



# Prevalence of the systemic inflammatory response syndrome in patients who underwent orthognathic surgery

Magno Liberato Silva<sup>1</sup> · Andréia Ferreira Ribeiro<sup>2</sup> · Fábio Ricardo Loureiro Sato<sup>3</sup> · Roger William Fernandes Moreira<sup>4</sup>

Received: 9 October 2017 / Accepted: 27 March 2018 / Published online: 11 April 2018  
© Springer-Verlag GmbH Germany, part of Springer Nature 2018

## Abstract

**Purpose** The systemic inflammatory response syndrome (SIRS) is the body's response to an insult, such as infection, trauma, burn, and surgical stress linked to several factors deemed potential for multiple organ failure if left untreated. Thus, the aim of this paper was a prospective study to examine the incidence of SIRS in postoperative patients who underwent orthognathic surgery from June/2013 to July/2016.

**Methods** The sample consisted of 80 patients who underwent bimaxillary orthognathic surgery, with data on vital signs and white blood cell count collected preoperatively, and the same data collected in the immediate postoperative period, in addition to CO<sub>2</sub> pressure in arterial blood by blood gas analysis. The data were tabulated and cases of SIRS (2 or more signs out of four pre-set signs) were identified within 24 h after surgery.

**Results** From the sample of 80 patients, 26 (32.5% of total) patients had SIRS with higher incidence in females who are 40 years old.

**Conclusion** The incidence of patients who develop SIRS after orthognathic surgery is relatively high and we should pay attention to the possible complications that these cases can evolve.

**Keywords** Systemic inflammatory response syndrome · Orthognathic surgery · Sepsis · Septic shock

## Introduction

The American College of Chest Physicians and the Society of Critical Care held a consensus conference in August 1991 (report published in 1992) [1, 2] in order to exclude and redefine some terms. At the conference, a new concept of disease called systemic inflammatory response syndrome (SIRS) was proposed, setting its physiological parameters and categorizing

each conditions of patients with such disease. SIRS is the body's response to a diverse trauma, such as infection, trauma, burns, and surgical stress, meeting at least two of the diagnostic criteria below:

1. Fever—body temperature > 38 °C or hypothermia, body temperature < 36 °C;
2. Tachycardia—heart rate > 90 bpm;
3. Tachypnea—respiratory rate > 20 bpm or PaCO<sub>2</sub> < 32 mmHg;
4. Leukocytosis or leukopenia—leukocytes > 12,000 cells/mm<sup>3</sup> or < 4000 cells/mm<sup>3</sup> or the presence of > 10% of young forms (band cells).

SIRS, regardless of etiology, has the same pathophysiology with minor differences in the inflammation cascade. Many consider the syndrome as a self-defense mechanism that uses inflammation and the body's response to nonspecific stimuli arising from chemical, infectious, or traumatic insults. The inflammatory cascade is complex and involves humoral and cellular responses. The relationship between these complex interactions of these cascades and SIRS is a three-stage process [3]:

✉ Fábio Ricardo Loureiro Sato  
fabio.sato@ict.unesp.br

<sup>1</sup> Resident of Oral and Maxillofacial Surgery, Brazilian Red Cross Hospital, São Paulo, Brazil

<sup>2</sup> Oral and Maxillofacial Surgeon, Brazilian Red Cross Hospital, São Paulo, Brazil

<sup>3</sup> College of Dentistry, São José dos Campos and Oral and Maxillofacial Surgeon, Oral and Maxillofacial Surgery Area, State University of São Paulo – UNESP, Brazilian Red Cross Hospital, Av. Eng. Francisco José Longo, 777, São José dos Campos, São Paulo 12245-000, Brazil

<sup>4</sup> Chief of Oral and Maxillofacial Surgery Department, Brazilian Red Cross Hospital, São Paulo, Brazil

- Phase I: After an insult, there is a local production of cytokines in order to induce an inflammatory response, thus promoting wound healing and recruitment of endothelial reticular system.
- Phase II: Small amounts of local cytokines are released into the circulation to improve local response. This leads to stimulation of the growth factor and the recruitment of macrophages and platelets. The acute phase response is typically well controlled by a decrease of the pro-inflammatory mediators and the release of endogenous antagonists. The goal is homeostasis.
- Phase III: If homeostasis is not restored, there is a significant systemic reaction. The release of cytokines leads to destruction rather than protection. The result is the activation of numerous humoral cascades and activation of the endothelial reticular system, leading to subsequent loss of circulatory integrity. This leads to the evolution of SIRS.

