Observational Study
Medicine®
OPEN

Effects of preoperative oral management by dentists on postoperative outcomes following esophagectomy

Multilevel propensity score matching and weighting analyses using the Japanese inpatient database

Jung-ho Shin, DDS, MPH[a], Susumu Kunisawa, MD, PhD[a], Kiyohide Fushimi, MD, PhD[b], Yuichi Imanaka, MD, PhD[a,*]

Abstract

The purpose of this study was to investigate the effects of preoperative oral management (POM) by dentists on the incidence of postoperative pulmonary complications (PPCs), length of hospital stay, medical costs, and days of antibiotics administration following both open and thoracoscopic esophagectomy.

Dental plaque is an established risk factor for postoperative pneumonia, which could be reduced by POM. However, few clinical guidelines for cancer treatment, including those for esophageal cancer, recommend POM as routine perioperative care.

We extracted data of esophagectomy cases from the Japanese Diagnosis Procedure Combination database. We subsequently conducted propensity score (PS) analyses for multilevel data, including matching, inverse probability of treatment weighting (IPTW), and standardized mortality ratio weighting (SMRW), to estimate the effect of POM by dentists on the outcomes of esophagectomy.

We analyzed 3412 esophagectomy cases of which 812 were open, and 2600 were thoracoscopic surgery. In IPTW analysis to estimate the average treatment effect, the risk difference of postoperative aspiration pneumonia ranged from –2.49% to –2.02% between the POM and control groups of both open and thoracoscopic esophagectomy cases. IPTW analyses indicated that the total medical costs of thoracoscopic esophagectomy were reduced by 221,200 to 253,100 Japanese Yen (equivalent to about \$2000–\$2200). In PS matching and SMRW analyses to estimate average treatment effect on treated, there was no difference in outcomes between the POM and control groups.

Our results suggested that in patients undergoing open or thoracoscopic esophagectomy, POM by dentists prevented the occurrence of postoperative aspiration pneumonia. It could also reduce the total medical costs of thoracoscopic esophagectomy. Thus, POM by dentists can be considered as a routine perioperative care for all patients undergoing esophagectomy, regardless of the expected risk for PPC.

Abbreviations: ADL = activities of daily living, ATE = average treatment effect, ATT = average treatment effect on treated, BMI = body mass index, CCA = complete case analysis, DPC = diagnosis procedure combination, FFS = fee-for-service, ICD-10 = International Classification of Diseases, Tenth Revision, IPTW = inverse probability of treatment weighting, JPY = Japanese Yen, LOS = length of hospital stay, MHLW = Ministry of Health, Labour and Welfare, NCD = National Clinical Database, NDB = National Database of Health Insurance Claims and Specific Health Checkups of Japan, PDPS = per-diem payment system, POM = preoperative oral management, PPC = postoperative pulmonary complication, PS = propensity score, SMRW = standardized mortality ratio weighting.

Keywords: clustered data, esophageal cancer, esophagectomy, multilevel analysis, preoperative oral management, propensity score

Editor: Feng Yang.

This study was supported by the Health, Labour, and Welfare Policy Research Grants H30-seisaku-sitei-004 from the MHLW and KAKENHI Grant Number JP16H02634 from the Japan Society for the Promotion of Science to Yuichi Imanaka.

The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

[a] Department of Healthcare Economics and Quality Management, Graduate School of Medicine, Kyoto University, Kyoto, [b] Department of Health Policy and Informatics, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan.

[*] Correspondence: Yuichi Imanaka, Department of Healthcare Economics and Quality Management, Graduate School of Medicine, Kyoto University, Yoshida Konoe-cho, Sakyo-ku, Kyoto 606-8501, Japan (e-mail: imanaka-y@umin.net).

