ESCVS article - Aortic and aneurysmal

Fast track management reduces the systemic inflammatory response and organ failure following elective infrarenal aortic aneurysm repair

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Abstract

Objectives: Systemic inflammatory response syndrome (SIRS) is common after abdominal aortic aneurysm (AAA) repair. The aim of this study was to analyze the impact of a multimodal fast track (FT) regimen on incidence rates of SIRS after elective infrarenal AAA repair. **Methods:** Post hoc analysis of a randomized controlled trial including 99 patients after either traditional (TC) or FT care. Basic FT elements were no bowel preparation, reduced preoperative fasting, patient controlled epidural analgesia, enhanced postoperative feeding and mobilization. The presence of SIRS, organ failure and mortality, length of stay (LOS) on intensive care unit (ICU) were analyzed during the postoperative course. **Results:** The incidence of SIRS in the FT treatment arm was significantly lower as compared to TC: 28% vs. 50%, $P=0.04$. The rate of any organ failure (AOF) and multiple organ failure (MOF) was lower in the FT group: AOF: 16% vs. 36%, $P=0.039$; MOF: 2% vs. 12%; $P=0.112$. LOS on ICU showed a slight advantage for FT care: 20 hours vs. 32 hours ($P=0.183$). **Conclusion:** An optimized patient care program in elective open AAA repair significantly decreases the postoperative incidence of SIRS as well as rates of organ failure.

1. Introduction

The systemic inflammatory response syndrome (SIRS) is an initial response to injury as well to surgical stress and reflects activation of inflammatory cascades with production of inflammatory markers [1]. After elective infrarenal aortic aneurysm repair 89% of the patients develop SIRS which usually precedes the development of organ failure [2]. SIRS can be rapidly assessed at the bedside without the need for special equipment and has therefore been proposed as an easy tool for the identification of patients at risk for organ failure [3]. Despite improvements of surgical techniques and perioperative management open repair of abdominal aortic aneurysms (AAAs) is associated with high rates of organ dysfunction and mortality: mortality rates after open elective aneurysm repair range between 6% and 8%, and morbidity is as high as 59% depending on pre-existing risk factors and age [4, 5]. In other surgical fields multimodal – so called – fast track (FT) recovery programs also referred to as enhanced recovery after surgery (ERAS) have been implemented in order to enhance recover, reduce morbidity and mortality and shorten hospital stay after major surgery [6]. Elements of FT recovery programs are no bowel preparation, no preoperative fasting and the use of epidural anesthesia (EDA) –

measurements that aim at reducing surgical stress, optimizing postoperative analgesia and adjusting postoperative care in order to reduce complication rates [7]. As for colonic surgery prospective randomized trials exist that favor FT patient care programs as compared to traditional care (TC) [8]. As for elective infrarenal aortic aneurysm repair we have shown that optimized perioperative management reduces postoperative morbidity [9]. The aim of the present post hoc analysis was to test whether the use of our proposed FT patient care program could decrease the incidence of SIRS and consequently the rates of organ and particularly multiple organ failure (MOF) after elective open AAA repair.

2. Patients and methods

A prospective randomization of 101 consecutive patients was performed for the evaluation of a FT regimen; randomization and inclusion/exclusion criteria had been described in detail previously (clinical trials. gov identifier NCT 00615888); patients were analyzed in an intention to treat analysis [9]. The study was approved by the local Ethics Committee and written informed consent of the patients was obtained preoperatively. There were no significant differences between the treatment groups concerning age, gender, American Society of Anesthesiologists (ASAs) classification, preoperative baseline laboratory tests and blood units transfused (Table 1).

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Table 1. Overview over patient characteristics

	TC ($n=50$)	FT ($n=49$)	P-value
Age (years)	68 (52–84)	67 (40–81)	>0.05
Gender ratio: male/female	47:3	46:3	>0.05
AAA-diameter (cm)	5.5 (4.4–8.5)	5.6 (4.2–7.4)	>0.05
Baseline serum creatinine (μmol/l)	103 (68–183)	87 (69–186)	>0.05
Homologous blood units transfused	0 (0–8)	0 (0–4)	>0.05
ASA-score			
ASA II	5	5	
ASA III	34	32	
ASA IV	3	0	

Patients were comparable concerning age, gender, aneurysm diameter, and ASA score. Values are given as median and range. TC, traditional care; FT, fast track; AAA, abdominal aortic aneurysm; ASA, American Society of Anesthesiologists.

