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M. Sander
M. Irwin
P. Sinha
E. Naumann
W.J. Kox
C.D. Spies

Suppression of interleukin-6 to interleukin-10 ratio in chronic alcoholics: association with postoperative infections

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M. Sander · E. Naumann · W.J. Kox
C.D. Spies (✉)
Department of Anesthesiology and Intensive Care,
University Hospital Charité,
Campus Charité Mitte, Humboldt University,
Schumannstrasse 20/21, 10117 Berlin, Germany
e-mail: claudia.spies@charite.de
Tel.: +49-30-450531012
Fax: +49-30-450531911

M. Irwin
Veterans Affairs San Diego Healthcare System and Department of Psychiatry,
University of California,
3350 La Jolla Village Drive, San Diego, CA 92161, USA

P. Sinha
Institute for Laboratory Medicine, and Pathobiochemistry,
University Hospital Charité,
Humboldt University,
Schumannstrasse 20/21, 10117 Berlin, Germany

Abstract *Objective*: To investigate the interleukin-6 (IL-6) to interleukin-10 (IL-10) ratio and levels of sE-selectin in patients undergoing elective surgery of the upper digestive tract and to define the differences in the perioperative immune response between chronic alcoholic and non-alcoholic patients. *Design*: Prospective pilot study. *Setting*: Single center, interdisciplinary intensive care unit (ICU) at a university hospital. *Measurement and main results*: The study compared chronic alcoholics (n=25) and non-alcoholics (n=20) before and after surgery for resection of upper digestive tract tumors. White blood cell counts, C-reactive protein and circulating levels of sE-selectin, the pro-inflammatory cytokine IL-6 and the inhibitory cytokine IL-10, were obtained at hospital admission, preoperatively, postoperatively at ICU admission and 2 and 4 days later. Rates of postoperative infectious complications including pneumonia and sepsis were determined. sE-selectin only differed between chronic alcoholics and non-alcoholics preoperatively. Compared to non-alcoholics, chronic alcoholic patients showed a fourfold increase in circulating levels of IL-10 (p<0.01) and a suppression of the IL-6/IL-10 ratio (p=0.001) immediately after surgery. Coincident with the immune alterations, chronic alcoholics had a prolonged ICU stay (p<0.01) and a threefold increased rate of wound infections (p<0.05) and pneumonia (p<0.01). Lower IL-6/IL-10 ratios were associated with increased rates of infectious complications (p<0.05). *Conclusion*: Chronic alcoholics had decreased IL-6/IL-10 ratios at ICU admission and increased rates of infectious complications in the postoperative ICU course. This may indicate immediate postoperative immune suppression before the onset of infections and may help to identify chronic alcoholic patients at risk.

Keywords Ethanol · Infection · Cytokine · ICU · Surgery

Introduction

Chronic alcoholism is prevalent in approximately 30–50% of patients who undergo surgery for upper digestive tract disease. Moreover, the rates of morbidity and mortality during the postoperative period are two to fivefold increased in alcoholic, as compared to non-alcoholic, surgical patients [1, 2, 3]. The high frequency of infectious disease complications in alcoholics stands in sharp contrast to the limited effort to determine the immunological mediators of this risk.

Compelling evidence suggests that the relative expression of pro-inflammatory versus inhibitory cytokines are involved in postoperative infectious complications.

For example, it is thought that the immediate postoperative increase of pro-inflammatory cytokines, such as interleukin-6 (IL-6) [4], and/or a compensatory increase in anti-inflammatory cytokines, such as interleukin-10 (IL-10) [5], are associated with a higher risk of developing a potentially devastating response to bacteremia [6] in patients who undergo surgery and anesthesia. Optimal response to surgery is seen only with the presence of IL-6 [4]. IL-10 is an important factor in the postoperative immune suppression as it is able to downregulate MHC class II antigen expression on antigen-presenting cells [5]. Different studies have reported adverse outcomes in patients with infections and high levels of circulating IL-10 [7, 8, 9]. In contrast to these findings, the IL-6/IL-10 ratio was higher in non-survivors 2 days after the onset of SIRS [10].

sE-selectin is considered to be a marker of endothelial activity [11, 12, 13]. A weak correlation between sE-selectin levels measured in the plasma and the number of bacteria in bronchoalveolar lavage fluid has been demonstrated [14]. Since chronic alcoholics have an increased gut permeability [15], preoperative fasting may be associated with an increased lipopolysaccharide (LPS) burden and, therefore, inflammatory response, which can be monitored by sE-selectin [16].

