<u>Fluid management after Laparoscopic colorectal surgery – Re-defining</u> <u>Enhanced Recovery</u>

Authors:

Mr B Levy	Surgical Registrar
Mr H Dowson	Surgical Registrar
Prof T Rockall	Consultant Surgeon

Institution:

Minimal Access Therapy Training Unit Post Graduate Medical School University of Surrey Manor Park Guildford Surrey GU2 7WG

Introduction

Enhanced recovery programmes have been shown to reduce the length of hospital stay after elective colorectal surgery with most of the evidence originating from open colo-rectal surgery^{1, 2}. The Enhanced Recovery criteria currently used for Laparoscopic Surgery have been adopted directly from open surgery with essentially no modification at all due to the current lack of evidence.

The elements of the Enhanced Recovery after Surgery (ERAS) protocol are shown in Table 1.

Table 1. Enhanced Recovery Protocol compliance

- 1) Pre-operative education regarding ERAS
- 2) Avoidance of bowel preparation
- 3) Pre-operative carbohydrate drink
- 4) Avoidance of pre-operative long acting sedatives
- 5) Intra-operative thoracic epidural started before skin incision
- 6) Upper body forced air heating cover
- 7) Avoidance of abdominal drains
- 8) Avoidance of NGT

9) Intra-operative fluid less than 3000mls

- 10) At least 800mls taken orally on the day of surgery
- 11) At least one unit of oral nutritional supplement taken on the day of surgery before midnight
- 12) At least two units of oral nutritional supplement taken on the first day after surgery before midnight
- 13) Intra-venous fluid terminated on Day 1
- 14) Termination of urinary drainage on post-operative day 2
- 15) Solid food eaten on day 1
- 16) Aperient given
- 17) Mobilisation on the day of surgery
- 18) Mobilisation of at least 6 hours on day 1
- 19) Post-operative thoracic epidural
- 20) Termination of thoracic epidural on day 2

Certain elements of the Enhanced Recovery Programme have been shown to be clearly beneficial, some make good common sense whilst others remain contentious. An example of a simple beneficial element would include the administration of 100g of carbohydrate drink (Pre-Load®, Vitaflo Limited, Liverpool, UK) in 800mls of water the night before surgery and 50g of carbohydrate in 400mls of water 2-3 hours prior to surgery. This has been shown to be safe³, to reduce the systemic response to surgery⁴⁻⁶ and to shorten the hospital stay⁷. In addition the pre-operative oral fluid helps prevent pre-operative dehydration, a factor that has also been reduced since the routine use of pre-operative bowel preparation was stopped^{8, 9}.

With regards to laparoscopic colorectal surgery, one of the contentious ERAS elements relates to the volume of intra-operative fluid used.

Fluid management

A key factor in the aetiology of post-operative morbidity is covert compensated hypovolaemia. This may not be detected by routine heart rate or blood pressure measurements due to compensatory vasoconstriction¹⁰ which maintains the blood pressure prior to surgery. This sympathetic vasoconstriction is unfortunately lost once anaesthesia commences¹¹. A background of dehydration from fasting, bowel preparation and evaporative losses from the abdomen during surgery exacerbates the situation. Consequently many initially_believed that liberal pre and intra-operative fluid therapy prevented organ hypoperfusion and improved outcome. There have been several studies¹²⁻¹⁶ investigating the intra-operative volume of fluid required in abdominal surgery. Three of the studies focussed on patients undergoing open colo-rectal surgery, one on general surgical patients undergoing upper and lower gastro-intestinal surgery and one on patients undergoing laparoscopic cholecystectomy. There have been several problems with analysis of these trials.

Firstly a variety of fluids have been used both pre-operatively and operatively as shown in table 2. In some cases a variety of fluids were used pre-operatively¹².

	Brandstrup	Kabon	Nisanevich	Holte	Holte
	(2003)	(2005)	(2005)	(2007)	(2004)
Study design	Effect of RF vs	Effect of RF vs	Effect of RF vs	Effect of RF vs	Effect of RF vs
	SF on	LF on wound	LF on adverse	LF on	LF on
	complication rate	infection rates	effects	physiological	physiological
				function	function
Type of surgery	Open colorectal	Open colorectal	Abdominal	Open colorectal	Laparoscopic
			(upper and lower		cholecytectomy
			GI)		
Pre-op fluid	5% gluocose or	? fluid given	Dextrose/saline	Ringers lactate	No pre-op fluid
	0.9% NaCl				
Intra-op fluid	HAES or HAES	Ringers lactate	Ringers lactate	Ringers lactate +	Ringers lactate
	+ NaCl			voluven	

Table 2 – Types of fluid administered in different trials

(RF – restricted fluid regime, SF – standard fluid regime, LF – liberal fluid regime)

Secondly the definitions of the fluid regimes used are extremely varied for the three types (restricted, standard and liberal).

