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

A multicenter retrospective analysis in Japan

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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 at 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 reveled 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

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Patient Consent was not required.

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

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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 managements (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 the 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,[17] 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 $\geq$ grade 3 of the New York Heart Association Classification.[18] 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.[19] 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 (Fig. 1). Patient characteristics are summarized in Table 1. Mean age was 57.8 ± 20.8 years. According to Eastern Cooperative Oncology Group Performance Status, score 0 was present in 6,169 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,[19] 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

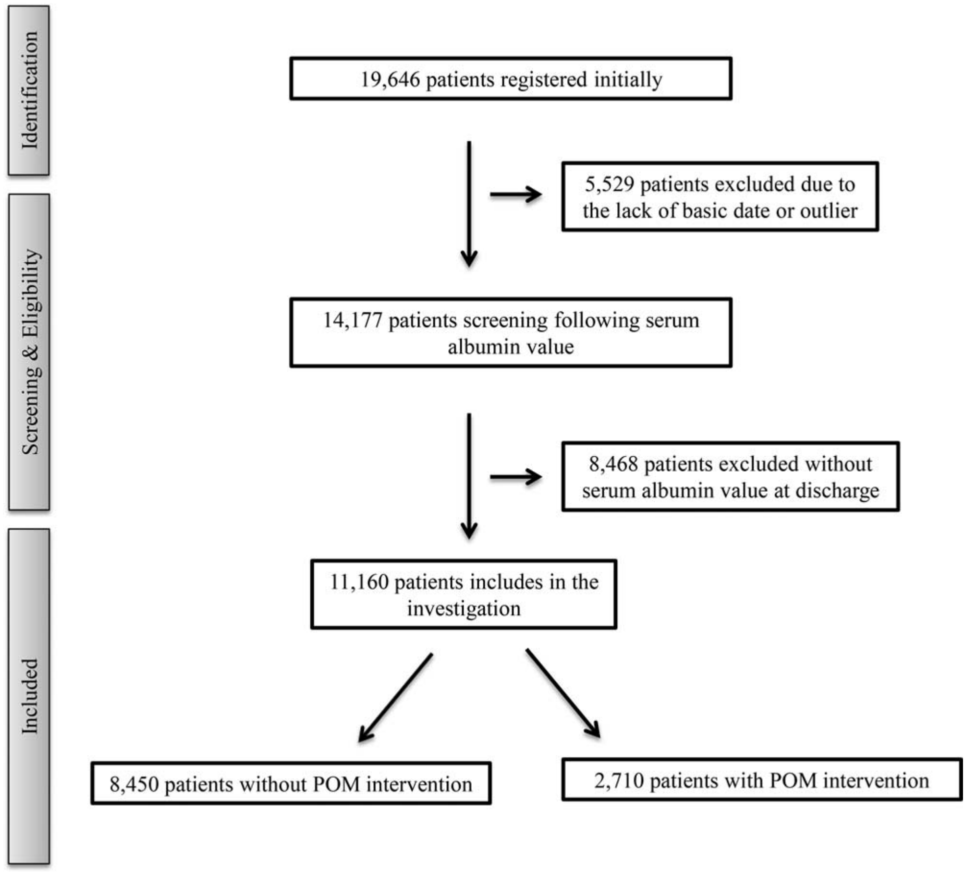

Figure 1. Flow-chart of the investigation. POMs = perioperative oral managements.