To our knowledge, there are no data that have evaluated the relative expression of pro-inflammatory and inhibitory cytokines during the postoperative period in relation to alcohol dependence, despite the increased risk of infectious complications in these patients. Nevertheless, other data suggest that chronic alcohol misuse is associated with immune alterations that might place patients at risk for developing infectious complications during their ICU stay [17, 18, 19]. Irwin et al. demonstrated in a recent study that the ex vivo stimulated IL-6/IL-10 ratio was significantly decreased in Afro-American men with chronic alcohol misuse compared to non-alcoholic controls, but not in white Americans [20]. IL-10 production was demonstrated to be increased and TNF-alpha mRNA levels were decreased by acute ethanol treatment [21]. Nevertheless, in patients with alcoholic liver inflammation elevated levels of pro-inflammatory cytokines such as sE-selectin, IL-6 and TNF-alpha were observed [22, 23, 24].

The aim of our study was to investigate the IL-6/IL-10 ratio and levels of sE-selectin in patients undergoing elective surgery of the upper digestive tract. Thereby, we wanted to define the differences between chronic alcoholic patients and a non-alcoholic group in their perioperative immune response and to elucidate whether altered cytokine levels correlate with postoperative infectious complications (wound infection, pneumonia, sepsis) in chronic alcoholic patients.

Methods

Patients

Following local ethics committee approval and informed written consent, 65 patients who were scheduled for surgery for upper digestive tract tumor were included in this prospective study according to the principles established in Helsinki. Of this total sample, 13 patients had inoperable disease (including all patients with liver dysfunction Child B and C) and were subsequently excluded. Another seven patients were excluded due to unresolved questions about the presence or absence of alcohol dependence. The remaining 45 patients with tumors of the upper digestive tract were stratified into two groups: chronic alcoholics and non-alcoholic controls. Basic patient characteristics such as age, gender, weight and alcoholism-related data are shown in Table 1, Acute Physiology and Chronic Health Evaluation scoring (APACHE III) [25] and Multiple Organ Failure Score (MOF) [26] are shown in Table 2. All patients were admitted to a surgical ICU after tumor resection.

Diagnosis of chronic alcohol abuse

The patients' histories as well as an alcoholism-related questionnaire, the CAGE questionnaire, were obtained preoperatively [27]. The patients' daily ethanol intake was documented. The Diagnostic and Statistical Manual of Mental Disorders (3rd edition, revised) (DSM-III-R) [28] criteria for alcohol dependence or alcohol abuse were obtained. Chronic alcoholics had a daily intake of more than 60 g ethanol per day at least 1 month preoperatively and met the DSM-III-R criteria of alcohol dependence or alcohol abuse. Patients with an ethanol intake less than 25 g per day, a CAGE score =1 and not meeting the DSM-III-R criteria were referred to the non-alcoholic group. Social drinkers (n=33) were not included in the study.

Laboratory markers

Routine laboratory parameters, such as hemoglobin, hematocrit, white blood count (WBC), mean corpuscular volume (MCV),

Table 1 Basic patients characteristics and alcoholism-related history; median (range) (*CAGE* alcoholism-related questionnaire [25], *CDT* carbohydrate-deficient transferrin (normal range 0–9), *GGT* gamma-glutamyltransferase (normal range 5–30), *MCV* mean corpuscular volume (normal range 76–96))

	Chronic alcoholics (n=25)	Non-alcoholics (n=20)	p value
Age (years)	59 (49–73)	59 (45–84)	0.79
Gender (F/M)	3/22	4/16	0.34
Weight (kg)	73 (40–108)	75 (51–95)	0.52
Ethanol intake (g/day)	110 (60–510)	10 (0–20)	<0.01
CAGE	3 (2–4)	0 (0–1)	<0.01
CDT (mg/l)	12.3 (3.9–64.4)	4.4 (2.0–23.4)	<0.01
GGT (U/l)	22 (8–894)	21 (8–93)	0.36
MCV (fl)	95.8 (82.6–110.1)	89.8 (80.6–96.8)	0.03

