High vs low urine output targets in elective surgical patients: a randomised controlled safety trial

Study Protocol 13 June 2011

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Background

A urine output (UO) below 0.5 ml/kg/h is routinely observed in otherwise well patients undergoing major surgery. This is traditionally regarded as a sign of impending acute kidney injury (AKI) and is therefore treated by liberal fluid infusion. However, several recent studies of perioperative renal function have shown no association between UO and AKI. For example, in a study of 15,102 patients undergoing non-cardiac surgery, intra-operative UO had no correlation to the development of perioperative AKI. In fact, it has long been known that oliguria is an important physiological response to injury, preserving sodium and water in recovering organisms. This response is mediated by antidiuretic hormone release, renin-angiotensin II-aldosterone activation and increased sympathetic nerve action on tubular cells in the nephron.

The current practice of maintaining a high UO in otherwise well patients by liberal fluid infusions can be therefore be questioned. More importantly, a series of recent randomised clinical trials demonstrate that liberal fluid therapy approximately doubles postoperative complication rates as compared to a more restricted fluid regime, confirming findings in animal studies of numerous detrimental effects of perioperative fluid overloading. Three clinical trials demonstrate a relative reduction of 46%, 45% and 84% of overall postoperative morbidity with restricted fluid therapy, clearly identifying fluid overloading as a major, iatrogenic and preventable cause of complications in contemporary surgical care. The main obstacle to fluid restriction in practice is maintaining the traditional high UO target. This study therefore aims to demonstrate that a lower UO target is not associated with renal impairment, confirming previous observational studies.

Aims

This study tests the hypothesis that a urine output target lower than the traditional 0.5 ml/kg/h (0.2 ml/kg/h) does not cause harm to the kidneys. Harm is defined in the widest sense of the word in order to detect any degree of harm. It is therefore evaluated by several highly sensitive methodologies beyond the routinely used serum concentrations of creatinine and urea. These methods include frequent sampling for novel, validated biomarkers of renal stress (neutrophil gelatinase-associated lipocalin (NGAL) and Cystatin C) in combination with renal clearance studies to directly measure renal plasma flow (para-aminohippurate (PAH) clearance) and glomerular filtration rates (Sinistrin clearance).

Table 1. Standardised fluid therapy in ERAS protocol

Day of surgery	*Preop*	≥400 ml clear liquids PO Oral bowel preparation not routinely used
	Intraop	5 ml/kg/h Plasma-Lyte 148 IV
		5 ml/kg/h Gelofusine IV
	Postop	0.5 ml/kg/h dextrose-saline IV
		600 ml liquids PO
	Total	*Approx 2500 ml IV + 1000 ml PO*
POD 1		IV fluids stopped at 8 am
		1500 ml liquids (and standard diet) PO
		If oral intake <800 ml by 6 pm, maintenance infusion of IV dextrose-saline with 20 mmol K/l restarted at 1 ml/kg/h
		In case of vomiting, replacement 1:1 with IV saline 0.9% with 20 mmol K/l is started
		If Hgb <80: Transfuse 2U RBCs If Hgb 80-100: Transfuse 2U RBCs only if symptomatic or ischaemic heart disease or evidence of ongoing bleeding

Importance

Approximately 45% of people in the industrialised world have abdominal surgery during their lifetime. Despite recent significant advances, such as minimally invasive surgery and enhanced-recovery protocols, people undergoing colorectal surgery still have a 35-55% risk of complications. As summarised above, recent trials have identified fluid overloading as a major, iatrogenic and preventable cause of complications in contemporary surgical care. The main cause of fluid overloading is the traditional emphasis on maintaining a high UO. This trial challenges this tradition by evaluating the non-inferiority of a lower UO target, with the ultimate goal of reducing the need for routine aggressive fluid resuscitation in elective surgery and the excess morbidity associated with such fluid excess. The potential impact on the practice and outcomes of surgery across most specialties is therefore large. In addition, this study will elucidate the regulators of renal function in contemporary surgical care, specifically evaluating the respective roles of renal perfusion changes *vs* changes in renoregulatory hormones.

Study design

This is a prospective randomised assessor-blinded non-inferiority trial. Forty patients undergoing elective bowel surgery will be studied.