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 effector 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			*P* < .05 (Student *t*-test)
Male	4873	− 0.422 ± 0.009	
Female	6287	− 0.525 ± 0.010	
Age			*P* < .01 (Pearson correlation test)
Mean ± SD	57.8 ± 20.8	r = − 0.103	
Diabetes mellitus			*P* < .01 (Student t-test)
No	9562	− 0.458 ± 0.007	
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		NS (Spearman rank correlation)	
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		NS (student t-test)	
No (NYHA < 3)	10,104	− 0.500 ± 0.006	
Yes (NYHA ≥ 3)	566	− 0.457 ± 0.027	
Unknown	490		
Sever pulmonary disease*		NS (student t-test)	
No	6981	− 0.440 ± 0.010	
Yes	286	− 0.406 ± 0.048	
Unknown	3893		
ASA physical status classification		NS (p = 0.057) (Spearmans rank correlation)	
class 1	2182	− 0.454 ± 0.599	
class 2	6395	− 0.523 ± 0.627	
class 3	1877	− 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			*P* < .01 (ANOVA)
Ophthalmic	203	−0.019 ± 0.050	
Oral and Maxillofacial	576	− 0.336 ± 0.029	
Thorax	1429	− 0.541 ± 0.019	
Musculoskeletal, limbs, and trunk	1273	− 0.439 ± 0.020	
Otorhinolaryngologic	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			*P* < .01 (Pearson correlation test)
Mean ± SD (g/dl)	4.02 ± 0.58	r = − 0.548	
Operation time			*P* < .01 (Spearman rank correlation)
Median (IQR) (min)	258 (182–363)	r = −0.085	
Blood loss			*P* < .01 (Spearman rank correlation)
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		p < 0.01 (Spearman rank correlation)	
Median (IQR) (days)	12 (8–22)	r = 0.056	
Difference of hospital			*P* < .01 (ANOVA)

(*continued*)

Table 1

(continued).

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
A	571	− 0.571 ± 0.029	
B	3911	− 0.515 ± 0.011	
C	25	− 0.348 ± 0.139	
D	923	− 0.598 ± 0.023	
E	883	− 0.366 ± 0.023	
F	1357	− 0.512 ± 0.019	
G	762	− 0.523 ± 0.025	
H	611	− 0.312 ± 0.028	
I	532	− 0.430 ± 0.030	
J	311	− 0.656 ± 0.039	
K	122	− 0.139 ± 0.063	
L	22	− 0.255 ± 0.148	
M	474	0.217 ± 0.032	
N	656	− 0.535 ± 0.027	

ANOVA = analysis of variance, NS = not significant.
No (%vital capacity ≥60% or FEV1.0% ≥50%) NS = not significant.
Yes (%vital capacity <60% or FEV1.0% <50%).
* severe pulmonary disease .

Table 2

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>|t|)	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					.600	
Continuing/stop smoking	−0.005	0.026	–	−0.004	.765	2.42
Never/stop smoking	0.009	0.030	–	0.013	.380	2.72
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	−0.072	−0.050	–	−0.077	<.0001	1.65
Surgical site (vs Abdomen)					< 0.01	
Ophthalmic	0.102	0.394	–	0.067	.496	116.40
Oral and Maxillofacial	0.037	0.134	–	0.029	.464	18.38
Thorax	−0.206	−0.115	–	−0.191	< .01	22.31
Musculoskeletal, limbs, and trunk	−0.053	0.039	–	−0.046	.260	20.14
Otorhinolaryngologic	0.027	0.129	–	0.020	.612	18.41
Cardiovascular	−0.113	−0.026	–	−0.113	<.05	24.11
Neuro and cranium	−0.019	0.075	–	−0.016	.688	19.40
Genital	−0.213	−0.122	–	−0.190	<.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 (g/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	0.001	–	0.016	.114	1.22
Difference of hospital (vs M & N)					<.01	
A	−0.093	−0.044	–	−0.060	<.01	3.13
B	0.022	0.133	–	0.011	.702	9.54
C	0.046	0.221	–	0.022	.610	22.00
D	−0.006	0.036	–	−0.005	.770	3.24
E	0.094	0.138	–	0.069	< .01	3.24
F	0.043	0.081	–	0.037	<.05	3.26
G	−0.112	−0.067	–	−0.081	<.01	3.17
H	−0.044	0.003	–	−0.029	.067	3.10
I	−0.036	0.012	–	−0.024	.139	3.15
J	−0.156	−0.091	–	−0.091	<.01	4.57
K	0.128	0.240	–	0.063	<.05	9.71
L	0.068	0.295	–	0.032	.555	35.91

95% CI = 95% confidence interval, POMs = perioperative oral managements.

