Effect of intraoperative fluid optimisation on renal function in patients undergoing emergency abdominal surgery; a randomised controlled pilot study (ISRCTN 11799696)

Fluid optimisation for emergency surgery

J Harten[1], JEM Crozier[2], B McCreath[1], A Hay[3], DC McMillan[2], CS McArdle[2], J Kinsella[1]

Departments of Anaesthesia[1] and Surgery[2], University of Glasgow, Glasgow, UK

University Departments of Anaesthesia[3], Royal Infirmary Edinburgh, Edinburgh, UK

Correspondence to:

Dr Johann Harten,

Department of Anaesthesia,

Gartnavel General Hospital,

Shelley Court, Glasgow G12 0YN

Phone No. 0141 211 4625

Fax No. 0141 211 1191

E-mail. jharten@doctors.org.uk

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Abstract

Background: Emergency abdominal surgery carries a high risk of postoperative morbidity and mortality. Goal directed therapy has been advocated to improve outcome in high risk surgery**.** The aim of the present pilot study was to examine the effect of goal directed therapy using fluid alone on postoperative renal function and organ failure score in patients undergoing emergency abdominal surgery.

Methods: This prospective randomized pilot study included patients over the age of 50 undergoing emergency abdominal surgery. In the intervention group pulse pressure variation measurements were used to guide fluid boluses of 6% Hydroxyethylstarch 130/0.4. The control group received standard care. Serum urea, creatinine and cystatin C levels were measured prior to and at the end of surgery and postoperatively on days 1&3&5.

Results: 30 patients were recruited. One patient died prior to surgery and was excluded from the analysis. The intervention group received a median of 750 ml of hydroxyethylstarch. The peak values of postoperative urea were 6.9 (2.7-31.8) vs 6.4 (3.5-11.5) mmol/l (p=0.425), creatinine 100 (60-300) vs 85 (65-150) umol/l (p=0.085) and cystatin C 1.09 (0.66-4.94) vs 1.01 (0.33-2.29) mg/dl (p=0.352) in the control and intervention group respectively.

Conclusions: In the present pilot study replacing the identified fluid deficit was not associated with a change in renal function. These results do not preclude that goal directed therapy using fluid alone may have an effect on renal function but they would suggest that the effect size of fluid optimization alone on renal function is small.

Keywords: Surgery abdominal, Kidney function, Fluid i.v.

Introduction

Despite improvements in surgery and peri-operative care, mortality following emergency abdominal surgery remains high with death rates in excess of 20% being reported consistently.[1 2] Few studies have identified factors which give prognostic information in patients undergoing emergency abdominal surgery. Recognised factors include magnitude of surgical insult, admission to intensive care unit, age and ASA status. [2 3] Biondo and coworkers reported, that following emergency abdominal surgery, multiple organ failure was also important risk factor for 30 day mortality. [4] It is of particular interest that renal failure, as indicated by a raised creatinine [5] or urea [3] were associated with an increased 30 day mortality.

Standard treatment for high-risk surgical patients is to maintain cardiovascular parameters such as blood pressure, heart rate, central venous pressure and urine output within the normal range using fluids initially and inotropic agents if required. "Goal directed therapy" aims to optimise the cardiovascular system and in particular oxygen delivery to support vital organs including renal function. [6 - 8] This treatment strategy employs fluids in addition to inotropes to achieve this cardiovascular goal. Although this approach has been associated with a reduced 30 day mortality it remained controversial for a number of reasons. Firstly, it involved complex and heterogenous protocols which were difficult to transfer from the research stage into clinical practice. Furthermore, the protocols involved invasive monitoring and inotropes and therefore required peri-operative admission to the intensive care unit with significant resource implications. As a consequence implementation of these strategies has not been widespread. Moreover the respective values of fluid optimisation and the provision of inotropes is also not well understood. [9] In several studies, in patients undergoing elective abdominal surgery, intraoperative optimisation with fluids alone and without the use of inotropes, was associated with improved outcomes such as reduced hospital stay and

improved gastrointestinal function. [10 - 12] Clearly, if it was shown that in emergency abdominal surgery goal directed therapy using fluid alone during the intraoperative period had significant value then this simplified low risk approach could then be more readily incorporated into clinical practice.

