Elsevier Editorial System(tm) for Journal of Prosthodontic Research
Manuscript Draft

Manuscript Number:

Title: Non-randomized controlled prospective study on perioperative levels of stress and dysautonomia during dental implant surgery-Comparative characteristics of patients with and without intravenous sedation-

Article Type: Original Article

Keywords: psychological stress; intravenous sedation; implant surgery; autonomic reflexes

Corresponding Author: Prof. Ryuji Hosokawa, D.D.S., Ph.D.

Corresponding Author's Institution: Kyushu Dental College

First Author: Miyuki Morino, D.D.S.

Order of Authors: Miyuki Morino, D.D.S.; Chihiro Masaki, D.D.S., Ph.D.; Yoshinori Seo, D.D.S., Ph.D.; Taro Mukaibo, D.D.S., Ph.D.; Yusuke Kondo, D.D.S., Ph.D.; Shunji Shiiba, D.D.S., Ph.D.; Tetsuji Nakamoto, D.D.S., Ph.D.; Ryuji Hosokawa, D.D.S., Ph.D.

Abstract: Purpose: The purpose of this study was to compare pre- and postoperative autonomic activities and changes in salivary stress biomarkers between patients who received sedation and those who received only local anesthesia in dental implant surgery.
Methods: A total of 21 patients were enrolled in this non-randomized controlled prospective study; 7 subjects underwent implant surgery under local anesthesia with intravenous sedation and 14 subjects underwent surgery under only local anesthesia. Stress was evaluated by measuring salivary levels of chromogranin A (CgA) and a spectral analysis of heart rate variability (HRV) at baseline, 1 h preoperatively, and 1 h postoperatively. HRV analysis yields low- (LF) and high-frequency (HF) components, the LF/HF ratio, and the component coefficient of variance (CCV[HF]), which provide indices of sympathetic and parasympathetic regulatory activity.
Results: CgA levels were significantly higher ($p<0.05$) at baseline in patients who received sedation than those who did not, but CgA levels did not differ prior to surgery. Also, the values of most parameters, including LF, HF, LF/HF, and CCV(HF), did not significantly differ between groups or among the three time points. Only ΔLF/HF and ΔCCV(HF) were significantly lower ($p<0.05$) at 1 h preoperatively in patients who received sedation than those who received only local anesthesia.
Conclusions: CgA levels were high in both groups immediately before surgery, and thus CgA values immediately before surgery may not be a reliable indicator of the need for intravenous sedation. Also, spectral analysis of HRV, especially ΔLF/HF and ΔCCV(HF), could be useful for assessing tension and anxiety.

Non-randomized controlled prospective study on perioperative levels of stress and dysautonomia during dental implant surgery

-Comparative characteristics of patients with and without intravenous sedation-

Short title: Perioperative stress and dysautonomia levels on implant surgery

Original article

Keywords: psychological stress; intravenous sedation; implant surgery; autonomic reflexes

The number of pages in the text: 14

The number of tables and figures: 5

Reprint requests: 50

Abstract

Purpose: The purpose of this study was to compare pre- and postoperative autonomic activities and changes in salivary stress biomarkers between patients who received sedation and those who received only local anesthesia in dental implant surgery.

Methods: A total of 21 patients were enrolled in this non-randomized controlled prospective study; 7 subjects underwent implant surgery under local anesthesia with intravenous sedation and 14 subjects underwent surgery under only local anesthesia. Stress was evaluated by measuring salivary levels of chromogranin A (CgA) and a spectral analysis of heart rate variability (HRV) at baseline, 1 h preoperatively, and 1 h postoperatively. HRV analysis yields low- (LF) and high-frequency (HF) components, the LF/HF ratio, and the component coefficient of variance (CCV[HF]), which provide indices of sympathetic and parasympathetic regulatory activity.

Results: CgA levels were significantly higher ($p<0.05$) at baseline in patients who received sedation than those who did not, but CgA levels did not differ prior to surgery. Also, the values of most parameters, including LF, HF, LF/HF, and CCV(HF), did not significantly differ between groups or among the three time points. Only ΔLF/HF and ΔCCV(HF) were significantly lower ($p<0.05$) at 1 h preoperatively in patients who received sedation than those who received only local anesthesia.

Conclusions: CgA levels were high in both groups immediately before surgery, and thus CgA values immediately before surgery may not be a reliable indicator of the need for intravenous sedation. Also, spectral analysis of HRV, especially ΔLF/HF and ΔCCV(HF), could be useful for assessing tension and anxiety.

Introduction

Stress surrounding dental treatment is one of the most important factors that induce accidental systemic symptoms such as shock and acute elevation of blood pressure during procedures [1–3]. Systemic complications during dental treatment can be readily provoked by these psychological stresses, and most emergencies such as blood pressure elevation, tachycardia, and vasodepressor syncope are related to autonomic nervous disturbances [4]. These generally cause stress and fear, which may affect patient physiology and increase perioperative anxiety [5]. Previous studies have confirmed that patients experience anxiety not only before invasive treatments such as tooth extraction, but also before general dental treatments such as root canals and periodontal scaling [6,7]. In fact, invasive or uncomfortable procedures sometimes require intravenous sedation or general anesthesia [5,8].

