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Positive Fluid Balance is Associated with Complications after Elective Open Infrarenal Abdominal Aortic Aneurysm Repair

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Background. *Open abdominal aortic aneurysm (AAA) repair is associated with cardiac and respiratory complications and an overall mortality rate of 2 to 8%. We hypothesised that excessive fluid administration during the perioperative period contributes to complications and poor outcome after AAA repair.*
Methods. *This was a retrospective cohort study. Medical records were analysed for fluid balance and complications in 100 consecutive patients treated by open AAA repair at a single centre between 2002–2005. Mortality and all major adverse events (MAE) such as myocardial infarction (MI), cardiac arrhythmia (Arr), pulmonary oedema (PO), pulmonary infection (PI), and acute renal failure (ARF) were included in the analysis. Level of care and hospital stay, were also recorded.*
Results. *There were no in-hospital deaths. MAE occurred in 40/100 (40%): MI (6%); Arr (14%); PO (14%); PI (25%); ARF (8%). Complications were not predicted by preoperative cardiovascular risk factors, operative and clamp time, or blood loss. Patients with complications had significantly greater cumulative positive fluid balance on postoperative day 0 ($p < 0.01$), day 1 ($p < 0.05$), day 2 ($p < 0.03$) and day 3 ($p < 0.04$). This relationship also existed for individual complications such as MI, and pulmonary oedema. These patients had significantly longer ICU/HDU ($p < 0.002$) and hospital stay ($p < 0.0001$).*
Conclusions. *Serious complications are common after elective open AAA repair, and we have shown that positive fluid balance is predictive of major adverse events increased HDU/ICU and overall hospital stay.*

Keywords: Abdominal aortic aneurysm; Vascular surgery; Fluid balance; Outcome; Complications; Mortality.

Introduction

The prevalence of abdominal aortic aneurysm (AAA) is between 4.5–7.7%,[1,2] and its incidence may be increasing.[3] The commonest complication of AAA is rupture, which is associated with massive internal haemorrhage, leading to death in up 80% of those affected.[1,3–6] Rupture-risk increases with maximum AAA diameter, and trials suggest that intervention should be considered for aneurysm greater than 5.5 cm.[7,8] In the absence of an effective pharmacotherapy, planned treatment is by open (OR) or endovascular aneurysm (EVAR) repair techniques. Several randomised trials have demonstrated that early mortality and morbidity is reduced after EVAR compared to OR.[9–11] However, this survival benefit is temporary, as procedural re-intervention rates and late medical complications are commoner after EVAR,[12] indeed mid-term outcomes may even favour OR.[13] Therefore, OR will remain an important treatment for AAA in selected patients, in particular those deemed unsuitable for EVAR in terms of age, anatomy, or patient preference.

Despite improvements in peri-operative care, OR for AAA is associated with a significant mortality of 4.6 to 9.6%.[4,10,14,15] Morbidity is also common after OR, in particular respiratory and cardiovascular complications.[4,10,14,15] Surgical outcomes are influenced by the age and medical fitness of the patient population treated,[16–19] and several predictive models have been designed to identify those patients at greatest risk of morbidity and mortality.[15,20,21] However, variations are also noted with the degree of specialisation and volume of the surgical unit,[4,16,22] which suggests that outcomes are also influenced by the type and quality of OR patients receive. OR of an AAA subjects

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the patient to the combined surgical insults of laparotomy incision, haemorrhage, and lower limb ischaemia-reperfusion. The resultant systemic inflammatory response, and increased microvascular permeability, combined with often massive intravenous fluid administration and haemodynamic effects of epidural anaesthesia makes these patients particularly vulnerable to harmful extravascular fluid accumulation.[23–25] Several recent clinical trials, in general surgical patients, have highlighted the beneficial effects of restricted perioperative fluid regimens, reporting reduced postoperative complications.[26–28] The aim of this study was to investigate the effect of perioperative excess fluid on outcome following elective open repair of AAA.

Patients and Methods

A consecutive series of 100 patients undergoing conventional open elective AAA repair between the years 2002–2005 at a single specialist vascular surgical unit, were included in this retrospective cohort study. Patients who underwent emergency surgery were excluded from the study.