Patients with known risk factors for AKI will be excluded. Baseline measures of effective renal plasma flow (ERPF), glomerular filtration rate (GFR), AKI biomarkers, plasma creatinine and renoregulatory hormones are obtained prior to surgery. Participants are randomised to the Low (0.2 ml/kg/h) or High (0.5 ml/kg/h) groups on induction of general anaesthesia. Randomisation is stratified by baseline renal function. Surgical techniques are per surgeon preference. Perioperative care is standardised according to the North Shore Hospital (NSH) enhanced-recovery after surgery (ERAS) protocol to minimise variation in ancillary care. This includes routine usage of epidural analgesia, routine urinary catheterisation until morning of postoperative day (POD) 2 and a standardised perioperative fluid protocol (see Table 1). During surgery and the next 48 hours, UO is monitored hourly. In both groups, an hourly UO <0.5 ml/kg/h prompts immediate anaesthetic or surgical team review to rule out evidence of potential hypoperfusion of any aetiology (see Figure 1). If this is not present, patients in the High group will receive 500-ml fluid boluses (Plasma-Lyte 148) until UO exceeds 0.5 ml/kg/h. In the Low group, fluid boluses will be only given if UO falls below 0.2 ml/kg/h.

Table 2. Exclusion criteria

Preexisting moderate or severe chronic kidney disease (eGFR <60 ml/min/1.73 m^2)
Pre-existing kidney damage regardless of eGFR (single functional kidney, renal transplant, significant proteinuria)
History of previous AKI due to any cause (AKI Network Stage 2)
Need for ongoing angiotensin-converting enzyme inhibitors, angiotensin receptor blockers or non-steroidal anti-inflammatory drugs (NSAIDs)
Nephrotoxic substance administration (including systemic radiocontrast dyes, aminoglycosides, glycopeptides and NSAIDs other than aspirin) within 48 h prior to surgery
Pre-existing hepatic failure (Child-Pugh Score >6)
ASA class IV
Morbid obesity (BMI>35)
Intraoperative ureteric injury
Intraoperative haemorrhage >50% of blood volume
Pregnant or lactating females

The main endpoint is the urinary NGAL on POD 1. Neutrophil gelatinase-associated lipoprotein, the best-validated and most sensitive biomarker of AKI, will be followed 12-hourly during 48 hours. In addition, plasma cystatin C and creatinine concentrations, urinary electrolytes and osmolality will be measured several times per day, and the ERPF and GFR measurements will be repeated on POD 1. Renoregulatory hormones will also be followed. The study nephrologist will acutely assess any participant with a persistently

low UO despite a total bolus volume of 2 l or a plasma creatinine increase by ≥2-fold compared to baseline at any point. Clinical outcomes will also be recorded.

Participants

Forty men and women aged between 18 and 85 years of age, able to give informed consent, undergoing elective segmental colectomy for benign or malignant disease, by laparotomy or laparoscopy will be studied. Participants will be recruited among patients undergoing bowel surgery at North Shore Hospital. Exclusion criteria are listed in Table 2.