Table 2 Intensive care unit and major intercurrent complications; median (range) (*APACHE III* Acute Physiology and Chronic Health Evaluation scoring, *MOF* Multi Organ Failure score, *AWS* alcohol withdrawal syndrome)

	Chronic alcoholics (*n*=25)	Non-alcoholics (*n*=20)	*p* value
APACHE III at ICU admission	39 (18–61)	32 (18–54)	0.12
MOF at ICU admission	1 (0–4)	1 (0–5)	0.94
MOF during ICU stay	2 (0–7)	1 (0–9)	0.32
AWS during ICU treatment [*n* (%)]	8 (32%)	0 (0%)	0.01
Period of mechanical ventilation (h)	20 (1–1872)	5 (1–903)	0.04
Period of ICU stay (days)	9 (1–108)	3 (1–49)	<0.01
Death [*n* (%)]	2 (8%)	0	0.20
Wound infection [*n* (%)]	9 (36%)	2 (10%)	0.04
Pneumonia [*n* (%)]	13 (52%)	3 (15%)	0.01
Severe sepsis/septic shock [*n* (%)]	2/6 (8% / 24%)	1/2 (5% / 10%)	0.19
Patients with any infections [*n* (%)]	17 (68%)	6 (30%)	0.02

gamma-glutamyltransferase (GGT) and carbohydrate-deficient transferrin (CDT) [29], were determined preoperatively. The concentration of IL-6 was determined by enzyme-linked immunosorbent assay (ELISA; Quantikine Human IL-6 Immunoassay kit from R & D Systems, Minneapolis, USA). The lower detection level according to the manufacturer was 0.7 pg/ml. Intra- and inter-assay variation coefficients were 2.4% and 3.8%, respectively. IL-10 concentration was determined by EIA with the TiterZyme IL-10 Enyme Immunoassay kit (PerSeptive Diagnostics, Cambridge, USA). The lower detection level was 1 pg/ml. Intra- and inter-assay variation coefficients were 7.4% and 4.6%, respectively. The concentration of sE-selectin was also determined by ELISA with a Human sE-selectin Immunoassay kit (R & D Systems, Minneapolis, USA). According to the manufacturer, the lowest measurable concentration was 2 ng/ml. Intra- and inter-assay variation coefficients were 3.2% and 6.4%, respectively.

Investigation protocol

Samples for the quantification of the cytokines were drawn on the day of admission, preoperatively and postoperatively and on days 2 and 4 after surgery in the ICU. Diagnosis, surgery, transfusion requirement and length of ICU stay were documented. Vital signs, routine laboratory parameters and intercurrent complications were recorded on a daily basis. The diagnosis of pneumonia was established according to the criteria recommended by the Center of Disease Control and Prevention (CDC) [30]. All patients with pneumonia had to have a new radiologically determined infiltrate, plus new onset of purulent sputum or a change in character of sputum as well as a typical finding in percussion and auscultation. Sepsis was defined according to the guidelines of the Society of Critical Care Medicine Consensus Conference [31]. All patients underwent a microbiological screening and were treated with cefotiam/metronidazole during their ICU stay. The antimicrobial therapy was changed according to the specific sensitivity of the strains in these microbiological screenings. If no microbiological agent was found in a case of pneumonia the antibiotic treatment was changed to cefotaxime, gentamicin and metronidazole. The differential diagnosis of alcohol withdrawal syndrome (AWS) was made according to the Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) scale [32]. The diagnosis was confirmed by a psychiatric consultant. The onset of AWS was documented in the study protocol.

