Oedema is associated with clinical outcome following emergency abdominal surgery

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ABSTRACT

INTRODUCTION Oedema is observed frequently following surgery and may be associated with worse outcomes. To date, no study has investigated the role of oedema in the emergency surgical patient. This study assesses the incidence of oedema following emergency abdominal surgery and the value of early postoperative oedema measurement in predicting clinical outcome.

METHODS A prospective cohort study of patients undergoing emergency abdominal surgery at a university unit over a two-month period was undertaken. Nutritional and clinical outcome data were collected and oedema was measured in the early postoperative period. Predictors of oedema and outcomes associated with postoperative oedema were identified through univariate and multivariate analysis.

RESULTS Overall, 55 patients (median age: 66 years) were included in the study. Postoperative morbidity included ileus ($n=22$) and sepsis ($n=6$) with 12 deaths at follow-up. Postoperative oedema was present in 19 patients and was associated with prolonged perioperative fasting (107 vs 30 hours, $p=0.009$) but not with body mass index (24kg/m^2 vs 27kg/m^2 , $p=0.169$) or preadmission weight loss (5% vs 3%, $p=0.923$). On multivariate analysis, oedema was independently associated with gastrointestinal recovery ($B=6.91$, $p=0.038$), artificial nutritional support requirement (odds ratio: 6.91, $p=0.037$) and overall survival ($\chi^2=13.1$, $df=1$, $p=0.001$).

CONCLUSIONS Generalised oedema is common after emergency abdominal surgery and appears to independently predict gastrointestinal recovery, the need for artificial nutritional support and survival. Oedema is not associated with commonly applied markers of nutritional status such as body mass index or recent weight loss. Measurement of oedema offers utility in identifying those at risk of poor clinical outcome or those requiring artificial nutritional support following emergency abdominal surgery.

KEYWORDS

Abdomen/surgery – Analysis of variance – Oedema/aetiology – Humans – Postoperative – Complications/aetiology – Postoperative period

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Generalised oedema is observed frequently following major surgery, and may be associated with an increase in postoperative morbidity and mortality.^{1–5} Pathological fluid accumulation has been shown to result in infective complications,¹ delayed wound healing,⁴ delayed gastrointestinal recovery⁵ and increased length of hospital stay.^{1,6} The physiological sequelae of fluid overload such as depressed myocardial function⁷ and reduced tissue oxygen tension^{8,9} may explain such associations.

Postoperative oedema occurs in part as a result of the cytokine response to surgical injury, which increases the permeability of the capillary membrane to proteins such as albumin, and results in a redistribution of plasma proteins and fluid from the intravascular to the interstitial space.^{10,11} In the 1960s, Shires *et al* suggested that crystalloid solutions should be administered perioperatively in order to compensate for the third-space losses associated

with surgical trauma and these recommendations have had a sustained impact on perioperative fluid prescription practices.^{12,15} However, we now know that overzealous fluid administration contributes to postoperative oedema,¹⁴ and it is therefore not surprising that recent evidence indicates a reduction in complications and length of hospital stay with restricted perioperative fluid regimens.^{5,15–18} As a result, accelerated recovery pathways, which are now commonplace following elective colorectal surgery, discourage prolonged and liberal fluid administration.¹⁹

A report by The Royal College of Surgeons of England has highlighted the disproportionate levels of morbidity and mortality associated with emergency surgery, with 80% of all surgical mortality arising from unplanned or emergency surgical intervention.²⁰ In the emergency surgical patient, the stress of surgery is compounded by acute illness. Furthermore, acute intra-abdominal pathology and

Table 1 Criteria for Malnutrition Universal Screening Tool (MUST) scoring (modified from Sutton *et al*)²⁶

MUST score	
Body mass index	
>20kg/m ²	(score = 0)
18.5–20kg/m ²	(score = 1)
<18.5kg/m ²	(score = 2)
Unplanned weight loss in past 3–6 months	
<5%	(score = 0)
5–10%	(score = 1)
>10%	(score = 2)
Acute disease effect	
No effect	(score = 0)
Acute illness and no nutritional intake >5 days	(score = 2)
Overall risk of malnutrition	
Low risk	(total = 0)
Medium risk	(total = 1)
High risk	(total = 2 or more)

perioperative starvation may result in a rapid decline in nutritional status, which will, in turn, affect fluid homeostasis. Despite recent interest in perioperative fluid administration and the significance of postoperative oedema in the elective surgical patient, no study to date has reported on the incidence or relevance of oedema in the high risk emergency surgical patient. This study aimed to determine the incidence of early postoperative oedema in patients undergoing emergency abdominal surgery at our institution, and to evaluate the role of postoperative oedema as a marker for postoperative morbidity and mortality.