Step-by-step protocol

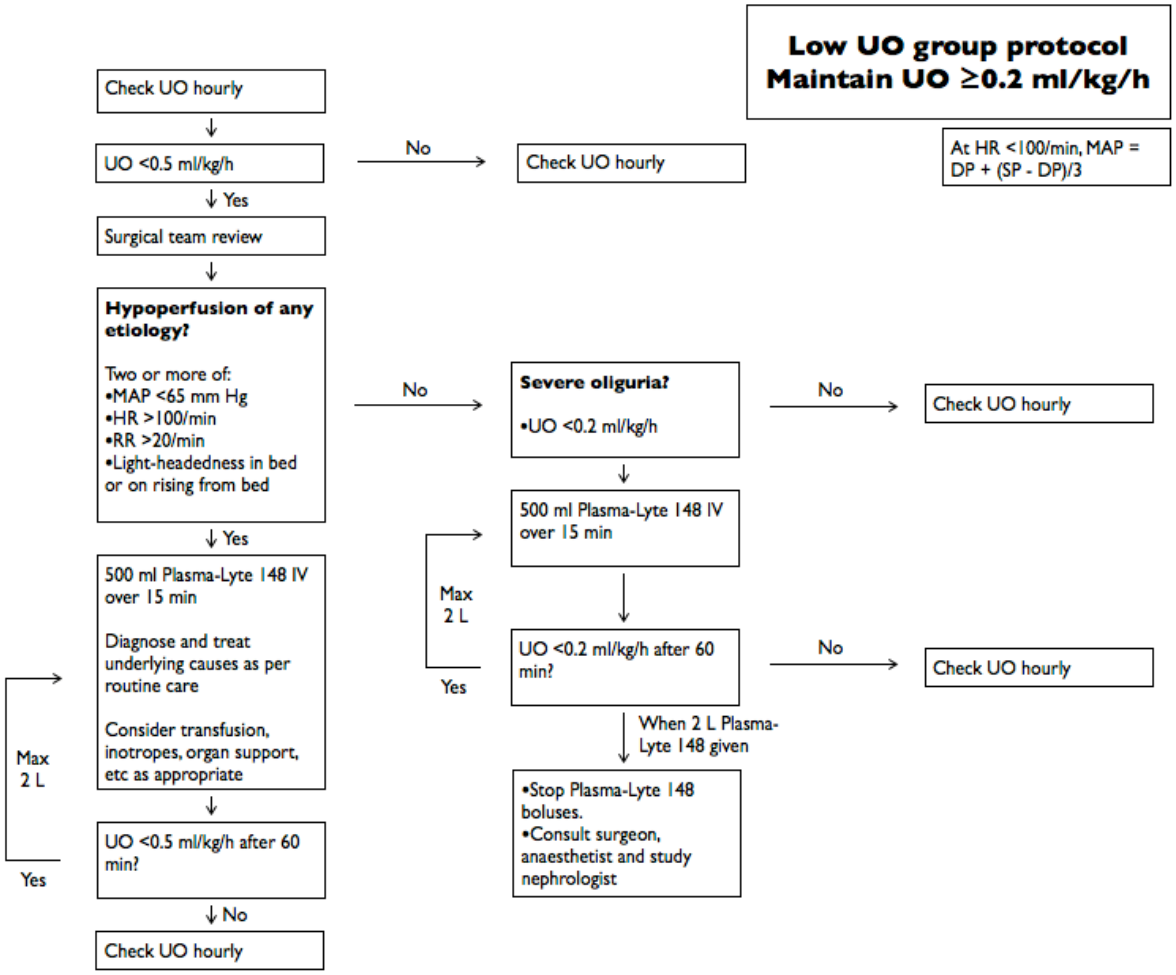
Recruitment: With the permission of the potential participant, a research fellow or research nurse gives a brief oral and written (Participant's Information Sheet) information about the study in outpatients clinic. The research fellow or research nurse telephones the potential participant 3-7 days later to further discuss the study and seek oral consent. If consent is given, patient attends a separate research visit approximately one week prior to surgery, where written consent is obtained prior to any test procedures.

Preoperative research outpatients visit: Baseline renal function measures will be performed on a dedicated research visit to outpatients clinic approximately one week prior to surgery. Patients present at 9 am overnight fasted. Two IV cannulas are placed. A 3-hour intravenous infusions of sinistrin and PAH is given with the participant resting in a reclining armchair (see Clearance Studies protocol). One urine sample and three blood samples will be taken on this occasion for baseline measures of urinary NGAL, plasma creatinine, cystatin C, electrolytes, osmolality, C-reactive protein (CRP), glucose, and renoregulatory hormones. Plasma concentrations of sinistrin and PAH are determined for calculation of ERPF and GFR. Body composition will be estimated using bioimpedance analysis (BIA).

Randomisation: Participants are randomised (allocation concealment by off-site computer randomisation, The University of Auckland) to the Low or the High group on induction of general anaesthesia.

Study period: The data collection period starts before surgery and ends on POD 30.

Study intervention: The only difference between the two study groups is the response to urine output below 0.5 ml/kg/min from start of anaesthesia until 8am on POD 1 (see Figure 1).



