

Impact of oedema on recovery after major abdominal surgery and potential value of multifrequency bioimpedance measurements

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Background: The consequences of generalized oedema following major abdominal surgery are under-recognized, and its causes are poorly understood.

Methods: Thirty-eight patients (21 men and 17 women) were observed for the occurrence of oedema after major abdominal surgery. Oedema formation was related to fluid balance, changes in whole-body bioimpedance (Z) measured at four frequencies (5, 50, 100 and 200 kHz), and clinical outcome.

Results: The 20 patients who developed oedema were older than those who did not (mean(s.d.) 73(9) versus 63(14) years; $P = 0.007$). Fluid intake over the first 5 days after surgery was similar in both groups, but those with oedema excreted less total fluid (16.9(2.4) versus 19.7(3.5) litres; $P = 0.022$). Oedema was associated with a delay in tolerating solid food ($P = 0.001$) and opening bowels ($P = 0.020$), a prolonged hospital stay (median 17 (range 8–59) versus 9 (range 4–27) days; $P = 0.001$) and more postoperative complications (13 of 20 versus four of 18 patients; $P = 0.011$). The preoperative ratio of whole-body impedance at 200 kHz to that at 5 kHz was higher in those who subsequently developed oedema (0.81(0.03) versus 0.78(0.02); $P = 0.015$).

Conclusion: The development of oedema after major abdominal surgery is associated with increased morbidity. Age and reduced ability to excrete administered fluid load are significant aetiological factors and bioimpedance analysis can potentially identify patients at risk.

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Introduction

Generalized oedema is often observed in patients with acute surgical complications¹ who are critically ill and require intensive supportive treatment after operation². Pathological fluid accumulation in the perioperative period in such patients is associated with an increased mortality rate^{3,4}. Generalized oedema may occur also in ward-based surgical patients who show no features of critical illness, but its significance in routine surgical practice is not clearly understood.

The tendency to accumulate fluid is a well recognized physiological response to surgical injury^{5,6}, but the mechanisms leading to generalized oedema are not entirely clear. The prevalence of generalized oedema following routine major surgery has not been established and, although there is anecdotal evidence to suggest that it may be associated with poor clinical outcome, this

has not been subjected to scientific evaluation. Early postoperative oedema may act as a warning sign for impending complications such as prolonged ileus, sepsis and prolonged recovery time⁷.

One aim of this study was to establish the incidence of generalized oedema after major abdominal surgery, and its relationship to postoperative ileus, infective and cardiopulmonary complications, and length of hospital stay. A further aim was to obtain greater insight into the processes that lead to postoperative oedema by using multifrequency bioimpedance analysis (BIA) to monitor the redistribution of total body water (TBW) after major abdominal surgery. This technique is based on the principle that the impedance of human tissue is inversely related to fluid volume and directly related to the square of the conducting length (or height²) when a small amount of current is applied. Fluid distribution can also be assessed

because the current does not penetrate the cell membrane at low frequencies, whereas it increasingly penetrates the intracellular space at higher frequencies^{8,9}.

Patients and methods

The study was approved by the local ethics committee and all participants gave informed consent. All patients included in the study underwent major abdominal surgery under general anaesthesia. Patients were excluded from the study if a vascular procedure was undertaken, if no major procedure was carried out after laparotomy, if an insufficient number of examinations was made to exclude the absence of oedema over the study period, and if the patient was unable to give informed consent. Age, weight, height and body mass index (BMI) were recorded at the preoperative evaluation. There was no evidence of oedema at this stage in any patient.

The anaesthetic agents used depended on the choice of the individual anaesthetist. Postoperative pain relief was by means of an epidural or patient-controlled analgesia comprising morphine and an anti-emetic.

Patients were subsequently grouped according to whether they developed oedema at any time within 5–7 days after surgery. The absence of oedema was confirmed by a minimum of three separate assessments during the study period. Oedema was identified by the presence of pitting on the limbs and/or trunk on clinical examination by the principal researcher, and verified by at least one independent clinician not involved in the study; there was 100 per cent agreement between observers.