Trauma, inflammation, or infections lead to activation of the inflammatory cascade. When SIRS is mediated by an infectious insult, the inflammatory cascade is often initiated by endotoxin or exotoxin. Tissue macrophages, monocytes, platelets, mast cells, and endothelial cells are able to produce a variety of cytokines. Thus, tumor necrosis factor- $\alpha$  (TNF) and interleukin 1 (IL-1) are released first and initiate various cascades. The release of IL-1 and TNF results in cleavage of the inhibitor of nuclear factor kappa B (NF- $\kappa$ B). Once the inhibitor is removed, NF- $\kappa$ B is able to start the production of mRNA that will induce the production of other pro-inflammatory cytokines. Interleukin 6 (IL-6), 8 (IL-8), and interferon gamma are the primary pro-inflammatory mediators induced by NF- $\kappa$ B. TNF and IL-1 have shown to be released in large amounts up to 1 h after an insult, and have both local and systemic effects. They are responsible for the fever and the release of stress hormones (norepinephrine, vasopressin, and activation of the renin-angiotensin-aldosterone system). Other cytokines, especially IL-6, stimulate the release of acute phase reactants, such as C-reactive protein [4].

The cumulative effect of these inflammatory cascades is a state of imbalance with inflammation and dominant coagulation. A hypercoagulable state induced by inflammation cascades leads to fibrin deposition in microvessels and is deemed to contribute to organ failure in pro-inflammatory state. To counteract the acute inflammatory response, the body is equipped to reverse this process via compensatory anti-inflammatory response syndrome (CARS), producing interleukin 4 (IL-4) and 10 (IL-10) cytokines that are responsible for the decrease in TNF, IL-1, IL-6, and IL-8. The acute phase response also produces TNF inhibitors and IL-1 receptors. Such inhibitors

are linked to cytokine and thus inactivate or block the receptors. The balance of SIRS and CARS is critical to determine an outcome in patients [4].

The aim of this paper was a prospective study to examine the prevalence of SIRS in postoperative patients who underwent bimaxillary orthognathic surgery from June/2013 to July/2016.

## Materials and methods

A prospective study was made in which patients were selected without distinction of gender and age who underwent bimaxillary orthognathic surgery (Le Fort I osteotomy and sagittal split ramus osteotomy) under general anesthesia. Even as inclusion criteria, patients should be ASA I, show no sign/symptom of infection, and not use drugs in the week prior to the surgical procedure. Cases that did not fit the inclusion criteria or whose data were incomplete were excluded from the sample.

All surgeries were performed by the same surgeon (RWFM), assisted by another two surgeons (FRLS and AFR). The data were registered by another assistant (MLS) in the pre, trans, and postoperative period.

Before the surgery, data were collected on vital signs (temperature, heart rate, respiratory rate) and leukocyte counts preoperatively. The patient's prescription requested verification of the same vital signs postoperatively with intervals of 08/08 h to the time of hospital discharge. Leukocyte count and blood gas analysis were also requested by means of laboratory tests. Preoperative data were analyzed and only patients within the normal range in these areas were included in the study. For study purposes, vital signs with greater deviation in the postoperative day were considered, and the white blood cell count and blood gas analysis collected after 24 h at the beginning of the surgical procedure.

Preoperatively, all patients received 10 mg intravenously of dexamethasone and 2 g of cefazoline. The patients that reported allergy to cephalosporin were medicated with clindamycin 600 mg.