Table 3

Final results of adjusted multivariate analysis of the effects of POMs on perioperative change of serum albumin level in all subjects.

Variables	Estimate	95% CI			Standard ß	*P* value (Prob>|t|)	Variance Inflation Factor
Gender (Female vs Male)	−0.038	−0.029	–	−0.064	−0.047	<.0001	1.018
Age (yr)	−0.009	−0.008	–	−0.311	−0.009	<.0001	1.200
Performance status	−0.022	−0.013	–	−0.037	−0.031	<.0001	1.064
ASA classification*	−0.066	−0.052	–	−0.077	−0.080	<.0001	1.254
Serum albumin level at admission (g/dL)	−0.673	−0.657	–	−0.669	−0.689	<.0001	1.153
Operation time (minutes)	−0.00015	0.000	–	−0.059	0.000	<.0001	1.100
Blood loss (mL)	−0.00001	0.000	–	−0.027	0.000	0.0005	1.102
Intervention of POMs (Yes vs No)	0.022	0.033	–	0.033	0.012	<.0001	1.057

95% CI = 95% confidence interval, POMs = perioperative oral managements.
* The American Society of Anesthesiologists (ASA) physical status classification.

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.[32]

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 those not receiving POMs.[15] 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.[15] 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,[33] and mean clinical attachment loss was also identified as a significant factor for lower albumin levels

Table 4

Japanese literature review of the effects of the POMs.

Author (Year)	Cancer site	Number of Patients	Effects of the POMs
Kataoka T, et al (2008)[21]	Oral cavity	112	Reduction of prevalence of postoperative pneumonia
Uejima S, et al (2009)[22]	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)[4]	Esophagus	86	Reduction of prevalence of postoperative pneumonia
Hiramatsu T, et al (2014)[5]	Esophagus	240	Reduction of prevalence of postoperative pneumonia
Tozawa S, etal (2015)[23]	Digestive system	464	Shortening of postoperative hospitalization days and postoperative fasting period (especially in stomach, small intestine, and large bowel)
Uruno, et al (2015)[24]	Oral cavity	100	Shortening of postoperative hospitalization days, antibiotics administration period and postoperative fasting period
Yamamura Y, et al (2016)[25]	Lung	27	Reduction of prevalence of postoperative pneumonia and fever of ≥38°C, and shortening of postoperative hospitalization days
Aizawa H, et al (2016)[26]	Liver	80	Shortening of postoperative hospitalization days, antibiotics administration period and postoperative fasting period
Soutome S, et al (2016)[27]	Esophagus	383	Reduction of prevalence of postoperative pneumonia and intervention of POMs as risk factor for postoperative pneumonia
Nishino T, et al. (2017)[28]	Lung	264	Reduction of prevalence of postoperative pneumonia, Shortening of postoperative hospitalization days, and lower postoperative CRP level
Soutome, et al (2017)[3]	Esophagus	539	Reduction of prevalence of postoperative pneumonia and intervention of POMs as risk factor for postoperative pneumonia
Kajihara R, et al. (2018)[29]	Lung	480	Reduction of prevalence of postoperative pneumonia and intervention of POMs as risk factor for postoperative pneumonia
Iwata E, et al. (2019)[6]	Lung	721	Reduction of prevalence of postoperative pneumonia and intervention of POMs as risk factor for postoperative pneumonia
Nobuhara H, et al. (2019)[30]	Large bowel	698	Reduction of prevalence of SSI, shortening of postoperative hospitalization days, and intervention of POMs as risk factor for postoperative pneumonia

CRP = C-reactive protein, POMs = perioperative oral managements, SIRS = systemic inflammatory response syndrome, SSI = surgical site infection.

in the elderly.[34] Furthermore, a close relationship has been reported between periodontitis and lower serum albumin levels.[34–37] Periodontal treatment had a positive influence on masticatory performance after conservative treatment.[38] Additionally, tooth loss may be a predictor for low energy and protein intake as well as serum albumin levels.[39] On the other hand, since serum albumin levels have been reported to significantly increase among individuals using partial dentures,[40] 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, exerts 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.

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