Methods

A prospective cohort study of patients undergoing emergency abdominal surgery at a university surgical unit over a two-month period was performed. Local audit and clinical effectiveness registrations were granted. All patients undergoing open or laparoscopic emergency abdominal surgery were identified and entered into the study. Clinical assessment occurred on weekdays only and so short-stay patients (<48 hours) discharged at the weekend were excluded.

Data were collected on patient demographics and comorbidities, body mass index (BMI) and Malnutrition Universal Screening Tool (MUST) score (Table 1)²¹ on admission, duration of perioperative fasting and ASA (American Society of Anesthesiologists) grade (Table 2). Operative data, the Bupa rating of the surgical severity (Table 2), postoperative C-reactive protein (CRP) and albumin levels, requirement for postoperative artificial nutritional support, and major and relevant morbidity and mortality data were collected prospectively.

Table 2 Criteria for the Bupa scores and ASA (American Society of Anesthesiologists) grades

Bupa	
Minor (1)	Removal of sebaceous cyst, skin lesions, oesophagoastroduodenoscopy
Intermediate (2)	Unilateral varicose veins, unilateral hernia repair, colonoscopy
Major (3)	Appendicectomy, open cholecystectomy
Major plus (4)	Gastrectomy, any colectomy, laparoscopic cholecystectomy
Complex major (5)	Carotid endarterectomy, abdominal aortic aneurysm repair, limb salvage, anterior resection, oesophagectomy
ASA	
1	No systemic disease
2	Mild systemic disease
3	Systemic disease affecting activity
4	Serious disease but not moribund
5	Moribund, not expected to survive

Clinical assessment and data collection was undertaken by a single specialist nutrition nurse (SJ). MUST scores were calculated independently by two authors (SJ and PVS) and disagreement was resolved through discussion with the senior author (ATK). Postoperative ileus (POI) was defined as a delay in gastrointestinal motility beyond three days evidenced by failure to tolerate solid food or sip feeds.²² The decision to prescribe artificial nutritional support was taken by a nutrition multidisciplinary team. Following discharge, clinical outcome data were extracted from electronic patient records until completion of the follow-up period (June 2012).

The primary outcome of interest was mortality. Secondary outcomes included the need for artificial nutritional support, time to oral intake, complications and factors that predicted incidence of postoperative oedema.

Statistical analysis

Data were analysed using Excel® (Microsoft, Redmond, WA, US), Prism® 3.03 (GraphPad Software, La Jolla, CA, US) and SPSS® 18.0 (SPSS, Chicago, IL, US). Univariate analysis using the Mann–Whitney, Kruskal–Wallis and chi-squared tests without Yates's correction was performed to identify significant variables between groups. Variables with potential ($p < 0.1$) on univariate analysis were included in a multivariate logistic regression analysis to identify predictors of oedema. The value of oedema in predicting clinical outcomes such as need for artificial nutritional support, complications and length of stay was investigated using multivariate logistic and linear regression including the variables age, ASA grade, Bupa score and postoperative CRP. Univariate survival analysis was undertaken using the Kaplan–Meier approach and significant differences were

Table 3 Demographics, nutritional and preoperative scoring data in patients with and without postoperative oedema

	All patients	Without oedema	With oedema	Univariate analysis*
Number of patients	55	36	19	
Median age (IQR)	66 (54–76)	64 (49–75)	70 (61–75)	0.182
Mean BMI in kg/m ² (95% CI)	24.9 (21.6–28.7)	26.0 (22.1–30.0)	23.1 (21.3–25.6)	0.169
Mean preadmission percentage weight loss (95% CI)	3.9 (1.5–6.2)	3.1 (0.9–5.3)	5.1 (-0.4–10.7)	0.923
Median duration of reduced oral intake in days (IQR)	2 (0–7)	2 (1–6)	5 (1–21)	0.067
Median MUST score on admission (IQR)	0 (0–1)	0 (0–2)	0 (0–1)	0.878
Median duration of preoperative fasting in hours (IQR)	16 (10–33)	14 (10–24)	26 (10–56)	0.167
Median duration of perioperative fasting in hours (IQR)	33 (19–104)	30 (16–69)	107 (33–136)	0.009
Bupa score				0.354
2	3	2	1	
3	23	17	6	
4	29	17	12	
ASA grade				0.039
1	18	15	3	
2	22	14	8	
3	13	6	7	
4	2	1	1	
Mean CRP in mg/l (95% CI)	144.7 (113.9–175.5)	159.0 (115.6–202.4)	111.7 (80.4–143.0)	0.436
Mean albumin in mg/l (95% CI)	23.7 (22.2–25.3)	24.7 (22.7–26.7)	22.0 (19.6–24.4)	0.143

