Observational Study

The effects of perioperative oral management on perioperative serum albumin levels in patients treated surgically under general anesthesia

A multicenter retrospective analysis in Japan

Shin-ichi Yamada, DDS, PhD, Kazuyuki Koike, DDS, PhD, Emiko Tanaka Isomura, DDS, PhD, Daichi Chikazu, DDS, PhD, Kenji Yamagata, DDS, PhD, Masahiro Iikubo, DDS, PhD, Satoshi Hino, DDS, PhD, Hideharu Hibi, DDS, PhD, Koju Katsura, DDS, PhD, Seiji Nakamura, DDS, PhD, Takeshi Nomura, DDS, PhD, Yoshiyuki Mori, DDS, PhD, Itaru Tojyo, DDS, PhD, Nariyoshi Kanamura, DDS, PhD, Kyo Yamamori, DDS, PhD, Keiko Aota, DDS, PhD, Shigeyuki Fujita, DDS, PhD, Kenji Yamagata, DDS, PhD, Hideki Tanzawa, MD, DDS, PhD, Hiroshi Kurita, DDS, PhD, the Japanese Stomatological Society

Abstract

The purpose of the present study was to investigate the efficacy of perioperative oral managements (POMs) on perioperative nutritional conditions in patients undergoing surgery with general anesthesia. Medical records were retrospectively reviewed and the effects of POMs were investigated based on a large number of cases using a multicenter analysis. The profile of serum albumin levels was assessed and compared between patients with and without POMs using the multivariate analysis. Seventeen Eleven thousand and one hundred sixty patients (4,873 males and 6,287 females) were reviewed. Of these, 2710 patients (24.3%) had undergone POMs. The results of a multivariate analysis revealed the significant positive effect of POMs on perioperative serum albumin level (change between admission and discharge, (Estimate: 0.022, standard error: 0.012, P < .0001). Patient gender, age, surgical site, performance status, the American Society of Anesthesiologists (ASA) physical status classification, operation time, amount of blood loss, and serum albumin level at admission were also significant predictors. Adjusted multivariate analysis of the effects of POMs on perioperative change of serum albumin level in all subjects revealed the significance of POMs intervention (estimate: 0.022, standard error: 0.012, P < .0001). These results suggest that POMs exerts significant positive effects on perioperative serum albumin levels in patients underwent surgery under general anesthesia.

Abbreviations: ASA = American Society of Anesthesiologists, POMs = perioperative oral managements.

Keywords: oral care, perioperative oral management, serum albumin, surgery

Editor: Luis Rato.

This study was approved by the Committee on Medical Research of Shinshu University (No.3788).

Patient Consent was not required.

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

1 Department of Dentistry and Oral Surgery, Shinshu University School of Medicine, Matsumoto, 2 Department of Oral Science, Graduate School of Medicine, Chiba University, Chiba, 3 First Department of Oral and Maxillofacial Surgery, Osaka University, Graduate School of Dentistry, Suita, 4 Department of Oral and Maxillofacial Surgery, Faculty of Medicine, Tokyo Medical University, Shinjuku, 5 Department of Oral and Maxillofacial Surgery, Faculty of Medicine, University of Tsukuba, Tsukuba, 6 Perioperative Oral Care Support Center, Tohoku University Hospital, Sendai, 7 Department of Oral and Maxillofacial Surgery, Ehime University Graduate School of Medicine, Toon Japan, 8 Department of Oral and Maxillofacial Surgery, Nagoya University Graduate School of Medicine, Nagoya, 9 Department of Oral Radiology, Niigata University Medical and Dental Hospital, Niigata, 10 Section of Oral and Maxillofacial Oncology, Division of Maxillofacial Diagnostic and Surgical Sciences, Faculty of Dental Science, Kyushu University, Fukuoka, 11 Department of Oral Medicine, Oral and Maxillofacial Surgery, Tokyo Dental College, Chiba, 12 Department of Dentistry, Oral and Maxillofacial Surgery, Ichi Medical University, Shimotsuke, 13 Department of Oral and Maxillofacial Surgery, Wakayama Medical University, Wakayama, 14 Department of Dental University Hospital, Kyoto Prefectural University of Medicine, Graduate School of Medical Science, Kyoto, 15 Department of Dentistry and Oral Surgery, Yamagata University Hospital, Yamagata, 16 Department of Oral Medicine, Tokushima University Graduate School of Biomedical Sciences, Tokushima, Japan.

* Correspondence: Shigeyuki Fujita, Department of Oral and Maxillofacial Surgery, Wakayama Medical University, 811-1, Kidera, Wakayama, 641-8509, Japan (e-mail: fujitashigyek@gmail.com).