Whole-body bioimpedance (Z) was measured at four frequencies (5, 50, 100 and 200 kHz) by means of four surface electrodes placed on the back of the hand and wrist, and foot and ankle on the right side with the patient lying in a recumbent position¹⁰. BIA was used to obtain estimates of TBW using a QuadScan[®] 4000 (Bodystat, Douglas, Isle of Man, UK). The impedance quotient (height^2/Z) was calculated.

Daily fluid balance was recorded in 30 patients who were admitted consecutively. The volume and type of fluid administered during surgery and the total fluid volume administered during the first 5 days after operation were documented. These patients were examined for the presence of oedema and had Z measurements on days 1, 3 and 5 after surgery. Z was measured only once after surgery in the remaining eight patients.

Fluid administration was controlled by the anaesthetist during surgery and by the surgical team thereafter, but neither followed a fixed fluid regimen. The fluid administered reflected typical clinical practice, and was

influenced by blood and fluid losses, urine output and cardiovascular signs. The daily total fluid intake by any route, urine output, and losses from the gastrointestinal tract and drains were documented. The daily cumulative fluid balance for the first 5 days after surgery was calculated from these values after allowing for insensible water loss of 1 litre per day, a value routinely used at this institution. No further adjustment was made for insensible water loss as none of the patients in this study had a prolonged period of pyrexia or ventilation¹¹.

The duration of postoperative ileus was estimated in two ways: as the time to the first bowel movement or passage of flatus, and the time to tolerate solid hospital food following surgery. Length of hospital stay was defined as the number of days spent in hospital after surgery until the patient was medically fit for discharge. Postoperative infections were diagnosed clinically and confirmed with microbiological or radiological tests. Superficial wound infections were classified as minor infective complications, whereas other infections, such as pneumonia and sepsis, were considered as major infective complications. Admissions to the intensive care or high-dependency unit were noted.

Statistical analysis

Unless otherwise stated, results are presented as mean(s.d.) for normally distributed data and median (range) for non-normally distributed data. Comparisons between the groups were made using the Student's t test for normally distributed data and the Mann–Whitney U test for continuous outcome variables that were not normally distributed. Rank analysis of co-variance (ANCOVA)¹² was used to adjust for differences in age between groups. Logistic regression was used to assess differences in binary outcome variables with and without age as a co-variate. Fisher's exact test was used to analyse differences in proportions in 2×2 contingency tables. ANOVA, one-way repeated measures ANOVA, two-way repeated measures ANOVA, split-plot ANOVA and ANCOVA were used, as appropriate. $P < 0.050$ was considered statistically significant. Statistical analyses were performed with SPSS[®] for Windows, version 10.0 (SPSS, Chicago, Illinois, USA).

Results

Of 38 patients enrolled in the study, 20 developed oedema. There were no differences in sex ratio, preoperative BMI or American Society of Anesthesiologists score¹³ between patients who developed oedema and those who did not

Table 1 Physical characteristics and laboratory findings in patients who did or did not develop oedema

| | No oedema | Oedema | P |
|-----------------------------------|-----------------|----------------|---------|
| All patients | 18 | 20 | |
| Sex ratio (M:F) | 11:7 | 10:10 | 0.547‡ |
| Age (years)* | 63(14) | 73(9) | 0.007§ |
| BMI (kg/m ²)* | 26.7(6.1) | 26.0(3.3) | 0.656§ |
| ASA score | | | 0.209‡ |
| 1 | 6 | 2 | |
| 2 | 9 | 13 | |
| 3 | 3 | 5 | |
| Use of epidural | 15 | 6 | 0.102¶ |
| Patients who had BIA measurements | 18 | 12 | |
| Sex ratio (M:F) | 11:7 | 6:6 | 0.547‡ |
| Age (years)* | 63(14) | 74(9) | 0.020§ |
| BMI (kg/m ²)* | 26.7(6.1) | 26.0(2.7) | 0.705§ |
| Preop. albumin (g/l)* | 38.3(5.1) | 36.5(3.5) | 0.301§ |
| Preop. total protein (g/l)* | 73.9(5.6) | 73.2(5.8) | 0.716§ |
| Preop. CRP (mg/l)† | 12.3 (3.9–61.5) | 8.1 (2.0–72.0) | 0.185** |
| ASA score | | | 0.082‡ |
| 1 | 6 | 0 | |
| 2 | 9 | 9 | |
| 3 | 3 | 3 | |

