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Clinical Report

Systemic Inflammatory Response Syndrome and Postoperative Complications after Orthognathic Surgery

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Abstract

Symptoms of Systemic Inflammatory Response Syndrome (SIRS) presenting immediately after surgery have lately been regarded as potential warnings of impending postoperative complications and multiple organ failure. Reports discussing the relationship between operative stress and SIRS are found in the field of digestive surgery, but not in that of oral surgery. Sixty-five patients with jaw deformity who had undergone maxillary and mandibular orthognathic surgery (Le Fort I osteotomy and sagittal splitting ramus osteotomy) between September 2003 and October 2006 were involved in this study. A search based on the SIRS diagnostic criteria resulted in assignment of 33 cases to the SIRS group and 32 cases to the non-SIRS group. Postoperative complications occurred in 27.3% of the SIRS group and 0.0% of the non-SIRS group ($p<0.01$). In four cases, a postoperative fluctuation in IL-6 level evaluated. These results suggest the importance of careful management of postoperative SIRS patients in preventing complications.

Key words: Systemic Inflammatory Response Syndrome (SIRS)—Postoperative complication—Jaw deformity—Orthognathic surgery—Interleukin 6

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Introduction

The American College of Chest Physicians and the Society of Critical Care Medicine co-hosted a consensus conference in 1991 (report published in 1992) to define sepsis and accompanying organ failure[13]. At the conference, a new disease concept called systemic inflammatory response syndrome (SIRS) was proposed. SIRS represents a state in which an attack induces systemic inflammatory reactions. More concretely, patients are diagnosed with SIRS when meeting at least 2 of the diagnostic criteria (Table 1). Besides infection, SIRS is induced by various causes, including trauma, burn and surgical stress.

In recent years, due to the simple diagnostic standards, SIRS has been interpreted as a warning sign for the onset of postoperative complications and organ failure, and prevention is clinically important[2,5,6,18,26,28,29]. Furthermore, to identify high-risk SIRS associated with organ injury, the relationship between SIRS duration and outcomes has also been investigated[10].

To date, the relationship between surgical stress and SIRS has been mostly reported in the field of gastrointestinal surgery[2,5,6,9,12,14,16,20,22,24,29,30]. In the field of oral surgery, the relationship has not been investigated at all, even though the mouth is the starting point of the gastrointestinal tract. In 2000 and 2002, we first introduced the concept of SIRS in the head and neck region and investigated the relationship between surgical stress and postoperative complications in oral cancer patients who underwent neck dissection[10,33]. The results clarified that postoperative SIRS also occurs in the field of oral surgery. The present study investigated SIRS and postoperative complications in orthognathic surgery, another form of oral surgery. Chronological changes in plasma interleukin (IL)-6 were also ascertained.

Patients and Methods

We selected 65 patients (13 men, 52 women) who underwent maxillary and mandibular orthognathic surgery (Le Fort I osteotomy and sagittal splitting ramus osteotomy) from among patients with jaw deformities undergoing surgery at Tokyo Dental College Chiba Hospital between September 2003 and October 2006. Mean patient age was 24.4 years (range, 16–45 years). All patients received intravenous steroid therapy a total of 3 times (8 mg during surgery and 4 mg each at 6 and 12 hr after surgery) to prevent facial edema.

Starting immediately after surgery, body temperature, heart rate and respiratory rate were monitored, and white blood cell count (WBC) was measured at different times. Patients who met ≥2 of the SIRS diagnostic criteria (Table 1) for ≥24 hr were classified as belonging to the SIRS group, while all other patients were classified as belonging to the non-SIRS group. Duration of SIRS was measured from return to the ward, and a duration ≥24 hr but <48 hr was considered as "2 days". Among these patients, the relationship of SIRS to surgical techniques was investigated, and SIRS and non-SIRS groups were compared in terms of age, operating time, blood loss and incidence of postoperative complications. We considered infection due to wound suture