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Yamada S, Koike K, Isomura ET, Chikazu D, Yamagata K, Iikubo M, Hino S, Hibi H, Katsura K, Nakamura S, Nomura T, Mori Y, Tojyo I, Kanamura N, Aota K, Fujita S, Tanzawa H, Kurita H. The effects of perioperative oral management on perioperative serum albumin levels in patients treated surgically under general anesthesia: a multicenter retrospective analysis in Japan. Medicine 2021;100:10(e25119). Received: 8 October 2020 / Received in final form: 18 January 2021 / Accepted: 17 February 2021 http://dx.doi.org/10.1097/MD.0000000000025119
1. Introduction

Pre-operative oral care has been reported as an effective and easy method to prevent post-operative pneumonia in patients undergoing esophagectomy. \[1,2\] The Surgeon General’s report on oral health in America showed that oral functional management prevented general complications during the perioperative period.\[3\]

In Japan, perioperative oral management (POMs) was introduced by the national health insurance system in 2012 and patients scheduled for surgery for cancer, cardiovascular diseases, and organ transplantation receive dental and oral functional management during the perioperative period. POMs may have an impact on the prevention of dental-related local and systemic infections in patients compromised by intensive surgery. The positive effects of POMs on the prevention of postoperative pneumonia, which has been attributed to aspiration of oral/oropharyngeal pathogens, have been reported in some cancer patients. \[1,2,4–6\]

Serum albumin has a number of roles, such as in cell growth stabilization, DNA replication, the maintenance of sex hormone homeostasis, and modulation of systemic inflammation. \[7\]

Albumin has been reported to be involved in inflammatory/stress reactions. \[8\] According to a study on colorectal cancer patients, hypoalbuminemia was reported to reflect the conditions of malnutrition and immunosuppression, and increase the risk of increased disease severity, tumor progression, and a poor prognosis. \[8\]

Inflammatory cytokines have been reported to trigger apoptosis and decrease the production of albumin mRNA by the liver, resulting in reductions in its synthesis and increases in albumin catabolism, and vascular permeability. \[9,10\] An early decrease in postoperative serum albumin was identified as an independent risk factor associated with severe postoperative complications and a poor prognosis. \[11,12\] Although early decreases in postoperative serum albumin levels are important for predicting the prognosis of patients, there is currently no information available on patients who received POMs. It has also been reported as a reliable systemic marker of malnutrition. \[13\]

Malnutrition and inflammatory responses strongly correlate with severe postoperative complications. \[14\] Increased oral bacteria, dental infections, oral mucositis, masticatory disorders due to the teeth loss result in the decline of the oral function. \[15\] As a result, the decline of oral function affects on the nutrition condition in cancer patients. Although oral and dental conditions play important roles in nutrition, the effects of POMs on perioperative serum albumin levels have not yet been investigated except for 1 recent report. \[15\] In this report, perioperative POMs intervention might have positive effects on the postoperative prognostic nutrition index (PNI), which was calculated using serum albumin and the peripheral lymphocyte count, in the patients with digestive systems or urinary cancer. \[15,16\] Therefore, the purpose of the present study was to investigate the efficacy of POMs on perioperative serum albumin levels in patients treated surgically under general anesthesia based on a large number of cases using a multicenter retrospective analysis.

2. Patients and methods

The present study was conducted by the Japanese Stomatological Society. The study protocol was approved by the Committee on Medical Research of Shinshu University (#3788). We published our research plan with a guaranteed opt-out opportunity on the homepage of each hospital.

A total of 19,646 patients who were scheduled for surgery under general anesthesia between April 2016 and March 2017 at 16 university hospitals were enrolled in the present study. The medical records of these patients were retrospectively reviewed. The objective variable was an increase or decrease of perioperative serum albumin level (change between at admission and at discharge). Since this was a retrospective observational study and the surgical invasion was different, the serum albumin levels at discharge was investigated at the time from which the general condition became calm and home treatment was possible. Predictor variables were defined as patient factors (age, sex, smoking habits, diabetes mellitus, severe heart disease, severe pulmonary disease, Eastern Cooperative Oncology Group Performance Status, \[16\] treatment factors (risk of general anesthesia, surgical site, operation time, days of hospital stay after operation, and blood loss), and the presence and absence of POMs. Severe heart disease was defined as ≥ grade 3 of the New York Heart Association Classification. \[17\] Severe pulmonary disease was defined as <60% of % vital capacity or <50% of % Forced Expiratory Volume in One Second. The risk of general anesthesia was evaluated with the American Society of Anesthesiologists (ASA) physical status classification. \[18\] Surgical sites were divided into 11 groups: ophthalmic, oral and maxillofacial, thorax, musculoskeletal, limbs, and trunk, otorhinolaryngologic, cardiovascular, neuro and cranium, genital, urinary tract and adrenal, skin and subcutaneous tissue, and abdomen. Operation times were classified by every 3 hours and blood loss by every 300 ml.

POMs was generally initiated from the time the decision for hospitalization was made. POMs included oral health instructions, the removal of dental calculus (scaling), professional mechanical tooth cleaning, removal of the tongue coating with a toothbrush, cleaning dentures, extraction of teeth with severe periodontitis showing pain, pus discharge, mobility, or marked alveolar bone loss by an X-ray examination. Basically, removal of the oral infected lesion was completed preoperatively, and oral care before and after surgery was continuously intervened by dental hygienists.