Statistical analysis

All data were expressed as medians and ranges or medians and 25^{th}, 75^{th} percentiles. The inter-group statistical analysis between the data of chronic alcoholics and non-alcoholics was performed with the Mann-Whitney U-test. Dichotomous variables were examined with the chi-square test or, as far as smaller case numbers were concerned, with Fisher's exact test of significance. The examination regarding significant changes in the course of sE-selectin, IL-6 and IL-10 was performed globally with the Friedman test and, if significant, with the Wilcoxon matched pairs signed rank sum test locally. A p less than 0.05 was considered statistically significant. The receiver operating characteristics (ROC) analysis was performed as described previously [33].

Results

Basic patient characteristics did not differ between the groups except for alcoholism-related data (Table 1). When admitted to ICU the chronic alcoholics and non-alcoholics did not differ with regards to their Acute Physiology and Chronic Health Evaluation Score III (APACHE III) and their Multiple Organ Failure (MOF) score (Table 2). Chronic alcoholics had no signs of liver dysfunction. All patients were mechanically ventilated at ICU admission. Chronic alcoholics had a prolonged need for mechanical ventilation and a prolonged ICU stay (Table 2).

The occurrence of infectious complication was threefold higher in the chronic alcoholics (Table 2). Infections developed on day 3 (median, range 1–17) in chronic alcoholics and on day 4 (median, range 1–12) in non-alcoholics (p=0.48) during ICU treatment. AWS only occurred in chronic alcoholics (n=8). Two deaths occurred in the chronic alcoholic group (Table 2).

At hospital admission and preoperatively the plasma levels of IL-6 and IL-10 did not differ between chronic alcoholics and non-alcoholics (Table 3). Postoperatively the IL-6 plasma levels increased in both groups, but to a 3 times higher extent in the non-alcoholic group than in the chronic alcoholic group (Table 3). The plasma level of IL-10 was 4 times higher in the chronic alcoholics compared to the non-alcoholics postoperatively (Table 3). The IL-6/IL-10-ratio was significantly increased in the non-alcoholics immediately after surgery (Fig. 1). sE-selectin did not differ between the groups except preoperatively, when it was significantly higher in the

Table 3 Interleukin-6, interleukin-10, sE-selectin, white blood count and C-reactive protein in chronic alcoholic and non-alcoholic patients; median (range)

	Chronic alcoholics (n=25)	Non-alcoholics (n=20)	p value
Interleukin-6 (pg/ml)			
At hospital admission	5.3 (2.5–34.1)	6.0 (2.4–10.4)	0.53
Preoperatively	6.9 (2.2–418.9)	5.6 (3.1–25.3)	0.32
At ICU admission	114.4 (10.6–987.0)*	343.5 (25.5–870.4)*	0.03
At day 2 ICU	127.4 (7.7–489.8)	229.4 (11.4–413.6)	0.41
At day 4 ICU	79.1 (17.8–410.4)	132.1 (48.6–270.6)	0.24
Interleukin-10 (pg/ml)			
At hospital admission	2.6 (0–105.0)	1.5 (0–22.2)	0.22
Preoperatively	2.5 (0–438.4)	2.5 (0–27.8)	0.64
At ICU admission	13.2 (0–189.1)*	3.0 (0–44.9)*	<0.01
At day 2 ICU	4.7 (0.7–139.2)	3.5 (1.6–77.7)	0.83
At day 4 ICU	5.4 (1.3–294.0)	3.6 (1.4–15.6)	0.38
sE-selectin (ng/ml)			
At hospital admission	16.6 (0–83.5)	15.3 (0–36.3)	0.42
Preoperatively	26.3 (0–90.4)*	15.9 (0–42.9)*	0.01
At ICU admission	23.9 (0–56.3)	18.1 (4.5–37.1)	0.25
At day 2 ICU	20.0 (0–126.1)	23.1 (8.8–52.7)	0.99
At day 4 ICU	10.5 (0–80.6)	9.6 (0–47.5)	0.77
White blood count (/µl)			
At hospital admission	8.0 (2.7–11.0)	6.7 (2.9–12.0)	0.81
Preoperatively	7.2 (3.1–14.1)	6.7 (3.8–18.0)	0.41
At ICU admission	11.0 (3.3–20.3)	9.2 (6.3–23.3)	0.42
At day 2 ICU	9.4 (3.1–19.4)*	12.6 (7.0–23.5)*	0.02
At day 4 ICU	14.6 (5.2–23.1)	13.7 (8.0–48.5)	0.40
C-reactive protein (mg/ml)			
At hospital admission	5 (1–19)	6 (1–15)	0.33
Preoperatively	5 (1–12)	7 (2–12)	0.22
At ICU admission	10 (3–21)	13 (5–25)	0.05
At day 2 ICU	12 (3–26)	11 (4–22)	0.21
At day 4 ICU	8 (2–31)	10 (3–29)	0.34