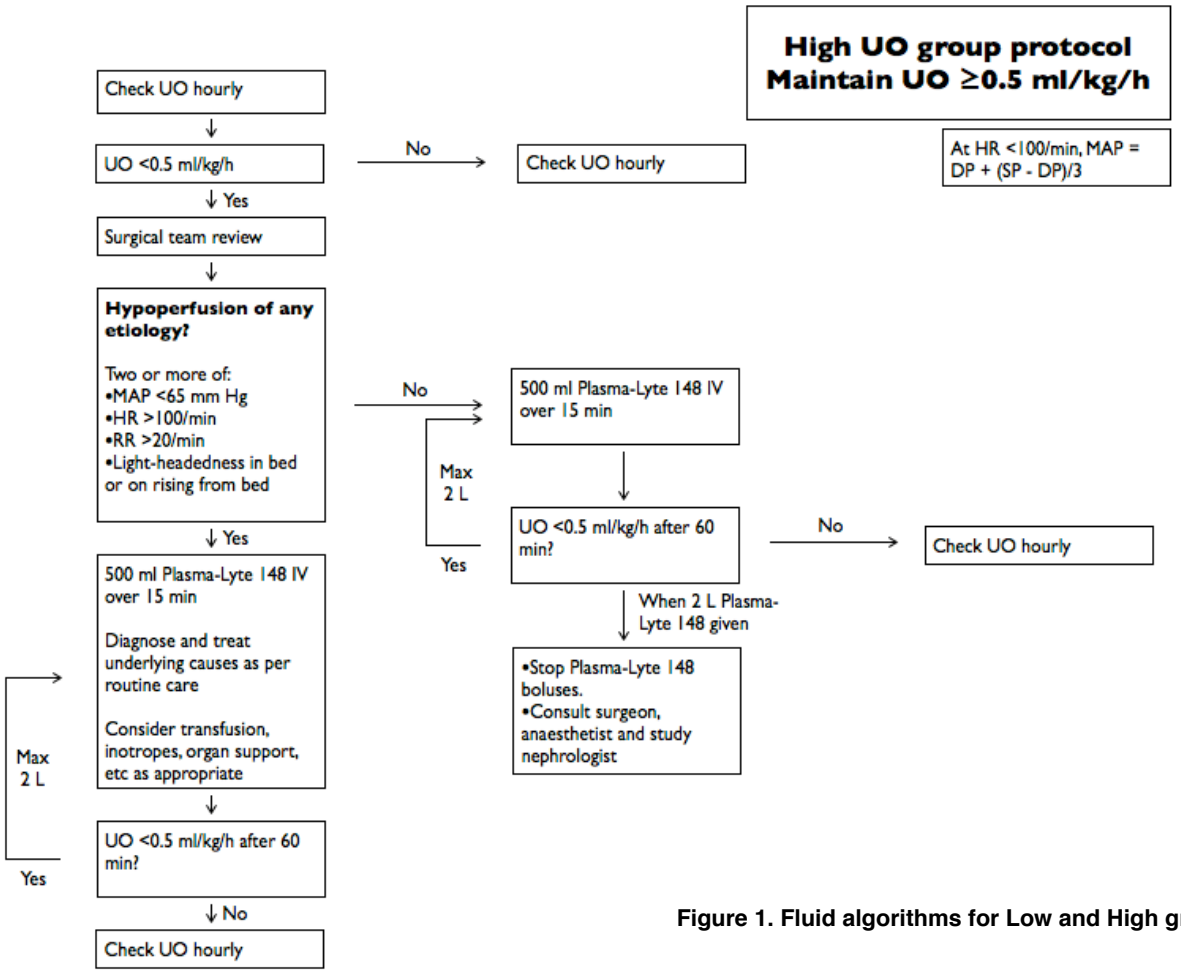


Figure 1. Fluid algorithms for Low and High groups

Urinary output is followed hourly. All anaesthetic and surgical teams providing care for participants will be educated face-to-face about the details of the fluid protocols. A research fellow will monitor compliance with protocols around the clock in person and over the phone. Participants with epidural-related hypotension will follow the standard ERAS protocol (a combination of fluid boluses and reduced epidural infusion rates). Participants with complications remain in the study. As per the study fluid algorithms (Figure 1), the UO target in the Low group will switch from 0.2 to 0.5 ml/kg/h if there are any signs of hypoperfusion.

Table 3. Secondary endpoints
Urinary excretion of NGAL 0800 POD1 - 0800 POD 2 and total excretion during intervention period
Urinary concentrations of NGAL and creatinine and osmolality during and after surgery
Plasma concentrations of cystatin C, creatinine, ADH, aldosterone, renin and angiotensin II and osmolality during and after surgery
ERPF and GFR before and 1 day after surgery
30-day incidence of complications (including AKI) classified and defined as per Auckland ERAS database, graded per Clavien-Dindo grading scale
Length of stay, time to repeated flatus
IV and oral fluid volumes and changes in body weight and lean tissue mass (BIA)

At the routine 30-day outpatients clinic followup, a final urine and plasma sample will be collected.

Nephrologist review triggers: The on-site study nephrologist Dr De Zoysa (or a named colleague in his absence) will urgently (within 12 hours) review any participant with an absent UO response to a 2L fluid bolus (see Figure 2), or with AKI Network (AKIN) stage 2 AKI per creatinine criteria (persistent elevations of plasma creatinine ≥100% above baseline despite adequate fluid resuscitation) within 30 days, and institute adequate therapy.

Independent Monitoring Committee: Two independent senior consultant nephrologists (Dr Ian Simpson at Auckland City Hospital and Dr David Voss at Middlemore Hospital) make up an independent Monitoring Committee, which will review individual clinical outcomes as well as postoperative changes in plasma creatinine in all participants after completion of four and 20 participants.