The effects of POMs on the perioperative serum albumin profile was statistically investigated with Student t-test, Pearson correlation test, Steel-Dwass test, Spearman rank correlation, analysis of variance in univariate analysis. A multiple regression analysis was performed for multivariate analysis. Statistical analyses were performed using JMP ver.13 (SAS Institute Inc., North Carolina). P-values <.05 were considered to be significant.

3. Results

Among 19,646 patients, 8,486 were excluded because of the lack of important data (serum albumin level at discharge) or any abnormal values such as outlier; therefore, 11,160 (4,873 males and 6,287 females) were ultimately examined in the present study. The median age was 57.8 ± 20.8 years. According to Eastern Cooperative Oncology Group Performance Status classification, \[16\] class 2 was noted in 6,395 patients (55.3%), 1 in 2,553 (22.9%), 2 in 1,054 (9.4%), 3 in 493 (4.4%), and 4 in 266 (2.4%). Regarding the ASA physical status classification, \[18\] class 2 was noted in 6,395 patients (57.3%), 1 in 2,182 (19.6%), 3 in 1,877 (16.8%), 4 in 199 (1.8%), 5 in 7 (0.06%), and 6 in 2 (0.02%). Mean serum albumin levels at admission and discharge were 4.02 ± 0.58 and 3.51 ± 0.55 g/dl, respectively. A total of 2,710 patients (24.3%) received
POMs. Median value of hospital days after the operation was 12 days (interquartile range: 8 – 22 days).

The results of univariate analyses were also summarized in Table 1. Change of serum albumin level significantly correlated with gender, age, presence of diabetes mellitus, smoking habit, surgical site, preoperative serum albumin level, operation time, blood loss, and days of hospitalization after the surgery. Decrease of serum albumin level was higher in those with female, older age, stop or never smoker, diabetes mellitus, higher preoperative albumin level, longer operation time, higher amount of blood loss, and longer hospital days. Performance status, ASA classification, and intervention of POMs showed no significant correlation with change of serum albumin level.

The results of a multivariate analysis of the effects of POMs on perioperative serum albumin levels in all subjects were summarized in Table 2. The results obtained revealed a positive impact with the intervention of POMs (estimate: 0.019, 95% confidence interval: 0.033 – 0.026, P < .05). A negative correlation was noted with other variables (gender, age, performance status, ASA classification, and preoperative serum albumin levels). The effects of POMs on perioperative serum albumin levels differed according to the surgical site. The effects of POMs on perioperative serum albumin levels investigated with adjusted multivariate analysis were summarized in Table 3. The intervention of POMs was a significant positive effect on perioperative serum albumin levels (estimate: 0.022, 95% confidence interval: .033 – 0.033, standard error: 0.012, P < .0001).

4. Discussion
To the best of our knowledge, this is the first study to demonstrate the positive effects of POMs on perioperative serum albumin levels in patients treated surgically under general anesthesia. In 2012, POMs was included in the national health insurance system in Japan and has since been widely performed on patients scheduled for cancer treatments, organ transplantation, cardiovascular surgery, and orthopedic implant surgery. Since professional oral care decreased the number of bacteria in the oropharynx, resulting in the prevention of aspiration pneumonia,[20] the efficacy of POMs at reducing the prevalence of postoperative pneumonia was demonstrated in Japanese patients with esophageal and lung cancers.[1,2,4,6,21] In a literature review on the effects of POMs in Japanese cancer patients,[2,4–6,21–30] various effects of POMs were reported, including reductions in the number of bacteria and bacterial species detected with an endotracheal bacteriological examination,[22] shorter postoperative hospitalization and fasting periods,[23] and reductions in the prevalence of surgical site infections (Table 4).[30] In recent retrospective study based on large number of Japanese cancer patients, the pre-treatment and completion of POMs were reported to reduce the risk of oral complications significantly.[31]
Table 1
The characteristics of patients and results of univariate analysis.