Medicine (2019) 98:17(e15376)

Received: 6 December 2018 / Received in final form: 22 February 2019 / Accepted: 27 March 2019

http://dx.doi.org/10.1097/MD.0000000000015376

1. Introduction

Esophageal cancer ranked ninth (11th in Japan) in the number of incident cases and sixth (7th in Japan) in the number of deaths globally, as of 2013.[1] Esophagectomy, an essential treatment modality for esophageal cancer, is a highly invasive procedure with a high risk of postoperative complications,[2] especially pulmonary complication as the independent predictor of poor long-term survival following esophagectomy.[2]

Postoperative pulmonary complications (PPCs) increase the mortality, health-care costs, and length of hospital stay (LOS).[3] Dental plaque, a biofilm that serves as a reservoir of oral bacteria, is a known risk factor for postoperative pneumonia including aspiration pneumonia and ventilator-associated pneumonia,[4,5] thus perioperative oral management could reduce the occurrence of postoperative pneumonia. In Japan, the treatment fees for perioperative oral management by dentists were newly included in the dental fee schedule of the National Health Insurance to prevent postoperative complications, such as aspiration pneumonia, in 2012.[6] Furthermore, additional fees for surgery preceded by preoperative oral management (POM) which can be claimed when conducted within 1 month prior to cancer surgery of the orofacial, neck, thoracic and abdominal areas, and cardiac surgery were imposed on the medical fee schedule in 2014 as incentives to promote POM.[7] However, few clinical guidelines for cancer treatment recommend oral management by dentists as routine perioperative care. Thus, the purpose of this study was to investigate the effects of POM by dentists on various postoperative outcomes, including PPCs, postoperative LOS, medical costs, and days of antibiotics administration following open and thoracoscopic esophagectomy.

2. Methods

2.1. Data source

We analyzed the Diagnosis Procedure Combination (DPC) data of esophagectomy cases from the database of the DPC research group,[8] which is funded by the Ministry of Health, Labour and Welfare (MHLW), Japan. The DPC/per-diem payment system (PDPS) is a Japanese prospective payment system applied to acute-care hospitals. DPC data comprise claims of inpatients, as well as patients' information of discharge summaries, such as height, weight, activities of daily living (ADL) indices, and International Classification of Diseases, Tenth Revision (ICD-10) codes, which are classified as the main diagnosis, cause of admission, most and the 2nd most medical resource-intensive diagnoses, up to 10 comorbidities, and 10 complications; in addition, it contains diagnosis-specific information, such as the TNM classification for cancer cases.

2.2. Inclusion and exclusion criteria

We included esophagectomy cases discharged between April 1, 2016, and March 31, 2017 (fiscal year 2016). We selected the surgical codes for open and thoracoscopic esophagectomy of the cervical, thoracic, and abdominal esophagus with ICD-10 codes of esophageal cancer (C15.x) as the cause of each admission. We included new esophageal cancer cases, not recurrent cases, in which the first surgery under general anesthesia during each admission period was esophagectomy. We excluded emergency and unexpected admissions, because the additional fees for surgery preceded by POM can be claimed only for those cases with POM administered within 1 month before the day of surgery. We further excluded cases with inconsistent data, such as having both codes of open and thoracoscopic esophagectomies, which were not considered as valid claims. To deal with missing values, we adopted complete case analysis (CCA) based on a recent simulation study which suggested that CCA could reduce the bias in propensity score (PS) matching and weighting.[9] For CCA, cases with missing values of the ADL indices, body mass index (BMI), and/or prescription information of antibiotics were excluded.

2.3. Outcomes of interests

In our study, the outcomes included the incidence of PPCs, postoperative LOS, medical costs, and days of antibiotics administration after esophagectomy. The cases with PPCs were defined as those with ICD-10 codes of pneumonia due to infectious organisms (J13.x–J18.x), aspiration pneumonia (J69.x), and/or postprocedural respiratory disorders (J95.8 and/or J95.9) as complications. We presented the incidence of aspiration pneumonia along with that of all PPCs. We calculated fee-for-service (FFS) costs as the medical costs, not the claimed costs by PDPS, to signify costs as the actual amount of consumed medical resources. The days of antibiotics administration was selected as a proxy of the days needed to treat postoperative infection.

2.4. Statistical analyses

We assigned cases with claims of additional fees for surgery preceded by POM as the POM group, and cases without these claims as the control group. We then performed PS matching and weighting analyses for clustered data, since the DPC data was considered to have a clustered structure of patients nested in each hospital.

