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PRO- AND ANTI-INFLAMMATORY CYTOKINE-RESPONSE IN ABDOMINAL AORTIC ANEURYSM REPAIR: A CLINICAL MODEL OF ISCHEMIA-REPERFUSION

René G Holzheimer, Jens Gross, and Moshe Schein‡

Department of General Surgery, University of Halle, Germany; and ‡Department of Surgery, New York Methodist Hospital, Brooklyn, New York 11215

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ABSTRACT—In traumatized and septic patients, excessive cytokine production may lead to organ dysfunction and death. Current understanding of cytokine kinetics with regard to clinical scenarios, however, is still limited by a paucity of studies investigating the cytokine levels in humans with inflammation–reperfusion injury in the absence of infection. Our hypothesis was that endotoxin is introduced into circulation during and after abdominal aortic aneurysm (AAA) repair and is associated with pro- and anti-inflammatory cytokine-response. The purpose of this prospective pilot study in 10 patients who underwent elective AAA repair was to assess organ function and immune response to systemic endotoxemia after the operation by measuring endotoxin, endotoxin neutralizing capacity (ENC), tumor necrosis factor (TNF)-α, interleukin (IL)-6, IL-10, and TNF-RI and II. Blood samples were obtained from indwelling catheters or direct venipuncture preoperatively, perioperatively (8 time points) until the second postoperative day. Endotoxin and ENC were determined by a special kinetic Limulus amoebocyte lysate (LAL) assay and TNF-α, IL-6, IL-10, and TNF-RI and II by commercial ELISA. Endotoxin levels were significantly elevated after declamping and 90 min after clamping of the aorta (2.3 + .9 pg/mL; 5.4 ± 3.6 pg/mL). ENC decreased to the lowest levels at 90 min after clamping. TNF-α levels were maximal, but not significantly elevated, 120 min after clamping. IL-6 increased significantly during the operation and reached maximum levels (189.8 ± 47 pg/mL) at the first postoperative day. Anti-inflammatory IL-10 and TNF-RI and II were elevated early during the operation. The changes in cytokine levels were associated with mild organ dysfunction. We conclude that AAA repair is associated with endotoxin, proinflammatory, and an almost coincidental anti-inflammatory cytokine release, providing baseline data about what constitutes an appropriate immune response. Such responses to trauma and ischemia-reperfusion need to be further investigated before attempting immunomodulation.

INTRODUCTION

The severity of Gram-negative infection seems to correlate with the release of endotoxin (LPS) from the disintegrating cell wall of Gram-negative pathogens (1), which is followed by the release of cytokines (2). Excessive cytokine production can lead to organ dysfunction, organ failure, and death (3). Gut ischemia followed by translocation of endotoxin and bacteria may induce the systemic release of mediators (4). Although the kinetics of cytokine release were mostly studied in the context of infection and sepsis, it is believed that cytokines are also associated with the systemic inflammatory response syndrome (SIRS) without pathogens (5).

In elective abdominal aortic aneurysm (AAA) repair, the production and release of endotoxin and cytokines can be studied in a controlled fashion (6). AAA repair may be a good clinical model to study the early phase of SIRS, the counter-regulatory immune response, and the potentials for immunomodulation. Cabie et al. demonstrated high levels of portal tumor necrosis factor (TNF)-α, originating from gut-associated macrophages activated by bowel manipulation, ischemia, and/or translocated LPS during an elective AAA repair (7). Ischaemia-reperfusion is a complex phenomenon that may lead to a local and remote tissue injury and, in the case of an excessive immune response, to death (8). This may be associated with a massive release of proinflammatory cytokines into the systemic circulation contributing to the development of vascular injury by up-regulation of adhesion molecules (9). Such response may be sufficient to cause organ dysfunction without the presence of pathogens (10). The pivotal role of proinflammatory cytokines has been demonstrated in trauma, shock, and sepsis (11). Most of these studies, however, focused on death as an endpoint; our knowledge of the development of multiorgan dysfunction with regard to cytokines is still rudimental (12).