The aim of the present pilot study was to examine the effect of intra-operative goal directed therapy using fluid alone on postoperative renal function and organ failure score in patients undergoing emergency abdominal surgery.

Patients and Methods

Study setting and patients

Local research ethics committee approval and written informed consent was obtained for this study. Patients, aged 50 years or over, who were to undergo emergency abdominal surgery at the Royal Infirmary, Glasgow between September 2003 and February 2005 were included in the study. Patients were recruited between the hours of 8 am to 8 pm on weekdays. Those patients who presented as an emergency following trauma, were to undergo vascular surgery, in whom surgery was expected to last less than 90 minutes or who were on lithium drug therapy were excluded from the study.

Study design and randomisation

Patients eligible for this randomised controlled study were allocated to control and intervention arms using opaque sealed envelopes immediately prior to surgery. The study group allocation was not blinded as the control group received no form of study intervention. Fluid optimisation was carried out by three investigators (JH, BMcC, AH) none of whom were present at the operations in the control group.

Intervention

In the intervention group an arterial line was sited and connected to the Lidco cardiovascular monitor according to manufacturer's instructions (Lidco plus system, Lidco Ltd., Cambridge, UK). This monitor displays cardiac output, stroke volume, heart rate, systemic vascular resistance, systemic oxygen delivery and pulse pressure variations. Fluid boluses of 250ml of 6% Hydroxyethylstarch 130/0.4 (Voluven, Fresenius Ltd, Cheshire, UK) were administered over 15 minutes during the operation if the pulse pressure varied by more than 10% (modified from Michard and colleagues [13]). This was in addition to the normal fluid administration by

the anaesthetist in charge of the patient. Data were recorded manually in 15-minute intervals throughout the operation.

The clinical team in charge of the patient in the intervention group did not have access to the data provided by the Lidco monitor or the volume of hydroxyethylstarch administered during the operation by the research team.

The control group received standard care by the clinical team in charge of the patient without the investigator being present in theatre. The type of anaesthesia in both study arms was at the discretion of the anaesthetist in charge of the patient. At the end of the surgical procedure, the pulse contour analysis monitor was disconnected. Postoperatively both patients, in the protocol and intervention group, were managed in the High Dependency or Intensive Care Unit and discharged to the ward when clinically deemed appropriate.

Outcome measures

Urea, creatinine and cystatin C were measured to assess renal function prior to surgery, immediately postoperatively, day 1, day 3 and day 5 following surgery. Arterial and venous blood gas samples were measured if an arterial or central venous line was clinically indicated (following the induction of anaesthesia (n=22), at the end of surgery (n=25), day 1 (n= 20), day 3 (n= 7) and day 5 (n=3)). The effects of serum electrolytes and weak acids on base excess were calculated using the simplified approach as described by Story. [14]

The Sequential Organ Failure Assessment (SOFA) score was calculated to assess organ function prior to and following surgery on days 1, day 3 and day 5 as described by Vincent and coworkers [15]. The score was modified in patients in whom arterial blood gases were not

available. In these patients the PaO2/FiO2 ratio was substituted with the oxygen flow required to obtain an oxygen saturation ≥94 % as follows: score of 0 if < 2 l/min; score of if 2-3 l/ min; score of 2 if 4-7 l/min; score of 3 if >7 l/min.

The Systemic Inflammatory Response Syndrome (SIRS) score were assessed prior to and following surgery on day 1, day 3 and day 5. [16] The Revised Cardiac Risk Index [17] and P-POSSUM [18] scores were documented immediately before emergency surgery.

The Postoperative Morbidity Survey is validated for patients following elective surgery usually associated with a short length of hospital. [19] We modified this score for emergency surgery, with a corresponding longer length of hospital stay, by assessing the incidence and pattern of postoperative complications on day 5, day 15 and day 30 rather than day 3, day 5 and day 7.

Mortality at 30 days and length of hospital stay was confirmed from Greater Glasgow Health Board.

Statistics

Data are presented as median (range). Where appropriate comparisons of data were carried out using the chi-square test and Mann Whitney test. Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, Illinois, U.S.A.).