Table 1 SIRS diagnostic criteria

Response is manifested by two or more of following conditions:	
Body temperature	<36°C or >38°C
Heart rate	>90 beats/min
Respiratory rate	>20 breaths/min or $Paco_2$<32 torr
WBC	>12,000 cells/μl, <4,000 cells/μl or >10% immature (band) forms

Table 2 Characteristics of SIRS group (33 cases)

case (No)	age	sex	operative procedures	time (min)	bleeding (g)	SIRS (days)	complications
1	17	F	Le Fort I osteotomy + SSRO (+Genioplasty)	317	857	1	
2	26	F	Le Fort I osteotomy + SSRO	274	659	1	
3	21	M	Le Fort I osteotomy + SSRO	301	1,042	1	
4	18	F	Le Fort I osteotomy + SSRO	313	712	1	
5	26	F	Le Fort I osteotomy + SSRO	319	394	1	
6	24	F	Le Fort I osteotomy + SSRO	260	382	1	
7	17	F	Le Fort I osteotomy + SSRO	304	210	1	
8	18	F	Le Fort I osteotomy + SSRO	262	838	1	
9	19	F	Le Fort I osteotomy + SSRO	279	692	1	
10	20	F	Le Fort I osteotomy + SSRO	184	257	1	
11	24	M	Le Fort I osteotomy + SSRO	281	408	1	
12	21	M	Le Fort I osteotomy + SSRO (+Genioplasty)	459	888	1	
13	27	F	Le Fort I osteotomy + SSRO	309	390	1	
14	36	F	Le Fort I osteotomy + SSRO	287	554	1	
15	19	F	Le Fort I osteotomy + SSRO	289	551	2	
16	21	M	Le Fort I osteotomy + SSRO	569	2,341	3	
17	39	F	Le Fort I osteotomy + SSRO (+Genioplasty)	262	1,264	2	
18	22	F	Le Fort I osteotomy + SSRO (+Genioplasty)	270	244	2	
19	25	F	Le Fort I osteotomy + SSRO (+Genioplasty)	270	400	4	
20	24	M	Le Fort I osteotomy + SSRO (+Genioplasty)	369	2,647	5	
21	30	F	Le Fort I osteotomy + SSRO	293	2,170	5	
22	18	F	Le Fort I osteotomy + SSRO	240	405	1	wound infection
23	29	F	Le Fort I osteotomy + SSRO	340	1,223	1	wound infection
24	24	M	Le Fort I osteotomy + SSRO	422	1,597	1	ununited wound
25	22	F	Le Fort I osteotomy + SSRO	285	762	1	pharyngitis
26	31	F	Le Fort I osteotomy + SSRO (+Genioplasty)	326	1,091	1	herpes labialis
27	20	F	Le Fort I osteotomy + SSRO (+Genioplasty)	473	1,019	3	wound infection
28	16	F	Le Fort I osteotomy + SSRO	316	397	1	
29	19	F	Le Fort I osteotomy + SSRO	242	283	1	
30	30	F	Le Fort I osteotomy + SSRO	367	497	1	herpes labialis
31	27	M	Le Fort I osteotomy + SSRO	312	369	1	sinusitis
32	30	F	Le Fort I osteotomy + SSRO	270	757	4	wound infection
33	22	F	Le Fort I osteotomy + SSRO	304	278	1	

SSRO: sagittal splitting ramus osteotomy

failure, suppurative inflammation secondary to local infection, and viral infection due to low immunity as postoperative complications. The Mann-Whitney *U*-test and Fisher's exact probability test were used to determine statistical significance on the SPSS Version 11 for Windows.

Furthermore, based on the perspective that SIRS represents hypercytokinemia, plasma levels of IL-6 were measured before and after surgery using chemiluminescent enzyme immunoassay (CLEIA).