| Variables                                | No. of patients, Median, or Mean ± SD | Change of (postoperation - preoperation) serum albumin level (Mean ± SE mg/dL) or Correlation coefficient | Result of univariate analysis |
|------------------------------------------|--------------------------------------|-----------------------------------------------------------------------------------------------------|------------------------------|
| Gender                                   |                                       |                                                                                                     |                              |
| Male                                     | 4873                                 | - 0.422 ± 0.009                                                                                     | P < .05 (Student t-test)     |
| Female                                   | 6287                                 | - 0.525 ± 0.010                                                                                     |                              |
| Age                                      |                                       | r = - 0.103                                                                                         | P < .01 (Pearson correlation test) |
| Mean ± SD                                | 57.8 ± 20.8                          |                                                                                                     |                              |
| Diabetes mellitus                        |                                       |                                                                                                     |                              |
| No                                       | 9562                                 | - 0.458 ± 0.007                                                                                     | P < .01 (Student t-test)     |
| Yes                                      | 1698                                 | - 0.520 ± 0.018                                                                                     |                              |
| Smoking                                  |                                       |                                                                                                     | P < .01 (Steel-Dwass test)   |
| Never                                    | 7315                                 | - 0.493 ± 0.631                                                                                     |                              |
| Stop smoking                             | 2712                                 | - 0.523 ± 0.628                                                                                     |                              |
| Continuing                               | 1113                                 | - 0.164 ± 1.196                                                                                     |                              |
| Performance status                       |                                       |                                                                                                     |                              |
| score 0                                  | 6169                                 | - 0.483 ± 0.656                                                                                     |                              |
| score 1                                  | 2553                                 | - 0.523 ± 0.561                                                                                     |                              |
| score 2                                  | 1054                                 | - 0.525 ± 0.641                                                                                     |                              |
| score 3                                  | 493                                  | - 0.434 ± 0.623                                                                                     |                              |
| score 4                                  | 266                                  | - 0.540 ± 0.745                                                                                     |                              |
| Unknown                                  | 625                                  |                                                                                                     |                              |
| Sever heart disease                      |                                       |                                                                                                     |                              |
| No (NYHA<3)                              | 10,104                               | - 0.500 ± 0.006                                                                                     |                              |
| Yes (NYHA≥3)                             | 566                                  | - 0.457 ± 0.027                                                                                     |                              |
| Unknown                                  | 490                                  |                                                                                                     |                              |
| Sever pulmonary disease*                 |                                       |                                                                                                     |                              |
| No                                       | 6081                                 | - 0.440 ± 0.010                                                                                     |                              |
| Yes                                      | 286                                  | - 0.406 ± 0.048                                                                                     |                              |
| Unknown                                  | 3893                                 |                                                                                                     |                              |
| ASA physical status classification       |                                       |                                                                                                     |                              |
| class 1                                  | 2182                                 | - 0.454 ± 0.599                                                                                     |                              |
| class 2                                  | 6395                                 | - 0.523 ± 0.627                                                                                     |                              |
| class 3                                  | 1977                                 | - 0.472 ± 0.676                                                                                     |                              |
| class 4                                  | 199                                  | - 0.403 ± 0.742                                                                                     |                              |
| class 5                                  | 7                                    | - 0.757 ± 0.707                                                                                     |                              |
| class 6                                  | 2                                    | - 0.000 ± 1.556                                                                                     |                              |
| Unknown                                  | 498                                  |                                                                                                     |                              |
| Surgical site                            |                                       |                                                                                                     |                              |
| Ophthalmic                               | 203                                  | - 0.019 ± 0.050                                                                                     | P < .01 (ANOVA)              |
| Oral and Maxillofacial                   | 576                                  | - 0.336 ± 0.029                                                                                     |                              |
| Thorax                                   | 1429                                 | - 0.541 ± 0.019                                                                                     |                              |
| Musculoskeletal, limbs, and trunk        | 1273                                 | - 0.439 ± 0.020                                                                                     |                              |
| Otolaryngologic                          | 584                                  | - 0.406 ± 0.029                                                                                     |                              |
| Cardiovascular                           | 1713                                 | - 0.407 ± 0.017                                                                                     |                              |
| Neuro and cranium                        | 680                                  | - 0.498 ± 0.027                                                                                     |                              |
| Urinary tract and adrenal                | 693                                  | - 0.519 ± 0.027                                                                                     |                              |
| Abdomen                                  | 2381                                 | - 0.459 ± 0.015                                                                                     |                              |
| Skin or subcutaneous tissue              | 288                                  | - 0.261 ± 0.042                                                                                     |                              |
| Genital                                  | 1332                                 | - 0.658 ± 0.019                                                                                     |                              |
| Others                                   | 8                                    |                                                                                                     |                              |
| Preoperative serum albumin               |                                       |                                                                                                     |                              |
| Mean ± SD                                | 4.02 ± 0.58                          | r = - 0.548                                                                                         | P < .01 (Pearson correlation test) |
| Operation time                           |                                       |                                                                                                     |                              |
| Median (IQR) (min)                       | 258 (182–363)                        | r = - 0.085                                                                                         | P < .01 (Spearman rank correlation) |
| Blood loss                               |                                       |                                                                                                     |                              |
| Median (IQR) (mL)                        | 100 (10–415)                         | r = 0.603                                                                                           |                              |
| Intervention of POMs                     |                                       |                                                                                                     | NS (student t-test)          |
| No                                       | 8450                                 | - 0.468 ± 0.008                                                                                     |                              |
| Yes                                      | 2710                                 | - 0.462 ± 0.014                                                                                     |                              |
| Days of hospital stay after operation    |                                       |                                                                                                     |                              |
| Median (IQR) (days)                      | 12 (8–22)                            | r = 0.056                                                                                           | P < .01 (ANOVA)              |
| Difference of hospital                   |                                       |                                                                                                     |                              |

(continued)
A multivariate analysis of the effects of POMs on perioperative change of serum albumin level in all subjects.