Results

During the study period 153 patients underwent emergency abdominal surgery; of these 19% of patients did not meet inclusion criteria of the study. A further 41 % presented for surgery out of hours and 20% could not give informed consent. 30 (20%) patients were recruited into the study (Figure 1). One patient who was randomised to the intervention group died prior to surgery and did not receive the intervention. This patient was excluded from the analysis.

The pre-operative characteristics of the control and intervention groups are shown in Table 1. The majority of patients were over the age of 60 years, male, and had Possum (physiological), ASA and Lee scores associated with increased risk of peri-operative mortality. Patient characteristics were similar in control and intervention groups.

The intra-operative characteristics of the control and intervention groups are shown in Table 2. The site, severity and duration of surgery and anaesthetic technique were similar between the groups. Also the administration of crystalloids, colloids and fluid balance were similar in both groups. The intervention group received a median of 750 ml hydroxyethylstarch. The median central venous pressure ($p<0.01$) and the hourly urine output ($p<0.05$) during surgery were higher in the intervention group.

At the end of surgery there were no differences in venous blood gases between the control and intervention groups. Both groups had a mild acidosis, normal central venous oxygen saturations and normal lactate concentrations.

Overall, the surgical Possum score was greater in the intervention group ($p<0.05$). This may have been due to a trend towards increased blood loss ($p=0.377$) and peritoneal soiling ($p=0.177$) in the intervention group.

The intra-operative haemodynamic characteristics of the intervention group are shown in Table 3. The data for 2 patients in the intervention was not collected. Pulse pressure variation ($p<0.01$) was higher, and cardiac output ($p< 0.05$) and stroke volume ($p<0.05$) were lower following induction of anaesthesia than at the end of surgery. The haemoglobin concentration and oxygen content of blood were lower at the end of surgery than following induction of anaesthesia ($p< 0.01$). There was no significant difference in oxygen delivery between the start and end of surgery.

The peri-operative characteristics of the control and intervention groups during the initial 24 hours are shown in Table 4. There were no significant differences in haemodynamic or fluid balance data for the groups.

Organ and renal function data in the peri-operative period are shown in Table 5. In both control and intervention groups the SOFA score peaked on day 1. The peak urea, creatinine and cystatin C occurred either pre-operatively or on day 1. There were no significant differences between the control and intervention groups in the peak values of urea ($p=0.425$), creatinine ($p=0.085$) and cystatin C ($p=0.352$).

The serum concentrations of albumin, sodium and chloride in the peri-operative period are shown in Table 6. The highest serum sodium and chloride concentrations values were either in recovery or on day 1 in both groups. The trough value for albumin occurred immediately

postoperatively. There were no differences in peak values of serum sodium ($p=0.112$) and chloride ($p=0.847$) and trough values of albumin ($p=0.425$) and calculated base deficit ($p=0.425$).

The PMS scores and length of hospital stay data of the control and intervention groups are shown in Table 7. There were no significant differences in the number of patients that remained in hospital on day 5 and 30. On day 15 more patients were in hospital ($p<0.05$). There was a trend towards more complications on day 15 in the intervention group (Table 8). There was no difference in overall length of stay ($p=0.252$). Also, hospital and 30 day mortality was similar in the control and intervention groups.

Discussion

In this randomised controlled pilot study, in patients undergoing emergency abdominal surgery, the effect of fluid optimisation alone on renal and organ function was examined. Based on increased pulse pressure variations of greater than 10 % we identified a median fluid deficit of 750 ml. However, the correction of the fluid deficit with hydroxyethylstarch was not significantly associated with either parameters of improved renal function or with reduced complications and hospital stay. This is, to our knowledge, the first study to examine the effect of fluid optimisation alone in patients undergoing emergency abdominal surgery and provide baseline information for future fluid alone intervention studies in these patients.