*p<0.05 significant intra-group difference to baseline

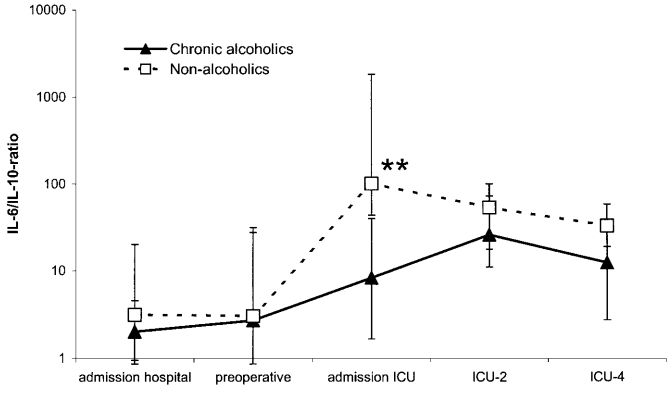

Fig. 1 Interleukin-6/IL-10 ratios in chronic alcoholics and non-alcoholics. Chronic alcoholics showed a significantly higher peak of their IL-6/IL-10 ratio immediately after surgery; median, 25th and 75th percentiles; **p=0.001

chronic alcoholics (Table 3). There were no significant differences in the WBC and CRP (Table 3).

Postoperative infectious complications in all patients were preceded by a decreased IL-6/IL-10 ratio at ICU admission (Fig. 2). This was, however, only significant for overall infectious complications (wound infection, pneumonia, sepsis).

The ROC analysis showed a significantly larger area under the curve (AUC) for the significantly decreased IL-6/IL-10 ratio at ICU admission in patients with any infectious complications (10 (0.2–6741) versus 61 (0.6–49350); p=0.02; AUC=0.70) compared to conventional laboratory markers such as CRP (AUC=0.37) and WBC (AUC=0.36). At ICU admission the level of IL-6 was significantly lower (114.4 (10.6–520.8) pg/ml versus 343.5 (18.3–987.0) pg/ml; p=0.02; AUC=0.71) and the level of IL-10 showed a tendency to increase, which was not statistically significant (9.5 (0–189.1) pg/ml versus 3.9 (0–72.0) pg/ml; p=0.18), in patients with infectious complications. At hospital admission patients with infectious complications had significantly higher levels of IL-10 (1.9 (0–22.2) pg/ml versus 3.5 (0–105.0) pg/ml; p=0.02; AUC=0.74). All other measurements showed no significant difference between the levels of IL-10 for patients with and those without infectious complications. The levels of sE-selectin were not significantly different between patients with and those without infectious complications.

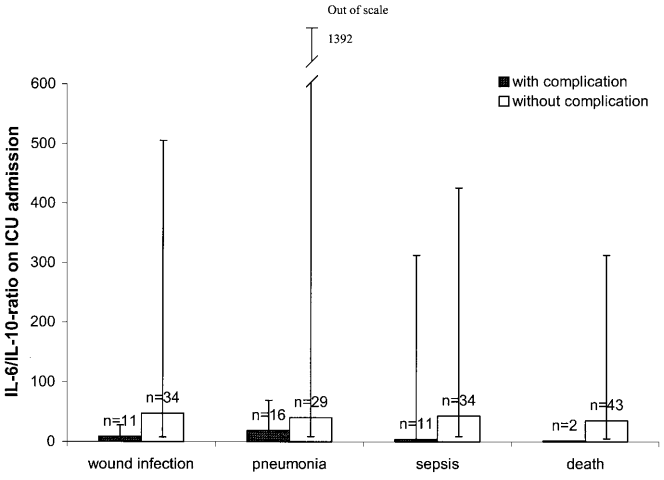

Fig. 2 Immediate postoperative IL-6/IL-10 ratio, infectious complications (wound infection, pneumonia and sepsis) and death; median, 25th and 75th percentiles. The median IL-6/IL-10 ratio after surgery was significantly decreased in all patients with any infectious complication (p=0.03)