| Variables | Estimate | 95% CI | P value (Prob > | Variance Inflation Factor |
|-----------|----------|--------|----------------|--------------------------|
| Gender (female/male) | -0.040 | -0.027 | -0.061 | < .01 | 1.27 |
| Age (years) | -0.006 | -0.005 | -0.136 | < .01 | 1.20 |
| Diabetes mellitus (presence/absence) | -0.012 | 0.003 | -0.015 | .114 | 1.07 |
| Smoking | | | | | |
| Continuing/stop smoking | -0.005 | 0.026 | -0.004 | .765 | 2.42 |
| Performance status | -0.022 | -0.009 | -0.037 | < .01 | 1.52 |
| Severe pulmonary disease (yes/no) | -0.014 | 0.013 | -0.010 | .316 | 1.25 |
| Severe heart disease (yes/no) | -0.022 | 0.011 | -0.012 | .190 | 1.04 |
| ASA physical status classification | -0.022 | 0.050 | < 0.007 | < .01 | 1.45 |
| Surgical site (vs Abdomen) | | | | | |
| Otorhinolaryngologic | 0.102 | 0.394 | 0.067 | .496 | 116.40 |
| Thorax | -0.026 | 0.134 | 0.029 | 0.464 | 18.38 |
| Musculoskeletal, limbs, and trunk | -0.053 | 0.039 | -0.046 | .260 | 20.14 |
| Oropharyngologic | 0.027 | 0.129 | 0.020 | .612 | 18.41 |
| Cardiovascular | -0.113 | 0.026 | -0.113 | < .05 | 24.11 |
| Neuro and cranial | -0.019 | -0.075 | -0.016 | .688 | 19.40 |
| Genital | -0.213 | -0.122 | -0.180 | < .01 | 20.68 |
| Urinary tract and adrenal | -0.145 | -0.047 | -0.112 | < .01 | 17.82 |
| Skin or subcutaneous tissue | -0.046 | 0.064 | -0.033 | .410 | 19.39 |
| Others | 0.813 | 1.688 | 0.534 | .069 | 1034.65 |
| Preoperative serum albumin (mg/dL) | -0.730 | -0.710 | -0.710 | < .01 | 1.18 |
| Operation time (minutes) | 0.000 | 0.000 | -0.039 | < .01 | 1.20 |
| Blood loss (mL) | 0.000 | 0.000 | -0.059 | < .01 | 1.34 |
| Intervention of POMs (presence/absence) | 0.019 | 0.033 | 0.026 | < .05 | 1.28 |
| Days of hospital stay after operation (days) | 0.000 | 0.000 | -0.016 | .114 | 1.22 |
| Difference of hospital (vs M & N) | -0.083 | -0.044 | -0.060 | < .01 | 3.13 |
| A | 0.022 | 0.133 | 0.011 | .702 | 9.54 |
| B | 0.046 | 0.221 | 0.022 | .610 | 22.00 |
| C | 0.006 | 0.036 | -0.005 | .770 | 3.24 |
| D | 0.094 | 0.138 | 0.069 | < .01 | 3.24 |
| E | 0.043 | 0.081 | 0.037 | < .05 | 3.26 |
| F | -0.112 | -0.067 | -0.081 | < .01 | 3.17 |
| G | -0.044 | 0.003 | -0.028 | .067 | 3.10 |
| H | -0.036 | 0.012 | -0.024 | .139 | 3.15 |
| J | -0.156 | -0.091 | -0.091 | < .01 | 4.57 |
| K | 0.128 | 0.290 | 0.083 | < .05 | 9.71 |
| L | 0.068 | 0.295 | 0.032 | .555 | 35.91 |

95% CI = 95% confidence interval, POMs = perioperative oral managements.
However, since difficulties are associated with conducting a prospective randomized controlled trial to investigate the efficacy of POMs in cancer patients, its efficacy based on a high evidence level has not yet been demonstrated.\textsuperscript{12}

In a recent report investigated the correlation between POMs and PNI score in cancer patients, patients who received POMs showed significantly higher PNI scores from the early postoperative period, compared to those not receiving POMs.\textsuperscript{13} Additionally, among patients who could resume oral intake within postoperative 3 days, those who received POMs intervention showed significantly higher PNI scores from the early postoperative period, compared to patients without POMs.\textsuperscript{13} Although these results might suggest the favorable effects of POMs on perioperative nutrition status in cancer patients, there was limitations such as a retrospective study based on relatively small number of cases at single institute. Therefore, in the present study, to obtain new evidence to support POMs for patients treated surgically under general anesthesia, perioperative serum albumin levels were examined in a large number of cases in a multicenter study. However, although, in multivariate analysis, POMs was associated with changes in perioperative serum albumin levels significantly, in a univariate analysis, POMs was not related to perioperative changes in serum albumin levels. This might be related to low intervention rate of POMs and variety of intervention rates at each institute. The differences of operation time, amount of blood loss, and risk of general anesthesia might also effect on results with low intervention rate of POMs.

In the present study, POMs appeared to exert positive effects on perioperative serum albumin levels. In a previous study, the number of decayed teeth was reported to be a significant factor for lower albumin levels,\textsuperscript{33} and mean clinical attachment loss was also identified as a significant factor for lower albumin levels.