IQR = interquartile range; CI = confidence interval; BMI = body mass index; MUST = Malnutrition Universal Screening Tool; ASA = American Society of Anesthesiologists; CRP = C-reactive protein

*Mann–Whitney U test

Table 4 Operative intervention and oedema scoring in the study cohort

Operative intervention	n
Large bowel resection	11
Appendicectomy	11
Repair of abdominal wall hernia	8
Small bowel resection	5
Repair of perforated peptic ulcer	4
Laparotomy and adhesiolysis	4
Laparotomy and stoma formation	4
Other	8
Clinical extent of oedema	n
No oedema	36
Detectable	7
Significant but localised	1
More extensive (knee +/- arm)	6
Trunk or thighs	5

identified with the logrank test. Finally, a multivariate survival model using a Cox regression (stepwise forward model) approach was performed adjusting for patient age, ASA grade, Bupa score and postoperative CRP.

Comparative statistics are presented as odds ratios (Exp(B) value, 95% confidence interval [CI]) for univariate chi-squared tests, multivariate logistic regression and Cox regression analyses while B values with 95% CI are expressed for linear regression analyses.

Results

Overall, 55 patients with a median age of 66 years (interquartile range: 54–75.5 years) were included in the study. The demographics are given in Table 3. Large bowel resection and appendicectomy were the most common surgical intervention (Table 4), with a median Bupa score of 4 (range: 2–4) and a median ASA grade of 2 (range: 1–4) indicating a high complexity of surgical intervention and moderate prevalence of co-morbidity in the cohort. Nineteen patients (35%) were found to have oedema, at a median of four days postoperatively (Table 4). POI occurred in 22 patients

Table 5 Clinical outcomes in patients with and without postoperative oedema

	All patients	Without oedema	With oedema	Univariate analysis
Number of patients	55	36	19	
Artificial nutritional support	16	7 (19%)	9 (47%)	0.030*
Parenteral nutrition	9	4 (11%)	5 (26%)	0.147*
Days to oral intake	3	2	5	0.040†
Complications	25	13 (36%)	12 (63%)	0.055*
Postoperative ileus	22	11 (31%)	11 (58%)	0.049*
Length of stay (days)	13	10	24	<0.001†
30-day mortality	3	0 (0%)	3 (16%)	$\chi^2=6.0$ df=1 p=0.014‡
6-month mortality	9	2 (6%)	7 (37%)	$\chi^2=10.2$ df=1 p=0.001‡
12-month mortality	9	2 (6%)	7 (37%)	$\chi^2=10.2$ df=1 p=0.001‡
Died at cessation of follow-up	12	3 (8%)	9 (47%)	$\chi^2=14.3$ df=1 p<0.001‡

*Chi-squared test; †Mann–Whitney U test; ‡Logrank test

while 16 patients were prescribed artificial nutritional support (Table 5).

Postoperative complications were recorded in 25 patients. In addition to the 22 cases of POI, complications included sepsis ($n=6$), wound dehiscence ($n=2$) and anastomotic leak ($n=1$). The in-hospital mortality rate was 7% ($n=4$) and 12 patients (21%) had died at follow-up (median: 576 days, range: 15–629 days).

Oedema and mortality

Death was significantly more likely in those with postoperative oedema (47% vs 8%) at cessation of the follow-up period ($\chi^2=14.3$, df=1, $p<0.0001$) (Table 5). On Kaplan–Meier curve analysis, presence of oedema predicted mortality at 30 days ($\chi^2=6.0$, df=1, $p=0.014$), 6 months ($\chi^2=10.2$, df=1, $p=0.001$) and 12 months ($\chi^2=10.2$, df=1, $p=0.001$). On multivariate analysis adjusting for age, admission MUST score, Bupa score, ASA grade and CRP, presence of oedema no longer predicted early mortality ($\chi^2=5.6$, df=1, $p=0.338$ at 30 days), yet independently predicted 6-month mortality ($\chi^2=11.6$, df=1, $p=0.009$), 12-month mortality ($\chi^2=10.3$, df=1, $p=0.011$) and mortality at cessation of the follow-up period ($\chi^2=13.1$, df=1, $p=0.006$) (Table 6 and Fig 1).