Discussion

The most important finding in this study was that chronic alcoholic patients had a significantly decreased IL-6/IL-10 ratio immediately following surgery, i.e. before the onset of any infectious complication. The predictive value of the IL-6/IL-10 ratio was superior to any other parameter at ICU admission for these selected patients developing infectious complications. Infections occurred in 17/25 (68%) chronic alcoholics and in 6/20 (30%) non-alcoholic patients. Infections developed on day 3 (median) in chronic alcoholics and day 4 (median) in non-alcoholics during ICU treatment. To the best of our knowledge this is the first study showing that the ratio of the pro-inflammatory cytokine IL-6 to the anti-inflammatory cytokine IL-10 in patients undergoing elective surgery can predict infectious complications. This is of major clinical relevance as it might be a marker with which to identify high risk chronic alcoholic patients, who had also a threefold increased infection rate in this study.

In chronic alcoholics the postoperative increase of the IL-6/IL-10 ratio observed in non-alcoholics was missing on the first postoperative day. Chronic alcoholic patients have a compromised immune system [18, 19, 34, 35]. Irwin et al. described, in a recent publication, how the IL-6/IL-10 ratio in chronic alcoholics of certain ethnic origin was significantly decreased compared to non-alcoholic controls in ex vivo stimulated lymphocytes [20]. This finding is consistent with a poor outcome of these chronic alcoholics after certain viral and other infections [20]. Previous studies have shown that acute ethanol treatment leads to increased levels of anti-inflammatory cytokines such as IL-10 and TGF-beta, which can cause a decreased activity of pro-inflammatory cytokines such as IL-1beta and TNF-alpha [21, 36].

In our study the levels of IL-6 increased after surgery in chronic alcoholics and in non-alcoholics as described previously [4, 37], but the concentration of IL-6 in chronic alcoholics was 3 times lower than in the non-alcoholic group early after surgery. Immediately after surgery chronic alcoholics had significantly higher levels of IL-10 than non-alcoholics. The levels of IL-10 were 2 times higher in chronic alcoholics. Chronic alcoholics have been demonstrated to suffer from a delayed type of hypersensitivity after surgery [3]. After surgery a pro-inflammatory response involving IL-6 seems to be necessary to initiate an optimal response to the trauma [4] and high levels of the anti-inflammatory cytokine IL-10 play a crucial role in the postoperative immune suppression [6].

At ICU admission the IL-6/IL-10 ratio was significantly decreased in the patients who developed any infectious complication after surgery. This result may be biased by the chronic alcoholic patients in our study as those patients developed more infections. However, as it was superior to any other parameter in predicting postoperative infectious complications in our patients, it might help to identify high risk patients like chronic alcoholics before the onset of infections. It has been stated that an increase of the IL-6/IL-10 ratio can predict a poor outcome in patients with systemic inflammatory response syndrome [10]. However, on the one hand this increase of the IL-6/IL-10 ratio was seen late after onset of sepsis and not before the onset of infectious complications, as observed in our study. On the other hand, intraoperative hemodynamic instability due to, e.g., bleeding may also be associated with increased IL-6/IL-10 ratios and, therefore, a worse outcome [38]. These different responses indicate that cytokine ratios may only be applicable to selected patient populations.