It has long been recognised that organ hypoperfusion has been associated with poorer outcome and this has been the basis for using goal directed therapy as a means to optimise organ perfusion and oxygen delivery. A number of workers [6 - 9] have shown that goal directed therapy using the combination of fluid and inotropes during the perioperative period reduced complications, length of hospital stay and mortality in patients undergoing high risk surgery. This effect has mainly been observed in patients undergoing high risk surgery with mortality rates in excess of 20%. [20] We have previously shown that, in almost 600 patients between 1998 and 2000, the 30-day mortality in patients undergoing emergency abdominal surgery was 26% and therefore represent a suitable target group for goal directed therapy. [3]

In the present study the operative mortality, at 10%, was lower than expected. The reasons for the difference in mortality rates between the two cohorts is not clear. However, this may reflect the small sample size. Alternatively, that 30 day mortality in these patients had decreased in the period between the two studies. Indeed, when we examined the outcome of all patients who underwent emergency surgery during the study period (n=153) 30 day

mortality was 21%. This confirms that a relevant high risk cohort was studied but raises the issue of why mortality in the experimental group (n=29) was only 10%. When we examined the study patients in detail, it would appear that obtaining consent was more problematical in the higher risk patients and that there was a tendency for high risk patients to present for surgery out with the daytime recruitment hours.

In this study the primary endpoint was renal function. In order to assess renal function in detail we measured serum urea, creatinine and cystatin C pre-operatively and throughout the postoperative period. Despite this detailed examination of renal function there were no differences between the control and intervention groups. Similarly, there was no beneficial effect on organ, gastrointestinal or hospital stay. The reasons for the lack of therapeutic effect of fluid therapy is unclear. It may be that the therapeutic effect of fluid optimisation is relatively small and would not have been detected in the present pilot study. Indeed, in recent randomised studies of elective surgical patients, undergoing fluid optimisation alone, the effect on hospital stay was only of the order of 10% to 15%. [10 - 12] This raises the issue of whether fluid optimisation alone can produce substantial benefits in the surgical patient. It is also of interest that the initial cardiac output was 5 l/min suggesting that these, and presumably also the patients in the control group, were well resuscitated prior to surgery and hence the effect size of fluid optimisation would be expected to be relatively small. Furthermore, there may be other factors that contribute to the lack of effect observed in this study. Previous studies have identified a therapeutic effect only when the oxygen delivery was raised to predefined targets. [6 - 9] It is of interest that in this study, although stroke volume and cardiac output increased in response to the fluid therapy, oxygen delivery, as a consequence of a decreased oxygen content, did not increase significantly. This could have accounted for the lack of effect seen in this study. Moreover, hydroxyethylstarch (Voluven),

the solution used in this study to optimise the cardiovascular system contains a high chloride contents which could result in a hyperchloraemic metabolic acidosis as a consequence of a reduced strong ion difference. Such a metabolic derangement has been associated with impaired organ and renal function. [21] It would therefore be possible that the potential beneficial effect of fluid optimisation was mitigated by an excessive chloride load. However, there was no evidence of a reduced strong ion difference measured in this study to support this explanation. In summary, the results of this pilot study would suggest that the effect of fluid optimisation alone on renal or organ function in well resuscitated patients undergoing emergency abdominal surgery is small. This would therefore indicate that further trials of the effect of fluid optimisation alone would not only require much larger cohorts of patients than have been studied to date but should also include those high-risk individuals who are presenting out of hours or who are unable to give consent for emergency surgery.

Perioperative fluid therapy is part of routine care. However, the optimal fluid strategy is unclear. It has long been recognised that fluid overload appears to be associated with increased complications and a prolonged hospital stay. [22] It is of interest that perioperative restriction of fluids was associated with improved outcome in some studies [23-25] but not others. [26] Taken together the results of studies examining fluid balance in high risk surgical patients would suggest that fluid should only be given to those patients with proven fluid deficit. However, the best method to demonstrate a fluid deficit in surgical patients is unclear. A number of workers [10-12] have examined the use of oesophageal Doppler guided fluid therapy during the intra-operative period in patients undergoing high risk surgery. In these studies fluid alone was associated with fewer complications, in particular gastrointestinal complications, and reduced length of hospital stay. However, when using this monitor we found that artefacts, in particular resulting from diathermy, which is extensively used

abdominal surgery, limited the usefulness of this device. More recently, pulse pressure variation in response to mechanical ventilation has been advocated to assess fluid volume status. [13] This technique has a number of advantages; it is simple to use, non-invasive and in addition this technology is free from interference by diathermy. Our study is the first to show that this method is a feasible approach to intraoperatively assessing fluid balance. We chose a pulse pressure variation of more than 10% as the trigger for the administration of a bolus. The optimal trigger is unknown. Previous work has identified patients to be fluid responsive if pulse pressure variation varied by more than 13%. [13] In the present study the volume of fluid administered was higher than described in previous work (750 ml vs $\leq$ 500ml) using the oesophageal Doppler monitor. It is of interest that in the intervention group of the present study a larger proportion of patients was in hospital on day 15 and there was a trend towards increased postoperative complications in the intervention group. It is therefore possible that a low threshold trigger could have led to excessive fluid administration and therefore be related to the trend towards prolonged hospitalisation. Further work is required to identify the optimal trigger for intraoperative fluid administration when using pulse pressure variation.

