Journal of Surgical Research 173, 68–74 (2012)
doi:10.1016/j.jss.2010.08.051

Impact of Restrictive Intravenous Fluid Replacement and Combined Epidural Analgesia on Perioperative Volume Balance and Renal Function Within a *Fast Track* Program[1]

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Originally submitted June 9, 2010; accepted for publication August 27, 2010

Background and Objective. **Key factors of *Fast Track* (FT) programs are fluid restriction and epidural analgesia (EDA). We aimed to challenge the preconception that the combination of fluid restriction and EDA might induce hypotension and renal dysfunction.**

Methods. **A recent randomized trial (NCT00556790) showed reduced complications after colectomy in FT patients compared with standard care (SC). Patients with an effective EDA were compared with regard to hemodynamics and renal function.**

Results. **61/76 FT patients and 59/75 patients in the SC group had an effective EDA. Both groups were comparable regarding demographics and surgery-related characteristics. FT patients received significantly less i.v. fluids intraoperatively (1900 mL [range 1100–4100] *versus* 2900 mL [1600–5900], $P < 0.0001$) and postoperatively (700 mL [400–1500] *versus* 2300 mL [1800–3800], $P < 0.0001$). Intraoperatively, 30 FT compared with 19 SC patients needed colloids or vasopressors, but this was statistically not significant ($P = 0.066$). Postoperative requirements were low in both groups (3 *versus* 5 patients; $P = 0.487$). Pre- and postoperative values for creatinine, hematocrit, sodium, and potassium were similar, and no patient developed renal dysfunction in either group. Only one of 82 patients having an EDA without a bladder catheter had urinary retention. Overall, FT patients had fewer postoperative complications (6 *versus* 20 patients; $P = 0.002$) and a shorter median hospital stay (5 [2–30] *versus* 9 d [6-30]; $P < 0.0001$) compared with the SC group.**

Conclusions. **Fluid restriction and EDA in FT programs are not associated with clinically relevant hemodynamic instability or renal dysfunction.**

Key Words: **enhanced recovery; *fast track*; epidural analgesia; fluid restriction; hemodynamics; renal function.**

INTRODUCTION

Optimal fluid management represents a key issue of perioperative care of patients undergoing major abdominal surgery. The successful advent of *fast track* (FT) programs has provided new aspects to the ongoing debate of perioperative fluid management [1–6].

Traditional fluid management aims to maintain blood pressure and heart rate in order to prevent hypovolemia-induced chances of microcirculation that may be associated with organ dysfunction [6, 7]. As a consequence, patients generally have a postoperative fluid overload that is reflected by a significant weight gain [1, 6, 8].

So called FT concepts or enhanced recovery after surgery (ERAS) programs have been increasingly implemented into clinical practice during recent years. By limiting patients' perioperative stress response, postoperative complication rates and length of hospital stay can be reduced [2, 3, 5]. FT programs are primarily based on the use of epidural analgesia (EDA) to minimize opioid consumption, restrictive perioperative fluid management, early postoperative oral nutrition, and early ambulation [2, 3, 5, 9, 10].

[1] PODIUM presentation (S63) at the 2009 ASCRS Annual Meeting, May 2–6, 2009, Hollywood, Florida.
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0022-4804/$36.00

The beneficial effects of thoracic EDA on pain reduction, pulmonary complications, and postoperative intestinal motility have largely been demonstrated [11–19]; drawbacks are transient arterial hypotension in about 10%, pruritus and urinary complications [14, 18–21]. However, the impact of a restrictive fluid management on organ function is still under debate, and opponents are concerned for hypovolemia-induced organ dysfunction like renal insufficiency, myocardial ischemia, and impaired wound healing [6, 7]. On the other hand, excessive perioperative fluid administration may exert deleterious effects on cardiopulmonary function, and prolong postoperative bowel arrest [1, 6, 22–25]. In fact, there is increasing evidence in the literature that restrictive fluid regimens are favorable to reduce cardiopulmonary complications and enhance postoperative recovery without compromising wound healing [1, 3, 5, 6, 9, 22, 23, 25, 26].

We were recently able demonstrate that patients undergoing elective open colonic surgery have a significantly reduced complication rate, if they were included in a FT program [27]. The two independent predictors for low postoperative complications were an efficient EDA and perioperative fluid restriction [27]. As outlined before, restrictive fluid management and EDA may both lead individually to arterial hypotension, renal dysfunction, and electrolyte disturbance. Their combined impact has not yet been examined in detail. Since this multicentric prospective randomized trial provided precise data on different organ function, we performed for the present study a *post hoc* analysis in patients with an efficient EDA.