Results

1. Comparison between SIRS and non-SIRS groups

The SIRS group comprised 33 patients (33/65, 50.8%; 7 men, 26 women) with a mean age of 23.7 years (range, 16–39 years) (Table 2). Mean operating time was 5 hr 14 min (range, 3 hr 4 min to 9 hr 29 min). Mean blood loss was 805.4 ml (range, 210–2,647 ml).

The non-SIRS group comprised 32 patients (32/65, 49.2%; 6 men, 26 women) with a

Table 3 Characteristics of non-SIRS group (32cases)

case (No)	age	sex	operative procedures	time (min)	bleeding (g)
34	17	F	Le Fort I osteotomy + SSRO (+Genioplasty)	319	709
35	20	F	Le Fort I osteotomy + SSRO	300	552
36	28	M	Le Fort I osteotomy + SSRO (+Genioplasty)	387	684
37	28	F	Le Fort I osteotomy + SSRO	204	1,151
38	23	F	Le Fort I osteotomy + SSRO	206	555
39	36	F	Le Fort I osteotomy + SSRO	198	939
40	21	F	Le Fort I osteotomy + SSRO	245	224
41	18	F	Le Fort I osteotomy + SSRO	257	796
42	18	M	Le Fort I osteotomy + SSRO	301	236
43	23	M	Le Fort I osteotomy + SSRO	211	270
44	26	F	Le Fort I osteotomy + SSRO	379	815
45	30	M	Le Fort I osteotomy + SSRO	192	213
46	33	F	Le Fort I osteotomy + SSRO	260	499
47	31	F	Le Fort I osteotomy + SSRO	319	322
48	26	F	Le Fort I osteotomy + SSRO	243	726
49	45	F	Le Fort I osteotomy + SSRO	195	281
50	21	F	Le Fort I osteotomy + SSRO	205	220
51	23	M	Le Fort I osteotomy + SSRO	332	254
52	30	F	Le Fort I osteotomy + SSRO	360	455
53	16	F	Le Fort I osteotomy + SSRO	268	310
54	20	F	Le Fort I osteotomy + SSRO	280	457
55	19	M	Le Fort I osteotomy + SSRO	168	190
56	19	F	Le Fort I osteotomy + SSRO	238	512
57	21	F	Le Fort I osteotomy (+Posterior alveolar osteotomy) + SSRO	316	1,768
58	31	F	Le Fort I osteotomy + SSRO	236	218
59	25	F	Le Fort I osteotomy + SSRO	287	860
60	34	F	Le Fort I osteotomy + SSRO	238	604
61	39	F	Le Fort I osteotomy + SSRO	265	90
62	29	F	Le Fort I osteotomy + SSRO	292	276
63	18	F	Le Fort I osteotomy + SSRO	361	620
64	17	F	Le Fort I osteotomy + SSRO	166	101
65	19	F	Le Fort I osteotomy + SSRO	365	725

SSRO: sagittal splitting ramus osteotomy

mean age of 25.1 years (range, 16–45 years) (Table 3). Mean operating time was 4 hr 29 min (range, 2 hr 46 min to 6 hr 27 min). Mean blood loss was 519.8 ml (range, 90–1,768 ml).

Based on these data, age, operating time and blood loss were compared between the SIRS and non-SIRS groups. The results showed that although no significant difference in age was present, operating time was significantly longer and blood loss significantly greater in the SIRS group (Table 4).

For the 33 patients in the SIRS group, duration of SIRS was 1 day in 24 patients (72.7%), 2 days in 3 patients (9.0%), 3 days in 2 patients (6.1%), 4 days in 2 patients (6.1%) and 5 days in 2 patients (6.1%), with a mean of 1.6 days. In all patients, SIRS occurred from postoperative day 1, and in no cases did SIRS occur after a postoperative period of non-SIRS.

2. Correlation with postoperative complications (Fig. 1)

Postoperative complications were seen in 9 of the 65 patients.