The objectives of this pilot study were to analyze the kinetics of endotoxin and endotoxin neutralizing capacity (ENC) before, during, and after AAA repair at multiple time points, to analyze the kinetics of pro- and anti-inflammatory cytokines in relation to endotoxin release and tissue ischemia, and to correlate the latter findings with organ dysfunction during the perioperative and postoperative period. Our hypothesis was that endotoxin is introduced into the circulation during and after AAA repair and is associated with pro- and anti-inflammatory cytokine response.

Address reprint requests to René Gordon Holzheimer, M.D., Ph.D., Klinik für Allgemeinchirurgie, Martin-Luther-Universität Halle-Wittenberg, D-82054 Sauerlach, Germany. E-mail: gresser.holzheimer@t-online.de

MATERIALS AND METHODS

Ours was a prospective study of 10 consecutive patients undergoing an elective infrarenal AAA repair at the Department of Surgery, University of Würzburg, Germany during 1996. All patients received a dose of prophylactic antibiotics—a third generation cephalosporin. The aorta was always clamped below the renal arteries after routine systemic heparinization. Colonic mucosal pH or inferior mesenteric artery stump pressures were not routinely measured.

Plasma samples were obtained preoperatively (baseline), 30 min after skin incision, 30, 60, 90, and 120 min after clamping of the aorta, after the release of the aortic clamp, 4 and 8 h after the operation, and on the first and second postoperative days. The samples were kept cool, centrifuged, and frozen within 30 min. The anticoagulant used to obtain the plasma was heparin. Samples were centrifuged in endotoxin-free tubes (Chromogenix, Essen, Germany) within 30 min and stored at −80°C until processing. The special software used to calculate results is described elsewhere (13). All procedures were performed in accordance with protocols approved by the Institutional Committee on Clinical Research.

Endotoxin assay

For measurement of endotoxin and endotoxin neutralizing capacity (ENC), we used the turbidimetric, kinetic LAL test with internal standardization as described by Urbaschek and Becker (13). Endotoxin standard (NP-3 (KSE) endotoxin standard, *Salmonella abortus equi*, 100 ng/mL) and lysate (Pyrospektro, Limulus amoebocyte lysate (LAL), Cape Cod, Falmouth, MA) were provided by Pyroquant Diagnostik (Walldorf, Germany). Each sample was spiked by a known concentration of endotoxin. The kinetic reaction was read continuously in an ELISA plate reader (Molecular Devices, MWG Biotech, Ebersberg, Germany), and the endotoxin concentration was calculated by a special software program. The sensitivity of the endotoxin test was .5 pg/mL. Unheated samples were tested in the same way for the measurement of ENC. In the absence of adequate references, it is difficult to assess the sensitivity and specificity of ENC measurements. ENC is an index describing the activity of human plasma to neutralize endotoxin added to the plasma in known quantities; it is influenced by plasma proteins and other factors known to neutralize endotoxin. Heating denaturates the proteins, interfering with ENC measurements.

Cytokines and TNF-RI and II

For the measurement of cytokines interleukin (IL)-6, IL-8, IL-10, TNF-α, and soluble TNF-RI p55 and TNF-RII p75, commercially available ELISA were used (Quantikine, R&D Systems Inc., Minneapolis, MN (DPC, Bad Nauheim, Germany)). The detection limits were .7 pg/mL for IL-6 and 1 pg/mL for IL-10, 4.4 pg/mL for TNF-α, and 1.5 pg/mL for sTNF-RI, and 5 pg/mL for sTNF-RII. As control, endotoxin and cytokines were also measured in five patients with laparoscopic cholecystectomy (data not shown); there was no endotoxin detectable and cytokine levels (e.g., IL-6 maximum level <100 pg/mL) remained well below the levels in AAA repair.

Statistical analysis

Data are indicated as mean and SEM. Statistical analysis was performed with a statistical package (Instat, Santa Monica, CA). For quantitative comparisons, we used the Wilcoxon analysis and for qualitative comparisons the Fisher exact test.