Values are *mean(s.d.) or †median (range). BMI, body mass index; ASA, American Society of Anesthesiologists; BIA, bioimpedance analysis; CRP, c-reactive protein. ‡ χ^2 test; §Student's *t* test; ¶Fisher's exact test; **Mann-Whitney *U* test.

Table 2 Surgical procedures in patients who did or did not develop oedema

| | No oedema <i>n</i> = 18 (18) | Oedema <i>n</i> = 20 (12) |
|--|---------------------------------|------------------------------|
| Resection of the colon (malignant disease) | 12 (12) | 12 (7) |
| Resection of the colon (benign disease) | 1 (1) | 1 (0) |
| Resection of other cancers | | |
| Liver | 1 (1) | 0 (0) |
| Stomach | 0 (0) | 2 (1) |
| Bladder or prostate | 2 (2) | 1 (1) |
| Other procedures | | |
| Small bowel resection | 1 (1) | 3 (2) |
| Pancreatic resection | 1 (1) | 1 (1) |

Values in parentheses are numbers of patients who had bioelectrical impedance measurements.

(Table 1), but the latter patients were significantly younger and age was related to the subsequent development of oedema (odds ratio 1.09 (95 per cent confidence interval 1.02 to 1.16); $P = 0.016$). The patients had major abdominal surgery for either malignant or non-malignant disease and there was no significant difference between groups in the type of surgical procedure undertaken (Table 2). There was no significant difference between groups in the use of epidural analgesia.

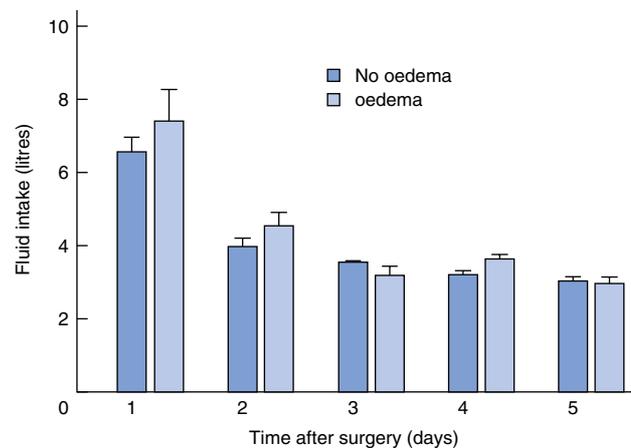
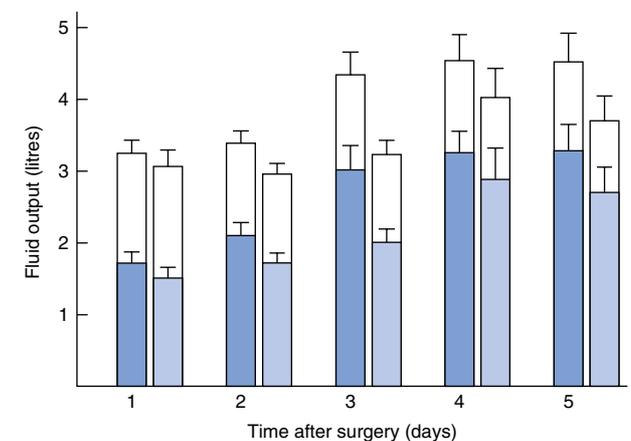
**a** Fluid intake**b** Fluid output

