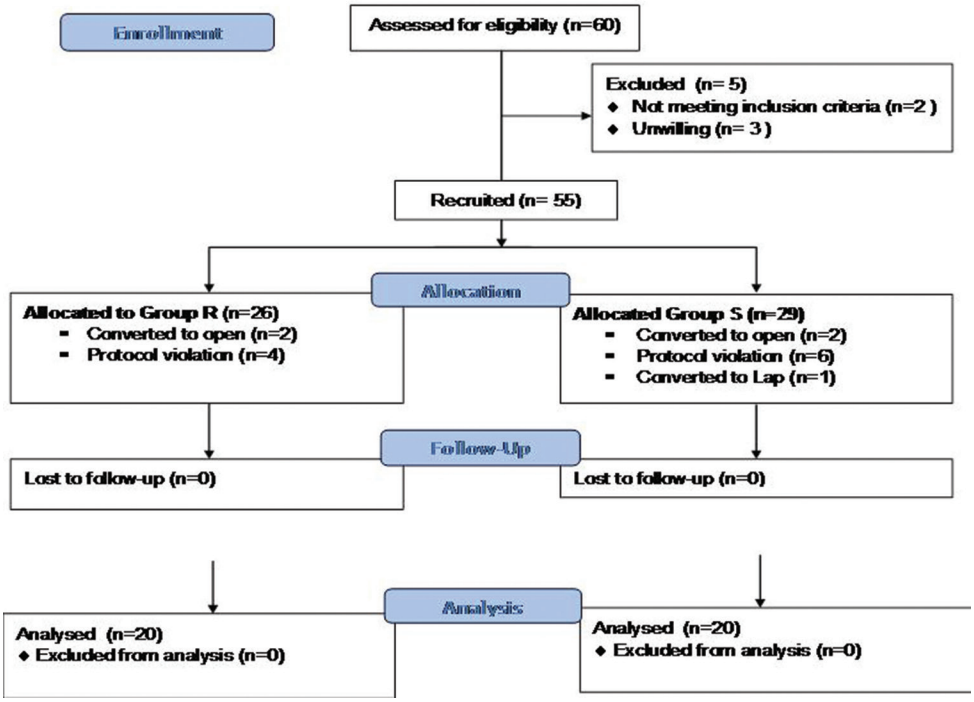

Figure 1: Consort flow diagram

boluses were administered when the mean arterial pressure (MAP) <65 mm Hg, and if no response was seen after 2 boluses over 15 min, noradrenaline infusion was started. Fluid boluses not exceeding two were administered over 15 min if urine output was <0.5 mL/kg/h, and over 30 min if lactate levels were >4.5 mmol/L. Patients were extubated and shifted to the post-operative ICU where they were monitored until shift to the surgical wards. The fluid management in both groups in the ICU was standardised to 2–2.5 L fluid in 24 h.

We also evaluated the $Pa0_2/Fi0_2$(P/F) ratio at the same 2 h intervals. The post-operative serum creatinine and length of ICU stay were also noted.

The surgical field was compared using a modified scoring system used for endoscopic sinus surgery, the Boezaart score.[4] We attempted to extrapolate the surgical field ooze to determine the impact of liberal fluids on the surgical field. This score was from 0 to 5, 0 implying a dry field and 5 constant oozing on the field.

The main surgeon's surgical field satisfaction at the end of surgery was graded from 1 to 5, with 5 implying extremely satisfied and 1 not at all satisfied by the Likertscale. The surgical team was blinded to the fluid policy used during surgery.

Sample size was calculated from a pilot study of twenty cases. The fourth hour lactate was compared between group R and L (1.05 mmol/L vs. 1.80 mmol/L) using a two means hypothesis. With a power of 90% and 5% alpha error the sample size was calculated as 17 in each group. We had included 40 patients, twenty in each group in our study.