As dental implant surgery can be very long, local anesthesia may be insufficient, and intravenous conscious sedation is an option [9]. Intravenous conscious sedation by the anesthetist is safe procedure and reduces the incidence of adverse events [9]. Consequently, intravenous sedation or general anesthesia is considered necessary for implant surgeries, particularly in patients who are highly susceptible to stress [10–12]. Stress may be evaluated by a variety of methods, including a self-administered questionnaire (SAQ) [5,6,13–15], statistical or dynamic analysis of electrophysiological signals of blood pressure and heart rate [16,17], and biochemical methods including measuring stress-related substances such as chromogranin A (CgA) and cortisol in blood or saliva samples [18–20]. The SAQ is employed most frequently, but it requires that subjects maintain reflective capability, and social preferences and subjects' tendency for self-conceit make its objective evaluation difficult. Moreover, levels of stress-related substances vary markedly among individuals and throughout the circadian cycle [19,20] and lack a baseline. Therefore, it is difficult to identify patients susceptible to stress from surgery in advance of a procedure or to reliably evaluate stress before, during, or after dental treatment; there are also no guidelines on which patients should be intravenously sedated.

On the other hand, HRV is widely used as an index of autonomic nervous activity. In humans, cardiac pulsation fluctuates constantly, even at rest, and is determined by the firing cycle of the sinus node. Sinus node firing is regulated by intracellular potassium (K^+) and calcium (Ca^{2+}) ion levels, which are adjusted by the autonomic nerves. Thus, autonomic nervous activity is assessable by frequency and time domain analyses of electrocardiogram data [21–26].

In this study, we attempted to identify biological distinctions between patients desiring intravenous sedation during implant placement and those who do not by evaluating salivary levels of the stress biomarker CgA and HRV immediately before, during, and after surgery.

Materials and methods

Subjects

A non-randomized controlled prospective study was performed with the approval of the Ethics Committee of Kyushu Dental University (No. 11-60). Twenty-one patients (15 females and 6 males; mean age, 61.4 years) were enrolled between August 2011 and August 2013 at Kyushu Dental University Hospital. Patients were given sufficient explanation of the study goals and signed a consent form. We excluded patients with certain criteria (severe diabetes, previous chemotherapy, previous irradiation of the head and neck region, progressive periodontitis, immunosuppression, human immunodeficiency virus infection), as well as those who had poor oral hygiene or were pregnant. Patients who needed bone grafting were also excluded. The differences between local anesthesia with and without intravenous sedation were explained to all patients before surgery, and the anesthetic methods were selected according to patient preference. In all, 7 patients received sedation during surgery and 14 received only local anesthesia.

Stress was evaluated by measuring salivary levels of the psychological stress biomarker CgA by immunoassay and by spectral analysis of heart rate variability (HRV) during orthostatic tolerance tests. HRV analysis yielded low- (LF) and high-frequency (HF) components, the LF/HF ratio, and the component coefficient of variance (CCV[HF]), providing indices of sympathetic and parasympathetic regulatory activity. Orthostatic tolerance tests were performed and saliva was collected at baseline (on a day other than the day of surgery), 1 h preoperatively, and 1 h postoperatively (Fig. 1).

Changes in salivary CgA related to psychological stress

Saliva was collected from each subject using a salivette. Subjects chewed on a small piece of cotton for 4 min, after which the cotton piece was placed in a tube. After collection, the samples were kept in an icebox until transport to the laboratory, where they were centrifuged and stored at -80°C until analysis. The concentration of CgA (pmol/mL) was measured using the YK070:CgA (Human) EIA kit (Yanaihara Institute).

CgA levels were corrected for protein concentration as measured by the Bio-Rad Protein assay kit and expressed as pmol/mg protein.

Autonomic reflex orthostatic tolerance test

HRV and blood pressure were measured for 5.5 min: 3 min while patients sat in a relaxed manner and 2.5 min while they stood (Fig. 2). Time domain analysis of HRV allowed direct evaluation of changes in the R-R interval, which then were converted into frequencies, and components in each frequency range were evaluated. The power spectrum was subsequently quantified using standard frequency-domain measurements, including HF power (>0.15 Hz) and LF power (between 0.05 and 0.15 Hz). LF/HF was used as an indicator of the balance between sympathetic and parasympathetic activities, that is, a relative sympathetic index. In addition, the coefficient of variance of R-R intervals (CVRR: SD of the R-R interval/mean of the R-R interval × 100), which represents fluctuations of heart beat, was measured as an index of autonomic activity [27,28].

With normal autonomic reflexes, sympathetic activity is increased and parasympathetic activity is suppressed immediately upon standing. On the other hand, while continuing to remain upright, sympathetic activity is suppressed and parasympathetic activity is increased. In addition, ΔL/H (L/H [just after standing] – L/H [sitting]), ΔCVRR (CVRR [just after standing] – CVRR [sitting]), and ΔnormCCVHF (normCCVHF [continued standing] – normCCVHF [just after standing]) were calculated to evaluate changes in the balance index with the change from sitting to standing, changes in autonomic activity with the change from sitting to standing, and changes in the percentage of the parasympathetic activity associated with continued standing, respectively. Systolic arterial and diastolic blood pressure was measured every minute, beginning 1 min after the beginning of the test, and heart rate was monitored throughout.

Statistical analysis

For comparisons between groups, the Mann-Whitney test was used, while for three groups (baseline, before, after), the Friedman's test followed by Dunn's post-test was used. A value of $p < 0.05$ was considered to indicate statistical significance.