In the <u>'restricted'</u> fluid regime defined by Nisanevich et al¹⁴, they found that an average of 1.4 +/-0.9 litres was given whilst the <u>'restricted'</u> fluid regime named by Kabon et al¹³ was more than twice this volume with an average of 3.1+/-1.5 litres.

Brandstrup et al's¹² defined fluid regime of *`standard'* fluid management resulted in an average of 5.4 (2.7-11.1) litres per patient whilst Nisanevich et al's¹⁴ definition of *"liberal"* fluid therapy gave an average of 3.8 +/-1.2 litres per patient. Similarly Kabon et al's¹³ *`liberal'* fluid regime resulted in an average of 5.7+/-2.0 litres , 50% more than Nisanevich et al's¹⁴ *'liberal'* protocol where an average of 3.8+/-1.2 litres were given

As the fluid regime definitions resulted in such a broad spectrum of fluid given, it is beneficial to look at the regimes in terms of the volume of fluid given and to re-classify them as shown below (see table 4).

	Restricted (<2 Litres)	Standard (2-4 Litres)	Liberal (>4 Litres)
Brandstrap ²⁷		2.7	5.4
Kabon ²⁸		3.1	5.7
Holte ³¹ (2007)	1.64		5.05
Nisanevich ²⁹	1.4	3.8	
Holte ³⁰ (2004)	0.99	2.9	

Table 3 Re-classification the studies according to fluid volumes given

Analysis of the four similar open studies using the re-classification system will be performed.

The most striking observation is the complication rates that are shown in table 4 below, which presents various aspects of the different studies for comparison.

	Restricted	Standard	Liberal
	group	group	group
Tot no. of pts	93	268	217
Pulmonary	1	0	(5)
oedema			
Intra-operative	27/93	1/75	9/16
hypotension	=29%	=1.3%	=56%
Post-operative		20/69	16/72
hypotension		= 28%	= 22%
Pneumonia	5	8	(10)
MI	1	1	(1)
Arrhythmia	3	3	(1)
Deaths	0	0	5
Total no of pts	29/93	48/268	58/217
with comps	=31%	=17%	=27%
Total no of	50/93	58/268	113/217
complications	=54%	=22%	=52%

Table 4 showing the complications in the three groups.

Numbers in brackets () indicate that the actual number from the studies may be greater, with many of these cases being picked out from the discussion.

"Deaths" were clearly reported in all the studies. The deaths, which were 5 in total, were all in the liberal fluid regime group. Four of the deaths were from Brandstrup et al's study where 2 of the cases died from pulmonary oedema, one from pulmonary embolus and one from pneumonia. The fifth patient died from another study¹⁴ due to pulmonary oedema. The liberal therapy group had at least 5 patients with pulmonary oedema.

The study by kabon et al¹³ only reports on wound infection rates, days till tolerating solid food, hospital stay and fluid volumes given in surgery. In their discussion there is mention that in the liberal volume group, several patients were admitted to intensive care. Three of these had surgical site infection, one had an MI and one had an arrhythmia. There is no formal list documenting the exact number of patients with specific complications. Despite this limitation, there were at least 5 patients that were admitted to the intensive care, all from the liberal fluid group with pulmonary oedema and none from the standard therapy group.

Only Nisanevich et al¹⁴ clearly reported on intra-operative hypotension that responded to fluid therapy. In this study, patients' in the restricted group had significantly more intra-operative hypotensive episodes that required fluid therapy to correct them. Holte et al¹⁵ gave 10mgs of intravenous ephedrine and 40mgs of intramuscular ephedrine at induction. They treated all hypotension with 10mgs of ephedrine intra-venously. The presence of hypotension in their '*restrictive group*" implies that there must be some degree of compensatory splanchnic vasoconstriction. This hypotension threatens an increased morbidity in terms of anastomotic healing¹⁷ and further vasoconstriction with ephedrine may worsen the problem. This may in part explain why their fluid restricted group had 3/16 anastomotic leaks whilst the liberal fluid group had 0/16 anastomotic leaks though this was not statistically significant . In Nisanevich et al's¹⁴ study the restricted (according to the re-classification in this discussion) fluid therapy regime did seem advantageous in terms of significantly shorter time to pass flatus and time in hospital (3 vs 4 and 8 vs 9 days respectively). This suggests that hypotension due to hypovolaemia is far less serious if treated with fluid than with inotropes. There was no significant difference in post-operative hypotension or hospital stay between the standard therapy and liberal therapy regimes.