Study halt triggers: In addition, the study will be halted pending urgent review by the independent Monitoring Committee if the following occurs: Two or more participants in the intervention arm develop AKI Network (AKIN) stage 3 AKI per creatinine criteria (persistent elevations of plasma creatinine ≥200% above baseline despite adequate fluid resuscitation) within seven days after surgery and in the absence of a clear-cut alternative cause (such as major systemic complication of surgery).

Depending on the findings of the independent Monitoring Committee, the study may then close or resume with changes as recommended.

Endpoints

The primary endpoint is urinary concentration of NGAL at 2 pm on POD 1. Secondary endpoints are listed in Table 3.

Urine samples are collected once at the preoperative research visit and at regular intervals during and 72 hours after surgery and once on POD 30 (See further Blood and urine sampling protocol).

Plasma samples are collected three times at the preoperative research visit, at regular intervals during and 72 hours after surgery and once on POD 30. In addition, two more samples are taken when the sinistrin-PAH test is repeated 0800-1100 on POD 1 (See further Blood and urine sampling protocol).

Clinical data including demographics, diagnosis, surgery, anaesthesia, complications and recovery parameters are prospectively collected as per standard practice by an ERAS Nurse Specialist in the Auckland ERAS database.

Sample handling and analysis

A research fellow or a research nurse will collect all samples. Some assays will be performed on collection by Waitemata DHB Laboratories; others will be stored in a dedicated -80°C alarmed research freezer at Waitemata DHB Laboratories for later batch analyses by the Christchurch co-investigators. All assays will be performed by staff unaware of participants' group allocation.

Statistical considerations

On the basis of a recent study in surgical trauma, the mean (SD) urinary NGAL concentration at 2pm on the first postoperative day in the control (High) group is assumed to be 10 (10) ng/ml, and the clinically significant cut-off in the Low group is assumed to be 25 ng/ml. To show non-inferiority with 90% power, a minimum of 18 participants completing the study per treatment group will be needed based on a margin of non-inferiority of 15 µg/L (25-10 ng/ml), a common SD of 15 ng/ml, and 0·05 one-sided significance level. Assuming 10% dropout, 20 participants per treatment group will be recruited (40 participants in total).

Certain data indicate that urinary NGAL follows a log-normal distribution. To ensure this will not increase the sample size required, a sample size calculation taking this into account

has also been performed. This indicates that a minimum of 31 participants, 15.3 in each treatment arm, will be needed based on a margin of non-inferiority of log 15 ng/ml and an SD of log 10 ng/ml, with 90% power using a one-sided statistical test with an alpha level of 0.05. A sample size of 40 patients will therefore be sufficient should urinary NGAL be log-normally distributed in the planned study. This sample size calculation was performed with the assistance of Dr Lifeng Zhou, Waitemata DHB statistician.

Repeated measures will be analysed by analyses of variance for repeated measures (time x treatment group with post-hoc Tukey's test as appropriate) or mixed regression models if appropriate. Student's unpaired t-test or, if non-normally distributed, Mann-Whitney U test and Fisher's exact test will be used as appropriate.

Planned subgroup analysis are: moderate vs no chronic kidney disease, patients with vs without epidural analgesia, patients undergoing surgery via laparotomy vs laparoscopy.