Basic FT elements were no bowel preparation, reduced preoperative fasting (2 h), pain control using EDA and postoperative intravenous (i.v.) fluid restriction (Table 2).

The development of SIRS was analyzed by a post hoc analysis of the patients' charts. The presence of SIRS was documented on postoperative days (POD) 1, 2, 3 and 7 according to the defined criteria published by Bown et al. [2] depicted in Table 3. Postoperative assisted mechanical ventilation (AMV) was defined as pulmonary failure within the SIRS criteria.

The occurrence of organ failure was documented during the in-hospital stay following the previous defined criteria as published by Knaus et al. 1985 (see below). Any organ failure (AOF) was defined as one organ systems failing during a single 24-hour period; MOF was defined as presence of two or more organ systems failing at the same time during the same 24-hour period.

2.1. Definition of variables (according to Knaus et al. 1985) [10]

2.1.1. Cardiovascular

Myocardial ischemia was suspected and documented if two of the following signs were noticed: chest pain and/or echocardiogram changes and/or elevated heart enzymes.

2.1.2. Respiratory

Pneumonia was confirmed if the patient showed clinical and radiological signs of infection (temperature >38 °C, infiltration on chest X-rays) that required administration of antibiotics.

Table 2. Overview realized FT elements

- Preoperative patient education
- No bowel preparation
- Reduced preoperative fasting
- Pain control via PCEA
- Prevention of heat loss
- Early removal of gastric tube
- Early enteral feeding
- Postoperative i.v. fluid restriction
- Early mobilization

FT, fast track; PCEA, patient controlled epidural anesthesia; i.v., intravenous.

Table 3. SIRS criteria according to Bown et al. [2]

SIRS criteria
Two or more of the following criteria
Temperature >38 °C or <36 °C
Heart rate >90 bpm
Respiratory rate >20 breaths/min or AMV
WCC >12 G/l or <4 G/l

SIRS, systemic inflammatory response syndrome; AMV, assisted mechanical ventilation; WCC, white blood cell count.

2.1.3. Acute renal failure (ARF)

According to the consensus conference of the acute dialysis quality initiative (ADQI) Group ARF was confirmed if urine output was <0.5 ml/kg/h or if serum creatinine showed an absolute acute increase of at least 44 μmol/l in the postoperative course which led to additional volume substitution and administration of diuretics (furosemide).

2.1.4. Gastrointestinal

Functional bowel obstruction (paralytic ileus) was confirmed if vomiting was present or the patient was not able to take oral food and horizontal fluid levels were documented on erect abdominal X-ray.

2.1.5. Infective

Urinary tract infection was confirmed if fever occurred in the postoperative course and bacteria were present in the urine probe and antibiotic medication was administered; i.v. line infection was confirmed with positive bacterial probes and elevated temperature to 39 °C.

2.2. Statistical analysis

The primary analysis was conducted in an intention to treat analysis. For discrete variables absolute and relative frequencies are given. For continuous frequencies median values and range are applied. To calculate significance of SIRS/morbidity/mortality and postoperative complications in the treatment groups Fisher's exact test was used. $P<0.05$ were considered to be significant. Statistical analysis was performed in collaboration with the Department of Biometry using the computer program SigmaStat (Systat, San Jose, CA, USA).

3. Results

3.1. Perioperative outcome

Table 4 shows our study results in terms of medical complications in the postoperative course of the patients:

Table 4. Incidence rate of organ failure in the treatment groups

	TC ($n=50$)	FT ($n=49$)	P-value
Organ system			
Cardiovascular	4 (8%)	3 (6.1%)	
ARF	3 (8%)	3 (6.1%)	
ARF requiring dialysis	1 (2%)	0	
Respiratory/AMV	17 (34%)	3 (6.1%)	
Functional bowel obstruction	9 (18%)	3 (6.1%)	
Infectious	5 (10%)	1 (2%)	
Summary	18/50 (36%)	8/49 (16%)	0.039*
Death	0	0	

