Electrolyte and Acid-base Disturbances in Emergency High-risk Abdominal Surgery, A Retrospective Study

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Abstract

BACKGROUND

Patients undergoing emergency high-risk abdominal surgery potentially suffer from both systemic dehydration and hypovolaemia. Data on the prevalence and clinical impact of electrolyte disturbances in this patient group, specifically the potential differences in patients with intestinal obstruction (IO) versus perforated viscus (PV) is lacking.

METHODS

In this retrospective single center cohort study, adult patients undergoing emergency high-risk abdominal surgery in a standardized perioperative pathway were included. Electrolyte and arterial blood gas analysis were measured prior to and just after surgery. Prevalence and clinical impact of electrolyte disturbances were assessed.

RESULTS

A total of 354 patients were included in the study. Acid-base and electrolyte disturbances had a high incidence in both groups with preoperative alkalemia dominating preoperatively, significantly more prevalent in IO (45 vs.32%, p<.001), and acidosis being most pronounced postoperatively in PV (49 vs. 28%, p<.0001). Preoperative hypochloraemia and hypokalemia were more prevalent in the IO group (34 vs 20 % and 37 vs 25 % respectively). Hyponatremia was highly prevalent in both IO and PV.

Of the electrolyte and acid-base disturbances pre- and postoperative hypochloremia were the only ones independently associated with day-30 postoperative major complications and/or death in patients with IO, OR 2.87 (1.35, 6.23) *p= 0.006* and OR 6.86 (1.71, 32.2) *p= 0.009* respectively.

Hypochloremic patients presented with reduced long-term survival as compared with the normo- and hyperchloremic patients, with postoperative hypochloremia having the most pronounced association (p<0.05). Neither plasma sodium nor potassium showed association with outcome.

CONCLUSION

These observations suggest that both acute high risk abdominal patient have frequent preoperative alkalosis shifting to postoperative acidosis, and that both pre- and postoperative hypochloremia are independently associated with both impaired short- and long-term outcome in patients with intestinal obstruction, which potential implications for the choice of resuscitations fluids. Research on pathophysiology and treatment strategies for electrolyte disturbances are needed in patients undergoing emergency high- risk abdominal surgery.

Background

Intravenous fluid therapy is one of the most frequent interventions in critically ill patients(1). All high-risk surgical patients are given intravenous fluid therapy(2) and abnormalities in acid-based homeostasis and electrolytes are common but insufficiently described.

Patients undergoing emergency high-risk abdominal surgery due to e.g. intestinal obstruction (IO) or perforated viscus (PV) potentially suffer from systemic dehydration due to inadequate fluid intake, vomiting ,pathological

vasodilation with subsequent hypotension and preload dependency as well as increased capillary permeability, but also hypovolemia due to blood loss and overwhelmingly sepsis(3,4).

Acute intestinal gut dysfunction resulting in malabsorption of macronutrients and/or water and electrolytes is almost universal in these patients, leading to a requirement for intravenous fluid and electrolyte supplementation(5). This condition is accompanied by both septic and metabolic complications as well as electrolyte shifts.

Further possible mechanisms for electrolyte disturbances include reduced kidney perfusion due to hypovolemia or hypotension; activation of hormonal systems such as renin-angiotensin-aldosterone system and vasopressin; and tubular dysfunction caused by ischemic or nephrotoxic kidney damage(6).

Sodium and chloride are the main ions of solutions used for volume expansion in critically ill and surgical patients. Due to the administration of large volumes of normal saline and/or a decreased urinary output, iatrogenic electrolyte disorders such as hyperchloremic acidosis or dysnatremia are common abnormalities in the clinical practice(7) and appear to be associated with worse outcome(8–10). This has led to a shift towards hypochloraemic fluids(balanced solutions)in perioperative care, but the impact of these on outcome is controversial, and their optimal use in the care of emergency abdominal surgery has not been established.

As such, detailed descriptive data on the prevalence and clinical impact of electrolyte disturbances in patients undergoing emergency high-risk abdominal surgery is lacking(11). This study aimed to assess the prevalence of electrolyte and acid-base disturbances and the associations with postoperative outcome in patients undergoing emergency high-risk abdominal surgery, treated within a standardized pathway, specifically focusing on potential differences in patients with IO versus PV.