Appendices

1. Blood and urine sampling protocol
2. Clearance studies protocol

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ALIQUOTS						Preop visit 1 wk preop				Surgery	Time 0 = induction				POD 1					POD 2		POD 3	POD 30
	Tube	Centrifuge within	Centrifuge at temp	Volume of spun blood or urine	Freeze Temperature	10am	11am	12:40pm	1pm	0h	1h	2h	6h	10h	8am	10am	12:40pm	1pm	8pm	8am	8pm	8am	10am
BLOOD - ANALYSE																							
Crea, Na, K	Li heparin	2 hours	20 degrees	500	N/A	X				X		X	X	X	X				X	X	X	X	X
Glucose	Li heparin	1h	20 degrees	500	N/A	X							X		X				X	X	X	X	X
CRP	Li heparin	8 hours	20 degrees	500	N/A	X							X		X					X		X	
Osmolality	Li heparin	8 hours	20 degrees	1500	N/A	X							X		X				X	X	X	X	X
Hct	EDTA	2 hours	20 degrees	500	N/A	X						X	X		X				X	X	X	X	X
URINE - ANALYSE																							
Creatinine, Na, K	Std	2 hours		10000	N/A	X						X	X	X	X				X	X	X	X	X
Osmolality	Std	2 hours		10000	N/A	X						X	X	X	X				X	X	X	X	X
PLASMA - FREEZE																							
Renin	EDTA	30m	20 degrees	500	-80	X						X	X		X					X		X	
Aldo	EDTA	30m	20 degrees	250	-80	X						X	X		X					X		X	
ADH	EDTA	30m	4 degrees	600	-80	X						X	X		X					X		X	
PAH	EDTA	15min	4 degrees	2000	-80			X	X								X	X					
Sinistrin	EDTA	15min	4 degrees	2000	-80			X	X								X	X					
Angiot-II	Special tube SST/Plain	immediate	4 degrees	3000	-80	X						X	X		X					X		X	
Cystatin C	Li heparin	jill	4 degrees	500	-80	X						X	X	X	X				X	X		X	X
Extra x3	Li heparin		4 degrees	100	-80	X				X	X	X	X	X	X				X	X	X	X	X
Extra	Li heparin		4 degrees	700	-80	X				X	X	X	X	X	X				X	X	X	X	X
Extra x2	EDTA		4 degrees	700	-80	X				X	X	X	X	X	X				X	X	X	X	X
URINE - FREEZE																							
PAH		15m	4 degrees	2000	-80				X									X					
Sinistrin		15m	4 degrees	2000	-80				X									X					
NGAL		24 hours	4 degrees	1500	-80	X						X	X	X	X				X	X	X	X	X
Extra x4					-80	X				X	X	X	X	X	X				X	X	X	X	X

Measured Renal Blood Flow and Glomerular Filtration Rate Protocol

- An intravenous cannula is inserted in to each forearm. One is for continuous infusion and the second is for venous blood drawing
- Each participant will receive a bolus loading dose and then infusion of *p*-aminohippurate sodium and sinistrin
- The infusions should be commenced prior to 0900 hours to control for the circadian rhythm of clearance of these substances
- After the cannula are inserted a venous blood sample will be drawn for sodium, creatinine, urea, chloride, haemoglobin, haematocrit, fasting lipids, fasting glucose, and neurohormones, sinistrin, and PAH

P-aminohippurate (PAH) infusion

a) Aim for 20mg of PAH / litre of extracellular fluid volume (ECF)

b) ECF volume (litres) = 16-20% of target body weight (kilograms)

c) If participant has oedema the ECF volume will be estimated as (16-20% of target body weight) + (estimated oedema weight)

d) Therefore in a 70 kg participant without oedema
Bolus dose
= 0.18 x 70 L x 20mg
= 280mg of 20% solution
= 1.4mL 20% solution PAH

e) PAH clearance (infusion rate in mg/hour)=estimated GFR (ml/min) by 0.02 (plasma PAH concentration expressed in mg/ml) x 5 (clearance factor) x 60

Sinistrin infusion

Bolus dose

a) Aim for 200mg/L of sinistrin in effective volume of distribution (extracellular fluid volume (ECF))

b) ECF volume (litres) = 16-20% of target body weight (kilograms)

c) If participant has oedema the ECF volume will be estimated as (18% of target body weight) + (estimated oedema weight)

d) Therefore in a 70 kg participant without oedema ECF volume = 12.6L to achieve sinistrin level of 200mg/L

Bolus dose of sinistrin
= 12.6 x 200/1000
= 2.52g

Infusion Rate

a) Sinistrin clearance (infusion rate in mg/hour) = estimated GFR (ml/min) by 0.2 (plasma PAH concentration expressed in mg/ml x 60

b) Therefore in a 70 kg person with a GFR of 80 ml/min the infusion rate/hour
= 80 ml/min x 0.2 mg/ml x 60min
= 960mg/hour
= 3.84ml/hour of sinitrin 25%

Plasma Sampling

After an equilibration period of 160 minutes a venous sample will be drawn for sinistrin, and PAH. These will be placed into chilled BD (EDTA) vacutainers and placed on ice. This will be centrifuged within 10 minutes. Venous samples will be drawn at 160 and 180 minutes after the start of the infusion for plasma PAH and sinistrin after which time the infusion will be stopped. Infusate volume from each ampoule will be sent for concentration.

Sinistrin and PAH clearance calculation

The clearance of sinistrin and hippurate will be calculated as follows

- All plasma concentrations will have the plasma concentration [blank] subtracted

$$\text{Clearance (sinistrin or hippurate)} = \frac{I \cdot V_i}{P \cdot \Delta t}$$

where I is the infusate concentration, V_I is the infusion volume, P is the arithmetic mean of the plasma concentrations.