Results

CgA levels were significantly greater ($p<0.05$) in patients who received sedation than those who did not at baseline. On the other hand, there was no significant difference between the two groups at 1 h pre- or postoperatively (Fig. 3). Autonomic functional measurements while sitting, including LF/HF, CCV (HF), and CVRR, did not differ significantly between patients who received the two methods of anesthesia (Fig. 4). In addition, there was no significant difference in autonomic functional measurements in other positions. As for changes in these variables between standing and sitting, the only significant difference between the two groups was in ΔLF/HF and ΔCCV (HF) at 1 h prior to surgery; both were significantly lower ($p<0.05$) in patients who received sedation; ΔCVRR did not vary between groups (Fig. 5). Moreover, heart rate, systolic arterial pressure, and diastolic blood pressure did not significantly differ between groups at any time point.

Discussion

In dental treatment, local anesthesia with intravenous sedation is reported to mitigate intraoperative stress and prevent accidental systemic symptoms [10–12]. However, there are no clear criteria regarding which patients would benefit from intravenous sedation. Generally, patients who feel fear tend to select intravenous sedation. In this study, baseline salivary CgA levels, which should correlate with fear, were significantly higher in these patients. Also, no significant difference was noted in the CgA level between the two groups 1 h prior to surgery, indicating that preoperative stress levels were also high in patients opting only for local anesthesia. These results suggest that CgA levels immediately before surgery are not reliable indicators of the need for intravenous sedation.

On the other hand, we also examined whether autonomic nervous activity signifies patients' preoperative stress susceptibility by comparing HRV before and after implant surgery between patients who underwent surgery with and without intravenous sedation. ECG R-R interval and HRV based on the pulse wave and first and second derivatives of photoplethysmogram have been shown to be reliable indicators of autonomic nervous activity [29,30]. Among these, we used the ECG R-R interval to analyze HRV. Frequency analysis of the R-R interval of ECG yields three spectral components: very LF (VLF; <0.05 Hz), LF (0.05–0.15 Hz), and HF (>0.15 Hz). Because the HF component reflects parasympathetic activity and the LF reflects both sympathetic and parasympathetic activities, the LF/HF ratio and HF are used as indices of the sympathetic and parasympathetic activities, respectively. In addition, in time domain analysis, the coefficient of variance of the dimension of fluctuation of the HRV (CVRR) is used as an index of the magnitude of autonomic activity. Moreover, in this study, perioperative autonomic nervous function was evaluated by analyzing HRV by means of the orthostatic tolerance test of autonomic reflexes. As a result, the ΔLF/HF, which reveals changes in sympathetic activity, and ΔnormCCVHF, changes in parasympathetic activity, were found to be significantly lower in patients who received sedation than those who elected not 1 h before surgery. Generally, upon standing, blood (0.5–1 L) is retained in the venous volume of the lower limbs and body trunk due to gravity, followed by an increase in sympathetic and suppression of parasympathetic activity due to the action of baroreceptors of the aortic arc and carotid body. These reactions induce increases in heart rate and contractile force and coarctation of the vascular volume to maintain blood pressure. If the standing position is maintained, the intravascular volume is expanded by activation of the renin-angiotensin-aldosterone system and secretion of antidiuretic hormones, and consequent suppression of sympathetic and enhancement of parasympathetic activity due to autonomic reflexes stabilize heart rate and coarctation of the vascular volume and maintain a standing-appropriate blood pressure. Because autonomic nervous function as indicated by ΔnormCCVHF and ΔLF/HF was unstable only in patients who received sedation immediately before surgery, pre-operative autonomic function tests may be effective to evaluate patients' fear of surgery and assess whether intravenous sedation should be used in addition to local anesthesia.

Conclusion

Patients who desire intravenous sedation for implant treatment may be prone to high levels of psychological stress that cause unstable autonomic nervous activity immediately before surgery. Also, autonomic function tests appear to be an effective evaluation of patients' fear and stress immediately before implant surgery. Implementation of this practice could mitigate the risk of accidents due to hemodynamic changes resulting from intraoperative psychological stress.

Acknowledgements

The authors express their special thanks to Dr. Seiji Watanabe (Professor, Department of Dental Anesthesiology, Kyushu Dental University) for his support of this study. The authors declare no conflicts of interest with this work.

Figure Legends

Figure 1

Study design. Orthostatic tolerance tests and measurement of salivary CgA levels were performed at baseline, 1 h before surgery and 1 h after surgery.

Figure 2

Principle of orthostatic tolerance test of the autonomic reflex.

Figure 3

CgA levels were significantly higher ($p<0.05$) in patients who received sedation than those who received only local anesthesia at baseline. There was no significant difference between groups at the pre- and post-operative timepoints.

Figure 4

Changes in baseline autonomic activity (in the sitting position) over the perioperative period. There was no significant difference between groups.

Figure 5

Changes in autonomic function over the perioperative period. ΔLF/HF and ΔCCV(HF) were significantly lower ($p<0.05$) in patients who received sedation than those opting for only local anesthesia 1 h before surgery, but did not differ at later time points. There was no significant difference in ΔCVRR.

References

[1] Montebugnoli L, Servidio D, Miaton RA, Prati C. Heart rate variability: a sensitive parameter for detecting abnormal cardiocirculatory changes during a stressful dental procedure. J Am Dent Assoc. 2004 Dec;135(12):1718–23.

[2] Romano MM, Soares MS, Pastore CA, de Oliveira Guaré R, Adde CA. Electrocardiographic changes during endosseous implant placement performed with local anesthetic agents. Int J Oral Maxillofac Implants. 2009 May-Jun;24(3):412–8.