The covariates for estimating PSs included the sex, age strata ($<$40, 40–49, 50–59, 60–69, 70–79, and $>$80 years old), BMI ($<$18.5 and $\geq$25), any dependency on ADL (Barthel index $<$100), smoking history (Brinkman index of 0, 1–399, 400–799, 800–1199, and $\geq$1200), TNM classification ($T\geq3$, $N\geq1$, and $M=1$), and preoperative respiratory rehabilitation during the same hospitalization period as that for surgery. The covariates of comorbidities included 32 categories suggested by Gagne et al,[10] which are the combined Charlson and Elixhauser comorbidities. We identified each comorbidity using ICD-10 coding algorithms described by Quan et al.[11] Using these covariates, logistic regression models were fitted to estimate single-level PSs. Fixed-effects PSs were estimated by fitting logistic regression models with the listed covariates and dummy variables of each hospital as intercepts, and random-effects PSs were estimated by fitting generalized linear mixed models with the covariates as fixed-effects and hospital codes as random-effects.[12,13] The dependent variables of 3 PS models were the indicator variables of the claims for additional fees of surgery preceded by POM.

We conducted 4 matchings to estimate the average treatment effect on treated (ATT) using the estimated PSs: single-level, preferential within-cluster, fixed-effects, and random-effects matching; the latter 3 are matching for clustered data described by Arpino and Cannas.[13] For single-level matching, which does not consider the clustered data structure, cases in the POM group were matched within all cases in the control group using single-level PSs. For preferential within-cluster matching, cases in the POM group were matched only within cases at the same hospital as that of the POM group using single-level PSs. This step might result in loss of many cases, so additional matching for unmatched cases in the POM group were conducted; cases that could not be matched within the same hospitals were matched with cases at hospitals other than the nested hospitals, using single-level PSs. For fixed-effects and random-effects matching, the fixed-effects PSs and random-effects PSs were used for matchings, respectively, where cases in the POM group were matched within all cases in the control group. For all matching, we performed one-to-one nearest-neighbor matching with replacement using a caliper of 0.2, as recommended by Austin.[14] In summary, the single-level matching ignored the clustered structure of the data, preferential within-cluster matching considered it by means of the matching method, and fixed-effects and random-effects matching considered it through estimation of PSs.

To estimate average treatment effect (ATE) and ATT by PS weighting, we used inverse probability of treatment weighting (IPTW) method and standardized mortality ratio weighting (SMRW) method,[15] respectively. For PS weighting analyses, as in matching analyses, considering the clustered structure at either the stage of estimating the PSs or treatment effects improved the quality of estimates.[16] Thus, we calculated the weights using 3 PSs estimated for matching. Using these weights, we estimated the ATE and ATT as risk differences, and differences in days or Japanese Yen (JPY).

The balances of covariates between the POM and control groups before and after matching and weighting were checked by standardized differences.[17,18] Charlson comorbidity index and Elixhauser/van Walraven comorbidity index[19] were presented instead of the 32 comorbidities to simplify the comparisons. To estimate *P* values between the groups, Student *t* test (or Welch–Satterthwaite *t* test for covariates with unequal variances) and Fisher exact test (if not applicable, χ^2 tests) were performed for baseline populations. After matching analyses, paired *t* test and McNemar test were performed. After weighting analyses, generalized linear models were fitted to estimate *P* values and confidence intervals using robust variances.[15]

SAS software version 9.4 (SAS Institute Inc, Cary, NC) was used for all analyses: PROC LOGISTICS and PROC GLIMMIX were used to estimate PSs, PROC PSMATCH for matchings, and PROC GENMOD for weighting analyses. Two-tailed significance level of 0.05 was used for all tests.

2.5. Sensitivity analyses

We used PS analyses methods for clustered data with unknown cluster-level confounders. However, we could calculate 1 cluster-level confounder of the hospital volume. Based on the annual cases at each hospital, we divided the hospitals into 3 categories of hospital volume: 1 to 11, 12 to 23, 24 or more cases per year. As the first sensitivity analysis, we incorporated these variables into the 3 PS models, and then conducted matching and weighting analyses.

Among several methods that deal with missing variables in PS analyses, the missing indicators method may reduce the bias.[9] As the second sensitivity analysis, we added the missing indicators of smoking index, BMI, and ADL scores into our PS models.

The third sensitivity analysis is a solution for the drawback of the PS weighting analyses. In PS weighting, the weight can be very big or small when the PS is near 0 or 1. Therefore, we used trimmed (or truncated) weights for the third sensitivity analysis. From among several ways to trim weights, we adopted the method using 1st and 99th percentiles of estimated weights.[18] The weights smaller than the 1st percentile of all weights were trimmed to the same values as the 1st percentile, and the weights bigger than the 99th percentile were trimmed to the same values as the 99th percentile.