Fig. 1 a Mean(s.e.m.) daily volume of fluid administered after operation in patients who did or did not develop oedema. There was no difference between groups ($P = 0.451$; split-plot ANOVA). **b** Daily urine and total fluid output in patients who did or did not develop oedema. Shaded bars represent urine output and unshaded bars above these correspond to the non-urinary output. Urine output and total fluid output were significantly lower in the oedema group ($P = 0.020$ and $P = 0.027$ respectively; split-plot ANOVA)

Fluid intake and output

The mean(s.e.m.) total volume of crystalloids and colloids administered during operation was similar in patients who did or did not develop oedema: 4.15(0.48) versus 3.40(0.29) litres respectively of crystalloids ($P = 0.322$) and 1.00(0.33) versus 0.63(0.33) litres of colloids ($P = 0.167$). The mean total daily fluid intake over the first 5 days after surgery did not differ significantly between groups (Fig. 1). In contrast, the mean daily urine output over the same interval was significantly lower in those

who developed oedema (mean(s.e.m.) 2.15(0.16) versus 2.69(0.14) litres; $P = 0.020$). There was an increase in diuresis between days 2 and 3 that was more marked in those without oedema (0.99 litres; $P = 0.036$) than in those with oedema (0.29 litres; $P = 0.114$). This pattern was repeated in the mean daily total fluid output over the same period (3.37(0.14) oedematous versus 3.98(0.18) litres non-oedematous; $P = 0.017$). Overall, the net fluid balance was significantly more positive in patients with oedema and maximum levels of fluid retention were achieved by the second day after surgery (Fig. 2).

Postoperative recovery and complications

The time taken to tolerate solid food, length of hospital stay and complication rate were significantly increased in the oedema group, before and after adjustment for age (Table 3). The time elapsed before opening bowels was not significantly different between the two groups after adjusting for age. Following exclusion of patients with major infective and/or cardiopulmonary complications, time to tolerate solid food and length of hospital stay

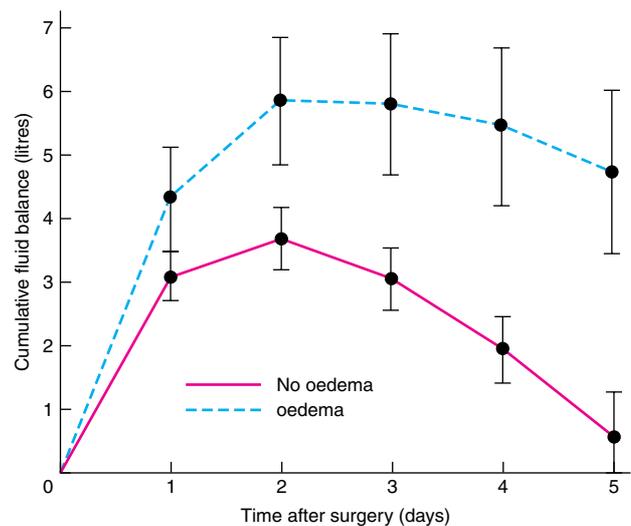


Fig. 2 Mean(s.e.m.) daily cumulative fluid balance after surgery in patients who did or did not develop oedema. The overall fluid balance was significantly more positive in patients who developed oedema ($P = 0.009$; split-plot ANOVA)