Limitations of the present study include the small number of patients recruited in a single centre. Nevertheless this is to our knowledge the largest study of fluid optimisation in patients undergoing emergency abdominal surgery. The study included patients undergoing a wide spectrum of clinical problems which was managed by varying anaesthetic and surgical staff. As a consequence of this it was unfeasible to standardise clinical management which resulted in larger variability of clinical care and this could have mitigated the potential effect of the intervention. The present study, although not fully blinded, was randomised and the collection of the postoperative data was carried out by an investigator (JEMC) who was unaware of the patient allocation. Furthermore, in order to minimise the potential bias in the

intervention group the additional haemodynamic data and volume of hydroxyethylstarch administered was concealed from the clinical team in charge of the patient. Clearly, in the control group the absence of additional cardiovascular monitoring reduced potential bias but also meant that no comparative intraoperative haemodynamic data could be recorded.

In summary, the results of the present pilot study show that fluid optimisation based on pulse pressure variation is feasible and identified a fluid deficit in patients undergoing emergency abdominal surgery. However, replacing such fluid was not associated with an improvement in renal or organ function. Although these results do not preclude that goal directed therapy using fluid alone may have an effect on renal function following emergency abdominal surgery, they would however suggest that the effect size of this intervention on renal function is small. Fluid optimisation was also associated with a prolongation of hospital stay and a trend towards increased complications that may be related to excessive volume of fluid.

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References

1. Cook TM, Britton DC, Craft TM, Jones CB, Horrocks M. An audit of hospital mortality after urgent and emergency surgery in the elderly. *Ann R Coll Surg Engl* 1997; **79**:361-367

2. Harten J, McCreath BJ, McMillan DC, McArdle CS, Kinsella J. The effect of gender on postoperative mortality after emergency abdominal surgery. *Gend Med* 2005; **2**:35-40

3. Harten J, Hay A, McMillan DC, McArdle CS, O'Reilly DS, Kinsella J. Postoperative serum urea is associated with 30-day mortality in patients undergoing emergency abdominal surgery. *Ann Clin Biochem* 2006; **43**:295-9

4. Biondo S, Ramos E, Deiros M, et al. Prognostic factors for mortality in left colonic peritonitis: a new scoring system. *J Am Coll Surg* 2000; **191**:635-42

5. Biondo S, Pares D, Frago R et al. Large bowel obstruction: predictive factors for postoperative mortality. *Dis Colon Rectum* 2004; **47**:1889-97

6. Boyd O, Grounds RM, Bennett ED. A randomized clinical trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high-risk surgical patients. *JAMA* 1993; **270**:2699-2707

7. Shoemaker WC, Montgomery ES, Kaplan E, Elwyn DH: Physiologic patterns in surviving and nonsurviving shock patients. Use of sequential cardiorespiratory variables in defining criteria for therapeutic goals and early warning of death. *Arch Surg* 1973; **106**: 630-6

8. Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM, Bennett ED. Early goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomised, controlled trial [ISRCTN38797445]. *Crit Care* 2005; **9**:687-93

9. Wilson J, Woods I, Fawcett J et al. Reducing the risk of major elective surgery: randomised controlled trial of preoperative optimisation of oxygen delivery. *BMJ* 1999; **318**:1099-1103

10. Wakeling HG, McFall MR, Jenkins CS, Woods WG, Miles WF, Barclay GR, Fleming SC: Intraoperative oesophageal Doppler guided fluid management shortens postoperative hospital stay after major bowel surgery. *Br J Anaesth*. 2005; **95**: 634-42

11. Noblett SE, Snowden CP, Shenton BK, Horgan AF. Randomized clinical trial assessing the effect of Doppler-optimized fluid management on outcome after elective colorectal resection. *Br J Surg* 2006; **93**:1069-76