2.6. Ethical considerations

This study was conducted in accordance with the Ethical Guidelines for Medical and Health Research involving Human Subjects of the MHLW, Japan. The Ethics Committee, Graduate School of Medicine Kyoto University approved the study (approval number: R0135).

3. Results

3.1. Study population

Figure 1 shows the flow of case selection. We extracted 3412 esophagectomy cases and excluded 812 cases; thus, 2600 cases were included in the final analysis. The number of hospitals was 202 for open surgery, and 220 for thoracoscopic surgery.

3.2. Patients' characteristics at baseline

Table 1 shows the comparison of patients' characteristics between the POM groups and control groups at baseline. The complete lists of comorbidities are presented in Supplemental Digital Content 1, http://links.lww.com/MD/C942. At baseline, the proportion of patients with preoperative respiration rehabilitation was higher in the POM groups for both surgery types. The proportion of patients with Barthel indices of <100 was higher in the control group of thoracoscopic surgery than that of the POM group.

3.3. Balance of covariates of the matched and weighted populations

Tables 2 and 3 show the standardized differences of the POM groups and control groups before and after matchings, and after weightings, respectively. For both surgery types, the mean absolute standardized differences of the PS weighting analyses were smaller than those of the PS matching analyses, which indicated that the 2 groups were balanced better in weightings than in matchings. Among the mean absolute standardized differences after matching, that of the random-effects matching was smallest for open esophagectomy, whereas that of the fixed-effects matching was smallest for thoracoscopic esophagectomy.

3.4. Outcomes

Table 4 shows the postoperative outcomes of the POM and control groups at baseline, and after matching. At baseline, the incidence of PPCs was higher in the control group of open esophagectomy (16.4% vs 10.6%), and the medical costs were lower in the POM groups of thoracoscopic surgery (3.4 vs 3.7 million Japanese Yen). Matching analyses revealed that none of the outcomes of the POM groups were better significantly than those of the control group except for all PPCs after open esophagectomy through fixed-effects matching. In contrast, the incidence of postoperative aspiration pneumonia was consistent-