RESULTS

All patients, with the mean age of 66 years (range 44–75 years), suffered from hypertension (Mean Arterial Pressure (MAP) 122–160 mmHg). With the exception of one patient who was admitted with a compensated renal insufficiency, no other co-morbidities were diagnosed. The mean operation time was 164 min (115–250 min), with a mean aortic clamping time of the aorta of 66 min (18–110 min). Mean blood loss was 2,110 mL (800–3,000 mL); blood was replaced with packed red cells (mean, 430 mL; 0–1,250 mL), fresh frozen plasma (mean, 275 mL; 0–1,250 mL), and other colloids (mean, 600 mL; 0–1,250 mL). We did not correlate the volume of blood-product transfusion with cytokine levels.

There were no perioperative complications recorded. The APACHE II score was not different preoperatively, on the day of operation, or on the first and second postoperative days (Table 1).

Mean arterial pressure was significantly decreased on the day of operation ($p < .001$); on the first and second postoperative days the values reached preoperative levels. Heart rate was increased on the day of operation (90 ± 2; $p < .01$) and remained so on the two consecutive days. Hemoglobin and thrombocytes were significantly low on the day of operation and on the first two postoperative days. Leukocytes were increased on Days 1 and II postoperation. There were also significant changes in the hemostatic system (Quick; Thrombin time) observed at the day of operation and thereafter. Bilirubin was significantly elevated on the day of operation, as well on the two postoperative days; liver enzymes (gamma-GT, GOT, GPT) remained within normal ranges. Creatinine showed no change; however, urea nitrogen was decreased on the day of operation (Table 1).

Endotoxin

Two patients were positive for endotoxin before the operation. Ninety minutes after clamping of the aorta and after the release of the aortic clamp, endotoxin levels were significantly elevated ($p < .05$) (2.4 + .9 pg/mL; 5.5 ± 3.6 pg/mL vs. .4 + .3 pg/mL baseline level). Nearly significant levels of endotoxin were detected at 30, 60, and 120 min after clamping of the

TABLE 1. **Pre- and perioperative characteristics of the patients**

	Preoperation	Day of operation	1 day after operation	2 days after operation
APACHE II	6	5	5	6
MAP (mmHg)	140 ± 4	118 ± 3	127 ± 6	131 ± 6
HF	81 ± 1	90 ± 1	92 ± 4	90 ± 5
Hb (g/dL)	14.5 ± .3	9.8 ± .2	9.7 ± .3	9.5 ± .3
Thr. (1,000)	263 ± 24	158 ± 16	163 ± 21	151 ± 21
Leukocytes (1,000)	8.3 ± .7	10.3 ± 1	12.3 ± 1.2	13 ± 1.5
Thrombin Time	14.6 ± .4	27.6 ± 3.2	24.3 ± 3.6	15.8 ± .9
Bilirubin (mg/dL)	.4 ± .1	1.2 ± 1.3	1.2 ± .2	.9 ± .1
Creatinine (mg/dL)	1 ± .1	.9 ± .1	1.1 ± .1	1.1 ± .1

Laboratory data (hemoglobin (Hb), thrombocytes (Thr.), leukocytes, thrombin time, bilirubin, creatinine), mean arterial pressure (MAP), heart frequency (HF) and acute physiology and chronic health evaluation (APACHE II) score. The MAP is above normal preoperatively and declines significantly at the day of operation ($p < .5$). There is a slight increase of bilirubin levels at the day of operation and the first postoperative day. All other laboratory data are in the normal range.