Table 4 Comparison between SIRS group and non-SIRS group regarding age, operation time and bleeding

	SIRS	non-SIRS	M±SE Mann-Whitney
Age	23.69±5.48	25.12±7.05	ns
Operation time (min)	314.18±73.51	268.53±62.13	$p<0.05$
Amount of bleeding (g)	805.39±602.25	519.75±346.02	$p<0.05$

ns: not significant

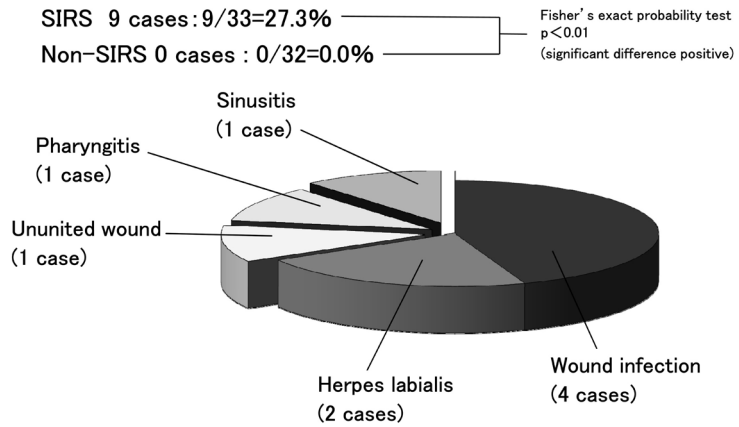

Fig. 1 Details of postoperative complications (SIRS: 9 cases)

Table 5 SIRS duration and postoperative complications

	complication negative	complication positive	M±SE Mann-Whitney
SIRS duration (days)	1.66±1.24	1.55±1.06	ns

ns: not significant

Nine (27.3%) of the 33 patients in the SIRS group developed complications, comprising wound infection (n=4), herpes labialis (n=2), ununited wound (n=1), pharyngitis (n=1), and sinusitis (n=1). In contrast, none of the 32 patients in the non-SIRS group experienced complications. The incidence of complications was significantly higher in the SIRS group than in the non-SIRS group.

The relationship between duration of SIRS and postoperative complications was investigated (Table 5). Mean duration of SIRS for patients who did not have postoperative complications was 1.7 days, compared to 1.6 days for patients with complications. No significant differences were identified between patients with and without complications.

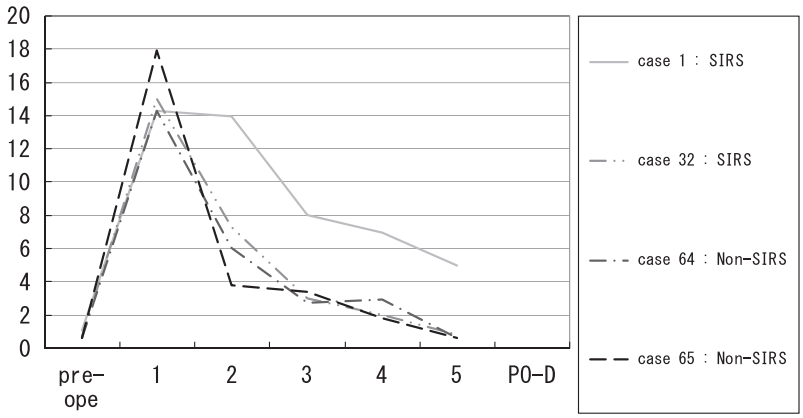

Fig. 2 Levels of IL-6 (pg/ml)

3. Changes in inflammatory cytokine levels (Fig. 2)

In the present study, plasma IL-6 was measured in 4 of the 65 patients: 2 patients (Cases 1 and 32) in the SIRS group and 2 patients (Cases 64 and 65) in the non-SIRS group. In all cases, IL-6 peaked on postoperative day 1 and began to decrease after postoperative day 2. In only 1 of the 4 cases (Case 1), IL-6 did not decrease much from postoperative day 1 to 2 (14.3 and 14 pg/ml, respectively). Maximum IL-6 in all cases was <20 pg/ml.