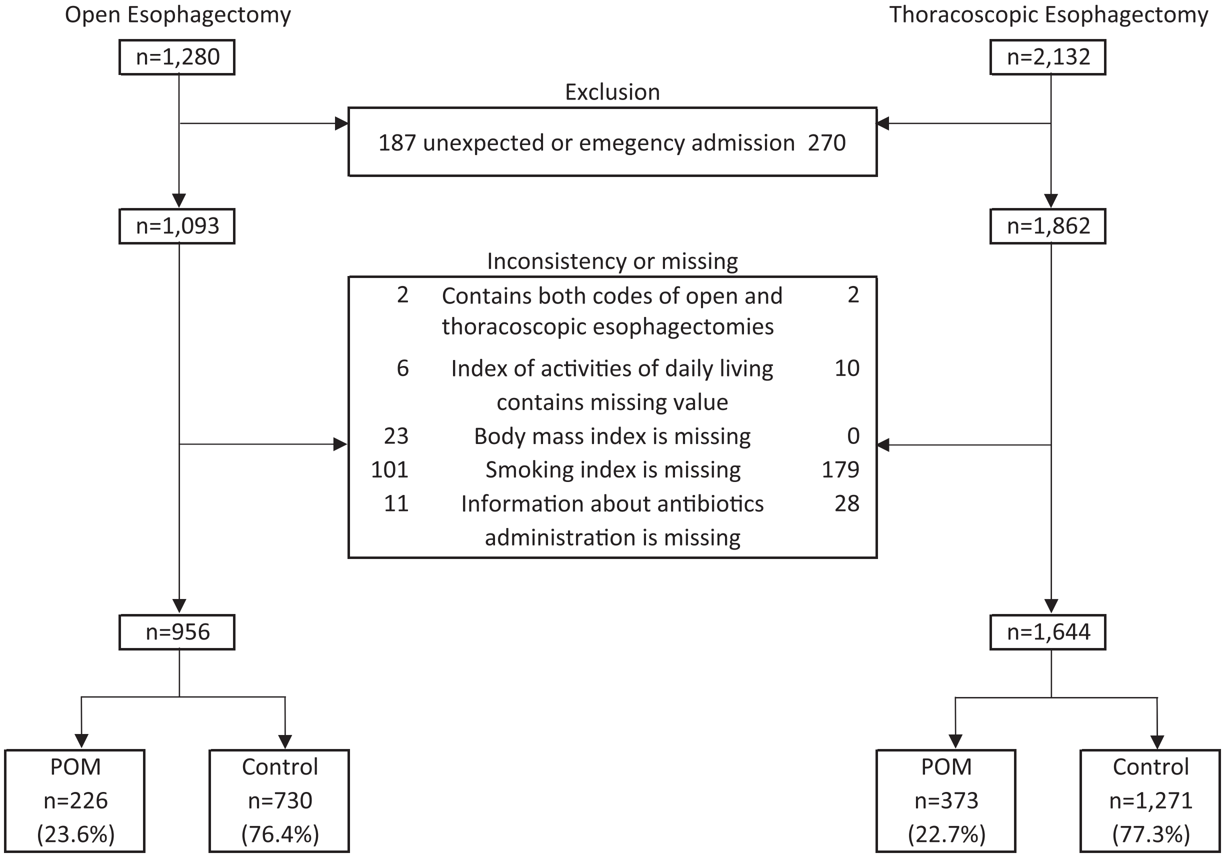

Figure 1. The flow of case selection. POM=preoperative oral management by dentists.

ly low by 2.0% to 2.5% in the POM groups through all IPTW analyses which estimated ATE, except for the analysis of open esophagectomy population using weights derived from single-level PSs (Table 5). The medical costs of thoracoscopic esophagectomy were significantly low by 221,200 to 253,100 Japanese Yen in the POM groups through the IPTW analyses (Table 5).

3.5. Sensitivity analyses

Supplemental Digital Contents 3 and 4, http://links.lww.com/MD/C942 show results of the sensitivity analyses of matching and weighting analyses, respectively. In the matching analyses of thoracoscopic esophagectomy, all outcomes showed no statistical significance except for the incidence of aspiration pneumonia through single-level matching adding missing indicators. For open esophagectomy, however, the postoperative LOS was longer in the POM groups through 3 matching analyses (37.6 vs 32.7 in single-level matching using missing indicator; 37.3 vs 31.7 in preferential within-cluster matching, and 36.8 vs 31.3 in fixed-effects matching using variables of hospital volume), whereas the incidence of PPCs was lower in the POM groups through 2 matching analyses (9.8% vs 18.0% in single-level matching and 9.8% vs 15.6% in preferential within-cluster matching using missing indicator). In the SMRW analyses, the outcomes showed no significant change. However, through the IPTW analyses using the trimmed weights derived from multilevel PSs and weights from the random-effects model with missing indicators, the *P* values for the incidence of aspiration pneumonia following thoracoscopic esophagectomy rose above .05 (relative differences and *P* values of the incidence of aspiration pneumonia using fixed-effects PS and random-effects PS in main analysis were −2.1%, $P=.031$ and −2.0%, $P=.039$, respectively; in analysis using trimmed weight, they were changed to −1.9%, $P=.060$, −1.9%, $P=.054$).

4. Discussion

We conducted multilevel PS analyses using the Japanese DPC data as clustered data to investigate the effects of POM by dentists on postoperative outcomes of esophagectomy. In the IPTW analyses, POM by dentists was related to the prevention of postoperative aspiration pneumonia for both open and thoracoscopic esophagectomy, and also related to the reduction of medical costs of thoracoscopic esophagectomy. The PS matchings and SMRW analyses indicated that POM by dentists had no effectiveness to improve the postoperative outcomes.

We estimated both the ATT and ATE of POM by dentists and showed that the risk reduction of postoperative aspiration pneumonia achieved in terms of ATE. These results suggested that POM by dentists for all esophagectomy patients, not just patients with expected high risk of PPC based on clinical factors that were not included in the DPC data, could be beneficial to prevent postoperative aspiration pneumonia. Although the preoperative oral management would cost 8000 to 16,000 JPY per person which is equivalent to around \$70 to \$140 based on

Table 1

Comparison of the baseline characteristics between the preoperative oral management groups and control groups of open and thoracoscopic esophagectomy.