### Table 3

| Variables                      | Estimate | 95% CI  | Standard ß | P value (Prob>|t|) | Variance Inflation Factor |
|--------------------------------|----------|---------|------------|----------------|--------------------------|
| Gender (Female vs Male)        | -0.038   | -0.029  | -0.026     | <.0001         | 1.018                     |
| Age (yr)                       | -0.009   | -0.008  | -0.009     | <.0001         | 1.200                     |
| Performance status             | -0.022   | -0.013  | -0.037     | <.0001         | 1.084                     |
| ASA classification\textsuperscript{a} | -0.066   | -0.052  | -0.077     | <.0001         | 1.254                     |
| Serum albumin level at admission (g/dL) | -0.673   | -0.657  | -0.669     | <.0001         | 1.153                     |
| Operation time (minutes)       | -0.00015 | 0.000   | -0.059     | <.0001         | 1.100                     |
| Blood loss (mL)                | -0.00001 | 0.000   | -0.027     | 0.0005         | 1.102                     |
| Intervention of POMs (Yes vs No) | 0.022     | 0.033   | 0.033      | <.0001         | 1.057                     |

\textsuperscript{a}95% CI = 95% confidence interval, POMs = perioperative oral managements.

\textsuperscript{b}The American Society of Anesthesiologists (ASA) physical status classification.

### Table 4

| Author (Year)          | Cancer site  | Number of Patients | Effects of the POMs                                      |
|------------------------|--------------|--------------------|----------------------------------------------------------|
| Kataoka T, et al (2008) | Oral cavity  | 112                | Reduction of prevalence of postoperative pneumonia       |
| Uejima S, et al (2009)  | Esophagus    | 51                 | Reduction of the number of bacterium and bacterial species detected with the endotracheal bacteriological examination and shortening of postoperative SIRS period |
| Akutsu Y, et al (2010)  | Esophagus    | 86                 | Reduction of prevalence of postoperative pneumonia       |
| Hiramatsu T, et al (2014) | Esophagus    | 240                | Reduction of prevalence of postoperative pneumonia       |
| Tocawa S, et al (2015)  | Digestive system | 464             | Shortening of postoperative hospitalization days and postoperative fasting period (especially in stomach, small intestine, and large bowel) |
| Uruno, et al (2015)     | Oral cavity  | 100                | Shortening of postoperative hospitalization days, antibiotics administration period and postoperative fasting period |
| Yamamura Y, et al (2016) | Lung        | 27                 | Reduction of prevalence of postoperative pneumonia and fever of ≥38°C, and shortening of postoperative hospitalization days |
| Aizawa H, et al (2016)   | Liver        | 80                 | Shortening of postoperative hospitalization days, antibiotics administration period and postoperative fasting period |
| Soutome S, et al (2016)  | Esophagus    | 383                | Reduction of prevalence of postoperative pneumonia and intervention of POMs as risk factor for postoperative pneumonia |
| Nishino T, et al (2017)  | Lung         | 264                | Reduction of prevalence of postoperative pneumonia, Shortening of postoperative hospitalization days, and lower postoperative CRP level |
| Soutome, et al (2017)    | Esophagus    | 539                | Reduction of prevalence of postoperative pneumonia and intervention of POMs as risk factor for postoperative pneumonia |
| Kajihara R, et al (2018) | Lung         | 480                | Reduction of prevalence of postoperative pneumonia and intervention of POMs as risk factor for postoperative pneumonia |
| Iwata E, et al (2019)    | Lung         | 721                | Reduction of prevalence of postoperative pneumonia and intervention of POMs as risk factor for postoperative pneumonia |
| Nobuhara H, et al (2019) | Large bowel | 698                | Reduction of prevalence of SSI, shortening of postoperative hospitalization days, and intervention of POMs as risk factor for postoperative pneumonia |

\textsuperscript{CRP} = C-reactive protein, POMs = perioperative oral managements, SIRS = systemic inflammatory response syndrome, SSI = surgical site infection.
in the elderly. Furthermore, a close relationship has been reported between periodontitis and lower serum albumin levels. Periodontal treatment had a positive influence on masticatory performance after conservative treatment. Additionally, tooth loss may be a predictor for low energy and protein intake as well as serum albumin levels. On the other hand, since serum albumin levels have been reported to significantly increase among individuals using partial dentures prosthodontic treatments may be of clinical significance for improving serum albumin levels. Therefore, the present results suggested that POMs, including oral care, the removal of chronic dental infections, and prosthodontic treatments, exerted positive effects on perioperative serum albumin levels by inhibiting decreases in early postoperative serum albumin levels in patients treated surgically under general anesthesia.