Oedema and clinical outcomes

The median time to tolerance of oral intake and incidence of POI was significantly greater in those with oedema (5 vs 2 days, $p=0.040$; and 58% vs 31%, $p=0.049$) (Table 5 and Fig 2). On excluding POI, there was no difference in incidence of other complications (16% vs 17%, $p=0.930$). The two cases of wound dehiscence occurred in patients without

postoperative oedema while the one anastomotic leak occurred in a patient with oedema. Artificial nutritional support was more commonly prescribed in those with postoperative oedema (47% vs 19%, $p=0.030$) and the median length of stay was significantly greater (24 vs 10 days, $p=0.0004$). On multivariate analysis adjusting for age, Bupa score, ASA grade and CRP, oedema independently predicted need for artificial nutritional support (odds ratio [OR]: 4.44, 95% confidence interval [CI]: 1.05–18.9, $p=0.037$) and days to oral intake ($B=6.91$, $p=0.038$) (Table 6). However, oedema was not associated with overall length of stay ($B=8.37$, $p=0.099$).

Factors associated with postoperative oedema

The median patient age was greater (70 vs 64 years, $p=0.182$) and the median BMI was less (23.7kg/m² vs 27.0kg/m², $p=0.169$) in those with oedema although neither difference was significant (Table 3). Prolonged perioperative fasting (107 vs 30 hours, $p=0.009$) and ASA grade (2 vs 2, $p=0.039$) were associated with postoperative oedema on univariate analysis and in a multivariate model (OR: 1.02, 95% CI: 1.0–1.03, $p=0.016$; and OR: 2.3, 95% CI: 1.03–5.06, $p=0.040$) (Table 6). Oedema was not correlated with postoperative CRP or albumin levels (111.7mg/l vs 159.0mg/l, $p=0.436$; and 22.0mg/l vs 24.7mg/l, $p=0.143$).

Discussion

Patients requiring emergency surgery are among the sickest treated in the National Health Service²⁵ and it is thought that around 80% of surgical mortality arises from unplanned or emergency surgical intervention.^{25,24} Identification and

Figure 1 Kaplan-Meier curves for survival at 30 days, 6 months and 12 months as well as at cessation of follow-up period

appropriate management of the sickest patients will improve outcomes. Two recent studies have demonstrated an association between oedema and outcomes following emergency surgery, reporting increased POI, complications and hospital stay in those with oedema.^{1,6} These findings highlight the importance of oedema assessment in the surgical patient.

It is likely that the overzealous administration of intravenous fluids traditionally guided by the findings and 'pro-fluid' recommendations of Shires¹⁵ compounds the body's response to injury, and contributes to postoperative oedema and a deterioration in outcome.¹ A meta-analysis of standard versus restrictive fluid regimes following elective colorectal surgery demonstrated a reduction in postoperative morbidity (but not mortality) with restrictive or goal directed therapy.¹⁷ However, while restrictive fluid regimens appear to be gaining widespread acceptance into practice in elective patients,¹⁹ there remain no data on the incidence and relevance of postoperative oedema in the emergency surgical patient. In addition, there is no evidence to date that suggests that fluid administration practices in the elective patient have been adopted in the emergency setting.

This present study demonstrates a high incidence of oedema following emergency abdominal surgery. The presence of postoperative oedema is independently associated with gastrointestinal recovery, the need for artificial nutritional support and late mortality. These results support those described in the meta-analysis by Rahbari *et al.*¹⁷ Fur-

thermore, a case review by Lowell *et al* reported a greater than 10% increase in body weight in 19/48 patients (40%) as well as an increase in vasopressor requirement and mortality in these patients.⁵

A cohort study similar to the present study considered oedema following major abdominal surgery and the role of bioimpedance measurements in oedema assessment. Here, Itobi *et al* demonstrated a slightly higher incidence (53%) of postoperative oedema and, in common with this present study, found an increase in postoperative oedema with increased age or ASA grade but no association with BMI, albumin or CRP.¹ In addition, Itobi *et al* reported an increase in cardiac and infective complications as well as delayed gastrointestinal recovery in patients with oedema. Of note, however, the cohort studied by Itobi *et al* was of greater median age and underwent only major gastrointestinal resections, which may explain the greater incidence of postoperative oedema and complications compared with the present study. Moreover, the need for artificial nutritional support and mortality were not reported by Itobi *et al* although they offer significant importance to the findings of the present study.