All patients were fasted from midnight prior to surgery. All patients received a general anaesthesia, and were given a single dose of a parental prophylactic antibiotic on induction of anaesthesia. All patients had a lumber epidural catheter placed pre-induction, but this was used only for postoperative analgesia. One of 4 specialist vascular surgeons operated on all patients with an attending specialist vascular anaesthetist. All patients underwent conventional open AAA repair through a standard midline laparotomy incision and transperitoneal approach with infra-renal interposition graft repair. A cell-saver device was routinely used, for collection and re-infusion of autologous blood. All patients returned to specialist beds on the vascular surgery unit in the postoperative period.

Patients' case notes were reviewed retrospectively, for demographic information, cardiovascular risk factors, and the Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM) score, and the operative indication. Operative factors were identified including the nature of surgery, duration of surgery, duration of clamp-time, and blood loss. The total fluid intake, intravenous fluid (including blood and blood products) and oral fluids, from midnight on the day of the operation (day 0) to the discharge date were recorded. The total fluid output (including urine, enteral losses, and surgical drains) during the same period was recorded. Outcome measures included in-hospital mortality, complications, fluid balance (daily and cumulative), and the length of postoperative stay (including ICU/HDU stay).

Statistical analysis

Means (standard deviation) values were calculated for continuous variables and categorical data were expressed as absolute numbers with percentages. Univariate analysis for continuous variables was conducted with unpaired Student's t test. Categorical variables were analysed by x^2 test, except when expected frequencies were less than 5, in which case Fisher's exact test was used. $P < 0.050$ was considered as significant. All statistical analyses were performed using SPSS® software (version 13; SPSS, Chicago, Illinois, USA).

Results

Morbidity and mortality

There were no in-hospital deaths (and no 30-day mortality). However, major complications occurred in 40% of patients, including: myocardial infarction, 6%; cardiac arrhythmia, 14%; pulmonary oedema, 14%; pulmonary infection, 25%; acute renal failure, 8%. Table 1 shows the major and minor complications in these patients.

Older patients (> 75 years), and current smokers were more likely to have major complications, and interestingly patients with hypertension were less likely to have a major complication, Table 2. Preoperative renal dysfunction (creatinine > 130 micromol/l), was present in 7 patients (range 133–231 micromol/l), but did not increase the risk of postoperative major complications, Table 2.

Influence of peri-operative factors on morbidity

The demographic profile, POSSUM scores, operative characteristics, and outcomes of patients are shown in Table 3. Patients who developed major complications were significantly older ($p < 0.002$), and had a significantly greater *POSSUM physiological score*, ($p < 0.02$). Operative characteristics and *POSSUM operative score* were not significantly different between those who developed major complications and those who did not (Table 3).

Level of care and hospital stay

Those patients with major complications had an ICU readmission rate of 27.5% compared to 2% in those

Table 1. Common Odds Ratio Estimate of prognostic factors for complications in 100 consecutive patients undergoing elective open infra-renal abdominal aortic aneurysm repair

Risk Factor	No complications† ($n = 60$)	Complications† ($n = 40$)	Odds Ratio‡	p-value
Old age (> 75 years)	10 (16.7)	18 (45.0)	4.091 (1.628, 10.280)	0.004*
Female	7 (11.7)	9 (22.5)	2.198 (0.745, 6.490)	0.245
Diabetes Mellitus	2 (3.3)	3 (7.5)	2.351 (0.375, 14.748)	0.641
Hypertension	35 (58.3)	14 (35.0)	0.385 (0.168, 0.880)	0.038*
Myocardial Infraction	16 (26.7)	15 (37.5)	1.650 (0.699, 3.894)	0.356
IHD	21 (35.0)	15 (37.5)	1.114 (0.485, 2.559)	0.966
COPD	6 (10.0)	8 (20.0)	2.250 (0.716, 7.072)	0.266
Smoker	40 (66.7)	35 (87.5)	3.500 (1.189, 10.305)	0.035*
Abnormal LVF	38 (63.3)	29 (72.5)	1.179 (0.480, 2.899)	0.896
CRF	5 (8.3)	2 (5.0)	0.579 (0.107, 3.141)	0.811