	Open esophagectomy				Thoracoscopic esophagectomy			
	POM (n=226)	Control (n=730)	*P*	SDif	POM (n=373)	Control (n=1,271)	*P*	SDif
Male	176 (77.9%)	607 (83.2%)	.076	**−0.133**	315 (84.5%)	1027 (80.8%)	.128	0.096
Age, y	66.4±8.7	66.9±8.1	.385	−0.065	67.0±8.4	66.8±8.5	.698	0.023
Median (1Q, 3Q)	68 (61, 72)	67 (62, 73)			68 (62, 73)	68 (61, 73)		
<40	1 (0.4%)	1 (0.1%)	.886	0.057	2 (0.5%)	4 (0.3%)	.634	0.034
40–49	6 (2.7%)	20 (2.7%)		−0.005	12 (3.2%)	37 (2.9%)		0.018
50–59	37 (16.4%)	101 (13.8%)		0.071	47 (12.6%)	192 (15.1%)		−0.073
60–69	97 (42.9%)	322 (44.1%)		−0.024	154 (41.3%)	532 (41.9%)		−0.012
70–79	76 (33.6%)	257 (35.2%)		−0.033	145 (38.9%)	449 (35.3%)		0.073
≥80	9 (4.0%)	29 (4.0%)		0.000	13 (3.5%)	57 (4.5%)		−0.051
BMI, kg/m^2	21.2±3.0	20.9±3.1	.248	0.088	21.5±3.1	21.5±3.3	.863	−0.010
Median (1Q, 3Q)	21 (19, 23)	21 (19, 23)			21 (19, 23)	21 (19, 24)		
<18.5	40 (17.7%)	154 (21.1%)	.298	−0.086	64 (17.2%)	228 (17.9%)	.759	−0.021
≥25	26 (11.5%)	69 (9.5%)	.374	0.067	41 (11.0%)	171 (13.5%)	.253	−0.075
Brinkman index	562.0±531.8	600.0±568.3	.372	−0.069	572.0±533.2	553.6±533.6	.557	0.035
Median (1Q, 3Q)	450 (0, 900)	600 (0, 920)			500 (0, 900)	500 (0, 870)		
0	62 (27.4%)	205 (28.1%)	.785	−0.014	101 (27.1%)	344 (27.1%)	.790	0.000
1–399	31 (13.7%)	87 (11.9%)		0.054	48 (12.9%)	193 (15.2%)		−0.067
400–799	58 (25.7%)	168 (23.0%)		0.062	98 (26.3%)	313 (24.6%)		0.038
800–1199	45 (19.9%)	166 (22.7%)		−0.069	86 (23.1%)	298 (23.4%)		−0.009
≥1200	30 (13.3%)	104 (14.2%)		−0.028	40 (10.7%)	123 (9.7%)		0.035
Barthel index	98.0±9.4	97.6±9.9	.531	0.048	99.6±3.8	98.5±8.4	**<.001**	**0.167**
Median (1Q, 3Q)	100 ((100, 100)	100 (100, 100)			100 (100, 100)	100 (100, 100)		
<100	15 (6.6%)	64 (8.8%)	.337	−0.080	8 (2.1%)	67 (5.3%)	**.010**	**−0.166**
Charlson comorbidity index	1.2±2.0	1.2±1.9	.812	0.018	1.0±1.5	1.1±1.6	.260	−0.067
Median (1Q, 3Q)	0 (0, 2)	1 (0, 1)			0 (0, 1)	1 (0, 1)		
Elixhauser/van Walraven comorbidity index	2.9±5.0	2.6±4.7	.376	0.066	2.0±4.0	2.4±4.4	.159	−0.085
Median (1Q, 3Q)	0 (0, 5)	0 (0, 4)			0 (0, 4)	0 (0, 4)		
T≥3	116 (51.3%)	425 (58.2%)	.077	**−0.139**	148 (39.7%)	528 (41.5%)	.550	−0.038
N≥1	133 (58.8%)	474 (64.9%)	.098	**−0.125**	200 (53.6%)	639 (50.3%)	.264	0.067
M=1	12 (5.3%)	31 (4.2%)	.468	0.050	18 (4.8%)	34 (2.7%)	**.043**	**0.113**
Preoperative respiratory rehabilitation	60 (26.5%)	124 (17.0%)	**.002**	**0.233**	84 (22.5%)	210 (16.5%)	**.009**	**0.152**
Comorbidities								