Nisanevich et al¹⁴ found that a restricted fluid regime resulted in a shorter hospital stay and less complications. However when Holte et al¹⁵ compared their restricted fluid regime with the liberal regime they found no difference in the length of hospital stay or the length of post-operative ileus. The only difference was slightly better respiratory function in the restricted group, but this was associated with significantly more complications in the restricted fluid therapy group. Holte et al's¹⁵ study was small in comparison with Nisanevich et al's¹⁴ which was five times larger.

Three of these studies¹³⁻¹⁵ have evaluated the effect of fluids on postoperative ileus. It was only Nisanevich et al's¹⁴ fluid restricted group that had a significant decrease in the time to ileus resolution when compared against their liberal therapy group, yet Holte ¹⁵ and Kabon¹³ found no benefit in their respective fluid therapy groups.

The ERAS protocol states that less than 3000mls of intravenous fluid be used intra-operatively, a volume which fits into the re-classified "standard therapy" group and which is consistent with the least complications overall for the trials above. The key issue with all the studies above is that fixed volume fluid regimes (in mls/Kg) have been used whilst failing to measure oxygen delivery. Excess fluid given in addition to volumes required for maximal oxygen delivery will predispose the patient to complications, whilst restrictive regimes will prevent maximal oxygen delivery from being achieved. The slowly evolving opinion is that a generic formula that covers all patients is not appropriate and that the correct amount of fluid needs be given to each individual patient at the correct time. This has been demonstrated by the trials that have used target driven oesophageal Doppler directed fluid replacement which have shown a reduction in hospital stay¹⁸⁻²⁵ or a reduction in critical care admissions²³ in all fields of surgery (see Table 5).

	No of pts	Type of surgery	Outcome
Mythen et al	60	Cardiac	37% reduction in stay
McKendry et al	174	Cardiac	39% reduction in stay
Sinclair et al	40	Orthopaedic	39% Reduction in stay
Venn et al	90	Orthopaedic	44% Reduction in stay (until medically fit)
Gan et al	100	Gen/gynae/ urology	29% Reduction in stay
Conway et al	55	Colorectal	Reduction in critical care admissions
Wakeling et al	128	Colorectal	13% Reduction in stay
Noblett et al	103	Colorectal	22% Reduction in stay

Table 5 – Randomized controlled studies using oesophageal Doppler

Conclusion

Studies examining fluid administration in abdominal surgery have primarily looked at the total volumes of fluid infused, with only a few studies looking at oxygen delivery and the timing of fluid administration in open surgery. Studies by Wakeling²⁴ and Conway²³ have shown oxygen delivery targeted by cardiac output to be the most significant factor in determining morbidity and length of stay. By giving enough fluid to achieve good oxygen delivery and normal oxygen extraction but restricting fluids beyond this point we would expect to see

- a) Benefits of the Restrictive fluid regimes
- b) Avoidance of pulmonary oedema/bowel oedema that exists after the liberal fluid regimes.

More recently it has been demonstrated that fluid replacement is not only dependent on the volume of fluid given but also on the timing with relation to surgery that it is given²⁵.

These volumes suggested for Enhanced recovery after open colorectal surgery have been transcribed directly to laparoscopic surgery without any modification whilst the evidence for fluid volumes to be administered during laparoscopic colorectal surgery has not yet described.

The use of the oesophageal Doppler during laparoscopic colorectal surgery optimizes the delivery of oxygen and prevents the un-necessary potentially harmful administration of additional fluid. Oesophageal Doppler directed fluid replacement has resulted in significantly less intra-operative fluid delivered compared to previously. It will be necessary to re-define the element of intra-operative fluid replacement within the Enhanced Recovery Programme for patients undergoing laparoscopic colorectal surgery as 3000mls is certainly excessive. Furthermore, stating a maximum volume that can be given re-introduces a fixed volume regime. Every patient is different and will require different volumes of fluid at different times. Therefore if the oesophageal Doppler were to be used routinely for laparoscopic surgery, it could be argued that a limit does not need to be set, as the correct volume of fluid would be given to that patient to optimise the stroke volume.

Although epidural anaesthesia is listed as one of the Enhanced recovery criteria, several forms of analgesia are currently being used for laparoscopic colorectal surgery. It is not clear at present what extent the type of analgesia (epidural, spinal or PCA) has on the intra-operative fluid requirement or patient outcome. Once these are known, the Enhanced Recovery Programme can be re-defined further.

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