Methods

Design, settings, patients

This was a planned sub-study of the principal trial(12) approved by the Danish Data Protection Agency (HVH-2013-014/052), though not addressed in the original study. In consensus with Danish law, The Regional Committee on Health Research Ethics waived the requirement for informed patient consent (H-19011165). The manuscript followed the Strengthening The Reporting of Observational Studies in Epidemiology (STROBE) statement.

Primary outcome was incidence of electrolyte disturbances in patients undergoing emergency high-risk abdominal surgery. Secondary outcomes were postoperative 30-day mortality and postoperative complications, as well as ICU stay. Exposure variables included but were not limited to age , ASA, functional performance, cardiac, pulmonary and renal comorbidities, serum electrolyte levels.

Data was be obtained from the electronic patient record (EPR) and documented using a standard report formula. There was a 100% follow-up on mortality through the Danish Civil Registration System. We evaluated patients undergoing emergency surgery due to suspicion of abdominal pathology from 1 June 2013 to 21 February 2015 (figure 1). The identification of these patients was done through electronic medical records.

Adults (18 years or over) undergoing emergency high-risk abdominal surgery for following abdominal pathology were included in the study: perforated viscus, intestinal obstruction, emergency re-operation after elective surgery, including anastomotic leak, postoperative perforated viscus owing to other than anastomotic leak and postoperative obstruction. Patients operated due to primary intestinal ischemia, primary abdominal bleeding, traumas, gynecological, urogenital and other vascular pathology, pregnant patients, reoperation owing to fascial separation with no other abdominal pathology identified and sub-acute colorectal cancer-surgery were excluded from the cohort. Appendectomies, cholecystectomies, negative diagnostic laparoscopies /laparotomies, herniotomies without bowel resections, sub-acute internal hernias after gastric bypass surgery, acute internal hernias without ileus, sub-acute surgery for inflammatory bowel diseases were excluded as well. Patients with missing data on fluid administration, vasopressor and inotropes administration, plasma electrolyte levels; as well as patients transferred to another hospital immediately following surgery were also excluded.

Perioperative management

At this surgical center, a multimodal standardized protocol(12) was applied to patients undergoing emergency high-risk abdominal surgery with focus on fast track surgery, with a senior surgeon and a senior anesthesiologist in charge of triage and preoperative treatment including preoperative resuscitation and optimization. Pre-operative high dose broad-spectrum prophylactic antibiotics, on-demand abdominal CT within 2 h, surgery within 6h after the decision to operate, peri-operative stroke volume(SV) guided fluid resuscitation (goal directed therapy (GDT)- via LiDCO Rapid guided fluid management (patients optimized by GDT had an arterial catheter placed through the radial or brachial artery) (LiDCOrapidTM; LiDCO, London, UK)(13–15), thoracic epidural analgesia when not contraindicated, Post-operative High Dependency Unit (PACU) stay for high risk patients, and early physiotherapy and mobilization.

Perioperative stroke volume guided fluid- and hemodynamic-management was applied through a standardized protocol for anesthesia and followed present NELA recommendations(3) during surgery and for first 24 hours after surgery.

Patients received a rapid sequence induction and intubation with Remifentanil, Propofol and muscle relaxant. General anesthesia was maintained with Remifentanil and Propofol, while subsequent intraoperative treatment was left to the discretion of the attending anesthesiologist guided by the institutional protocol.

The electronic medical records of enrolled patients were reviewed, and pre-, intra-, and postoperative data were collected, including demographics; comorbidities; intraoperative hemodynamics and hemodynamic therapy; surgery characteristics; pre- and postoperative blood analysis, postoperative defined as drawn up to two hours after end of surgery. Fluid administration and sensible fluid losses (output: urine, fecal, aspirate, drainage) were registered (crystalloids, colloids, blood products separately) through intraoperative anesthesia charts and postoperative PACU charts, calculated in milliliters.

Fluid administration

The preoperative resuscitation fluid amount constitutes a part of the intraoperative fluid balance and fluid administration. Intraoperative fluid balance and fluid balance for up to 24 hours postoperatively was calculated as the total fluid input (volume of colloids, crystalloids, transfusions) minus fluid output (urine output, fluid from

drains and gastric aspiration). Intra- and postoperative fluid balances were calculated in 6- hour intervals, maximal for 24 hours after surgery.