Enhancing recovery after surgery
Surgical team protocol: Small bowel and colon surgery

Scope: This clinical pathway outlines the standard care for elective open or laparoscopic small bowel or colon surgery (including high anterior resection without dissection below peritoneal reflection).

Deviations: Protocol deviations are authorised by the patient's surgeon or anaesthetist, and documented by the nurse on the *Care Plan.*

Length of stay: Expected length of postoperative hospital stay is 4 nights.

Before surgery

- Preoperative patient education 1-2 weeks before surgery.
- Bowel preparation according to Departmental *Bowel Preparation Protocol.*
- Same-day admission.
- Normal diet allowed until 6 hours before anaesthesia. Clear oral fluids allowed until 2 hours before anaesthesia.
- Preoperative oral carbohydrate treatment 2 hours before anaesthesia. **Exceptions:** pts with insulin-treated diabetes; pts with signs of gastrointestinal obstruction (bloating, nausea).
- Admitting nurse ensures that time oral carbohydrate is taken is documented on the *How to take your Nutricia PreOp® Drink* form.

Surgery

- Minimally invasive techniques and short incisions are used.
- Abdominal wound drainage is avoided.

Day of surgery

- After surgery, 500 ml dextrose-saline until 8 am POD 1. Diabetics on GIK infusion (approx 80 ml/h) need no other IV fluids.
- Free oral fluids and a sandwich offered 4 h after surgery.
- Postoperative oral fluid intake target: 600 ml (including 400 ml Fortisip).
- Postoperative nutritional target: 2 cartons (400 ml) of Fortisip.

- Urine output target is >0.5 ml/kg/h (for 50 kg patient, 25 ml/h; for 75 kg, 33 ml/h; for 100 kg, 50 ml/h). *See Anaesthetic Team Protocol for poor urine output action plan.*
- Mobilisation target: 2 hours out of bed (in chair or walking).
- Ensure paracetamol and Clexane (8 pm) charted.

Postoperative day 1

- IV infusion stopped at 8 am.
- Check body weight by 10 am.
- Standard (not postoperative) diet.
- Oral fluid intake target: 1500 ml (including 600 ml Fortisip).
- Nutritional target: 3 cartons (600 ml) of Fortisip. Some cooked food.
- Urine output target is >0.5 ml/kg/h (for 50 kg patient, 25 ml/h; for 75 kg, 33 ml/h; for 100 kg, 50 ml/h. *See Anaesthetic Team Protocol for poor urine output action plan.*
- Mobilisation target: 8 hours out of bed (in chair or walking). Four short walks (10 minutes each).

Postoperative day 2

- Urinary catheter removed at 8 am.
- Make sure epidural stopped (and oral etoricoxib and tramadol started) by 10 am.
- Check body weight by 10 am.
- Standard diet.
- Oral fluid intake target: 1500 ml (including 600 ml Fortisip).
- Nutritional target: 3 cartons (600 ml) of Fortisip. Half a cooked meal
- Mobilisation target: 8 hours out of bed (in chair or walking). Four short walks (10 minutes each)

Postoperative day 3 and onwards

- Check body weight by 10 am.
- Standard diet.
- Oral fluid intake target: 1500 ml (including 600 ml Fortisip).
- Nutritional target: 3 cartons (600 ml) of Fortisip. Half a cooked meal.
- Mobilisation target: 8 hours out of bed (in chair or walking). Four short walks (10 minutes each).

Discharge criteria (pt to be discharged when all three criteria are fulfilled)

1. No need for IV fluid infusions or nutrition (able to drink and eat).

2. No need for epidural or IV analgesia (pain scores ≤4 on oral analgesia).

3. No need for continued observation: normal temperature and vital signs, resumed bowel function (repeated flatus or stool, through stoma if patient has stoma).

After discharge

- Colorectal nurse specialist calls pt 48 hours after discharge.
- Patient telephones Ward 8 directly during first 7 days after surgery in case of concerns.
- Surgical clinic follow up 4 weeks after surgery (Oncology referral sooner as appropriate).

Waitemata District Health Board
Te Wai Awhina

Enhancing recovery after surgery

Anaesthetic team protocol: Colorectal surgery

Scope: This clinical pathway outlines the standard care for elective open or laparoscopic small bowel, colon and rectal surgery.

Premedication: No routine premedication. Midazolam in highly anxious patients.