†Values in parenthesis are sum (percentages), except ‡values are Mantel-Haenszel Common Odds Ratio Estimate (95% confidence interval), *$p < 0.05$; risk of complications. IHD: Ischaemic heart disease; COPD: Chronic obstructive pulmonary disease; LVF: Left ventricular function (LV ejection fraction < 50%); CRF: Chronic renal failure (creatinine > 130 micromol/l).

without major complications ($p < 0.0001$). Patients who developed major complications also spent significantly longer in ICU ($p < 0.002$), an average of 4 days, and had a significantly longer postoperative hospital stay, ($p < 0.0001$), Fig. 1.

Fluid balance and morbidity

Patients who developed major complications had greater daily fluid administered and had significantly greater cumulative positive fluid balance on postoperative day 0 ($p < 0.01$), day 1 ($p < 0.05$), day 2 ($p < 0.03$) and day 3 ($p < 0.04$), as shown in Fig. 2.

Table 2. Type and characteristics of major complications after elective open infra-renal abdominal aortic aneurysm repair

Complication	Complications ($n = 100$)	Time to symptom development in days*	No. of deaths (within 30 days)
Major			
Myocardial infarction	6	3.7 (2.3)	0
Cardiac arrythmia	14	2.1 (1.2)	0
Pulmonary oedema	14	2.6 (1.1)	0
Pulmonary infection	25	4.0 (2.2)	0
Cerebrovascular accident	0	-	0
Renal dysfunction	8	1.5 (0.7)	0
Minor			
Wound infection	2	4.7 (2.3)	0
Infection (other)	3	5.1 (2.2)	0
Prolonged ileus	4	5.0	0
Wound dehiscence	1	5.0	0
Hepatic dysfunction	1	5.0	0
Total	78	-	0

*Values are means (standard deviation).

Discussion

In this retrospective study of 100 consecutive patients we have shown that patients who develop major complications after OR of AAA were administered significantly greater fluid volume in the early postoperative period than those who did not.

Identifying those patients at greatest risk, to allow correct patient selection,[15,20,21] combined with improved perioperative care.[16–19] has improved outcomes for vascular surgical patients. Fortunately, there was no mortality during the study period in these 100 consecutive patients. However, our units 30-mortality for the last 400 OR of AAA was 3.9% (personal communication, DW Harkin), which is representative of our tertiary specialist vascular practise and case mix, and comparable with published series.[1,6,17] Patients who developed complications in our series had a slightly greater *POSSUM* physiological score and were slightly older, which may account for some of the increased risk. The adverse effect of age and medical co-morbidities is well known for vascular surgical patients.[1,6,16,17] However, in this study there was no significant difference between the groups in terms of serious medical co-morbidities such as diabetes mellitus, ischaemic heart disease, chronic obstructive airways disease, or chronic renal dysfunction. Interestingly patients with known hypertension were less likely to develop complications, and it is possible that instituted medical and lifestyle therapies may have improved outcomes in this group. During the study period it was the unit policy that all patients considered high cardiovascular risk were commenced on beta-blockers, two-weeks

Table 3. Demographics, operative factors, and outcome of 100 consecutive patients undergoing elective open infra-renal abdominal aortic aneurysm repair

Parameter	All patients ($n = 100$)	No complications ($n = 60$)	Complications ($n = 40$)	p-value
Age (years)	71 (52–86)	68.52 (66.71–70.32)	72.78 (70.88–74.67)	0.002*
Sex (M:F)	84:16	53:7	31:9	
POSSUM				
Physiology score	19 (12–30)	18.44 (17.41–19.47)	20.33 (18.93–21.74)	0.028*
Operative score	16 (14–20)	15.13 (14.54–15.72)	16.03 (15.17–16.00)	0.076
Creatinine (micromol/l)	97 (90–103)	99.80 (90.67–108.94)	91.90 (83.75–100.05)	0.245
Epidural analgesia	100 (100%)			
Operating time (minutes)	180 (90–360)	181.72 (169.24–194.21)	166.58 (147.22–185.94)	0.168
Clamp time (minutes)	59 (26–135)	60.52 (55.32–65.73)	60.58 (52.67–68.48)	0.991
Blood loss (ml)	1100 (250–4000)	1482 (1002–1961)	1373 (912–1833)	0.736
Intraoperative fluid (ml)	4600 (1500–9300)	4471 (4113–4830)	5056 (4521–5591)	0.060
Time in ICU (days)	0 (0–54)	0.06 (−0.01–0.15)	4.23 (0.97–7.48)	0.002*
Time in HDU (days)	0 (0–28)	0.52 (0.13–0.90)	1.85 (0.30–3.40)	0.048*
Postoperative stay (days)	11 (6–104)	11.03 (9.81–12.26)	20.20 (14.27–26.13)	0.000*