Chloride rich vs. chloride restrictive fluids

In this study, chloride rich (hyperchloremic) fluids included 0.9% saline (chloride concentration, 154 mmol/l), 4% succinylated gelatin solution (chloride concentration, 154 mmol/l). Chloride restrictive (hypo/normochloremic) fluids included Ringer's acetate crystalloid solutions (chloride concentration, 110 mmol/l), a balanced buffered solution (chloride concentration, 45 mmol/l), and a 20% albumin solution (chloride concentration, 19 mmol/l).

Selection of plasma sodium, potassium and chloride cut-offs

Patients were divided into groups based on admission plasma sodium, potassium and chloride concentrations for the purpose of analysis. The normal range for plasma sodium, potassium and chloride in our laboratory is 137-144 mmol/l and 3,5-4,4 mmol/l and 98-106 mmol/l respectively and were chosen as the initial cut-off points. The normal reference range represents the "rounded of" 95% confidence interval of sodium, potassium and chloride values for a standardized group of normal subjects selected from the local population.

All patients with admission plasma sodium value of 145 mmol/l or higher were classified as having hypernatremia and those with an initial plasma sodium within the normal range were included in the control group. Hyponatremia is generally defined as a sodium concentration of less than 135 mmol/L, with severe hyponatremia being below 120 mmol/l14, cut-off values of 130 and 120 mmol/l were chosen to divide the hyponatremic patients into mild, moderate and severe categories.

All patients with admission plasma potassium value over 4,6 mmol/l were classified as having hyperkalemia and those with initial plasma potassium within the normal range were included in the control group. Levels below 3.5 mmol/L defined as hypokalemia and defined severe when levels are less than 2.5 mmol/L(16).

All patients with admission plasma chloride value less than 98 mmol/l were considered hypochloremic, while hyperchloremia was defined as plasma chloride value above 106 mmol/l.

Statistics

Statistical analysis was performed using R Statistical Software. Patients were classified into hypo- normo- and hyper-condition as previously described, based on their baseline levels.

Continuous variables were presented as means ± standard deviation or median (interquartile range), categorical variables as numbers and %ages. T-test was applied in comparison of normally distributed data, and Wilcoxon signed-rank for non-normally distributed data. For categorical variables, a chi-square test was used.

Logistic regression was used to test for association of chloride, potassium and sodium parameters with postoperative outcome.

Univariate logistic regression was used to test for unadjusted association between chloride/sodium/potassium and outcome. Multivariate logistic regression was used to test for association between chloride/sodium/potassium and outcome after adjusting for potential confounders. Independent variables from univariate models were incorporated as covariates in the multivariate regression model.

Results

During the inclusion period, 600 patients underwent surgery for emergency high risk abdominal condition. Three-hundred and fifty-four (354) patients were included in the analysis, 192 patients with intestinal obstruction(IO) and 162 patients with perforated viscus (PV) (figure 1).

Patient demographics are presented in table 1.

Comparison of electrolyte levels and acid base status in patients with intestinal obstruction and perforated viscus

Patients with PV were significantly more acidotic both prior to and after the surgery (p <.0001), while patients with IO presented with more prevalent alkalemia compared to PV (p=0.0007) but normalizing postoperatively . Furthermore, there was an increase in proportion of acidemia in both cohorts pre- to postoperatively, most pronounced in patients with PV (figure 2).

Patients with IO had higher incidence of hypochloraemia and hypokalemia preoperatively, whereas higher proportion of patients with PV presented with preoperative hyponatremia (figure 1). In total, preoperative hypochloremia was observed in 99 patients (28 %) of the cohort, while 88 patients (25 %) were hyperchloremic. Preoperative hypochloremia was significantly more frequent in those with IO (p=0.002). Preoperative hyponatremia was prevalent in 57 % of the overall cohort, with 52 % in the OI, and 64 % of those with PV (p=0.016). Significantly higher number of hypokalemic patients was also seen in the intestinal obstruction cohort, both prior and after surgery (p=0.013 and p=0.002 respectively).

Impact of electrolyte levels and acid-base status on outcome

Both cohorts had similar outcomes regarding day-30 adverse events incl. death (41.1 vs 51.2 %; p=0.050), Acute Kidney Injury (AKI) (15.1 vs 15.4 %; p=0.932) and need for Renal Replacement Therapy (RRT) (6.3 vs 11.7 %; p=0.668) (table 1).