Data were tabulated and placed in a worksheet and submitted to a descriptive analysis of the data. The sample was separated into two groups (SIRS and non-SIRS) in accordance with the criteria and then were subjected to statistical analysis by the Mann-Whitney test for age variable and chi-square test for gender using SPSS software Version 11 (SPSS Inc., Chicago, IL, USA) for comparison between the two groups.

The Local Research Ethics Committee assessed and approved the work, and all participants signed the free and informed consent agreeing to participate.

**Table 1** Descriptive statistics

Study variable	Descriptive statistics
Sample Size ( <i>n</i> )	80
Gender—male/female	39 (49%)/41 (51%)
Age	30.6 ± 9.1
Length of hospital stay	1.3 ± 0.6 days
Presence of comorbidities	28 cases (35%)

## Results

The sample consisted of 80 patients, 41 females (51%), and 39 males (49%). Table 1 describes the data for the sample characteristics.

After tabulating and analyzing the data, it was possible to identify the samples that, according to the criteria of the consensus established in 1991, changed in at least two of the following criteria: temperature, heart rate, respiratory rate, CO<sub>2</sub> pressure in blood, and leukocyte counts.

A total of 26 patients (32.5% of the total) out of 80 patients had changes in at least two of their results, thus were included in the category of patients with SIRS—Table 2.

The sample data of SIRS and non-SIRS patients were then separated, tabulated, and subjected to statistical analysis and presented in Table 3.

The average age of the sample was approximately 30 years old with an average of patients with modifications, of 40 years old. Among the group with at least two factors of SIRS, 15 were female (66%) and 11 were male (34%), while in the non-SIRS group, the prevalence was higher for males (28 or 52%) and lower for females (26 or 48%), but no statistically significant difference. Besides this gender difference, age was also a different issue, with prevalence for the 4th decade of life for SIRS group, while the non-SIRS was most prevalent in half of the 2nd decade of life, with a statistically significant difference between SIRS and non-SIRS groups. Regarding the type of change, the majority was related to the number of leukocytes and body temperature (9 cases), followed by the change of leukocyte and respiratory rate (8 cases).

Fortunately, no major complication was found in the 80 procedures performed in this study. However, the incidence of SIRS in oral and maxillo-facial surgery procedure was

elevated as demonstrated in this study (32.5%), and all surgeons must pay attention to this fact, as SIRS is the first step to the stage of sepsis and multiple organ dysfunction syndrome (also known as multiple organ failure).

## Discussion

The symptoms of systemic inflammatory response syndrome (SIRS) shown immediately after surgery were recently considered as potential warnings of impending postoperative complications of multiple organ failure [5]. As this is a highly prevalent worldwide disease with high morbidity and mortality rate, standardization of diagnostic criteria is necessary in order to achieve early diagnosis and influence the improved survival of patients, thus preventing the disease from becoming worse [1, 2].

Several papers discuss the relationship between operative stress and SIRS in the field of general surgery and internal medicine. A hospital research with SIRS patients by Pittet et al. [6] revealed an intra-hospital overall incidence of 542 episodes/1000 days of hospitalization. In comparison, the incidence in the ICU was 840 episodes/1000 days of hospitalization. Rangel-Fausto et al. [5] published in the same year a prospect survey of patients admitted to a tertiary hospital, which revealed that 68% of hospital admissions of surveyed units met the criteria for SIRS. SIRS progression was as follows: 26% developed sepsis, 18% developed severe sepsis, and 4% developed septic shock within 28 days of hospitalization. Mortality rates were 7% (SIRS), 16% (sepsis), 20% (severe sepsis), and 46% (septic shock). Pittet et al. [6] also showed that control group patients had the lowest time of hospitalization, while SIRS patients, as well as patients who had sepsis and severe sepsis required, respectively, and on a progressive basis, longer hospitalization. But these studies are scarce in the field of maxillo-facial surgery.

The first description of SIRS in maxillo-facial surgery was done by Yajima et al. [7], but in other medical specialties, especially in gastrointestinal surgery, it has already been discussed for a long time with consolidated data in the literature. For example, the incidence of SIRS in gastrectomy is about 73%, for gastroesophageal cancer resection 67%, 54% for colon resection, and 37% for cholelithiasis.