12. Gan TJ, Soppitt A, Maroof M et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. *Anesthesiology* 2002; **97**:820-826

13. Michard F, Boussat S, Chemla D et al. Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. *Am J Respir.Crit Care Med* 2000; **162**: 134-8

14. Story DA, Morimatsu H, Bellomo R. Strong ions, weak acids and base excess: a simplified Fencl-Stewart approach to clinical acid-base disorders. *Br J Anaesth* 2004; **92**:54-60

15. Vincent JL, Moreno R, Takala J et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 1996; **22**:707-10

16. Bone RC, Balk RA, Cerra FB et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest* 1992; **101**: 644-55

17. Lee TH, Marcantonio ER, Mangione CM et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999; **100**:1043-9

18. Prytherch DR, Whiteley MS, Higgins B et al. POSSUM and Portsmouth POSSUM for predicting mortality. Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity. Br J Surg 1998; **85**:1217-20

19. Bennett-Guerrero E, Welsby I, Dunn TJ et al. The use of a postoperative morbidity survey to evaluate patients with prolonged hospitalization after routine, moderate-risk, elective surgery. *Anesth Analg* 1999; **89**: 514-9

20. Kern JW, Shoemaker WC. Meta-analysis of hemodynamic optimization in high-risk patients. *Crit Care Med* 2002; **30**:1686-92

21. Wilkes NJ, Woolf R, Mutch M et al. The effects of balanced versus saline-based hetastarch and crystalloid solutions on acid-base and electrolyte status and gastric mucosal perfusion in elderly surgical patients. Anesth Analg. 2001; **93**:811-6

22. Holte K, Sharrock NE, Kehlet H. Pathophysiology and clinical implications of perioperative fluid excess. *Br J Anaesth* 2002 ;**89**:622-32

23. Lobo DN, Bostock KA, Neal KR, Perkins AC, Rowlands BJ, Allison SP. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. *Lancet* 2002; **359**:1812-8

24. Nisanevich V, Felsenstein I, Almogy G, Weissman C, Einav S, Matot I. Effect of intraoperative fluid management on outcome after intraabdominal surgery. *Anesthesiology* 2005;**103**:25-32

25. Brandstrup B, Tonnesen H, Beier-Holgersen R et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid

regimens: a randomized assessor-blinded multicenter trial. *Ann Surg* 2003; **238**:641-8

26. MacKay G, Fearon K, McConnachie A, Serpell MG, Molloy RG, O'Dwyer Randomized clinical trial of the effect of postoperative intravenous fluid restriction on recovery after elective colorectal surgery. *Br J Surg* 2006 **93**:1469-74

Table 1. Pre-operative characteristics of control and intervention groups in patients undergoing emergency abdominal surgery (n=29)

	Control (n=15)	**Intervention (n=14)**	**p-value**
Age (years)	64 (51-76)	66 (56-75)	0.377
Gender (female/male)	3/12	3/11	0.666
BMI	26 (18-38)	23 (17-37)	0.172
POSSUM (physiological)	18 (13-40)	22 (13-44)	0.189
ASA	3 (1-4)	3 (1-4)	0.937
LEE	3 (2-4)	3 (2-4)	0.589
SOFA	1 (0-3)	1 (0-6)	0.399
SIRS	1 (0-4)	1.5 (0-4)	0.467

Table 2. Intra-operative characteristics of control and intervention groups in patients undergoing emergency abdominal surgery (n=29)