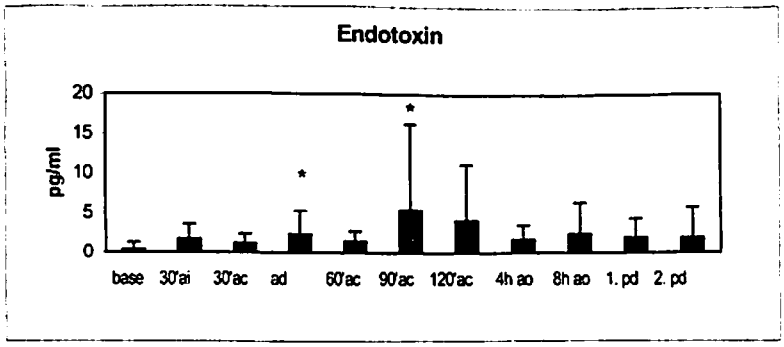

FIG. 1. **Endotoxin plasma levels at aortic aneurysm repair.** Endotoxin levels (pg/mL) at baseline (base), 30 min after incision(30'ai), 30 min after clamping of the aorta (30'ac), after declamping (ad), 60 min after clamping of the aorta (60'ac), 90 min after clamping of the aorta (90'ac), 120 min after clamping of the aorta (120'ac), 4 h after operation (4 h ao), 8 h after operation (8 h ao), first postoperative day (1. pd), second postoperative day (2. pd). Endotoxin is not detectable in most patients preoperatively. There is a significant increase in endotoxin at after declamping of the aorta and 90 min after clamping of the aorta ($p < .05$).

aorta and 4 h after operation. Thirty and 90 min after clamping of the aorta and 4 h from the end of operation, there were almost significant differences ($p = .053$, $p = .056$) with regard to endotoxin-positive versus endotoxin-negative results (Fisher's exact test) (Fig. 1).

Endotoxin neutralizing capacity

ENC levels were comparable preoperatively, 30 min after skin incision, and on the two postoperative days (357 ± 306; 342 ± 308; 221 ± 126). Thirty minutes after clamping the aorta, ENC decreased and was almost significantly reduced on declamping ($p = .059$). Ninety minutes after clamping, ENC reached the lowest level ($p < .05$). From the first postoperative day on, ENC increased slowly to reach normal values on the second postoperative day (Fig. 2).

Tumor necrosis factor-α

The preoperative baseline level was 28.7 ± 13.6 pg/mL. During the whole observation period, no significant differences were detectable. The maximum TNF level was measured 120 min after clamping the aorta (85.8 ± 60 pg/mL) (Fig. 3A).

Interleukin-6

Baseline level of IL-6 was 5.2 ± 1.8 pg/mL. It was significantly elevated 60 min after clamping the aorta (13.3 ± 2.4) and after declamping (19.3 ± 6.7 pg/mL; $p < .05$). It's maximal level was detected on the first postoperative day (189.8 ± 46.7 pg/mL; $p < .001$), decreasing on the second postoperative day (56 ± 12 pg/mL; $p < .01$) (Fig. 3B).

Interleukin-10

Preoperatively and 30 min after skin incision, IL-10 remained at low levels (10.8 ± 2.1 pg/mL; 8.9 ± 2.1 pg/mL). Thirty minutes after aortic clamping and unclamping, it was elevated (52.1 ± 40.6 pg/mL; 26 ± 5.7 pg/mL; $p < .05$). IL-10 increased to reach maximum levels at 4 h after operation (53.9 ± 18.6 pg/mL; $p < .05$). On the first and second postoperative days, it returned to baseline levels (Fig. 4A).

TNF-α RI and RII

The preoperative baseline level for TNF-RI was 1,752 ± 403 pg/mL. It increased 30 min after skin incision (3,164 ± 577 pg/mL; $p = .06$) and reached significantly elevated levels at 4 h after operation (7,280 ± 3,519 pg/mL; $p < .05$). Maximal levels were measured 8 h after operation (9,142 ± 2,880 pg/mL). On the second postoperative day, TNF-RI was still elevated (6,111 ± 2,046 pg/mL; $p < .05$). (Fig. 4B) Ninety minutes after clamping, there were only minor changes of TNF-RII: from baseline (1,628*–140 pg/mL to 1,896 ± 254 pg/mL). 120 min after clamping TNF-RII reached a significant elevation (2,367 ± 346 pg/mL: $p < .05$) and was maximally elevated on the first postoperative day (3,435 ± 203 pg/mL: $p < .001$). It remained elevated on the second postoperative day (3,249 ± 345 pg/mL; $p < .001$) (Fig. 4C).