*Fisher's exact test. TC, traditional care; FT, fast track; ARF, acute renal failure; AMV, assisted mechanical ventilation.
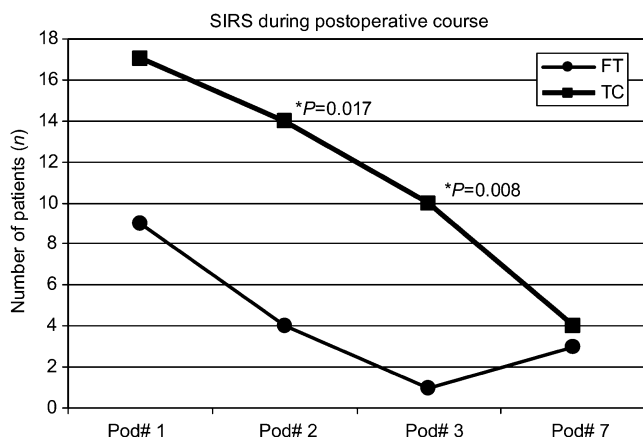
Fig. 1. Incidence rate of SIRS on pod# 1, 2, 3 and 7; on pod# 2 and 3, the rate of SIRS in the fast track group (FT) is significantly lower as compared to the traditional care (TC) group: 14 vs. four patients and 10 vs. one patient; *Fisher's exact test. SIRS, systemic inflammatory response syndrome.

we found cardiac complications in 4/50 (8%) patients in the TC treatment group and in 3/49 (6%) in the FT treatment group. ARF occurred in three patients in each group of whom one in each group had had elevated baseline creatinine prior to surgery; dialysis due to ARF was necessary in one patient in the TC group who had had normal renal function as judged by serum creatinine prior to surgery. Respiratory failure or need for postoperative AMV, respectively, occurred in 17 patients in the TC and three patients in the FT group. With respect to functional bowel obstruction we had nine patients in the TC and three patients in the FT group that showed signs of paralytic ileus. Infectious complications – urinary tract, i.v. line and pneumonia – occurred in 5/50 patients in the TC and in one patient in the FT group. In summary 18/50 patients in the TC and 8/49 in the FT group experienced postoperative medical complications (36% vs. 16%; $P=0.039$). No death occurred during the observation period in both groups. There were no re-admissions within 30 days after patients had been discharged. Surgical complications that required reoperation were postoperative bleeding, peripheral embolization, graft occlusion, ischemic colitis, cholecystitis and incisional hernia with no difference between the groups (data not shown).

3.2. SIRS during postoperative course

On pod# 1, 17 patients in the TC group and nine in the FT group showed signs of SIRS; during the following days on pod# 2 and 3, 14 and 10 patients in the TC group compared to four and one patient in the FT group developed SIRS ($P=0.017$ and $P=0.008$); on pod# 7, four and three patients showed signs of SIRS (Fig. 1).

3.3. SIRS and organ failure

During the postoperative course 50% (25/50) of TC patients developed SIRS, 28% (14/49) of the FT patients ($P<0.05$). As for organ failure 36% of TC patients and 16% of FT patients experienced AOF – including cardiovascular, respiratory, renal and infective complications – during in hospital stay ($P<0.05$); MOF was recorded in 12% and 2%,

respectively (n.s.) (Fig. 2). Mortality rates in both groups was 0% during the observation period.

4. Discussion

This post hoc analysis of a prospective randomized trial investigated the incidence of the SIRS rate after elective open infrarenal aneurysm repair depending on perioperative management. For this purpose we compared 'TC perioperative care' to an optimized 'FT care' regimen. The main differences between the groups were duration of preoperative fasting (2 h vs. 6 h, no bowel preparation and use of EDA in the FT group). Earlier studies that focused on SIRS after aneurysm repair reported about incidence rates of 89% after elective repair [2]. In our series, we found that 50% of the patients managed by TC developed SIRS, whereas only 28% of the FT patients showed SIRS ($P=0.04$). SIRS usually occurs with or before AOF after an initial insult, e.g., blunt trauma with hemorrhage or surgery. This leads to activation and priming of pro-inflammatory pathways mediated by interleukin (IL)-6, IL-8, pro-calcitonin and the LPS-binding protein (LBP) [11]. These pro-inflammatory pathways are counterbalanced by anti-inflammatory pathways – a phenomenon which has been described as concept of a compensatory anti-inflammatory response syndrome (CARS) [12]. As long as SIRS and CARS are in balance patients' homeostasis is maintained; if SIRS predominates pro-inflammatory pathways become activated. After priming of inflammatory pathways a second hit later – insult may cause a degree of inflammation which is even greater and finally results in MOF: the so called two-hit phenomenon [13]. As for the timing of first and second hit it has been shown that inflammation can occur in the first few hours after an initial insult [14]. This is underlined by our findings that show the highest rate of SIRS in both groups on pod# 1 – in the TC group being even higher than in the FT group. On POD 2 and 3, the difference between the groups was significant. Bown et al. also described the highest number of patients experiencing SIRS within the first three days gradually decreasing over time [2]. It has to be stressed that development of SIRS is not necessarily associated to organ failure as not any patient with SIRS
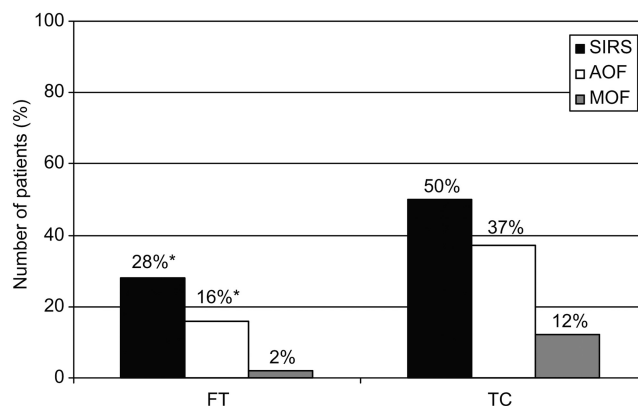