	Control (n=15)	**Intervention (n=14)**	**p-value**
Type of surgery			
Duodenal ulcer repair	1	1	
Small bowel resection	3	2	
Choelcystectomy	1	1	
Large bowel resection	9	8	
Others	1	2	
Duration of surgery (mins)	120 (45-240)	100 (40-295)	0.497
Epidural catheter (yes/no)	6/9	7/7	0.588
CVP (yes/no)	14/1	10/4	0.119
IBP (yes/no)	12/3	(14/0)	0.077
Crystalloids (ml)	2000 (0-4000)	1750 (1000-3500)	0.947
Intraop inotropic support	1	1	1.0
Colloids (ml)	1000 (0-3500)	1000 (0-3000)	0.627
Hydroxyethylstarch (ml)	0	750 (0-1750)	<0.001
Fluid balance (ml)	1910 (-280 to 4543)	1515 (-650 to3250)	0.481
Blood loss	250 (0-750)	400 (0-2000)	0.172
Haemoglobin			
Postinduction	10.7 (6.8-16.0)	11.1 (6.9-14.0)	0.838
End of operation	10.7 (7.4-13.5)	8.6 (6.9-13.5)	0.095
CVP highest (mmHg)	9 (0-12)	13 (9-17)	0.002
BP mean lowest (mmHg)	59.9 (46.5-83.2)	61.8 (39.9-93.2)	0.949
HR highest (beats/minute)	100 (80-120)	100 (70-120)	0.715
Urine output (ml/hr)	69 (0-333)	109 (57-393)	0.014
Temperature lowest (C)	36.5 (35.7-37.8)	36.4 (34.8-37.9)	0.576
End of Surgery VBGs			
H^+ (nmol/l)	47.0 (41.0-65.0)	49.4 (39.0-55.0)	0.910
BE (mmol/l)	-0.10 (-8.0 - 7.0)	-3.0 (-7.0 - 2.0)	0.616
CV SpO_2 (%)	74.0 (54.0 - 83.0)	74.6 (65.0-89.0)	0.793
Lactate (mmol/l)	1.4 (0.6 - 4.0)	1.2 (0.7 - 2.0)	0.319
Possum (surgical)	15	20	0.014

VBGs Venous blood gas sample,

CVP =central venous pressure monitoring, IBP=invasive arterial pressure monitoring

Table 3. Haemodynamic characteristics in the intervention group at postinduction and at the end of surgery.

	Postinduction (n=12)	**End of Surgery (n=12)**	**p-value**
Pulse Pressure Variation (%)	14.0 (3.3-33.0)	6.6 (3.3-14.5)	0.005
Cardiac Output (l/min)	5.05 (3.2-12.6)	5.95 (3.2-12.6)	0.023
Stroke Volume (ml)	72.0 (44.0-137.0)	82.0 (43.0-136.0)	0.030
Haemoglobin (g/dl)	11.1 (6.9-14.0)	8.6 (6.9-13.5)	0.007
Oxygen content (ml/l)	147.6 (105.5-178.4)	119.3 (95.2-176.4)	0.007
Oxygen delivery (ml/min/m^2)	352.5 (251.0-925.0)	440 (197-918)	0.799

Table 4. Immediate postoperative (24 hours) haemodynamic and fluid balance data of control and intervention groups in patients undergoing emergency abdominal surgery (n=29).

	Control (n=15)	**Intervention (n=14)**	**p-value**
Crystalloids (ml)	3100 (2200-4000)	3687 (1500-7500)	0.235
Colloids (ml)	0 (0-2250)	0 (0-1500)	0.403
Fluid balance (ml)	2055 (500 to 6205)	2935 (610 to 9570)	0.105
CVP lowest (mmHg)	1 (-3 to12)	2 (-4 to 6)	0.979
BP mean lowest (mmHg)	63.1 (49.9-89.9)	63.1 (50.2-91.2)	0.892
HR highest (beats/minute)	100 (70-126)	100 (70-125)	0.821
Urine output (ml/hr)	20 (0-50)	20 (0-50)	0.339

Table 5. Peri-operative organ function scores and renal function parameters of control and intervention groups in patients undergoing emergency abdominal surgery (n=29).

Control (n=15)	SOFA	SIRS	Urea (mmol/l)	Creatinine (umol/l)	Cystatin C (mg/dl)
Preop	1 (0-3)	1 (0-4)	5.6 (2.3-30.0)	100 (70-260)	1.19 (0.74-3.95)
Recovery			5.2 (2.1-28.1)	95 (60-280)	0.99 (0.59-3.73)
Day 1	3 (0-10)	2 (0-4)	6.7 (2.2-31.8)	95 (60-300)	0.91 (0.71-4.94)
Day 3	2 (0-10)	2 (0-4)	3.8 (1.6-24.0)	80 (55-300)	0.91 (0.61-4.41)
Day 5	1 (0-5)	1 (0-3)	4.4 (2.1-23.8)	75 (37-260)	0.96 (0.69-3.64)
Intervention (n=14)	SOFA	SIRS	Urea (mmol/l)	Creatinine (umol/l)	Cystatin C (mg/dl)
Preop	1 (0-6)	1 (0-4)	6.4 (2.3-12.3)	85 (55-160)	0.87 (0.64-2.48)
Recovery			5.2 (2.8-9.8)	77 (60-140)	0.8 (0.47-2.10)
Day 1	3 (1-4)	2 (0-4)	5.7 (3.5-10.5)	85 (60-150)	1.01 (0.63-2.29)
Day 3	2 (0-4)	1 (0-4)	4.2 (1.3-10.3)	68 (50-110)	0.86 (0.39-1.72)
Day 5	1 (0-3)	1 (0-2)	3.1 (1.2-11.9)	75 (43-140)	0.85 (0.53-1.52)