DISCUSSION

This study confirms that AAA surgery, which represents a clinical model of temporary ischemia and reperfusion, is associated with pro- and anti-inflammatory cytokine mediated response. It also may correlate the pro-inflammatory response to postoperative organ dysfunction.

Ischemia of the gut may induce translocation of bacteria and/or endotoxin. (14). Although it is known that endotoxin may not be the only trigger, there is evidence that it plays an important role in the development of SIRS, sepsis, and multiorgan failure (15). In AAA repair, the effect of translocation of endotoxin and/or bacteria and the onset of SIRS and organ dysfunction may correlate with the onset of ischemia by clamping of the infrarenal aorta.

In this study, we observed endotoxin to be significantly elevated 90 min after clamping of the aorta and the release of the clamp. The presence of endotoxin after surgical procedures was also demonstrated by van Deventer et al. (4) and Cabie et al. (7) who detected LPS in the portal vein following aortic clamping. That endotoxin was not present in all patients may be explained by the detection limit of the LAL test used, the

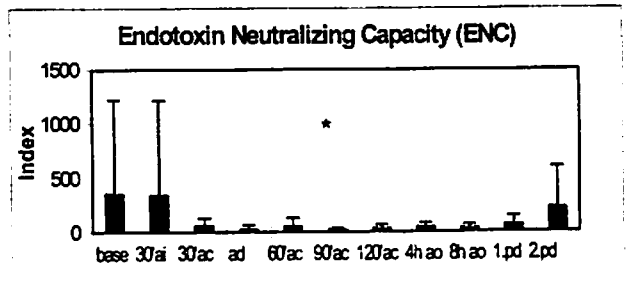

FIG. 2. **Perioperative endotoxin neutralizing capacity (ENC) in aortic aneurysm repair.** ENC index at baseline (base), 30 min after incision (30'ai), 30 min after clamping of the aorta (30'ac), after declamping (ad), 60 min after clamping of the aorta (60'ac), 90 min after clamping of the aorta (90'ac), 120 min after clamping of the aorta (120'ac), 4 h after operation (4 h ao), 8 h after operation (8 h ao), first postoperative day (1. pd), second postoperative day (2. pd). There is the lowest level of ENC detectable at 90 min after clamping of the aorta.