Study limitations

A number of limitations exist for this study. First, the small sample size risks type II statistical error and may have resulted in some variations failing to reach statistical significance. Second, more selective inclusion criteria (including only major and major complex cases) would have created

Table 6 Multivariate analysis of potential predictors of oedema and outcomes with oedema

	Univariate		Multivariate	
	Odds/B value	p-value	Odds/B value	p-value
Duration reduced oral intake in days (95% CI)	1.01 (1.00–1.02)	0.171*	1.00 (0.99–1.02)	0.777 [†]
Perioperative fasting (95% CI)	1.01 (1.00–1.02)	0.009*	1.02 (1.00–1.03)	0.016[†]
ASA grade (95% CI)	2.11 (1.04–4.29)	0.039*	2.28 (1.03–5.06)	0.042[†]
Outcome				
Artificial nutritional support (95% CI)	3.73 (1.10–12.65)	0.035*	4.44 (1.05–18.90)	0.037[†]
Days to oral intake (95% CI)	6.91 (0.40–13.41)**	0.038**	6.91 (0.40–13.41) [‡]	0.038[‡]
Complications (95% CI)	3.03 (0.96–9.62)	0.059*	3.27 (0.90–11.98)	0.079 [†]
Postoperative ileus (95% CI)	3.13 (0.99–9.91)	0.053*	3.34 (0.94–11.87)	0.054 [†]
Length of stay in days (95% CI)	12.91 (-0.65–26.48)**	0.062**	8.37 (-5.78–22.52) [‡]	0.099 [‡]
30-day mortality (95% CI)	–	$\chi^2=6.0$ df=1 p=0.014[#]	169.97 (0.00–>1,000)	$\chi^2=5.6$ df=1 p=0.338 [§]
6-month mortality (95% CI)	8.38 (2.46–43.52)	$\chi^2=10.2$ df=1 p=0.001[#]	8.48 (1.76–40.95)	$\chi^2=11.6$ df=1 $\pi=0.009^{\S}$
12-month mortality (95% CI)	8.38 (2.46–43.52)	$\chi^2=10.2$ df=1 p=0.001[#]	8.48 (1.76–40.95)	$\chi^2=10.3$ df=1 $\pi=0.011^{\S}$
Died at cessation of follow-up (95% CI)	8.11 (3.32–43.65)	$\chi^2=14.3$ df=1 p<0.001[#]	8.08 (2.31–33.63)	$\chi^2=13.1$ df=1 $\pi=0.001^{\S}$

ASA = American Society of Anesthesiologists

*Binary logistic regression

**Linear regression (B value reported)

[#]Logrank test[†]Multinomial logistic regression[‡]Multivariate linear regression (B value reported)[§]Cox regression

a more homogeneous group and firmer conclusions. Third, exclusion of short-stay patients discharged at the weekend, who undoubtedly underwent less major operative intervention, may have falsely elevated the baseline oedema prevalence but should not have significantly affected observed associations between oedema, patient factors and clinical outcome.

Finally, while we have adjusted for potential confounders of outcome such as age, Bupa score and ASA grade, we have not considered the underlying pathological process in each case (eg malignancy). Other clinical data of importance would include perioperative fluid administration, which is known to contribute to postoperative oedema,^{1,25} and change in postoperative total body weight, which is often reported in the literature in preference to clinically evident oedema.

Despite these limitations, our study shows that oedema, morbidity and mortality are all common following emergency abdominal surgery. A number of correlations have been demonstrated between oedema and outcome although the

direction of causality and effect of confounders may be debated. Nevertheless, this study highlights the potential utility of oedema in predicting outcome and the importance of oedema assessment in emergency surgical patients. Having demonstrated a significant association between oedema and mortality, larger studies focusing on the aetiology of postoperative oedema in the emergency setting, particularly with regard to fluid regimens, and the identification of strategies to reduce this process are essential.

Conclusions

Oedema occurs frequently following emergency abdominal surgery, and is associated with the requirement for artificial nutritional support and death. Attention to fluid management in this high risk cohort must be integral to modern surgical practice. Meanwhile, it is imperative that clinicians assess the emergency surgical patient regularly for oedema, and implement appropriate management to help reduce the high rates of morbidity and mortality in this cohort.

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