Cerebrovascular disease	13 (5.8%)	17 (2.3%)	.083	**0.175**	9 (2.4%)	40 (3.1%)	.603	−0.045
Myocardial infarction	0 (0.0%)	0 (0.0%)	–	0.000	2 (0.5%)	10 (0.8%)	1.000	−0.031
Congestive heart failure	8 (3.5%)	17 (2.3%)	.341	0.072	9 (2.4%)	31 (2.4%)	1.000	−0.002
Cardiac arrhythmias	20 (8.8%)	49 (6.7%)	.303	0.080	20 (5.4%)	75 (5.9%)	.801	−0.023
Valvular disease	8 (3.5%)	22 (3.0%)	.666	0.030	11 (2.9%)	31 (2.4%)	.577	0.032
Pulmonary circulation disorders	1 (0.4%)	2 (0.3%)	.555	0.028	1 (0.3%)	7 (0.6%)	.691	−0.044
Peripheral vascular disorders	1 (0.4%)	9 (1.2%)	.467	−0.087	3 (0.8%)	10 (0.8%)	1.000	0.002
Hypertension	44 (19.5%)	171 (23.4%)	.236	−0.096	87 (23.3%)	300 (23.6%)	.945	−0.007
Other neurological disorders	0 (0.0%)	4 (0.5%)	.578	**−0.105**	0 (0.0%)	6 (0.5%)	.347	−0.097
Chronic pulmonary disease	15 (6.6%)	68 (9.3%)	.227	−0.099	14 (3.8%)	86 (6.8%)	**.036**	**−0.135**
Diabetes, uncomplicated	23 (10.2%)	118 (16.2%)	**.031**	**−0.178**	45 (12.1%)	188 (14.8%)	.205	−0.080
Diabetes, complicated	3 (1.3%)	17 (2.3%)	.438	−0.075	8 (2.1%)	17 (1.3%)	.333	0.062
Hypothyroidism	5 (2.2%)	5 (0.7%)	.062	**0.128**	2 (0.5%)	9 (0.7%)	1.000	−0.022
Renal failure	4 (1.8%)	6 (0.8%)	.259	0.084	2 (0.5%)	9 (0.7%)	1.000	−0.022
Liver disease	12 (5.3%)	33 (4.5%)	.594	0.037	14 (3.8%)	72 (5.7%)	.185	−0.090
Peptic ulcer disease	32 (14.2%)	79 (10.8%)	.191	**0.101**	50 (13.4%)	190 (14.9%)	.505	−0.044
Any malignancy except malignant neoplasm of skin	27 (11.9%)	78 (10.7%)	.626	0.040	49 (13.1%)	151 (11.9%)	.529	0.038
Metastatic cancer	17 (7.5%)	54 (7.4%)	1.000	0.005	16 (4.3%)	60 (4.7%)	.781	−0.021
Rheumatoid arthritis/collagen vascular diseases	2 (0.9%)	4 (0.5%)	.631	0.040	2 (0.5%)	6 (0.5%)	1.000	0.009
Coagulopathy	2 (0.9%)	2 (0.3%)	.239	0.081	1 (0.3%)	10 (0.8%)	.473	−0.072
Obesity	0 (0.0%)	1 (0.1%)	1.000	−0.052	0 (0.0%)	3 (0.2%)	1.000	−0.069
Weight loss	3 (1.3%)	8 (1.1%)	.728	0.021	6 (1.6%)	10 (0.8%)	.224	0.076
Fluid and electrolyte disorders	4 (1.8%)	4 (0.5%)	.095	**0.114**	1 (0.3%)	10 (0.8%)	.473	−0.072
Blood loss anemia	1 (0.4%)	1 (0.1%)	.417	0.057	2 (0.5%)	4 (0.3%)	.624	0.034
Deficiency anemia	5 (2.2%)	25 (3.4%)	.512	−0.073	10 (2.7%)	40 (3.1%)	.734	−0.028
Alcohol abuse	0 (0.0%)	19 (2.6%)	**.011**	**−0.231**	1 (0.3%)	17 (1.3%)	.093	**−0.120**
Psychoses	2 (0.9%)	6 (0.8%)	1.000	0.007	5 (1.3%)	17 (1.3%)	1.000	0.000
Depression	1 (0.4%)	10 (1.4%)	.474	−0.098	5 (1.3%)	19 (1.5%)	1.000	−0.013
Dementia	2 (0.9%)	2 (0.3%)	.239	0.081	1 (0.3%)	4 (0.3%)	1.000	−0.009