The strength of the present study is that it is the first to clarify the positive efficacy of POMs on perioperative serum albumin levels in patients treated surgically under general anesthesia based on a large number of cases. The limitation of the present study is the differences observed in POMs criteria and treatment protocols at each institute because of its retrospective nature. Additionally, the intervention rate of POMs was low at 24.3% in the present study. The reason for the low intervention rate of POMs was probably due to the lack of coordination between doctors and dentists, the treatment schedule, and patient awareness of significance of POMs. However, difficulties are associated with ethically conducting a prospective randomized control study to evaluate the efficacy of POM because POMs has been covered by the Japanese national health insurance system since 2012, and most Japanese patients now receive POMs before cancer treatments. The protocol and intention of dental interventions for patients remain controversial. The establishment of guidelines for POMs in patients scheduled for surgery is needed for the standardization of dental interventions. Additionally, although periodontal conditions might affect on perioperative serum albumin levels, effects of periodontal conditions were uncertain, due to low intervention rate of POMs and large population based study.

In conclusion, the intervention ratio of POM was 24.3%. In the multivariate analysis, perioperative serum albumin levels positively correlated with POMs. Therefore, the POMs may prevent reductions in postoperative serum albumin levels and contribute to patients treated with surgery under general anesthesia. The POMs may play a possible role in reducing the side effects of preoperative malnutrition.

Acknowledgments
We wish to thank Medical English Service (https://www.med-english.com/) for English proofreading of this manuscript. This study was supported by the Japanese Stomatological Society.

Author contributions
Conception and design of the study: Kurita H, Tanzawa H, Fujita S
Analysis and interpretation of data: Kurita H
Collection and assembly of data: Yamada S, Koike K, Isomura E, Chikazu D, Yamagata K, Ikukhu M, Hino S, Hibi H, Katsura K, Nakamura S, Nomura T, Mori Y, Tojyo I, Kanamura N, Yamamori I, Aota, K Fujita S

Drafting of the article: Yamada S
Critical revision of the article for important intellectual content: Yamada S
Final approval of the article: Kurita H

Conceptualization: Shigeyuki Fujita, Hideki Tanzawa, Hiroshi Kurita.

Data curation: Kazuyuki Koike, Emiko Tanaka Isomura, Daichi Chikazu, Kenji Yamagata, Masahiro Ikukhu, Satoshi Hino, Hideharu Hibi, Kouji Katsura, Seiji Nakamura, Takeshi Nomura, Yoshiyuki Mori, Itaru Tojyo, Narisato Kanamura, Ikuko Yamamori, Keiko Aota, Shigeyuki Fujita, Hideki Tanzawa.

Investigation: Shin-ichi Yamada, Hiroshi Kurita.

Writing – original draft: Shin-ichi Yamada.

Writing – review & editing: Shin-ichi Yamada, Hiroshi Kurita.