Discussion

Most of the parameters required for a diagnosis of SIRS are routinely measured as vital signs at the bedside after surgery. In the past, physicians intuitively assessed vital signs and predicted the risk for various postoperative complications, including infection, empirically. The introduction of SIRS is clinically very useful in systemically ascertaining the degree of surgical stress and predicting postoperative complications. Yajima *et al.* were the first to report SIRS in the field of oral surgery[33]. Here, we thoroughly investigated the relationship of SIRS to surgical stress and postoperative complications in different groups of subjects by comparing oral and gastrointestinal surgeries.

1. SIRS and non-SIRS groups

In the field of gastrointestinal surgery, the incidence of SIRS has been reported at 73.0% for gastrectomy, 67.0% for esophageal cancer resection, 54.1% for colon resection and 37.5% for cholelithiasis surgery[32,34]. In our study on maxillary and mandibular orthognathic surgery, incidence of SIRS was 50.1%. This suggests that the incidence of SIRS after orthognathic surgery is not necessarily low.

Mean duration of SIRS is 6.9 days for esophageal cancer surgery and 5.9 days for all gastrointestinal surgeries[32]. In the present study on orthognathic surgery, mean duration was 1.6 days. The duration of SIRS thus appears shorter for orthognathic surgery.

SIRS and non-SIRS groups were compared. Hagiwara *et al.*[6] studied patients who underwent surgery for esophageal cancer and reported no significant differences in age, blood loss or nutritional state, but operating time for SIRS patients was significantly longer. Likewise, our study on orthognathic surgery revealed no significant difference in age, and operating time was significantly longer and blood loss significantly greater in the SIRS group. The incidence of postoperative SIRS thus seems to be substantially affected by operating time and blood loss. This is because orthognathic surgery is an osteotomy, so blood

loss increases with operating time.

2. SIRS and postoperative complications

In esophageal cancer surgery, the incidence of complications in the non-SIRS group was 31.0%, compared to 83.0% in the SIRS group[3]. In the present study on orthognathic surgery, complications were confirmed in 9 patients (27.3%) in the SIRS group and none in the non-SIRS group, representing a significantly higher incidence of complications in the SIRS group. Caution must, therefore, also be exercised regarding the onset of postoperative complications in SIRS patients in orthognathic surgery, and screening patients using the concept of postoperative SIRS appears clinically significant.

Studies have shown that longer duration of SIRS is associated with a higher incidence of organ damage and multiple organ failure[1,6]. Kitamura *et al.*[12] reported that the mean duration of SIRS in patients who did not have complications following gastrointestinal surgery was 3.3 days, compared to 8.5 days in patients with multiple organ failure. In our study, no significant correlation was seen between duration of SIRS and incidence of postoperative complications. This might have been because patients with SIRS lasting only 1 day accounted for 72.7% of the total, and the longest duration was a relatively short 5 days.

Hirasawa *et al.*[7] documented multiple organ failure in 11 (4.8%) of 231 patients who had SIRS following gastrointestinal surgery and in 4 (12.9%) of 31 patients who had SIRS following emergency surgery. In our study on orthognathic surgery, none of the patients developed multiple organ failure. These results thus suggest that the incidence of SIRS following orthognathic surgery is relatively high, but because of the short duration, severe complications are less likely. Another factor was that many patients with jaw deformities were otherwise healthy and young.