Adjusted for age, gender, ASA, physical performance, co-morbid disease, sepsis and fluids administered, pre- as well as postoperative hypochloremia was significantly associated with day-30 postoperative major complications, including death in patients with IO, OR 2.87 (1.35, 6.23) *p= 0.006* and OR 6.86 (1.71, 32.2) *p= 0.009* respectively (appendix 1). This was not seen in patients with PV. Neither plasma sodium nor potassium changes were associated with 30-day complications.

Furthermore, after adjusting for age, gender, ASA, physical performance, co-morbid disease, sepsis and fluids administered, preoperative hypochloremia was associated with postoperative major complications, specifically pulmonary complications (adjusted OR 1.25 95%CI [1.05, 2.60], p= 0.035) in patients with IO. No association was found in patients with PV.

In both cohorts, preoperative hyperlactatemia was associated with an increased risk of postoperative major complications, including death within the first 30 days(intestinal obstruction: OR 4.39 [1.42, 15.3], *p=0.013*; perforated viscus: OR 2.44; 95%CI, 1.24, 4.92, *p=0.010*) (appendix 1).

Figure 3 illustrates Kaplan Meier survival curve for (A) preoperative and (B) postoperative chloride levels and day-30 mortality for patients undergoing emergency abdominal surgery. Hypochloremic patients presented with

reduced long-term survival as compared with the normo- and hyperchloremic patients, with postoperative hypochloremia having the most pronounced association.

Chloride and interaction with fluid administration

Patients with IO presenting with hypochloremia received significantly more hyperchloremic fluids during (estimate 173 mL, 95%CI(50-296), p=0.005) and after surgery (estimate 476 mL, 95%CI(151-801), p=0.004), normochloremic fluids after surgery (estimate 698 mL, 95%CI(520-1526), p=0.048), as well as overall 24 hour fluid administration (estimate 1604 mL, 95%CI(402-2807), p=0.009), when compared to patients with normo- and hyperchloremia (linear regression models).

Discussion

In this retrospective analysis of 354 patients undergoing emergency high-risk abdominal surgery, perioperative electrolyte derangement was frequent, with a high incidence of hyponatremia and hypochloremia. We found significant associations between preoperative as well as postoperative hypochloremia and both overall morbidity and short- and long-term morbidity in patients with intestinal obstruction, which was not found in patients with perforated viscus. Neither sodium nor potassium derangement had statistically significant impact on postoperative outcome.

Data from a recent prospective observational investigation demonstrate that temporary hyperchloremia may occur in 75% of ICU patients during the first 24 hours of ICU stay(17). However, despite a rather high prevalence in critically ill patients, few outcome-related data regarding systemic chloride levels exist.

The available data suggest that, increased disease severity may be associated with abnormal chloride levels, however, in various cohort studies discrepant results exist(17–20). Our findings seem to be coincide with several negative retrospective cohorts assessing the role of hyperchloremia in critically ill patients(21–24), where hyperchloremia was not associated with worse outcome.

Although chloride is one of the major electrolytes, it is not measured routinely in daily practice and optimal management of hypochloremia is inadequately understood in the critically ill surgical patient(25). Emerging evidence shows that low chloride levels affects outcome in heart failure patients, (26,27). Furthermore, several studies have found hypochloremia associated with impaired outcome in critically ill patients(25,28).

In patients with IO, we found a higher degree of electrolyte imbalances than in those with PV, specifically hypokalemia and hypochloremia. Thus, almost 35 % of patients with IO presented with preoperative hypochloremia, compared to only 24 % of the patients with PV (p=0.002). The manifestations of *IO* and its *degree* of severity generally depend on the site of obstruction(29), however, both obstructive but also paralytic ileus are associated with profound effects on body fluid balance. Accumulation of fluids and gases drives elevated intraluminal pressure and inflammation, microcirculatory dysfunction of the bowel wall and disruption of the mucosal barrier results leading to fluid sequestration into the intestinal wall lumen, potentially accounting for several liters of fluid and promoting hypovolemia and electrolyte derangement(30,31). It could be argued that patients with PV all have a degree of IO, either an obstruction as the underlying cause of perforation or paralysis of the intestines as a result of inflammation and stress, partly explaining the preoperative electrolyte derangement in patients with PV.