[3] Georgelin-Gurgel M, Diemer F, Nicolas E, Hennequin M. Surgical and nonsurgical endodontic treatment-induced stress. J Endod. 2009 Jan;35(1):19–22.

[4] Tsugayasu R, Handa T, Kaneko Y, Ichinohe T. Midazolam more effectively suppresses sympathetic activations and reduces stress feelings during mental arithmetic task than propofol. J Oral Maxillofac Surg. 2010 Mar;68(3):590–6.

[5] Seto M, Sakamoto Y, Takahashi H, Kita R, Kikuta T. Does planned intravenous sedation affect preoperative anxiety in patients? Int J Oral Maxillofac Surg. 2013 Apr;42(4):497–501..

[6] Nair MA, Shankarapillai R, Chouhan V. The dental anxiety levels associated with surgical extraction of tooth. Int J Dent Clin 2009:1(1):20–23

[7] Sanikop S, Agrawal P, Patil S. Relationship between dental anxiety and pain perception during scaling. J Oral Sci. 2011 Sep;53(3):341–8.

[8] Silay E, Candirli C, Taskesen F, Coskuner I, Ceyhanli KT, Yildiz H. Could conscious sedation with midazolam for dental procedures be an alternative to general anesthesia? Niger J Clin Pract. 2013 Apr-Jun;16(2):211–5.

[9] González-Lemonnier S, Bovaira-Forner M, Peñarrocha-Diago D, eñarrocha-Diago MA. Hemodynamic and ventilatory changes during implant surgery with intravenous conscious sedation. Med Oral Patol Oral Cir Bucal. 2011 Jul 1;16(4):e541–5.

[10] Coolidge T, Irwin SP, Leyster KA, Milgrom P. Determinants of receiving intravenous sedation in a sample of dentally fearful patients in the USA. SAAD Dig. 2012 Jan;28:52–60.

[11] Collado V, Faulks D, Nicolas E, Hennequin M. Conscious sedation procedures using intravenous midazolam for dental care in patients with different cognitive profiles: a prospective study of effectiveness and safety. PLoS One. 2013 Aug 5;8(8):e71240.

[12] González-Lemonnier S, Bovaira-Forner M, Peñarrocha-Diago M, Peñarrocha-Oltra D Relationship between preoperative anxiety and postoperative satisfaction in dental implant surgery with intravenous conscious sedation. Med Oral Patol Oral Cir Bucal. 2010 Mar 1;15(2):e379–82.

[13] Pohjola V, Lahti S, Suominen-Taipale L, Hausen H. Dental fear and subjective oral impacts among adults in Finland. Eur J Oral Sci. 2009 Jun;117(3):268–72.

[14] Takahashi H, Masaki C, Makino M, Yoshida M, Mukaibo T, Kondo Y, Nakamoto T, Hosokawa R. Management of sleep-time masticatory muscle activity using stabilisation splints affects psychological stress. J Oral Rehabil. 2013 Dec;40(12):892–9.

[15] Albanidou-Farmaki E, Poulopoulos AK, Epivatianos A, Farmakis K, Karamouzis M, Antoniades D. Increased anxiety level and high salivary and serum cortisol concentrations in patients with recurrent aphthous stomatitis. Tohoku J Exp Med. 2008 Apr;214(4):291–6.

[16] Ilies C, Gruenewald M, Ludwigs J, Thee C, Höcker J, Hanss R, Steinfath M, Bein B. Evaluation of the surgical stress index during spinal and general anaesthesia. Br J Anaesth. 2010 Oct;105(4):533–7.

[17] Uehara N, Takagi Y, Miwa Z, Sugimoto K. Objective assessment of internal stress in children during dental treatment by analysis of autonomic nervous activity. Int J Paediatr Dent. 2012 Sep;22(5):331–41.

[18] Shigeyama C, Ansai T, Awano S, Soh I, Yoshida A, Hamasaki T, Kakinoki Y, Tominaga K, Takahashi T, Takehara T. Salivary levels of cortisol and chromogranin A in patients with dry mouth compared to age matched controls. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008 Dec;106(6):833–9.

[19] Giampaolo B, Angelica M, Antonio S. Chromogranin 'A' in normal subjects, essential hypertensives and adrenalectomized patients. Clin Endocrinol (Oxf). 2002 Jul;57(1):41–50.

[20] Hong RH, Yang YJ, Kim SY, Lee WY, Hong YP. Determination of appropriate sampling time for job stress assessment: the salivary chromogranin A and cortisol in adult females. J Prev Med Public Health. 2009 Jul;42(4):231–6.

[21] Severi S, Cavalcanti S, Avanzolini GPhysiol Meas. Heart rate variability spectral indices for haemodynamic classification of haemodialysis patients. 1997 Nov;18(4):339–53.

[22] Shinba T, Kariya N, Matsui Y, Ozawa N, Matsuda Y, Yamamoto K. Decrease in heart rate variability response to task is related to anxiety and depressiveness in normal subjects. Psychiatry Clin Neurosci. 2008 Oct;62(5):603–9.

[23] Battipaglia I, Barone L, Mariani L, Infusino F, Remoli R, Careri G, Pinnacchio G, Tarzia P, Lanza GA, Crea F. Relationship between cardiac autonomic function and sustained ventricular tachyarrhythmias in patients with an implantable cardioverter defibrillators. Europace. 2010 Dec;12(12):1725–31.

[24] Huang WL, Lin YH, Kuo TB, Chang LR, Chen YZ, Yang CC. Methadone mediated autonomic functioning of male patients with heroin dependence: the influence of borderline personality pattern. PLoS One. 2012;7(5):e37464.