Chi square test was used to compare the categorical variables by group. For normally distributed continuous variables, Independent sample *t*-test was used to compare by group. The Analysis of covariance (ANCOVA) test was used to compare the adjusted lactate levels between the groups. Mann–Whitney U test was done to compare the surgical field scores between the groups. Statistical analysis was done using IBM SPSS Statistics 20 Windows (SPSS Inc., Chicago, USA).

RESULTS

The demographics were comparable between the groups [Table 1]. All patients in this study underwent surgery for primary colorectal malignancies. The comorbidities in group R vs. L, i.e., diabetes 7:5, hypertension 4:5 and coronary artery disease (CAD) 2:2 appeared similar. Age >50 y was 15:18 in group R versus L, although the mean age was comparable.

Table 1: Demographic variables

Variable	Group R (*n*=20)	Group L (*n*=20)	*P*
Age years	58.3±16.5	60.3±10.2	0.640
Gender M:F	9:11	12:8	0.527
Weight Kg	61.85±16.41	62.65±9.91	0.853

The primary outcome, the measure of lactate was compared at baseline and 2 h during surgery. The baseline lactate (mmol/L) was 0.81 ± 0.21 in group R versus 1.11 ± 0.45 in group L ($P = 0.011$). An adjusted mean was calculated using this baseline differences in lactate. The values of lactate at 2h, 4h and 6h were comparable between the groups, [Table 2].

The fasting replacement was higher in group L in comparison to group R. The basal fluid used was 2.08 ± 0.29 mL/kg/h in the restrictive versus 4.47 ± 1.04 mL/kg/h in the liberal group. The total fluids given during the surgery were 1694.3 ± 445.49 mL in group R versus 2773 ± 708 ml in group L. Boluses were administered at defined points and were comparable between the groups, [Table 3]. The urine output and pre and post-operative creatinine between the groups were comparable [Table 3].

One patient in each group needed transfusion with 1 unit of packed red blood cells. The pre and post-operative haemoglobin between the groups was comparable. Three patients in group L needed noradrenaline as per protocol. One patient in group L was ventilated for 3 h post-operatively on account of hypothermia, but this was not significant [Table 3].

The length of ICU (LOICU) stay was significantly shorter in group R. Two patients, one in each group underwent re-exploration post-operatively for bleeding.

Three patients in group L had minor post-operative complications, wound infection, bronchospasm and paralytic ileus. One patient in group R had a neurological incident (parietal lobe infarct) on 4th postoperative day (POD) in the ward from which he recovered with conservative management.

The modified scale was used to assess the surgical field by the assistant surgeon at 2 h intervals. The score

Table 2: Comparison of lactate values among groups adjusted by the baseline lactate values								
Time points	Group R (*n*=20)			Group L (*n*=20)			Adj. mean difference from baseline mmol/L	*P*
	Observed mean	Adjusted mean*	SD	Observed mean	Adjusted mean*	SD		
Baseline	0.81		0.21	1.11		0.45		0.011
2 H	1.03	1.14	0.37	1.44	1.32	0.66	0.18	0.270
4 H	1.22	1.34	0.57	1.67	1.54	0.80	0.20	0.383
6 H	1.39	1.56	0.71	2.04	1.88	1.05	0.32	0.335

was superior in group R at the 4th h and comparable at all other points during surgery. The main surgeon's assessment was superior in group R at the end of surgery [Table 4].

DISCUSSION

We inferred that a restrictive fluid policy in robotic surgery did not affect lactate levels or affect renal functions in comparison to the liberal group.

Dynamic monitoring indices guide fluid replacement[5] but are not very reliable in the context of minimally invasive surgery.[6,7] This obligates a fluid management based upon haemodynamic profile, urine output and metabolic parameters such as lactate, which is an early indicator of tissue hypoperfusion.[8] The restrictive versus liberal fluid therapy in major abdominal surgery (RELIEF) trial[9] while comparing a restrictive versus liberal fluid administration strategy has shown increased risk of renal failure, renal replacement therapy and surgical site infection in the restrictive group. We did not find a negative impact of fluid restriction in our patients as interventions were introduced to maintain blood pressure and urine output throughout the study.