We aimed to assess whether additional fluid restriction had a negative impact on preservation of hemodynamics and renal function in patients having an effective EDA. Furthermore, electrolyte disturbances as well as clinical outcome were separately assessed.

METHODS

A prospective randomized trial (NCT00556790) assessing a FT regimen *versus* standard care (SC) was performed in 156 patients undergoing open elective colon resection at four surgical departments in Switzerland (Fig. 1) [27].

Patients in the SC group received a fixed restricted fluid regime according to institutional guidelines that were based on established recommendations [6, 28]. They received Ringer's lactate at 2 mL per kg bodyweight per h for preoperative loading, and 10 mL per kg bodyweight per h during the surgery, respectively. The actual bodyweight was measured usually the day before surgery. In the FT group, preoperative fasting (nil per mouth) time was 2–6 h for clear liquids. Loading volume to compensate external and internal loss caused by preoperative fasting, vasodilatation, and epidural analgesia (pre-block hydration) was performed by using Ringer's lactate solution at 1 mL per kg bodyweight per h. Intraoperatively, crystalloid fluid administration was limited to 5 mL per kg bodyweight per h. Preoperative fluid loading according to the reported formulas was initiated upon entry in the operation room area. The epidural catheter was habitually placed before induction of general anesthesia; therefore, fluid loading was administered approximately 30–45 min prior to use of the EDA and for a total time of about 45–60 min before skin incision. Intravenous fluid administration in the FT group was discontinued at postoperative d 1, unless there were medical indications to do otherwise. In the SC group, patients received 2000 mL Ringer's lactate per 24 h until postoperative d 3.

Additional colloid fluids or low-dose vasopressors were given, when mean arterial pressure dropped permanently (>1 h or three consecutive measurements) below 60 mm Hg or urine output was (3×) lower than 0.5 mL/kg/h. Vasopressors were privileged in order to avoid fluid overload. Low-dose vasopressors were norepinephrine up to 5 μg/min or ephedrine at a bolus dose of 10–25 mg intravenously (maximum 150 mg/24 h). Blood transfusion was limited to a hematocrit <25%. Patients in the FT group were allowed to drink immediately after surgery and to resume an oral diet on postoperative d 1, while the SC group started drinking and oral nutrition on postoperative d 2 and full oral nutrition on postoperative d 4. An epidural catheter with ropivacaine 0.33% or bupivacaine 0.25% was placed at thoracic level 6–9 preoperatively and removed on postoperative d 2. For additional analgesia, paracetamol was given intravenously at a fixed rate (4 × 1 g/d). A failure of EDA (inefficient EDA) was defined by the need for additional intravenous opioids. Perioperative fluid administration was recorded for the first 24 h after surgery. At postoperative d 1, the urinary catheter was removed according to the study protocol.

Outcome of primary interest in the present study was perioperative vasopressor requirements and/or need for additional fluid administration indicating clinically relevant hemodynamic instability. Of note, patient's outcome was assessed in this study by a *per protocol* analysis; as we were interested in the effect of EDA with and without additional fluid restriction, we included only patients with an efficient EDA in the present subgroup analysis. Secondary outcome parameters included plasma concentrations of sodium, potassium, creatinine, and hematocrit values pre- and postoperatively that served as surrogate parameters for perioperative fluid shifts. Furthermore, perioperative creatinine values were used to assess for risk of renal dysfunction according to the AKIN classification system (RIFLE criteria) [29]. Postoperative complications (30-d morbidity) were graded according to its severity, and a validated therapy-orientated complication score on a five-point scale described was used [30].

Statistical analysis was performed using standard software package SPSS 14.0 (SPSS, Inc., Chicago, IL). Descriptive statistics are expressed as mean [± standard deviation] or median [range] as appropriate. The Mann-Whitney U test was used to compare continuous variables, Chi-square and Fischer's exact tests were used for comparison of discrete variables. P-value < 0.05 was considered statistically significant.

RESULTS

Overall, 156 patients were included in the study and randomly assigned to either FT ($n = 78$) or SC ($n = 78$). There were two patients in the FT group and three patients in the SC group who were excluded due to withdrawal or other protocol violation. Another 31 patients (FT: 15, SC: 16) were excluded in the present study for EDA failure. Finally, 61 out of 76 FT patients (80%) and 59 out of 75 SC patients (79%) had an effective EDA and were included in the present per protocol analysis (Fig. 1).

Patients' Characteristics

The FT and SC groups matched well regarding gender, body mass index, American Society of Anesthetists