Fig. 2. Incidence rate of SIRS, any organ failure (AOF) and multiple organ failure (MOF) during the postoperative course; in the fast track group rates of SIRS and AOF were significantly lower as compared to the traditional care group; *$P<0.005$; Fisher's exact test. SIRS, systemic inflammatory response syndrome; FT, fast track; TC, traditional care.

later develops organ failure – a finding that has already been described in patients of the general intensive care unit (ICU) [15]. Open AAA repair represents a complex surgical procedure including surgical trauma, aortic cross-clamping and ischemia/reperfusion injury (I/R). The surgical trauma itself can be regarded as first hit which leads to activation and priming of inflammatory pathways inducing SIRS; experimental studies have shown a positive relationship between inflammatory markers and magnitude of surgery and blood loss [16]. The second hit in AAA repair is considered to be the I/R injury which subsequently can lead to organ dysfunction, morbidity and mortality. Experimental studies support this theory of I/R injury as second hit [17]. There are attempts to diminish I/R injury after aortic cross-clamping but these have been proven of value only in animal models and are far from being clinical routine [18].

FT patient care programs aim at reducing the surgical stress response by a number of means: reduced preoperative fasting, minimal incisions, avoidance of hypothermia and the use of regional anesthetic techniques, i.e., EDA. Several systematic reviews about the value of preoperative fasting found that avoiding preoperative fasting is related to a substantial reduction in postoperative stress and insulin resistance [19]. As a consequence a two-hour preoperative fast for clear fluids and a carbohydrate-rich beverage given before anesthesia and surgery can be recommended because the catabolic response (insulin resistance) after surgery is reduced which in turn may have implications for postoperative recovery [20]. Hence, in our FT concept as in others preoperative fasting was reduced to two hours. Another tool to diminish the surgical stress response is the use of epidural anesthesia: in patients undergoing coronary artery bypass grafting (CABG) supplementation of general with thoracic epidural anesthesia has been shown to attenuate epinephrine release [21]. In addition, by this means the incidence of myocardial ischemia as judged by troponin T measurements could be reduced [22]. To date regional anesthesia is regarded to be the ideal technique available to attenuate endocrine metabolic responses with extended effect on postoperative analgesia [23]. As for infrarenal aortic reconstructive surgery the use of EDA is favored as it has been associated to decreased rates of morbidity and mortality [24]. In our analysis we found that FT patients had significant lower rates of SIRS and organ failure during the postoperative course as compared to TC. As for SIRS we found 28% vs. 50% ($P=0.04$) and in terms of organ failure we had 16% vs. 36% ($P=0.039$). Reported organ failure after elective open AAA repair rates range between 35% and 59% [5, 25].

In summary, in the context of the two-hit theory an optimized multimodal perioperative patient management including reduced preoperative fasting and the use of EDA appears to be able to significantly reduce incidence rates of SIRS after elective AAA repair. The combination of these measurements leads to reduction of the first hit – the surgical trauma. Subsequently, inflammation after the second hit – I/R injury – may be reduced and finally (multiple) organ failure prevented. Our data support the implementation of an optimized perioperative patient care regimen in order to reduce the surgical trauma in elective AAA

repair and consequently to decrease rates of SIRS and organ failure. Nonetheless, a larger number of patients and better definition of supportive perioperative tools is required before broad implementation can be justified.

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