Values are either medians (range) or mean (95% confidence interval for mean). *$p < 0.05$, one-way analysis of variance (ANOVA); patients with no complications versus patients with complications.

preoperatively and continued for six-weeks postoperatively or on medical advice.[29]

Pulmonary complications were commonest problem in our series, including acute pulmonary oedema, which may be directly associated with harmful hypervolaemia. Prior pulmonary dysfunction[30] and smoking[5] are poor prognostic indicators for patients undergoing elective AAA repair and in this study those who developed complications were more likely to be smokers although rates of diagnosed pulmonary disease were not significantly different. As expected for this patient population many in this study had ischaemic heart disease and impaired left ventricular function, although neither predicted major complication. Renal dysfunction is a poor prognostic indicator in patients considered for elective OR of AAA.[17] Of 7 patients in our series with preoperative renal dysfunction, only 2 developed a major complication, and indeed the 2 patients with highest creatinine levels (> 200 micromol/l) underwent OR without complication. A recent prospective review of 1,559 patients undergoing vascular surgery, has shown that of patient with normal preoperative renal function, renal failure occurred in only 7%.[31] Importantly, mortality in this group was 32%, compared to only 4% in those without renal failure, and often associated with multiple organ failure.[31] In our study acute renal failure occurred in 8%, but was temporary in all cases, with no

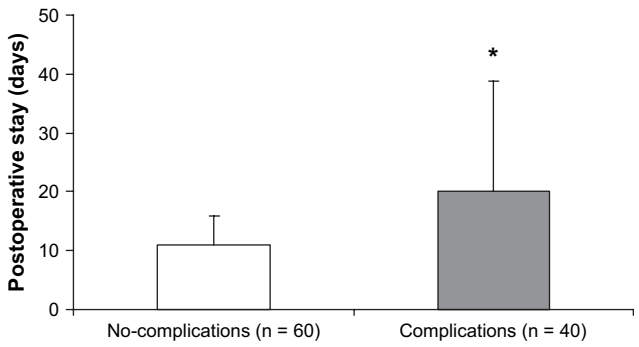

Fig. 1. Patients who developed major complications had a significantly longer postoperative hospital stay, 20.2 (14.3–26.1) days compared to 11 (9.8–12.3) days for those patients without complications, ($p < 0.0001$). Data represents mean (95% Confidence Interval of mean).