Table 3 Clinical outcomes in patients who did or did not develop oedema

| | No oedema (n = 18) | Oedema (n = 20) | Unadjusted P | P (adjusted for age) |
|---|-----------------------|--------------------|--------------|-------------------------|
| Time to tolerate solid food (days)* | 5 (1–8) | 6 (5–25) | 0.001† | 0.030‡ |
| Time to bowel movement (days)* | 5 (1–13) | 6 (3–17) | 0.020† | 0.124‡ |
| Hospital stay (days)* | 9 (4–27) | 17 (8–59) | 0.001† | 0.030‡ |
| Admission to high-dependency unit | 4 | 7 | 0.389§ | 0.433§ |
| Patients with any complications | 4 | 13 | 0.011§ | 0.018§ |
| Patients with infective complications | 3 | 9 | 0.069§ | 0.060§ |
| Patients with cardiopulmonary complications | 1 | 4 | 0.217§ | 0.359§ |

*Values are median (range). †Mann–Whitney U test; ‡rank analysis of co-variance; §binary logistic regression.

Table 4 Clinical outcomes when patients with major infective and cardiopulmonary complications were excluded from the analysis

| | Non-oedematous | Oedematous | Unadjusted P* | P (adjusted for age)† |
|--|----------------|--------------|---------------|--------------------------|
| Major infective complications excluded | n = 16 | n = 12 | | |
| Time to tolerate solid food (days) | 5 (1–7) | 6 (5–25) | 0.015 | 0.103 |
| Time to bowel movement (days) | 4.5 (1–13) | 6 (3–17) | 0.100 | 0.479 |
| Hospital stay (days) | 8.5 (4–27) | 17 (8–50) | 0.001 | 0.020 |
| Cardiopulmonary complications excluded | n = 17 | n = 16 | | |
| Time to tolerate solid food (days) | 5 (1–8) | 7 (5–25) | < 0.001 | < 0.001 |
| Time to bowel movement (days) | 5 (1–13) | 7 (3–17) | 0.012 | 0.045 |
| Hospital stay (days) | 9 (4–27) | 17.5 (12–47) | 0.001 | 0.001 |
| Major infective and cardiopulmonary complications excluded | n = 16 | n = 8 | | |
| Time to tolerate solid food (days) | 5 (1–7) | 7 (5–9) | 0.006 | 0.030 |
| Time to bowel movement (days) | 4.5 (1–13) | 6 (3–17) | 0.061 | 0.235 |
| Hospital stay (days) | 8.5 (4–27) | 17.5 (12–22) | 0.001 | 0.006 |

Values are median (range). *Mann–Whitney U test; †rank analysis of co-variance.

remained significantly prolonged in the oedema group (Table 4).

Changes in impedance and impedance quotient

Whole-body bioimpedance Z decreased significantly after surgery at all measured frequencies in the cohort as a whole ($P < 0.001$, split-plot ANOVA), and in the oedema and no oedema groups. At all frequencies the decrease in Z was greater in the former group (mean change from baseline 135 versus 53 ohms) and such changes were more exaggerated at lower frequencies (Fig. 3). The percentage decrease relative to the preoperative value was greater at 5 kHz than at 200 kHz in both groups: 28.4 versus 24.1 per cent in patients who developed oedema ($P = 0.003$) and 12.6 versus 8.7 per cent in those who did not ($P < 0.001$). The change in impedance quotient followed a similar pattern at each frequency and was greater in the oedema group (Fig. 4).

The preoperative ratio of Z obtained at 200 kHz to that measured at 5 kHz (Z_{200}/Z_5) was higher in those who went on to develop oedema than in those who did not (0.81(0.03) versus 0.80(0.02); $P = 0.015$). There was an increment in the value of this ratio after surgery which was greater in patients who developed oedema, although this did not reach statistical significance (Fig. 5).