[25] Tanosoto T, Arima T, Tomonaga A, Ohata N, Svensson P. A Paced Auditory Serial Addition Task evokes stress and differential effects on masseter muscle activity and haemodynamics. Eur J Oral Sci. 2012 Aug;120(4):363–7.

[26] Ptaszynski P, Kaczmarek K, Klingenheben T, Cygankiewicz I, Ruta J, Wranicz JK. Noninvasive assessment of autonomic cardiovascular activity in patients with inappropriate sinus tachycardia. Am J Cardiol. 2013 Sep 15;112(6):811–5.

[27] Mochizuki H, Okahashi S, Ugawa Y, Tamura T, Suzuki M, Miyatake S, Shigeyama T, Ogata K, Kawai M. Heart rate variability and hypercapnia in Duchenne muscular dystrophy. Intern Med. 2008;47(21):1893–7. Epub 2008 Nov 4.

[28] Nomura K, Ikeda H, Mori K, Hamamoto Y, Honjo S, Kawasaki Y, Wada Y, Koshiyama H. Less variation in R-R interval of electrocardiogram in nonobese type 2 diabetes with nocturnal intermittent hypoxia. Endocr J. 2

[29] Chan GS, Fazalbhoy A, Birznieks I, Macefield VG, Middleton PM, Lovell NH. Spontaneous fluctuations in the peripheral photoplethysmographic waveform: roles of arterial pressure and muscle sympathetic nerve activity. Am J Physiol Heart Circ Physiol. 2012 Feb 1;302(3):H826–36.

[30]Wang X, Chen X, Ye S, Feng Y, Huang C, Hou L, Liu J, Chen H. Changes in the photoplethysmogram with tracheal intubation and remifentanil concentration. Anaesthesia. 2012 Dec;67(12):1332–6.

*Title Page

Non-randomized controlled prospective study on perioperative levels of stress and dysautonomia during dental implant surgery

-Comparative characteristics of patients with and without intravenous sedation-

Short title: Perioperative stress and dysautonomia levels on implant surgery

Miyuki Morino, DDS[a], Chihiro Masaki, DDS, PhD[b], Yoshinori Seo, DDS, PhD[c], Chisato Mukai, DDS, PhD[c], Taro Mukaibo, DDS, PhD[b], Yusuke Kondo, DDS, PhD[b], Shunji Shiiba, DDS, PhD[e], Tetsuji Nakamoto, DDS, PhD[d], Ryuji Hosokawa DDS, PhD[f]

[a]PhD Candidate, Department of Oral Reconstruction and Rehabilitation, Kyushu Dental University, Graduate School, Japan

[b]Assistant Professor, Department of Oral Reconstruction and Rehabilitation, Kyushu Dental University, Japan

[c]Research Associate, Department of Oral Reconstruction and Rehabilitation, Kyushu Dental University, Japan

[d]Associate Professor, Department of Oral Reconstruction and Rehabilitation, Kyushu Dental University, Japan

[e]Associate Professor, Department of Dental Anesthesiology, Kyushu Dental University, Japan

[f]Professor, Department of Oral Reconstruction and Rehabilitation, Kyushu Dental University, Japan

Original article

Keywords: psychological stress; intravenous sedation; implant surgery; autonomic reflexes

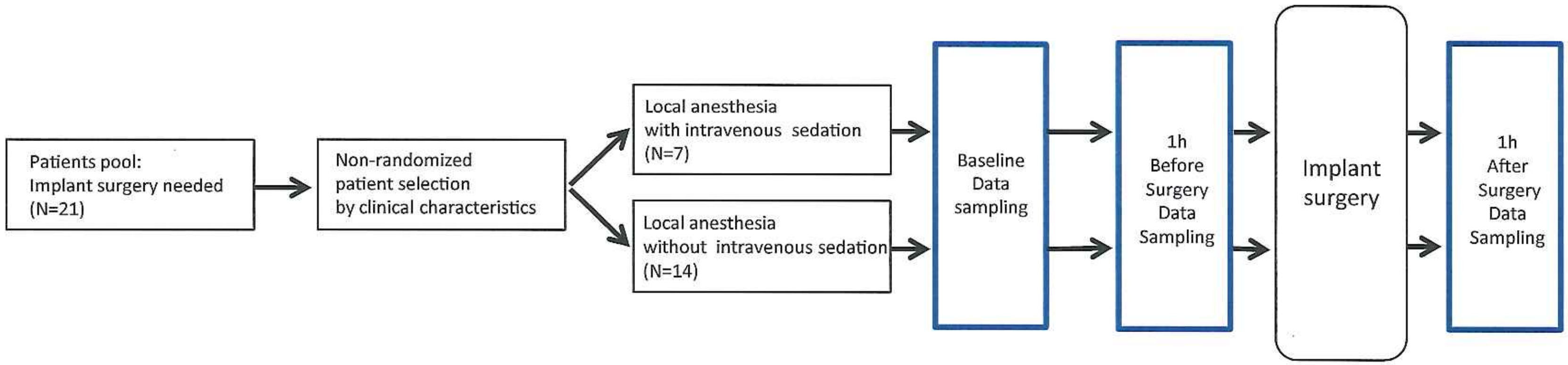
The number of pages in the text: 14

The number of tables and figures: 5

Reprint requests: 50

Reprint Requests and Correspondence to: Ryuji Hosokawa, DDS, PhD, Department of Oral Reconstruction and Rehabilitation, Kyushu Dental University, 2-6-1 Manazuru, Kokurakita, Kitakyushu, Fukuoka 803-8580, Japan. Fax: +81-93-592-3230.