At ICU admission the level of IL-6 was significantly lower in patients with infectious complications. The decreased level of IL-6 in patients developing infectious complications may be biased by the study design and can only be applied to chronic alcoholic patients. Nevertheless, it may be consistent with a previous study of patients with an acute phase response preoperatively where a decreased TNF-alpha and IL-6 release after lipopolysaccharide stimulation ex vivo was found [39]. The authors concluded that this might alter the patients' resistance to invasive microorganisms in the perioperative period and could therefore lead to infectious complications. The decreased level of IL-6 in our patients seems to be in contrast to other previous findings. Increased levels of IL-6 were observed in patients with pneumonia, sepsis, hemorrhagic shock and multiple injury [40, 41]. High levels of IL-6 were associated with a fatal outcome in these studies. As we only measured cytokines until

day 4 in the ICU and the median of the onset of infectious complications was day 3 and day 4 (chronic alcoholics and non-alcoholics, respectively), we cannot comment on levels of cytokines after the development of these complications.

Another study showed an increase in IL-6 levels during and directly after major abdominal surgery, which was associated with postoperative complications [42]. However, in this study by Donati et al. the group with complications were only four patients and the mean difference was probably only due to one patient whose IL-6 peak was 10 times higher than the median in this group. As nothing is said about the prevalence and severity of ethanol abuse in their patients, the two studies are difficult to compare. A different study demonstrated a positive correlation between the APACHE II score and both peak and postoperative IL-6 levels in patients with preoperative infection [43]. However, as the authors themselves concluded, this exaggerated IL-6 response could be due to an activation of the immune system due to the preoperatively ongoing infection. Therefore, this finding is hard to compare with our results as our patients did not show any evidence of infection preoperatively. In our study the early postoperative IL-6 response in patients with infectious complications could have been influenced by the high prevalence of chronic alcoholics in our study population. In accordance with previous studies, patients with infectious complications had significantly higher levels of IL-10 at hospital admission than patients who did not develop infections [6, 21, 37]. This supports the theory that increased levels of anti-inflammatory cytokines could compromise the host's ability to react adequately to potentially harmful events. Lyons et al. have seen a significant association between elevated levels of IL-10 and the development of sepsis/SIRS in trauma patients [44].

Chronic alcoholics had only significantly elevated sE-selectin levels immediately before surgery. No significant difference in sE-selectin levels could be found after surgery. Chronic alcoholics were shown to have an increased gut permeability [15]. Therefore, during the preoperative fasting period these patients might be exposed, due to relative hypovolemia, to an LPS challenge after bacterial translocation. This could have led to a preoperative inflammatory response with increased levels of sE-selectin as described previously [16]. The sE-selectin levels of patients with infectious complications were no different from those of patients without infections. Other studies have shown increased levels of sE-selectin in septic patients [11, 12]. In our study septic patients showed no differences in the levels of sE-selectin compared to patients who did not develop sepsis. The discrepancy in our study could be in part due to differences in the severity in sepsis. Only 2/11 patients with sepsis in our study died. In our study the WBC and CRP could not predict patients who would develop infections. Our results are supported by a study which showed no significant differences in WBC in survivors and non-survivors of patients at ICU admission and a study which found that CRP was not able to discriminate between patients with and without postoperative infection [45, 46].

Chronic alcoholics had a threefold increased rate of postoperative infectious complications, a significantly increased duration of ventilatory support, by a median of 15 h, and a prolonged ICU treatment, by a median of 6 days. The prolonged need for ventilatory support and the prolonged ICU treatment were related to the increased infection rate in chronic alcoholics. Chronic alcoholics developed significantly more wound infections and pneumonia, which confirmed the results of previous studies [1, 2, 3, 47]. This prolonged ICU stay accounted for an additional median cost of US$ 7000 in each chronic alcoholic for ICU treatment alone.

In conclusion, for the first time, to the best of our knowledge, this study has shown that chronic alcoholics have a suppressed IL-6/IL-10 ratio, whereas non-alcoholics showed a physiological pro-inflammatory cytokine profile immediately after surgery. The immediate postoperative IL-6/IL-10 ratio was superior to any other conventional parameter in predicting infectious complications in this study design considering chronic alcoholics and non-alcoholics. These findings support the theory that chronic alcoholics could suffer from an immune paralysis immediately following surgery that makes them more susceptible to the harmful effects of exogenous events and leaves them more vulnerable to infectious complications. Due to the threefold increase in infection rate and the prolonged ICU stay of chronic alcoholics, interventional immune modulating trials may be considered critically in patients with inadequate IL-6/IL-10 ratio increases following surgery.

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