With subject as fixed variable when ANCOVA was used to predict intraindividual fluid balance from the impedance quotient (independent variable), the overall value of r^2 for the whole cohort was high at all frequencies ($r^2 = 0.925-0.949$). Previous analysis had established no

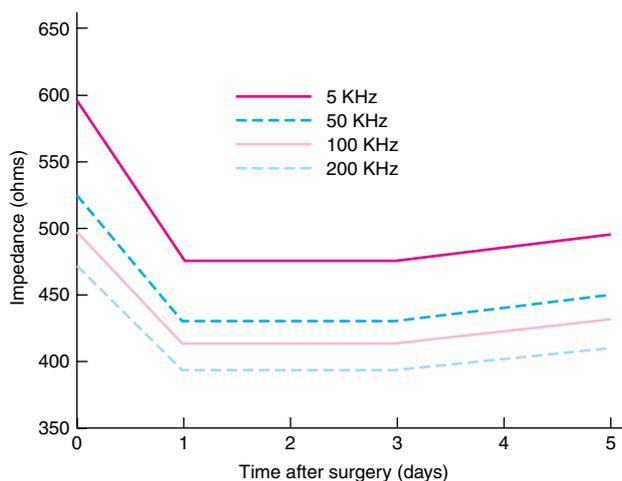


Fig. 3 Mean changes in impedance at 5, 50, 100 and 200 kHz after surgery. The reduction in impedance over time was significant at each frequency ($P < 0.001$; repeated measures ANOVA)

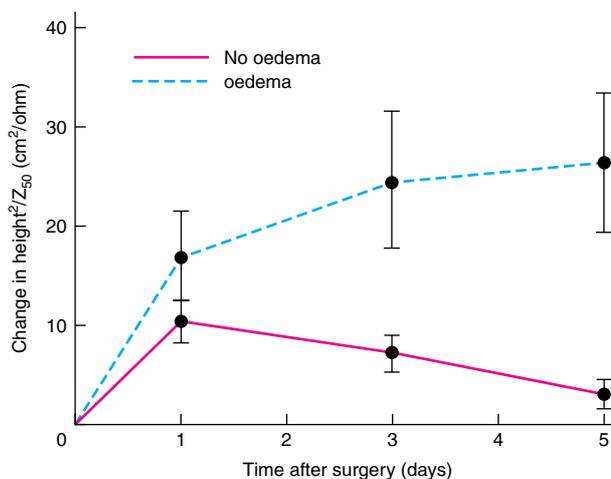


Fig. 4 Mean (s.e.m.) change in the impedance quotient ($\text{height}^2/\text{impedance at } 50 \text{ Hz } (Z_{50})$) after surgery in patients who did or did not develop oedema. The increments were significantly greater in the oedema group ($P < 0.001$; split-plot ANOVA)

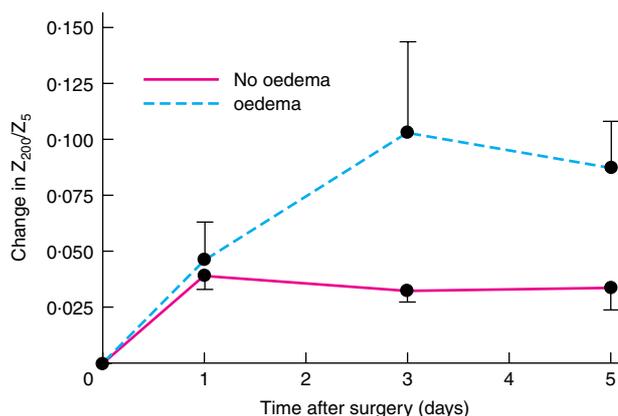


Fig. 5 Mean (s.e.m.) change in the ratio of impedance at 200 kHz to impedance at 5 kHz (Z_{200}/Z_5) after surgery in patients who did or did not develop oedema. The change was greater in patients who developed oedema, but there was no significant difference between the two groups ($P = 0.089$; split-plot ANOVA). Within each group there were significant increments at each time point relative to the preoperative value (day 0) ($P < 0.001$; split-plot ANOVA)

significant effect of sex, and so men and women were analysed together. There was significant between-subject variation in the gradient (Δ fluid balance/ Δ impedance quotient) ($P < 0.050$ at 5, 50 and 100 kHz; $P = 0.054$ at 200 kHz). When patients who did or did not develop oedema were analysed separately, there was no significant difference in gradients (homogeneity of regression) at