Table 6. Peri-operative albumin, electrolytes and calculated base deficit of control and intervention groups in patients undergoing emergency abdominal surgery (n=29).

Control (n=15)	Albumin (g/l)	Sodium (mmol/l)	Chloride (mmol/l)	$BDE_{Nacl+\ Albumin}$
Preop	36 (19-47)	138 (130-142)	102 (84-108)	-0.5 (-9.5 to 7.8)
Recovery	24 (11-40)	140 (134-145)	107 (95-115)	0.8 (-6.5 to 8.3)
Day 1	26 (13-48)	140 (132-146)	104 (100-111)	1.8 (-4 to 6.3)
Day 3	28 (15-34)	139 (133-146)	102 (99-114)	2.0 (-3.3 to 10.3)
Day 5	28 (17-35)	139 (134-150)	105 (97-116)	1.8 (-2.3 to 6.3)
Intervention (n=14)	Albumin (g/l)	Sodium (mmol/l)	Chloride (mmol/l)	$BDE_{Nacl+\ Albumin}$
Preop	37 (16-43)	137 (132-142)	100 (95-109)	1.0 (-7.3 to 7.5)
Recovery	20 (13-28)	140 (130-144)	104 (100-112)	0.5 (-6.5 to 11.5)
Day 1	21 (15-35)	140 (133-146)	106 (97-114)	-0.1 (-6.8 to 5.0)
Day 3	26 (21-35)	139 (130-144)	102 (99-111)	2.3 (-6.0 to 5.8)
Day 5	27 (21-36)	138 (132-144)	101 (89-107)	2.5 (-3.8 to 12.7)

$BDE_{Nacl+\ Albumin}$=calculated Base deficit (Story 2004)

Table 7. Post-operative characteristics of control and intervention groups in patients undergoing emergency abdominal surgery (n=29).

	Control	**Intervention**	**p-value**
PMS Day 5	3 (0-6)	3 (0-6)	0.982
In hospital (yes/no)	15/0	14/0	1.000
PMS Day 15	0 (0-5)	1 (0-7)	0.328
In hospital (yes/no)	4/11	9/5	0.042
PMS Day 30	0 (0-1)	0 (0-1)	1.000
In hospital (yes/no)	1/12	1/12	1.000
Hospital stay (days)	12 (7-55)	17.5 (7-41)	0.122
ITU (yes/no)	4/11	5/10	0.690
HDU (yes/no)	14/1	14/0	0.326
30 day mortality (alive/dead)	13/2	13/1	0.584

PMS =postoperative morbidity score, ITU=intensive care unit, HDU=high dependency unit

Table 8. Characteristics of post-operative morbidity score (day 15) of control and intervention groups in patients undergoing emergency abdominal surgery (n=29).

	Control	**Intervention**	**p-value**
Pulmonary (yes/no)	2/13	2/12	0.941
Infection (yes/no)	4/11	3/11	0.742
Renal (yes/no)	2/13	5/9	0.159
Gastrointestinal (yes/no)	1/14	4/10	0.119
Cardiovascular (yes/no)	1/14	1/13	0.960
Neuro (yes/no)	0/15	2/12	0.129
Wound (yes/no)	2/13	1/13	0.584
Haematology (yes/no)	0/15	1/13	0.292
Pain (yes/no)	2/13	1/13	0.584
Total number of patients with complications (yes/no)	4/11	7/7	0.196

Figure 1 Flow chart of patients presenting for emergerncy abdominal surgery