Figure



Patients pool:
Implant surgery needed
(N=21)
Non-randomized
patient selection
by clinical characteristics
Local anesthesia
with intravenous sedation
(N=7)
Local anesthesia
without intravenous sedation
(N=14)
Baseline
Data
sampling
1h
Before
Surgery
Data
Sampling
Implant
surgery
1h
After
Surgery
Data
Sampling

Fig. 1

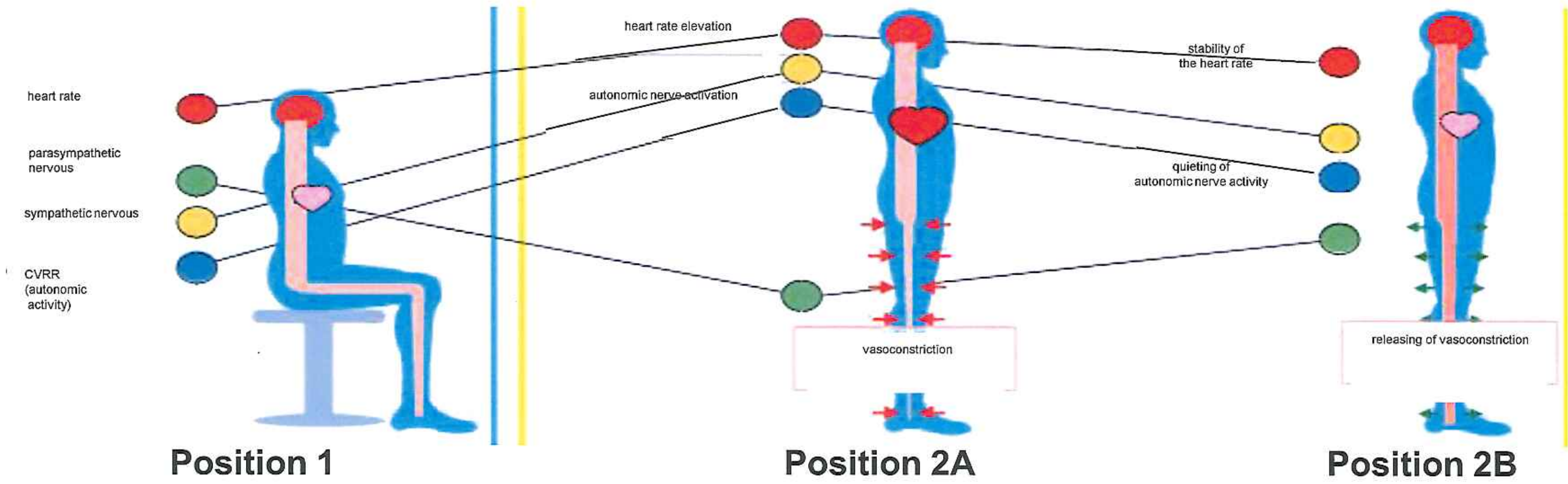

heart rate
parasympathetic nervous
sympathetic nervous
CVRR (autonomic activity)
heart rate elevation
autonomic nerve activation
stability of the heart rate
quieting of autonomic nerve activity
vasoconstriction
releasing of vasoconstriction
Position 1
Position 2A
Position 2B