any frequencies, apart from 50 kHz in the oedema group ($P = 0.023$). The common intraindividual gradient (Δ fluid balance/ Δ impedance quotient) tended to be steeper in patients who developed oedema; at 5 kHz the mean(s.e.m.) values were 0.291(0.068) versus 0.059(0.053) litre ohms per cm² ($P < 0.050$), whereas at 100 kHz they were 0.265(0.061) versus 0.094(0.071) litre ohms per cm² ($P = 0.080$), in the oedema and no oedema groups respectively. There were significant differences between subjects in the intercepts on the y axis (fluid balance). In all cases, the overall r^2 value obtained with the ANCOVA model was significant in both the no oedema ($r^2 = 0.667$ – 0.677 , depending on the frequency) and oedema ($r^2 = 0.811$ – 0.817) groups.

The QuadScan[®] 4000 provided estimates of TBW using equations derived by the manufacturer (not released to users). The changes in TBW calculated directly from measured fluid balance were compared with those predicted by BIA. The mean fluid balance on days 1, 3 and 5 established through clinical measurements and BIA predictions were similar for patients who did not develop oedema (2.31 versus 2.62 litres respectively; mean(s.e.m.) difference 0.30(0.75) litres). The difference was larger in the oedema group (5.00 versus 8.65 litres; mean(s.e.m.) difference 3.65(s.e.m. 1.82) litres). The overall difference between the two methods was strongly related to the magnitude of the fluid imbalance ($r = 0.882$); BIA progressively overestimated the direct estimates of fluid balance as the fluid balance became more positive.

Clinical outcome, urine output and impedance

The results were analysed with respect to presence or absence of complications. There was no significant difference in age between patients who had complications and those who did not (mean 68 versus 67 years respectively). Patients with complications tended to have a lower urine output (mean(s.e.m.) 29.7(2.1) versus 38.6(3.6) litres per kg per day; $P = 0.049$), a more positive fluid balance on day 5 (3.8(1.9) versus 1.0(0.9) litres; $P = 0.148$), and a larger change in impedance quotient at 50 kHz (21 versus 5 m² per ohm; $P = 0.201$; split-plot ANOVA) and Z_{200}/Z_5 ratio (0.057 versus 0.035; $P = 0.082$; split-plot ANOVA).

The sensitivity of oedema as a diagnostic test for the development of complications was 76 per cent, with a specificity of 67 per cent, positive predictive value 65 per cent and negative predictive value 78 per cent.

Discussion

This study showed that development of oedema in patients undergoing major abdominal surgery is common, affecting

up to 40 per cent of consecutive patients. Lowell *et al.*⁴ reported a similar incidence of fluid overload in patients managed in an intensive care unit after surgery, although they did not indicate whether these patients had oedema.

Fluid balance calculations in this study indicated that some patients are capable of accumulating large volumes in the postoperative period without developing clinically obvious oedema. Such fluid might have accumulated in parts of the body that are not easily accessible clinically. Fluid retention within the gastrointestinal tract following major abdominal surgery has been attributed to a combination of albumin sequestration and reduced motility^{14,15}, with potentially adverse consequences¹⁶.

The most important clinical finding of this study is that the presence of oedema was associated with a slower postoperative recovery. Patients with oedema had significantly more complications, a slower recovery of bowel function and a longer hospital stay. This does not necessarily mean that oedema is responsible for the delayed recovery. It is possible that the complications caused both oedema and delay in return of gastrointestinal function. To examine this possibility further, we analysed the clinical outcome data after exclusion of patients with overt complications (infective plus cardiovascular complications). Recovery remained slower in patients with oedema, even after adjustment for age. Similar results were obtained when patients with infective complications alone were excluded.