Metabolic alkalosis, as was seen to be prevalent in the preoperative phase in patients with IO, could be caused by both hypochloremia and hypokalemia, while plasma contraction could further aggravate hypochloremic metabolic alkalosis especially in patients who loose high quantities of chloride-rich fluids(32) both via inadequate renal Cl– reabsorption or via dilution following infusion of hypotonic fluids(33,34). Another cause of abnormality of chloride concentration might be the derangement of adrenal hormones triggered by surgical stress. As the current study is a retrospective observational study, the cause of hypochloremia was not ascertained. Future prospective studies focusing on the preoperative loss of chloride, as well as the postoperative adrenal function and inflammatory response, should be conducted to refute or confirm these considerations. In this context, a recently published retrospective study did find a statistically significant positive correlation between fluid balance and inflammation in patients with OI, as well as association between high pre- and postoperative C-reactive protein and a high positive fluid balance with worse outcome in patients with IO, but not in patients with PV(35).

Linear regression models found an association between preoperative hypochloremia and the amount of fluid administrated during the observational period in patients with IO. The severity of hypochloremia could be indicative of the severity of the IO and the associated degree of dehydration and potential hypovolaemia, explaining the association between preoperative hypochloremia and postoperative major complications, specifically pulmonary complications. As such, the potential iatrogenic fluid overload as a result of treatment of hypovolemia with hypochloremic fluids could promote postoperative complications. Buffered intravenous fluids do indeed reduce the incidence of hyperchloremia and metabolic acidosis(36,37), however, the question remains if normal saline has a more advantageous position when treating patient with IO.

This is the first analysis describing electrolyte derangement and the potential role of hypochloremia on the outcome of patients undergoing emergency high-risk abdominal surgery. However, this is a retrospective cohort, thus prone to selection bias. The patients were classified into three groups hypo-, normo- and hyperchloremia according to our hospital laboratory reference; There are no clearly established cutoff values, hypochloremia is usually defined as serum chloride levels below 96–101 mmol/l, while hyperchloremia normally is defined as serum chloride levels higher than 106–111 mmol/l(38). The definition varies depending on the local laboratory. Indeed, some studies showed an independent effect of hypochloremia defined as plasma chloride level below 100 mmol/l, on cardiovascular, non-cardiovascular, and all-cause mortality(39–41). Also, we analyzed only change in chloride level pre-to immediate post operatively and data cannot be extrapolated beyond that.

We should note that this study is a hypothesis-generating study, indicating the need for future prospective research, which may assess the preoperative cause of hypochloremia and the mechanisms of its association with worse outcome. We also note that our results showed just the association of hypochloremia and higher mortality, but not the causality link.

Conclusions

Perioperative hypochloremia may have clinical importance as an indicator of prognosis in patients undergoing emergency high-risk abdominal surgery, with a significant association with morbidity in patients who have IO. Further studies should examine the pathophysiological similarities and more importantly differences in patients with IO and perforated viscus as well as potential effects of different resuscitation strategies for acute fluid and electrolyte disturbances emergency abdominal surgery.

Abbreviations

IO Intestinal Obstruction

PV Perforated viscus

ICU Intensive Care Unit

PACU Post-anesthesia Care Unit

Declarations

Ethics approval and consent to participate

In consensus with Danish law, The Regional Committee on Health Research Ethics waived the requirement for informed patient consent.

Consent for publication

Not applicable.

Availability of data and materials

Original data is available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MC, NBF, HK, JH and ML conceived and designed the study; MC, NBF and HK contributed in data management; MC, NBF, HK and JH collected and analyzed the data; MC, NBF, HK, JH and ML contributed in data analysis, interpretation of the data and drafting the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1: Perioperative characteristics of 354 patients who underwent high-risk emergency abdominal surgery categorized by intraoperative pathology