Fig. 2

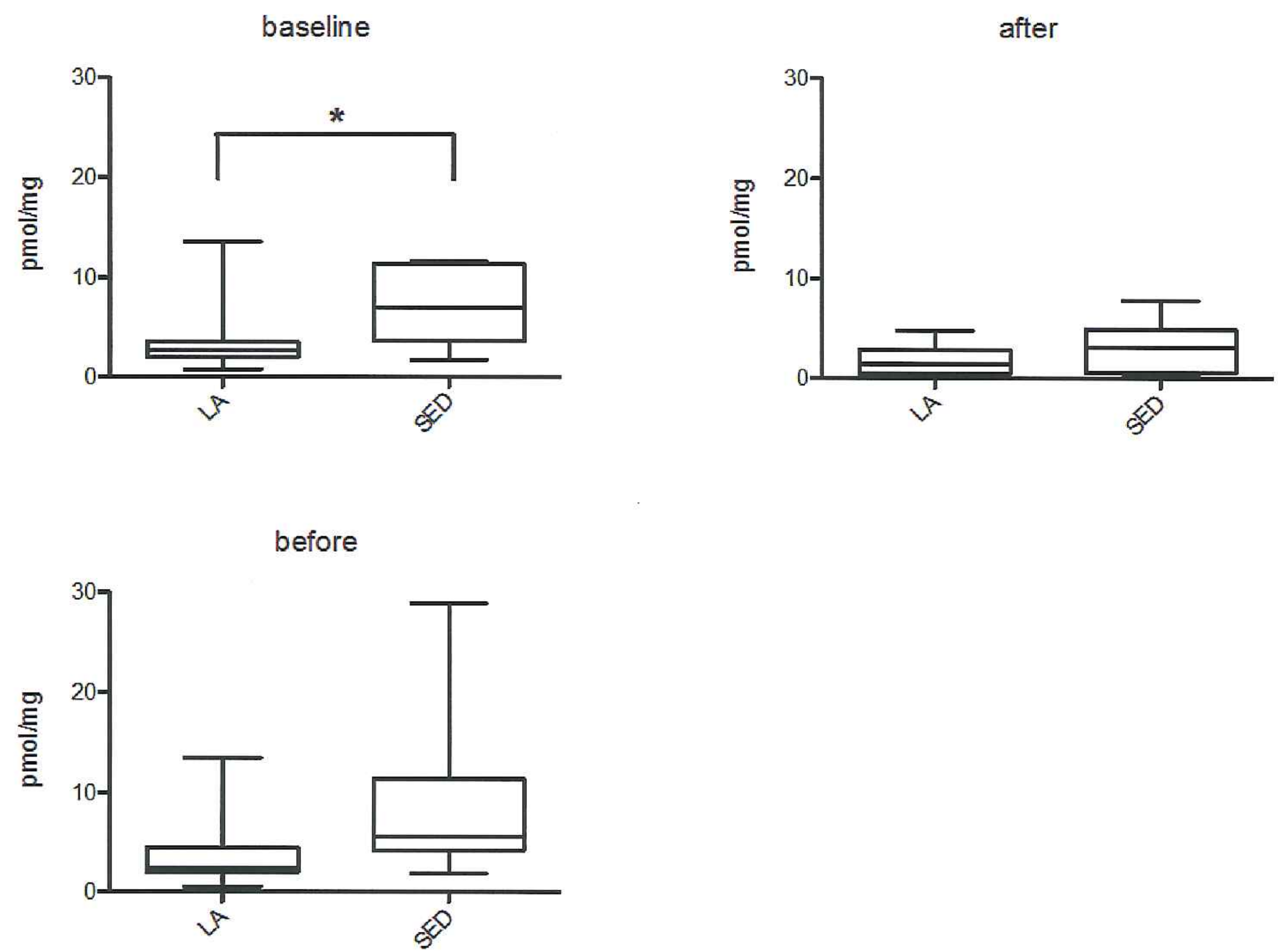


Fig. 3

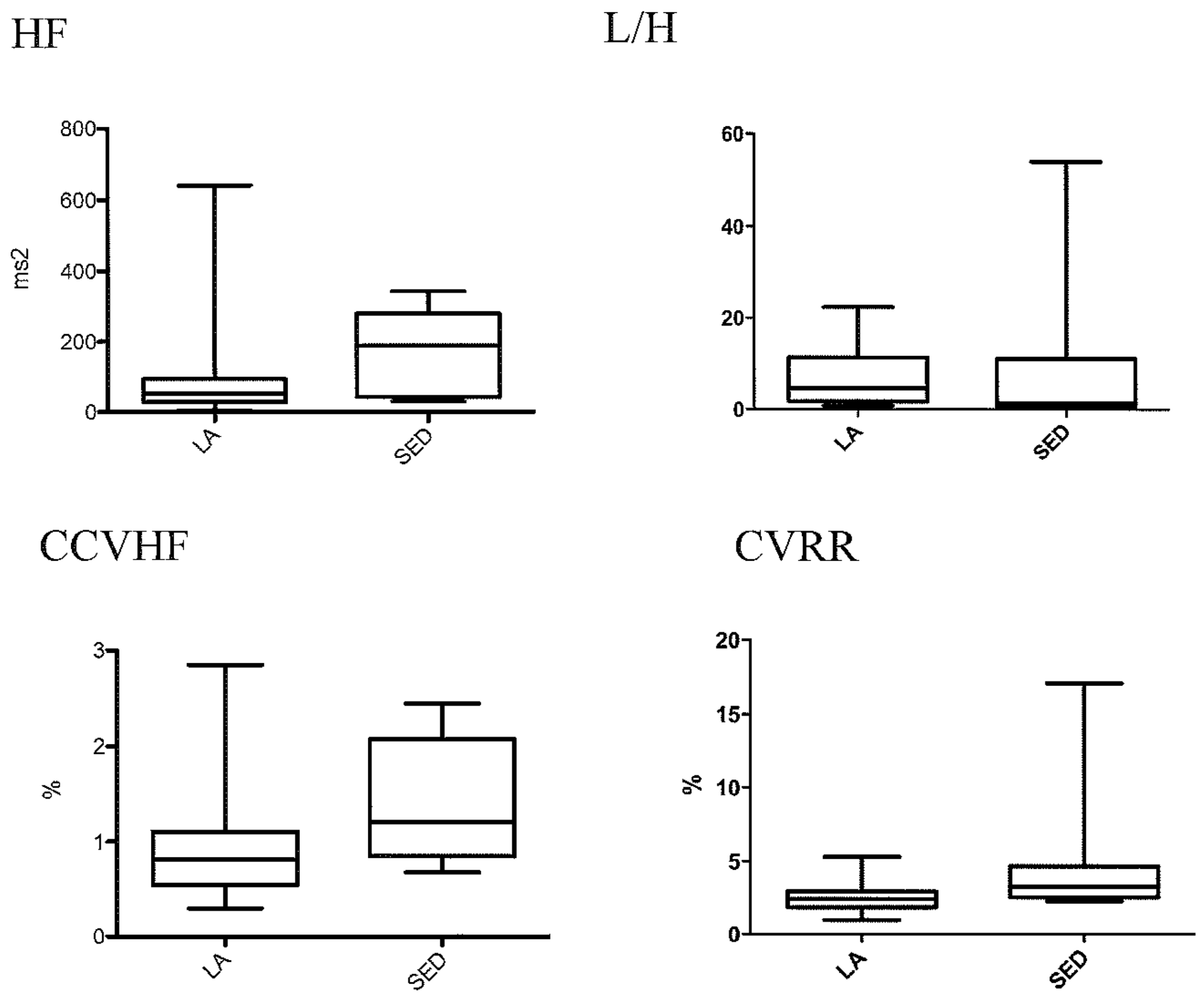
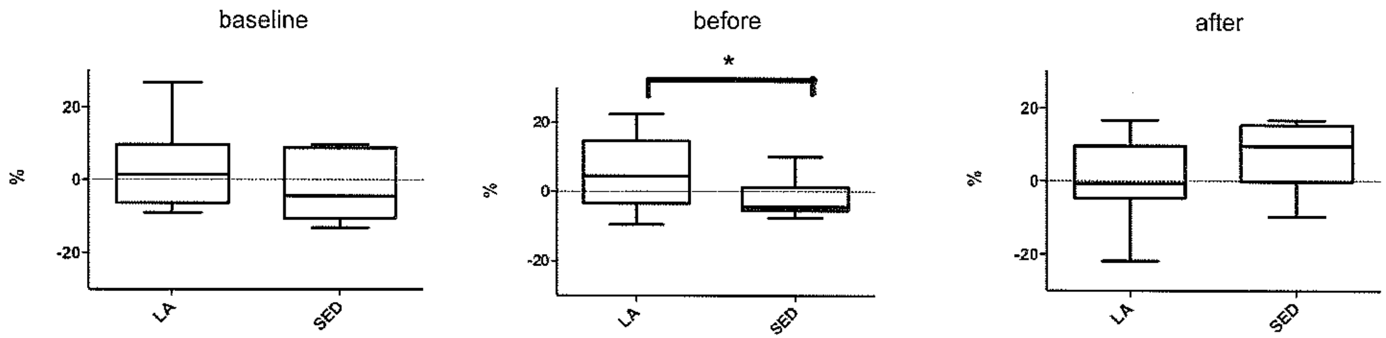
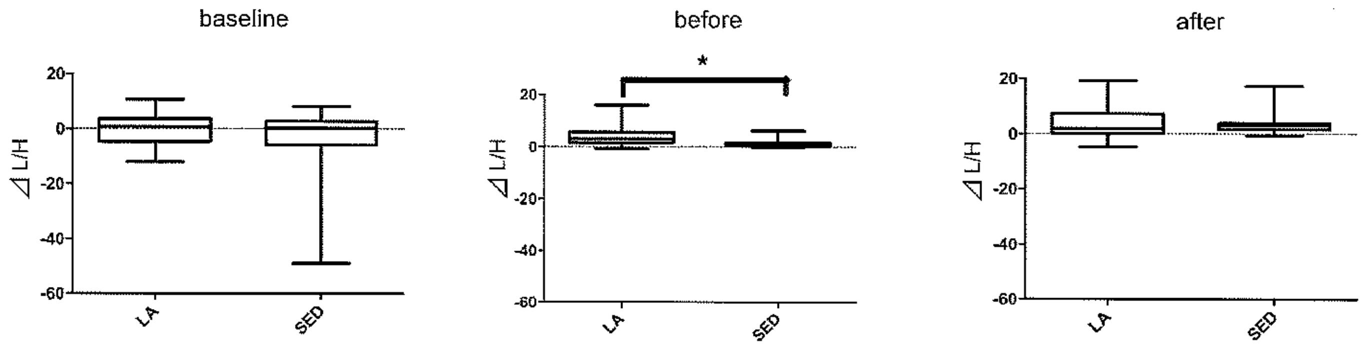

HF
800
600
400
200
0
ms2
LA
SED
L/H
60
40
20
0
LA
SED
CCVHF
3
2
1
0
%
LA
SED
CVRR
20
15
10
5
0
%