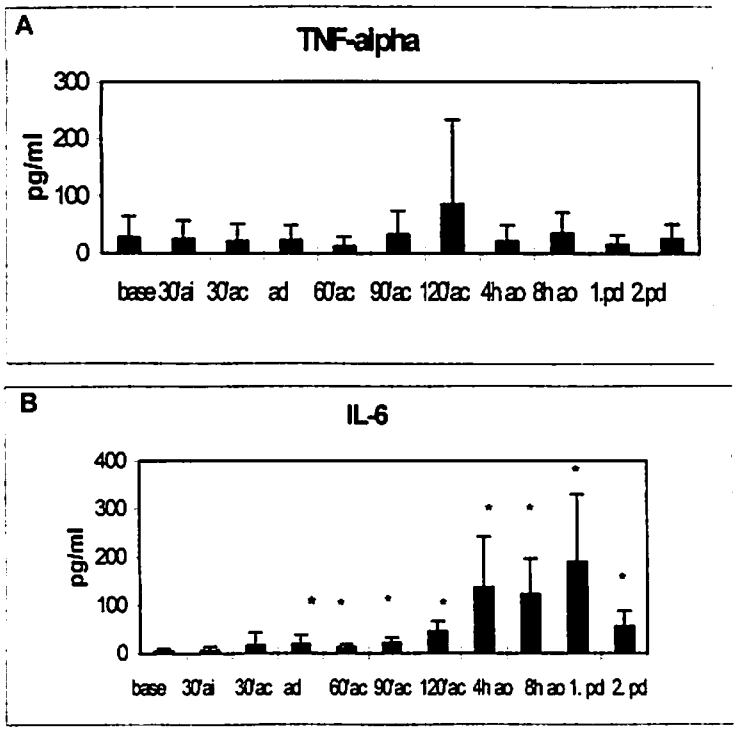

FIG. 3. ***A:*** **Perioperative TNF-α plasma levels in aortic aneurysm repair.** Tumor Necrosis Factor (TNF)-α levels at baseline (base), 30 min after incision (30'ai), 30 min after clamping of the aorta (30'ac), after declamping (ad), 60 min after clamping of the aorta (60'ac), 90 min after clamping of the aorta (90'ac), 120 min after clamping of the aorta (120'ac), 4 h after operation(4 h ao), 8 h after operation (8 h ao), first postoperative day(1. pd), second postoperative day (2. pd). There is no difference detectable between the levels at different time points. ***B:*** **Perioperative IL-6 plasma levels in aortic aneurysm repair:** Interleukin-6 (IL-6) levels at baseline (base), 30 min after incision (30'ai), 30 min after clamping of the aorta (30'ac), after declamping (ad), 60 min after clamping of the aorta (60'ac), 90 min after clamping of the aorta (90'ac), 120 min after clamping of the aorta (120'ac), 4 h after operation (4 h ao), 8 h after operation (8 h ao), first postoperative day (1. pd), second postoperative day (2. pd). There is a slight, but significant increase of IL-6 detectable after declamping of the aorta and 60 min after clamping of the aorta ($p < .5$). The maximum IL-6 levels are detected at the first postoperative day.

heterogeneous reactivities of LPS from different origin in the LAL assay, as compared with the *Escherichia coli* LPS standard, and the persistence of low flow circulation among patients with intrarenal clamping (16). In contrast, we detected endotoxin in all patients at some time during the operation, which may be due to the different and more sensitive test system used by us (17). Factors in human plasma, such as natural LPS-antibodies, high density lipoproteins, lipoprotein associated esterases, antithrombin III and α 2-Macroglobulin, can neutralize endotoxin (18). Therefore, negative samples do not exclude the involvement of endotoxin in the underlying disease, nor do high levels reflect the severity of disease.

It has been demonstrated in kinetic follow-up determinations of septic patients that a decrease of ENC may be associated with a clinical deterioration whereas an increase of ENC is associated with a better prognosis (19). In an animal model of intra-abdominal infection, ENC decreased after cecal ligation and puncture and was significantly elevated when animals were pretreated to induce endotoxin tolerance (20). In this study, ENC decreased rapidly, reaching a minimum at 90 min after aortic clamping; this occurred when endotoxin concentrations reached a maximum.

The clinical significance of endotoxin is in dispute. Cabie et al. have demonstrated LPS release during AAA but did not report the correlation with the organ's function (7). The failure of several clinical studies to improve the mortality rate in septic patients with anti-endotoxin antibodies added to the doubts concerning the clinical significance of endotoxin. There is, however, evidence for a correlation of endotoxemia with pulmonary and infectious complications in surgical patients (21). The presence of intra-abdominal pathogens was reported to be associated with high local and systemic levels of endotoxin (22).

The results of this study suggest that a small increase in endotoxin and decrease in ENC may have been associated with minor organ dysfunction. This, however may be an epiphenomenon as other known (surgical technique, tissue injury, hemorrhage, anesthesia) or unknown parameters may influence the inflammatory response. Trauma, shock, and infection initiate a complex inflammatory response in which the proinflammatory cytokines are thought to play a pivotal role. Consecutive multiorgan failure may be caused by a systemic inflammatory response leading to autodestruction (horror autotoxicus) and death (23). Whereas the release of cytokines has been studied in sepsis and infections, the association of cytokines and organ dysfunction after trauma and hemorrhage has been less clear (24). In this study, the increase of TNF-α after aortic crossclamping was small and not significant. Following surgical procedures, TNF-α is rarely detected (25), whereas it has been observed in animal models of hemorrhage or ischemia-reperfusion injury (26). The correlation of LPS levels with the amount of circulating TNF-α has been investigated with different results. The biological activity of TNF may be counteracted by specific inhibitors such as soluble TNF receptors. Furthermore, the localization of the sample may have an effect on cytokine determination. Cabie et al. reported differences in cytokine concentrations in the different blood compartments—systemic circulation and portal vein (7). TNF-α may be produced by gut associated macrophages after LPS translocation. In animals, shock was the main factor leading to the production and release of TNF-α by macrophages. Intestinal ischemia and reperfusion injury is likely to be responsible for the elevated levels of proinflammatory cytokines found in patients after elective aortic aneurysm repair. However, medication or chronic heart failure can influence the production of proinflammatory cytokines (27). Furthermore, the role of anesthesia and antibiotic prophylaxis needs further investigation.