Fluid guidelines in prostatic surgery recommend use of less than 2.0 L fluid to avoid field flooding and facial oedema.[10,11] We used the restrictive policy recommended in robotic prostatic surgery of 2 mL/kg/h and compared it with a more liberal policy of 4 mL/kg/h in our patients.

As per the enhanced recovery after surgery (ERAS) guidelines for rectal surgery,[12] oral polyethylene glycol was administered for bowel preparation. To avoid effects of dehydration on lactate we had infused bolus fluids prior to intubation. The pre-operative baseline lactate in the groups was less than 1.00 mmol/L suggesting adequate hydration in our patients.

The rescue fluid boluses administered were similar in both groups but the total fluids averaged 1.7 L in the group R and 2.7 in group L. Three patients in the group L needed noradrenaline to maintain the MAP >65 mm Hg, but this was not significant.

Table 3: Intraoperative Fluids, P/F ratio, urine output and postoperative variables			
Variable	Group R (*n*=20)	Group L (*n*=20)	*P*
Duration h	6.95±1.88	6.70±1.78	0.668
Fasting ml/patient	452.50±54.95	495±22.36	0.003
Basal Fluids ml/patient	906.8±416.47	1866±22.36	*P*<0.001
Basal ml/kg/h	2.08±0.29	4.47±1.04	*P*<0.001
Bolus ml/patient	478.57±162.57	484.38±213.48	0.935
Total Fluids ml/patient	1694.3±445.49	2773±708.02	*P*<0.001
Urine output/patient	677.75±362.5	648.75±304.7	0.786
Urine ml/kg/h	1.56±0.59	1.56±0.69	0.984
P/F_0	385.79±93.62	341.55±125.33	0.214
P/F_2	365.68±83.09	328.7±99.06	0.209
P/F_4	340.60±103.97	332.68±132.04	0.836
P/F_6	314.87±85.50	303.82±101.26	0.743
Noradrenaline (*n*)	*n*=0	*n*=3	0.231
Extubation on table (*n*)	20	19	0.3173
Creatinine mg/dL_0	1.04±0.16	1.00±0.2	0.542
Creatinine mg/dL_1	0.93±0.16	0.92±0.23	0.937
Haemoglobin g/dL_0	11.9±1.39	11.89±1.58	0.876
Haemoglobin mg/dL_1	11.06±1.73	11.0±1.39	0.909
LOICU days	1.45±0.51	2.25±1.12	0.007

Table 4: Assessment of surgical field			
Scoring Surgical field	Group R (*n*=20)	Group L (*n*=20)	*P*
Score 0	0.26±0.45	0.20±0.410	0.644
Score 2 h	1.37±0.831	1.40±0.681	0.988
Score 4 h	1.32±0.671	2.25±0.851	0.001
Score 6h	2.00±0.926	2.21±0.83	0.48
Surgeon satisfaction (Likert)	4.2±0.696	3.08±1.004	*P*<0.001

The lactate levels in both groups showed an increase with increasing duration of surgery, but the mean values were well within the normal range and did not need intervention. Lactate levels are reflective of tissue perfusion and can increase with hypovolemia. Wenkui and associates[13] compared post-operative lactate-guided fluid replacement versus clinical decisions to replace fluid and concluded that the former could reduce post-operative complications.

We had evaluated the effects of peri-operative fluid restriction as it was a minimally invasive surgery and

had protocolised interventions for lactate increases. However the maximal values of lactate at 6 h 1.56 ± 0.71 vs. 1.88 ± 1.05 mmol/L in group R vs. group L were in the acceptable range for our study. We inferred that the restrictive fluid strategy did not compromise tissue perfusion in comparison to the liberal group.