LA
SED

Fig. 4

ΔnormCCVHF（Parasympathetic function changes: Position 2B to Position 2A.)



ΔL/H（Sympathetic function changes: Position 2 A to Position 1.）



ΔCVRR（Amount of autonomic activity changes: Position 2A to Position 1.）

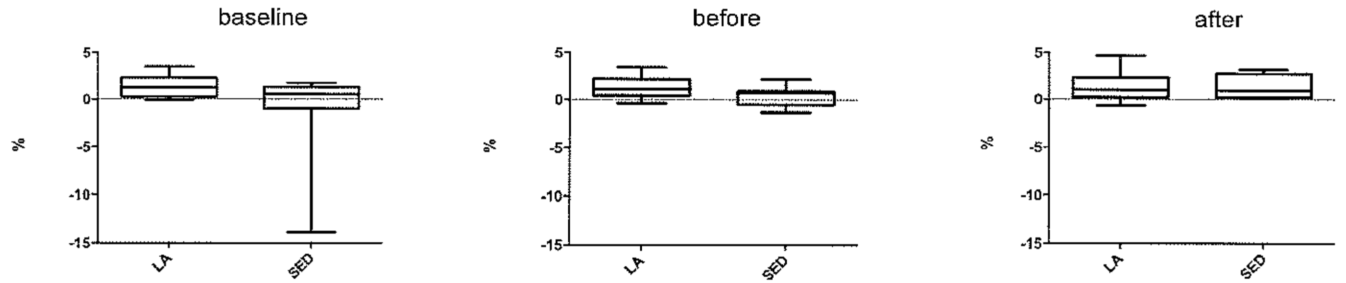


Fig. 5