In contrast to TNF-α, the presence of IL-6 is associated with

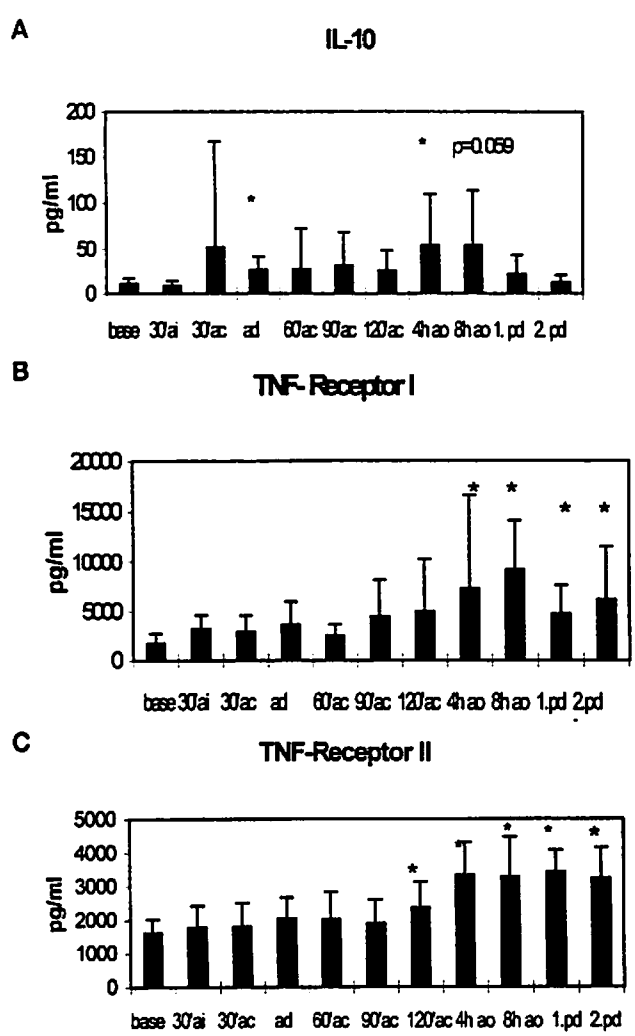

FIG. 4. ***A:*** **Perioperative IL-10 plasma levels in aortic aneurysm repair.** Interleukin (IL)-10 levels at baseline (base), 30 min after incision (30'ai), 30 min after clamping of the aorta (30'ac), after declamping (ad), 60 min after clamping of the aorta (60'ac), 90 min after clamping of the aorta (90'ac), 120 min after clamping of the aorta (120'ac), 4 h after operation (4 h ao), 8 h after operation (8 h ao), first postoperative day (1. pd), second postoperative day (2. pd). IL-10 plasma levels are slightly, but significantly increased after declamping of the aorta and 90 min after clamping of the aorta ($p < .05$). There is a almost significant difference 120 min after clamping of the aorta ($p = .059$). ***B:*** **Perioperative TNF-RI plasma levels in aortic aneurysm repair:** Tumor Necrosis Factor-α Receptor I (TNF-RI) levels at baseline(base), 30 min after incision (30'ai), 30 min after clamping of the aorta (30'ac), after declamping (ad), 60 min after clamping of the aorta (60'ac), 90 min after clamping of the aorta (90'ac), 120 min after clamping of the aorta (120'ac), 4 h after operation (4 h ao), 8 h after operation (8 h ao), first postoperative day (1. pd), second postoperative day (2. pd). There is a small increase in TNF-RI levels 30 min after incision ($p = .06$), after declamping ($p = .059$), 90 and 120 min after clamping of the aorta ($p = .06$; $p = .08$). TNF-RI levels are significantly increased 4 h ($p < .05$), 8 h ($p < .05$) after operation, the first postoperative day ($p < .01$) and the second postoperative day ($p < .05$). ***C:*** **Perioperative TNF-RII plasma levels in aortic aneurysm repair:** Tumor Necrosis Factor-α Receptor II (TNF-RII) levels at baseline (base), 30 min after incision (30'ai), 30 min after clamping of the aorta (30'ac), after declamping (ad), 60 min after clamping of the aorta (60'ac), 90 min after clamping of the aorta (90'ac), 120 min after clamping of the aorta (120'ac), 4 h after operation (4 h ao), 8 h after operation (8 h ao), first postoperative day (1. pd), second postoperative day (2. pd). TNF-RII rises 120 min after clamping of the aorta ($p < .05$) and stays elevated until the second postoperative day ($p < .05$).

surgery and can be detected throughout the clinical course (28). The prognostic value of IL-6 after trauma has been reviewed elsewhere (29). In this study, systemic IL-6 has been detected early during operation. This differs from the results of Cabie et al., who did not observe high levels of systemic or portal IL-6 during surgery (7). Others (30) found that traumatized and postoperative patients exhibited the