References
[1] Soutome S, Yanamoto S, Funahara M, et al. Preventive effect on post-opera-tive pneumonia of oral health care among patients who undergo esophageal resection: a multi-center retrospective study. Surg Infect (Larchmt) 2016;17:479–84.
[2] Soutome S, Yanamoto S, Funahara M, et al. Effect of perioperative oral care on prevention of postoperative pneumonia associated with esophageal cancer surgery: a multicenter case-control study with propensity score matching analysis. Medicine (Baltimore) 2017;96:e7436.
[3] Grass J. Oral health policy development since the Surgeon General’s Report on Oral Health. Acad Pediatr 2009;9:476–82.
[4] Akutsu Y, Matsubara H, Okazumi S, et al. Impact of preoperative dental plaque culture for predicting postoperative pneumonia in esophageal cancer patients. Dig Surg 2008;25:9–7.
[5] Hiramatsu T, Sugiyama M, Kowabara S, et al. Effectiveness of an outpatient preoperative care bundle in preventing postoperative pneumonia among esophageal cancer patients. Am J Infect Control 2014;42:385–8.
[6] Iwata E, Hasegawa T, Yamada S, et al. Effects of perioperative oral care on prevention of postoperative pneumonia after lung resection: Multicenter retrospective study with propensity score matching analysis. Surgery 2019;165:1003–7.
[7] Gupta D, Lis CG. Pretreatment serum albumin as a predictor of cancer survival: a systematic review of the epidemiological literature. Nutr J 2016;9.
[8] Nazha B, Moussaly E, Zaarour M, et al. Hypoalbuminemia in colorectal cancer prognosis: nutritional marker or inflammatory surrogate? World J Gastrointest Surg 2015;7:370–7.
[9] Jensen GL. Inflammation as the key interface of the medical and nutrition universes: a provocative examination of the future of clinical nutrition and medicine. JPN J Parenter Enteral Nutr 2006;30:453–63.
[10] Friedman AN, Fadem SZ. Reassessment of albumin as a nutritional marker in kidney disease. J Am Soc Nephrol 2010;21:223–30.
[11] Wang Y, Wang H, Jiang J, et al. Early decrease in postoperative serum albumin predicts severe complications in patients with colorectal cancer after curative laparoscopic surgery. World J Surg Oncol 2018;16:192.
[12] Tang Y, Liu Z, Liang J, et al. Early post-operative serum albumin level predicts survival after curative nephrectomy for kidney cancer: a retrospective study. BMC Urol 2018;18:111.
[13] Fouque D, Pelletier S, Mafra D, et al. Nutrition and chronic kidney disease. Kidney Int 2011;80:348–57.
[14] Mohri Y, Inoue Y, Tanaka K, et al. Prognostic nutritional index predicts postoperative outcome in colorectal cancer. World J Surg 2013;37:2688–92.
[15] Otagiri H, Yamada S, Hashidume M, et al. A clinical investigation of the association between perioperative oral management and prognostic nutritional index in digestive and urinary cancer patients. Curr Oncol 2019;26:92.
[16] Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. Jpn J Gastroenterol 1984;85:1001–5.
[17] Oken MM, Creech RH, Torney DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982;5:649–55.
[18] Fisher JD. New York Heart Association Classification. Arch Intern Med 1972;129:836.
[19] American Society of Anesthesiologists. ASA Physical Status Classification System (original approval: October 15, 2014). URL: Available at: https://www.asahq.org/standards-and-guidelines/asa-physical-status-classification-system April 26, 2020 accessed
[20] Ishikawa A, Yoneyama T, Hirota K, et al. Professional oral health care reduces the number of oropharyngeal bacteria. J Dent Res 2008;87:594–8.
[21] Ishikawa A, Yoneyama T, Hirota K, et al. Prophylactic effect of oral health care of postoperative pneumonia after oral cancer surgery. Jpn J Oral Diag 2008;21:1–6.
[22] Uejima S, Sakai K, Naganawa Y, et al. Efficacy of professional oral care for the patients who underwent esophagectomy. J Jpn Soc Surg Infect 2009;6:183–8.
[23] Uejima S, Nishimaki F, Kamijou R, et al. A retrospective clinical study on the effect of perioperative oral management for patients who underwent gastrointestinal cancer surgery. J J M C P 2015;24:214–23.
[24] Uruno H, Nakashima D, Kasamatsu T, et al. Evaluation of the effectiveness of perioperative oral care in patients with oral cancer. Oral Sci Jpn 2015;93–6.
[25] Yamamura Y, Takizawa H, Matsumoto F, et al. Effects of perioperative oral management in thoracoscopic lung lobectomy: retrospective study. Oral Care 2016;1:106–10.
[26] Azawa H, Shimane T, Uehara S, et al. Clinical study on the effect of the perioperative oral management in surgical patients of liver cancer. Oral Care 2016;11:43–7.
[27] Soutome S, Funahara M, Oho T, et al. The effect of perioperative oral management on prevention of postoperative pneumonia in patients undergoing esophageal resection: —Analysis by a multicenter, retrospective study—. J Jpn Stomatol Soc 2016;65:324–9.
[28] Nishino T, Takizawa H, Sawada T, et al. Perioperative oral management can prevent postoperative pneumonia after lung cancer surgery. Jpn J Chest Surg 2017;31:432–8.
[29] Kajihara R, Yamada S, Nishimaki F, et al. A retrospective study of the efficacy of perioperative oral management on prevention of postoperative pneumonia associated with lung cancer surgery. Shinshu Med J 2018;66:249–56.
[30] Nobuhara H, Yamamoto S, Funahara M, et al. Effect of perioperative oral management on the prevention of surgical site infection after colorectal cancer surgery: a multicenter retrospective analysis of 698 patients via analysis of covariance using propensity score. Medicine (Baltimore) 2018;97:e12545.
[31] Yamada S, Soutome S, Hasegawa T, et al. A multicenter retrospective investigation on the efficacy of perioperative oral management in cancer patients. Medicine (Baltimore) 2020;99:e19129.
[32] Hong CH, Napeñas JJ, Hodgson BD, et al. A systematic review of dental disease in patients undergoing cancer therapy. Support Care Cancer 2010;18:1007–21.
[33] Yoshihara A, Hanada N, Miyazaki H. Association between serum albumin and root caries in community-dwelling older adults. J Dent Res 2003;82:218–22.
[34] Ogawa H, Yoshihara A, Amarasena N, et al. Association between serum albumin and periodontal disease in community-dwelling elderly. J Clin Periodontol 2006;33:312–6.
[35] Maruyama T, Yamanaka R, Yokoi A, et al. Relationship between serum albumin concentration and periodontal condition in patients with head and neck cancer. J Periodontol 2012;83:1110–5.
[36] Kaur N, Kaur N, Sarangal V. A study to evaluate the correlation of serum albumin levels with chronic periodontitis. Indian J Dent Res 2015;26:11–4.
[37] Terashima T, Chubachi S, Matsuzaki T, et al. The association between dental health and nutritional status in chronic obstructive pulmonary disease. Chron Respir Dis 2017;14:334–41.
[38] Pereira LJ, Gazolla CM, Magalhães IB, et al. Influence of periodontal treatment on objective measurement of masticatory performance. J Oral Sci 2012;54:151–7.
[39] Ioannidou E, Swede H, Fares G, et al. Tooth loss strongly associates with malnutrition in chronic kidney disease. J Periodontol 2014;85:899–907.
[40] Kanehisa Y, Yoshihara M, Taj T, et al. Body weight and serum albumin change after prosthodontic treatment among institutionalized elderly in a long-term care geriatric hospital. Community Dent Oral Epidemiol 2009;37:534–8.