Although this study was not designed to establish causality, the data suggest that oedema might be involved in a chain leading to delayed clinical recovery. Fluid overload in experimental animals¹⁷ and humans¹⁸ can reduce gastrointestinal motility and delay gastric emptying, depress myocardial function¹⁹, reduce oxygen tension in tissues²⁰ and delay wound healing²¹. Oedematous tissues are more susceptible to infection and breakdown as a result of poor blood flow and impaired leucocyte function²². A recent randomized controlled trial demonstrated that restricting fluid and salt intake after colonic surgery to no more than 2 litres and 77 mol sodium per day reduced the postoperative gastric emptying time, time to tolerate food, rate of infective complications and length of hospital stay¹⁸. Another multicentre randomized controlled trial restricted fluid intake to maintain bodyweight in one group, whereas the other group received routine fluid therapy. The fluid-restricted group had a significantly lower incidence of cardiopulmonary and wound-healing complications²³. The presence of oedema was not reported in these two studies.

This study examined several ways in which BIA could be employed to monitor fluid redistribution and disturbances in the postoperative period. First, the postoperative

decrease in Z and the increase in the impedance quotient were found to be more sensitive indicators of fluid overload than clinical examination for the presence of oedema. Significant changes in impedance suggestive of fluid retention (also reflected by the fluid balance calculations) were established well before the appearance of clinical oedema. The changes in impedance were also noted in patients who did not develop oedema, although they were more marked in those who did. Second, both the absolute and fractional increase in the impedance quotient was greater at 5 kHz than at higher frequencies, with the result that the ratio Z_{200}/Z_5 also increased significantly over time. These data suggest that the extracellular fluid compartment increased more than the intracellular fluid compartment. Third, patients who developed oedema not only showed a greater increase in impedance quotient, but a greater increase per litre of fluid accumulated. The reason for this is not clear, but it may be explained by differences in tissue impedance and in the distribution of retained fluid within and between body segments. The trunk contributes only about 10 per cent of Z but contains a much greater proportion of body water. Accumulation of fluid here would make a much smaller difference to Z than accumulation of the same amount of fluid in the limbs, which offer greater impedance to the flow of current. Thus accumulation of fluid in the trunk, including gastrointestinal fluid which increases during postoperative ileus, would be expected to have little effect on Z ²⁴. In contrast, accumulation of additional fluid in the limbs (known to have occurred in patients with oedema) would be expected to have a greater effect on Z and impedance quotient. A study that measured segmental bioelectrical impedance on the day of gastrointestinal surgery concluded that most fluid accumulated within the trunk²⁵.

Because quantitative relationships between changes in impedance quotient and changes in fluid status differ between individuals, the use of a single equation to predict changes in fluid balance is limited. This study demonstrated a discrepancy between measured fluid balance and that predicted by BIA, which progressively increased as the fluid balance became more positive. This draws attention to the problems of extrapolating equations relating impedance measurements of body water and body composition derived in healthy subjects to patients with fluid disturbances. Other clinical indices such as microalbuminuria have been used to measure the increased systemic capillary permeability precipitated by the inflammatory response to trauma and this has been shown to be of use in predicting outcomes in patients with burns and surgical patients admitted to intensive care^{26,27}. The present study has shown that BIA represents an additional bedside tool

with the potential to identify and monitor patients who are susceptible to pathological fluid shifts after major surgery.

The study has several limitations. First, the sample size was small, which means that the risk of Type II statistical error was high. Second, although there was complete agreement between observers in diagnosis of oedema, it is recognized that detection of oedema can be affected by such factors as skin elasticity and interstitial tissue compliance, which are known to be age-dependent. Third, although this study was observational, it adds weight to the findings from previous studies in which fluid intake was restricted after surgery. A clinical trial is now needed, in which patients are randomized to receive either fluid to strictly maintain fluid balance or routine fluid therapy, with segmental and whole-body BIA undertaken before and after surgery, and simultaneous monitoring of clinical outcome and fluid balance.

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