highest concentrations of IL-6 immediately after injury and 6 h later, supporting the notion that IL-6 production is more closely related to soft tissue trauma. The delay in IL-6 release may be related to the vascular reconstruction while IL-6 release follows that of TNF and IL-1 (31). In this study, we observed higher plasma levels to be associated with organ dysfunction. It should be noted, however, that plasma cytokine levels may only be the tip of the iceberg, not reflecting the inflammatory response at the local level (32).

IL-10, a potent anti-inflammatory mediator that inhibits the production of cytokines from activated macrophages and T-helper cells, has been shown to prevent death caused by experimental endotoxemia, presumably by reducing the release of TNF-α from macrophages. IL-10 may also have a counter-regulatory effect in ischemia-reperfusion injury or endotoxin-induced inflammatory response (33). To our knowledge, this has not been studied in this clinical model before. We observed a significant rise in IL-10 immediately after the declamping of the aorta and 4 h after operation. Such anti-inflammatory response is rapid and timely-correlated with the endotoxin and pro-inflammatory cytokine release. This may partially explain why we did not detect any significant rise in TNF-α. From our preliminary results, however, we cannot conclude that this or the lack of complications is only due to the IL-10 response.

Soluble TNF receptors (sTNFR) from the p55 and p75 surface receptor bind to the TNF-α molecule and prevent ligand binding to the cellular TNF receptors, thereby blocking the cytotoxic and inflammatory effects induced by TNF-α *in vitro* (34). The inhibition of the effects induced by TNF-α may be stronger by sTNFRp55 than by sTNFRp75. There may be elevated levels of sTNFRp55 and p75 after intravenous administration of *E. coli* endotoxin in critically ill patients following major surgical procedures and in septic patients. Elevated release of sTNFR may represent a marker for the severity of sepsis and outcome (35). During and after AAA, we detected elevated levels of sTNFRp55 and p75. TNFRp55 showed a trend to be released faster than TNFRp75 after endotoxin translocation or inflammatory response. This receptor showed a slower increase and stayed elevated until the second postoperative day.

With the small sample size and lack of complications, this study provides only limited data about the importance or role of endotoxin and cytokines in AAA surgery. It does, however, show the natural history of the inflammatory response when "things go well." This provides baseline data about what constitutes an appropriate immune response.

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