Variables, [n(%)] unless otherwise indicated	Intestinal obstruction *N=192*	Perforated viscus *N=162*	p-value[a]
Sex, female	103 (53.6)	90 (55.5)	0.719
Age, median (IQR), y	68 (54-79)	67 (54-78)	0.749
ASA class ≥3	76 (39.6)	68 (42.0)	0.648
ECOG >1	58 (30.2)	38 (23.5)	0.155
Preoperative sepsis*	18 (9.3)	28 (17.3)	0.030
History of:			
Congestive heart failure	16 (8.3)	14 (8.6)	0.917
Chronic kidney disease	11 (5.7)	9 (5.5)	0.955
Cerebrovascular disease	27 (14.1)	13 (8.0)	0.074
Cirrhosis	5 (2.6)	6 (3.7)	0.553
Diabetes	25 (13.2)	17 (10.5)	0.464
Diuretics., all	59 (30.7)	39 (27.1))	0.281
Intraoperative fluid administration (H_{intra}) median (IQR), L			
Hyperchloremic fluids	0.8 (0.5-1.25)	1.0 (0.5-1.4)	0.226[b]
Hypo/normochloremic fluids	1.8 (1.3-2.5)	2.0 (1.5-3.0)	0.007[b]
Blood products, mean (SD)	121 (328)	253 (798)	<.001
Fluid balance, end of surgery, median (IQR), L	1.9 (1.3-2.7)	2.5 (1.8-3.5)	<.0001[b]
Vasopressor infusion[h] (yes)			
Intraoperatively	50 (26.0)	70 (43.2)	0.001
6 hours postoperatively	35(18.2)	55 (34.0)	<.001
24 hours postoperatively	39 (20.3)	59 (36.4)	<.001
Norepinephrine dose intraoperatively, µg/kg/min[d]	0.20 (0.12-0.47)	0.28 (0.14, 0.46)	0.412
Duration of surgery, median (IQR), min	87 (37-124)	124 (80-156)	0.011
Postoperative fluid administration (H_{24}) median (IQR), L			

Hyperchloremic fluids	1.8 (0.6-3.1)	2.0 (1.0-3.7)	0.120[b]
Hypo/normochloremic fluids	1.8 (0.5-3.7)	2.2 (0.8-4.6)	0.037[b]
Blood products, mean (SD)	110 (548)	372 (2232)	0.005[b]
ICU stay No.(%)	34 (17.7)	46 (28.4)	0.017
Length of ICU stay, median, (IQR)	1.5(0-0)	3(0-1)	0.016
Length of hospital stay, median, (IQR)	9 (5-16)	13 (6-26)	<.0001
Outcomes No. (%)			
AKI	29 (15.1)	25 (15.4)	0.932
Need for RRT	12 (6.3)	19 (11.7)	0.668
Day-30 postoperative major complications incl death [c]	79 (41.1)	83 (51.2)	0.050
Day-30 mortality	34 (17.7)	17 (10.4)	0.050

AKI; Acute kidney injury; RRT: renal replacement therapy; $H_{intra:}$ time during surgery; Hyperchloremic fluids: Isotone Sodium chloride, Human Albumin 5%, Voluven®; Hypo/normochloremic fluids: Ringers acetate, Human albumin 20%; a: chi square ; b: mann-whitney; h: Phenylephrine or Norepinephrine infusion; *severe sepsis, septic shock defined by 2016 Sepsis-3 guidelines
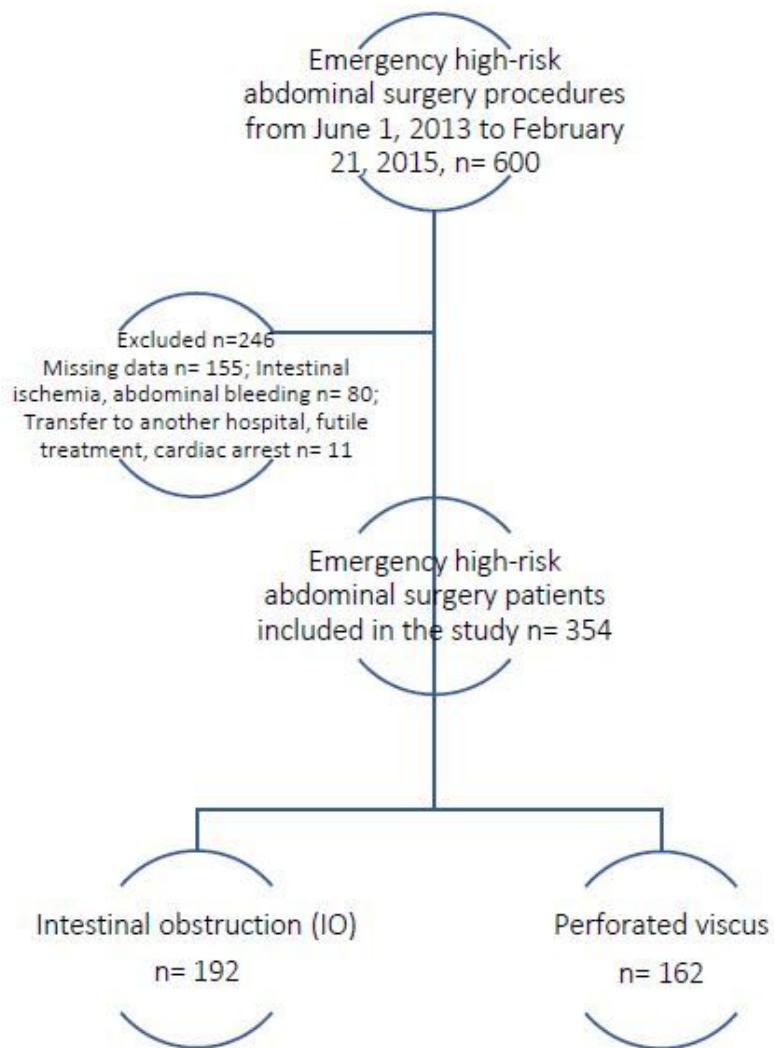
Figures