**Table 2** Sample with alteration in the vital signals or in the laboratory exam

Item	Sample ( <i>n</i> )	Values		
		Minimum	Mean	Maximum
Tachycardia (bpm)	7	60	85.25	105
Tachypnea (bpm)	9	17	18.77	22
Fever (°C)	11	35.1	36.41	38
Leukocytosis/leukopenia (leukocytes)	24	8060	15,129	27,370

**Table 3** Comparison between the SIRS and non-SIRS group

Variable	Non-SIRS group	SIRS group	<i>p</i> value
Sample size	54 (67.5%)	26 (32.5%)	–
Gender—male/female	28/26	11/15	<i>p</i> = 0.42
Age	26.1 ± 6.9	40.0 ± 4.9	<i>p</i> < 0.01

The work proposed by Kasahara et al. [8] evaluated 65 patients with jaw deformity, who underwent maxillary and mandibular orthognathic surgery (Le Fort I and sagittal split ramus osteotomy) between September 2003 and October 2006. A survey based on SIRS diagnostic criteria resulted in the transfer of 33 cases for SIRS group and 32 cases for non-SIRS group (50% incidence of SIRS), showing an incidence slightly higher than the one found in this work, which also proves that SIRS should always be considered by maxillo-facial surgeons. Postoperative complications occurred in 27.3% of SIRS group and 0.0% among non-SIRS (*p* < 0.01). In four cases, a postoperative fluctuation in IL-6 levels was detected.

Although the authors had used the criteria of the American College of Chest Physicians and the Society of Critical Care to classify the systemic inflammatory response syndrome (SIRS) cases [1, 2], the results may have some false-positive cases, as postoperative fever can be normal (mainly due to atelectasis), and some changes in heart rate due to pain, especially in surgeries of higher morbidity.

## Conclusion

SIRS is a disease that can and must be combated when diagnosed early, as its evolution is dangerous to the patient and can have fatal damage.

Based on the data of this work, we can identify that its incidence is relatively high in the case of bimaxillary orthognathic surgery, and the surgeon should always be aware of the clinical and laboratory parameters of normality in the postoperative period, in order to identify cases of SIRS earlier as possible, preventing their progression to more serious cases such as sepsis and septic shock.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

## References

1. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, Schein RM, Sibbald WJ (1992) Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest* 101:1644–1655
2. Bone RC (1992) Toward an epidemiology and natural history of SIRS (systemic inflammatory response syndrome). *JAMA* 268: 3452–3455
3. Bone RC (1997) Systemic inflammatory response syndrome: a unifying concept of systemic inflammation. In: Fein A, Abraham A et al (eds) *Sepsis and Multiorgan Failure*. Lippencott, Williams, & Wilkins, Philadelphia, pp 1–10
4. Bone RC (1996) Toward a theory regarding the pathogenesis of the systemic inflammatory response syndrome: what we do and do not know about cytokine regulation. *Crit Care Med* 24:163–172
5. Rangel-Fausto MS, Pittet D, Costigan M, Hwang T, Davis CS, Wenzel RP (1995) The natural history of the systemic inflammatory response syndrome (SIRS). A prospective study. *JAMA* 273:117–123
6. Pittet D, Rangel-Fausto MS, Li N, Tarara D, Costigan M, Rempe L, Jebson P, Wenzel RP (1995) Systemic inflammatory response syndrome, sepsis, severe sepsis and septic shock: incidence, morbidities and outcomes in surgical ICU patients. *Int Care Med* 21:302–309
7. Yajima Y, Noma H, Kasahara K, Takeda E (2000) Systemic inflammatory response syndrome and postoperative complications after oral cancer surgery. *Bull Tokyo Dent Coll* 41:187–194
8. Kasahara K, Yajima Y, Ikeda C, Kamiyama I, Takaki T, Kakizawa T, Shibahara T (2009) Systemic inflammatory response syndrome and postoperative complications after orthognathic surgery. *Bulletin of Tokyo Dental College* 50:41–50