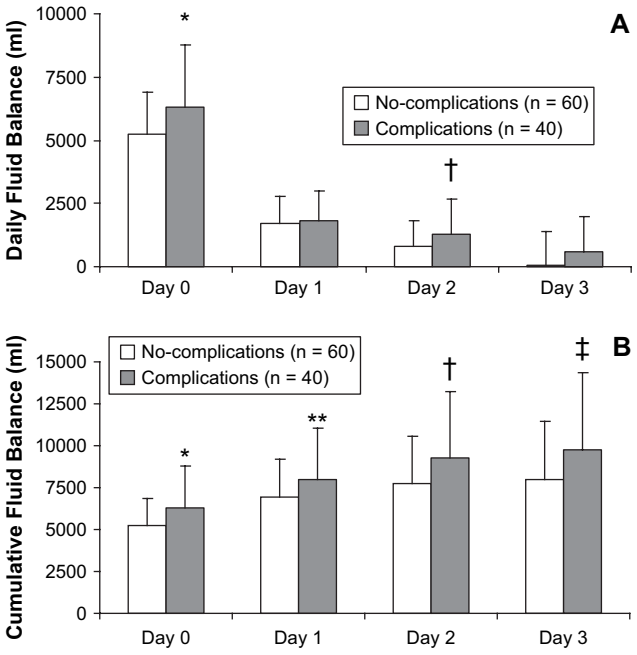

Fig. 2. A: Daily fluid balance for patients who developed major complications compared to those with no major complications. B: Cumulative fluid balance for patients who developed major complications compared to those with no major complications. Data represents mean ± standard deviation. Analysis of variance: *$p < 0.003$, †$p < 0.05$, **$p < 0.008$, ‡$p < 0.015$.

patient requiring renal replacement therapy. The mainstay of preventative therapy against renal dysfunction is maintenance of adequate renal perfusion. However, excessive fluid administration may be harmful if it leads to congestive failure and pulmonary oedema, whilst failing to achieve adequate renal perfusion.[32]

OR of an AAA subjects the patient to the combined surgical insults of laparotomy incision, haemorrhage, and lower limb ischaemia-reperfusion. The resultant systemic inflammatory response, and increased microvascular permeability, combined with often massive intravenous fluid administration and haemodynamic effects of epidural anaesthesia makes these patients particularly vulnerable to harmful extravascular fluid accumulation.[23–25] Our study has shown that patients who develop complications after elective OR of AAA received significantly more fluid in the early post-operative period, despite having no significant difference in surgical factors such as blood loss, intra-operative fluid replacement, clamp time, and total surgery time. There are no established guidelines on perioperative fluid management for patients undergoing elective OR for AAA, and significant variation exists in respect to the of types and volumes of fluid administered within the United Kingdom.[33] However, there is a broadly-held perception that patients who undergoing surgery associated with haemorrhage require liberal fluid replacement to maintain extracellular fluid volume (ECV).[34] However, this practise is not evidence-based and indeed there is ample evidence from systematic review of the literature that ECV is well maintained and may even be expanded after surgery.[35] Neuro-endocrine responses (anti-diuretic hormone (ADH, aldosterone, and renin-angiotensin system) help protect ECV and as such excessive fluid administration in the early peri-operative period after AAA repair may not improve organ perfusion, and may indeed be harmful. Several recent clinical trials, in general surgical patients, have highlighted the beneficial effects of restricted perioperative fluid regimens, reporting reduced postoperative complications and hospital stay.[26–28] Indeed in a recent national review of perioperative fluid and electrolyte management amongst general surgeons would suggest that this important component of surgical care is often delegated to junior inexperienced staff and not optimally delivered.[36] Whilst it is not possible to support a causal link between excessive intravenous fluid administration and complications in this retrospective series, it is clear that over hydration may have contributed to deleterious effects on a number of organ systems in these high-risk surgical patients.

In our series all patient returned to high-dependency beds on a specialist vascular surgical ward for the first three postoperative days, and early fluid management was based upon standard physiological parameters (including invasive blood pressure and central venous pressure), fluid balance, urine output, and clinical characteristics. However, it is clear that it is difficult to assess individual patients ECV or cardiac preload, without advanced or invasive monitoring equipment, and as such current fluid administration is at best an educated clinical guess. In our series 11 patients (11%) were readmitted to intensive care unit (ICU), major complications requiring respiratory support accounted for 10 admissions (25% readmission rate in this group), staying for an average of 4 days. A single patient was readmitted to ICU without a major complication, with hypotension for inotrope support and monitoring, staying for less than 1 day. Whilst it is common practice in many units to admit elective OR of AAA to ICU, others have proposed the selective use of ICU, with comparable surgical outcomes.[37]

Serious complications are common after elective open AAA repair, and we have shown for the first time that positive fluid balance is predictive of major adverse events (in particular cardiac and respiratory complications), increased ICU, and overall hospital stay. It is evident that optimal fluid balance is necessary in these high-risk vascular surgical patients if outcomes are to be further improved, and the authors feel it is time for a robust prospective assessment of the role of fluid balance on outcome following open infra-renal abdominal aortic aneurysm repair.

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