Besides the duration of SIRS, the number of SIRS-positive criteria influences the incidence of postoperative complications. A higher number of SIRS-positive criteria reportedly correlates with a higher incidence of complications[25]. Ogawa[19] retrospectively investigated this point and reported that an increase in the number of positive criteria at the time of onset was also included. Furthermore, even when the number of SIRS-positive criteria was low, incidence of complications increased when duration was longer, and emphasis would thus be better placed on duration (a time factor indicating failure to remove SIRS). We agree with this perspective and did not investigate the relationship between number of SIRS-positive criteria and incidence of postoperative complications. Hirasawa[8] also reported the following parameters for "dangerous SIRS": 1) SIRS lasting ≥4 days; 2) plasma level of IL-6 ≥800–1,000 pg/ml on postoperative day 5; 3) damaged tissue oxygen metabolism; and 4) appearance of cytotoxicity. However, SIRS remains a warning sign that can be assessed using simple criteria. Instead of determining whether SIRS is dangerous, ascertaining whether a patient has SIRS and quickly eliminating the state represent the most important steps in avoiding postoperative complications. Ogawa proposed the second attack theory to clarify this point[18]. In other words, in the state of SIRS, cytokines that are induced due to a first attack (surgical stress) cause the adherence of neutrophils to vascular endothelial cells and aggregation of neutrophils to important organs. Under such circumstances, when cytokines are again released by a second attack (mainly infection), easily irritable neutrophils attack the organs, hindering organ function. Therefore, when preventing postoperative complications and organ failure, shortening the duration of SIRS as much as possible and quickly eliminating states in which a second attack could cause body injury is important.

3. Changes in cytokines

Surgical stress has been known to cause various changes in the endocrine and metabolic systems. Besides these neuroendocrine reactions, stress-induced cytokine induction reaction has been most closely examined in recent years and is thought to play a central role in inflammatory reactions. Stating that

hypercytokinemia is the essence of SIRS is thus no exaggeration[3,7,8,17,22]. When the body is subjected to surgical stress, levels of inflammatory cytokines such as TNF-α, IL-1β, IL-6 and IL-8 are known to increase, while at the same time, levels of anti-inflammatory cytokines such as IL-4 and IL-10 are also elevated. From the perspective of measurement sensitivity, IL-6 in the plasma can be easily detected after surgery, and is frequently used as a SIRS marker[3,7,11,15–17,21–23,27,31]. Studies have shown that plasma levels of IL-6 are significantly higher in patients with postoperative SIRS[7,20,22,31], remain high in deceased patients with SIRS[7,20], and closely reflect degree of surgical stress[4].

In the present study, changes in plasma IL-6 before and after surgery were only seen in 4 of the 65 patients. In our previous study on oral cancer surgery, the highest level of IL-6 was >100 pg/ml[10]. However, the highest level of IL-6 was much lower with orthognathic surgery, at 17.9 pg/ml. In the present study, all patients who underwent orthognathic surgery received steroids to prevent postoperative edema, and this could have suppressed increases in plasma cytokines.

Conclusion

In 65 patients with jaw deformities who underwent maxillary and mandibular orthognathic surgery (Le Fort I osteotomy and sagittal splitting ramus osteotomy), SIRS and postoperative complications were investigated, and the following conclusions reached:

1. Incidence of SIRS was 50.8%, and comparisons with non-SIRS showed no significant difference in age, but operating time and blood loss were significantly greater in the SIRS group.

2. Duration of postoperative SIRS was 1 day in 72.7% of patients, 2 days in 9.0%, 3 days in 6.1%, 4 days in 6.1% and 5 days in 6.1%. Duration of SIRS was thus only 1 day in more than two-thirds of cases.

3. Incidence of postoperative complications was 27.3% in the SIRS group, compared to 0.0% in the non-SIRS group, representing a significant difference between groups.

4. Postoperative complications comprised wound infection (n = 4), herpes labialis (n = 2), ununited wound (n = 1), pharyngitis (n = 1), and sinusitis (n = 1) in the SIRS group.

5. No significant correlation was observed between duration of SIRS and incidence of postoperative complications.

6. Compared with oral cancer surgery, levels of inflammatory cytokine IL-6 were lower in orthognathic surgery.

7. Focus needs to be placed on identifying and carefully monitoring SIRS patients while taking into consideration the risk of postoperative complications.

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