Figure 1

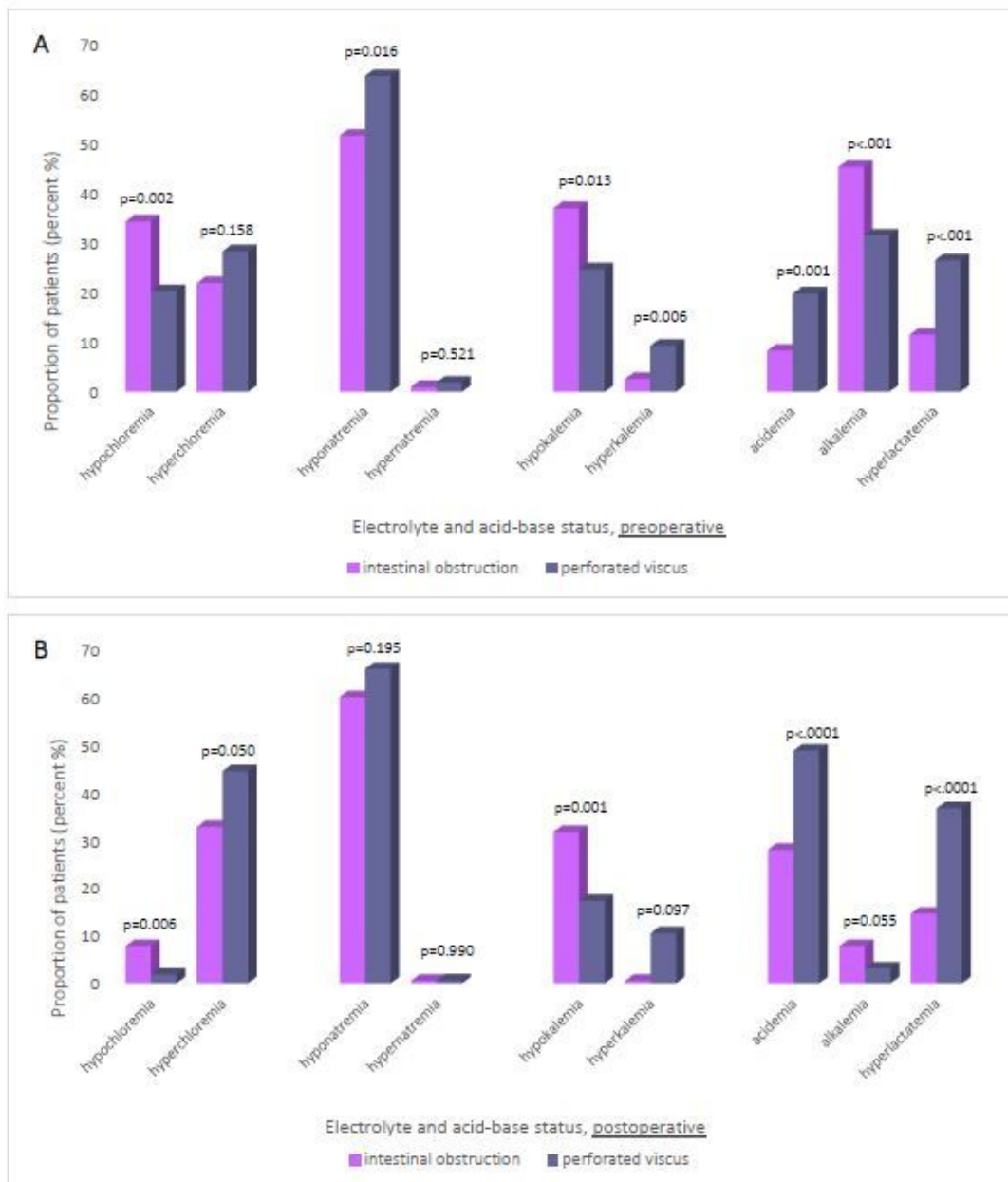Flow diagram of patient selection during the study