Preoperative fluid management:

- Normal diet allowed until 6 hours before anaesthesia. Clear oral fluids allowed until 2 hours before anaesthesia. IV fluids not used prior to surgery.
- Most pts will have no oral bowel prep. Most pts will have 400 ml oral carbohydrate solution 2 hours prior to anaesthesia.

Epidural analgesia (currently used for all cases including laparoscopic):

- Insertion level T7-9 (all small bowel, colon and rectal surgery).
- Test before induction: 5-10 ml bupivacaine 5 mg/ml, check bilateral block (sensory loss to touch over dermatomes to be affected).
- Intraop block: 5-10 ml/h bupivacaine 0.125% + fentanyl 2 mcg/ml.
- End of surgery - 8am POD1: PCEA + basal rate (5 ml bolus / 20 mins lockout / 5 ml/hr).
- 8am POD1 - 8am POD2: PCEA (5 ml / 20 min lockout). Remove epidural by 10 am POD2. Ensure Clexane given more than 12 h prior to removal and not within 4 hours after removal.
- Epidural to be resited – if possible – if analgesia ineffective before 8pm on day of surgery. Otherwise start IV PCA with oxycodone 1mg bolus, 5 min lockout.

Induction and maintenance of general anaesthesia:

- TIVA using propofol (2.5-4.5 mcg/ml target range) or desflurane (0.6-1.5 MAC), along with either remifentanil (0.2-0.4mcg/kg/min) or fentanyl (up to 5mcg/kg) with BIS or entropy monitoring (target range 20-60 units).

Nasogastric tube:

- Only on indication (gastric distension).
- Pull before extubation.

Active warming: Core temp target >36°C by upper body warming and warm infusions

Antiemetics: Follow routine hospital protocol

Intraop maintenance fluid therapy:

- Avoidance of fluid and sodium overload is top priority. For a 75-kg patient:

- Duration of surgery <180 min: 1000 ml Plasma-Lyte 148 + 1000 ml Gelofusine
- Duration of surgery >180 min: 1500 ml Plasma-Lyte 148 + 1000 ml Gelofusine

Postop maintenance fluid therapy and transfusions:

- Start a bag of 500 ml dextrose-saline with 10mmol KCl to run until 8 am POD 1, at which time IV fluids are discontinued. (Diabetics on GIK infusion (approximately 80 ml/h) need only their GIK.)
- Note that total fluid intake on day of surgery is about 1000 ml PO (PreOp® + postop oral fluids) + 2500 ml IV = 3500 ml in total.
- If Hgb <80, transfuse 2U RBCs. If Hgb 80-100, transfuse 2U RBCs only if symptomatic or ischaemic heart disease or evidence of ongoing bleeding.

Urine output:

- Target is ≥0.5 ml/kg/h (for 50 kg patient, 25 ml/h; for 75 kg, 33 ml/h; for 100 kg, 50 ml/h).
- If urine output <0.5 ml/kg/h: 1) examine patient, review fluid balance and fluid status, and contact patient's anaesthetist and surgeon if any signs or symptoms of hypoperfusion (for example, sepsis or heart failure); 2) give 500 ml of Plasma-Lyte 148 IV over 15 min; 3) review urine output over next hour; 4) if urine output still <0.5 ml/kg/h go back to 1) repeating until 2 L Plasma-Lyte 148 has been given; 5) obtain senior review.

Epidural-related symptomatic hypotension in theatre, PACU, HDU:

1) Metaraminol infusion per protocol, 2) ephedrine IV if bradycardic,
3) noradrenaline infusion

Epidural-related symptomatic hypotension on ward:

1) Review patient and liaise with patient's anaesthetist and surgeon,
2) 500 ml of Plasma-Lyte 148 IV over 15 minutes, 3) Stop epidural basal rate,
4) 500 ml of Plasma-Lyte 148 IV over 15 minutes, 5) consider other causes

Postoperative multimodal analgesia *- these are prescribed by patient's anaesthetist on day of surgery in theatre:*

From surgery - POD 1 8 am: paracetamol 1g IV (or PO if tolerated) 6-hrly

From POD1 8 am: paracetamol 1g PO 6-hrly

From POD2 8 am - POD7: etoricoxib 60-90 mg PO OD

From POD2 8 am - POD7: tramadol SR 100mg PO 12-hrly

Breakthrough pain:
1) Assess epidural function and liaise with patient's anaesthetist,
2) Tramadol 50-100mg 6rly PO/IV,
3) oxycodone sustained release (Oxycontin) PO 10-20mg PRN,
4) oxycodone 0.5-1mg IV PRN