We chose a balanced salt solution that contained acetate as the buffer (Kabilyte) for replacement and excluded patients who had received fluids containing lactate or normal saline. We believe that acetate solutions are more physiologic than normal saline based on earlier studies.[14] A study comparing Ringer's lactate with an acetate containing fluid in donor hepatectomy showed no differences in lactate, but an increased metabolic acidosis in the Ringer's lactate group.[15]

A study by Holte[16] on restrictive versus liberal strategies in fast-track colorectal surgery has shown transient improvements in post-operative pulmonary functions in the restrictive group. We had monitored the $Pa0_2$/$Fi0_2$ (P/F) ratio 2nd hourly as a surrogate of fluid overload or early pulmonary congestion in the Trendelenburg position[17] and also for ventilatory compromise in this position combined with a pnuemoperitoneum.[18] We found the values comparable at all points in the study implying there were there was no evidence of pulmonary fluid overload.

One patient in each group had needed transfusion of blood. The policy for transfusion in this group of ASA I and II was restrictive and transfusions were administered only if haemoglobin <8.0 gm/dL.

Noradrenaline was introduced after two fluid boluses. Three patients in the liberal group versus none in the restrictive needed noradrenaline transiently for maintenance of mean arterial pressure ($P = 0.231$).

The length of ICU stay was significantly shorter in the group R, ($P = 0.007$). The intensive care team and surgical team were both blinded to the fluid strategy employed intra-operatively. Three patients in the group L had extended ICU stay due to wound related complications, protracted bronchospasm (patient with history of asthma) and paralytic ileus respectively. One patient in the group R developed a parietal infarct in the ward and was managed conservatively without shift to the ICU. The prolongation in the group L could have occurred because of prolongation of stay in a few patients. Although it appeared that group L was associated with delayed wound healing and ileus, prospective studies with larger numbers may be able to highlight this association more accurately.

This study was conducted at the time of introduction of robotic colorectal surgery in our institute and we were uncertain of the impact of liberal fluid on the visual field on account of oozing from the tissues during surgery. Piegeler[10] in his review of robotic prostatectomy comments on the negative impact of additional fluids in an elderly cohort and states that additional crystalloid can reach the interstitial tissue. The integrity of the endothelial glycocalyx layer dictates fluid transudation across and occurrence of tissue oedema.[19] We proposed to evaluate the negative impact of liberal fluid on oozing from tissues consequent to tissue oedema. Noradrenaline was introduced when the MAP was less than 65 mm Hg, and we do not believe that this could have impacted the oozing on the surgical field. At 4 h into surgery, the field in group R was superior with less ooze although this difference was not seen at the 6 h of surgery.

We believe that ours is one of the few studies to have objectively looked at fluid management in an emerging field of robotic colorectal surgery. We did not come across the assessment of visual field in surgeries other than prostatic surgeries and this may provide us with some insight of tissue oedema with liberal fluids in robotic surgery.

Our study had its limitations. The numbers were limited in view of the nature of surgery in an emerging speciality. The need for additional fluid and management was at the discretion of the anaesthesiologist and individual variations could have occurred. The measurements of weights of patients in the ICU may have helped in assessment of fluid gain at the end of surgery. The post-operative ICU stay was prolonged in group L on account of ileus and bronchospasm and may have affected the overall length of ICU stay. The impact on the surgical field was based upon a presumption of ooze secondary to tissue oedema and could have been affected by learning curve of the surgeon in transecting planes during surgery. We did not follow or evaluate post-operative analgesia between the groups and are unsure of the implications of restricting fluid on post-operative pain. A prospective larger study and the exclusion of younger patients may bring out clearly the impact of restricting fluids on post-operative outcomes.

CONCLUSION

Restrictive fluid strategy of 2mL/kg/h basal fluid (group R) does not increase lactate levels per-operatively or affect post-operative creatinine, improves surgical field at 4 h, and shortens length of ICU stay in comparison to 4 mL/kg/h (Group L) in robotic colorectal surgery.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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