Figure 2

Electrolyte derangement, preoperative (A) and postoperative (B), for patients with intestinal obstruction and perforated viscus; Legend: Hypochloremia: <98 mmol/l; Hyperchloremia: >106 mmol/L; Hyponatremia: < 135 mmol/L ; Hypernatremia: >144 mmol/L ; Hypokalemia: <3.5 mmol/L ; Hyperkalemia: >4.5 mmol/L ; Acidemia: pH <7.35; f: Alkalemia: pH >7.45; g: Hyperlactatemia: lactate > 2.1 mmol/L;
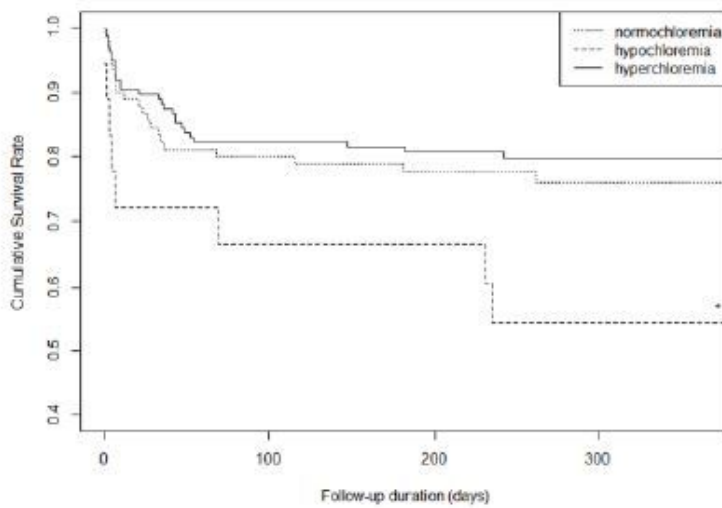
(A)
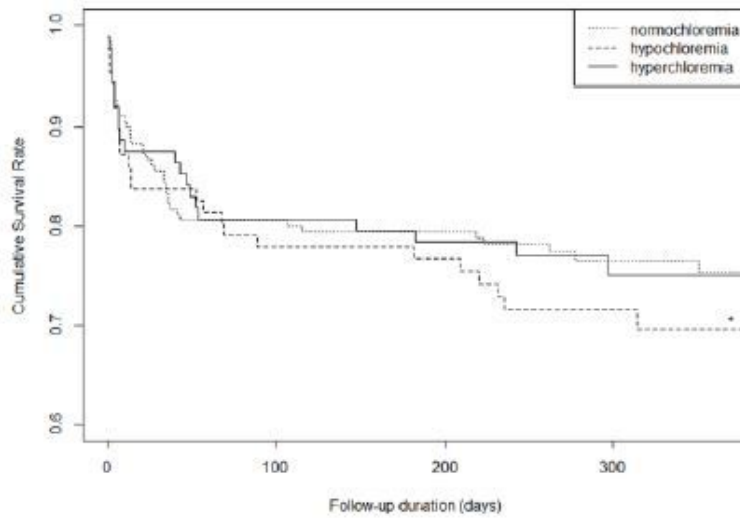
(B)

Figure 3

Kaplan Meier survival curve for (A) preoperative chloride levels and (B) postoperative chloride levels and day-30 mortality in patients undergoing emergency abdominal surgery for either intestinal obstruction or perforated viscus. Hypochloremic patients had reduced survival as compared with the normo- and hyperchloremic patients (* p <0.05)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Appendix1.docx