Values are presented as mean ± standard deviation, and n (%), unless otherwise indicated.

Values in bold indicate $P<.05$ or absolute standardized difference >.1.

1Q=1st quartile, 3Q=3rd quartile, POM=preoperative oral management by dentists, SDif=standardized difference.

Table 2

Standardized differences of the selected covariates of the preoperative oral management groups and control groups at baseline and after matching.

	Baseline			Single-level matching			Preferential within-cluster matching			Fixed-effects matching			Random-effects matching		
Open esophagectomy	**POM (n=226)**	**Control (n=730)**	**SDif**	**POM (n=225)**	**Control (n=225)**	**SDif**	**POM (n=225)**	**Control (n=225)**	**SDif**	**POM (n=205)**	**Control (n=205)**	**SDif**	**POM (n=224)**	**Control (n=224)**	**SDif**
Male	77.9%	83.2%	**−0.133**	77.8%	84.9%	**−0.183**	77.8%	80.9%	−0.077	77.6%	77.6%	0.000	78.1%	78.1%	0.000
Age (years)	66.4	66.9	−0.065	66.4	66.2	0.020	66.4	65.6	0.097	66.5	66.1	0.036	66.3	65.0	**0.156**
Body mass index	21.2	20.9	0.088	21.2	21.7	**−0.177**	21.2	21.3	−0.046	21.3	21.8	**−0.165**	21.2	21.6	**−0.146**
<18.5	17.7%	21.1%	−0.086	17.3%	11.6%	**0.165**	17.3%	11.6%	**0.165**	16.6%	14.6%	0.054	17.4%	14.3%	0.086
≥25	11.5%	9.5%	0.067	11.6%	12.9%	−0.041	11.6%	8.4%	**0.104**	11.7%	14.1%	−0.073	11.2%	12.5%	−0.041
Brinkman Index	562.0	600.0	−0.069	561.1	605.1	−0.078	561.1	534.4	0.050	546.2	554.4	−0.015	561.8	575.8	−0.028
Barthel index	98.0	97.6	0.048	98.0	98.0	0.007	98.0	98.3	−0.030	97.9	98.1	−0.026	98.0	99.0	**−0.130**
<100	6.6%	8.8%	−0.080	6.7%	6.7%	0.000	6.7%	5.3%	0.056	6.8%	8.8%	−0.073	6.7%	4.0%	**0.119**
Charlson index	1.2	1.2	0.018	1.2	0.7	**0.278**	1.2	0.9	**0.176**	1.3	1.4	−0.059	1.2	1.1	0.056
Elixhauser/van Walraven index	2.9	2.6	0.066	2.9	2.3	**0.128**	2.9	2.1	**0.187**	3.0	2.8	0.042	2.9	2.6	0.064
T≥3	51.3%	58.2%	**−0.139**	51.1%	49.3%	0.036	51.1%	52.0%	−0.018	50.2%	50.7%	−0.010	50.9%	51.3%	−0.009
N≥1	58.8%	64.9%	**−0.125**	59.1%	60.0%	−0.018	59.1%	64.9%	**−0.119**	58.0%	58.0%	0.000	59.4%	55.4%	0.081
M=1	5.3%	4.2%	0.050	5.3%	6.2%	−0.038	5.3%	10.2%	**−0.183**	5.9%	3.9%	0.091	5.4%	5.8%	−0.019
Preoperative respiratory rehabilitation	26.5%	17.0%	**0.233**	26.2%	28.9%	−0.060	26.2%	28.4%	−0.050	26.8%	30.7%	−0.086	25.9%	26.8%	−0.020
Mean Absolute SDif*			0.071			0.063			0.061			0.067			0.058

	Baseline			Single-level matching			Preferential within-cluster matching			Fixed-effects matching			Random-effects matching		
Thoracoscopic esophagectomy	**POM (n=373)**	**Control (n=1,271)**	**SDif**	**POM (n=370)**	**Control (n=370)**	**SDif**	**POM (n=370)**	**Control (n=370)**	**SDif**	**POM (n=361)**	**Control (n=361)**	**SDif**	**POM (n=369)**	**Control (n=369)**	**SDif**
Male	84.5%	80.8%	0.096	84.3%	84.6%	−0.007	84.3%	86.8%	−0.069	84.8%	85.0%	−0.008	84.3%	87.0%	−0.077
Age (years)	67.0	66.8	0.023	67.0	67.5	−0.061	67.0	66.9	0.019	67.2	67.8	−0.072	67.0	67.0	−0.005
Body mass index	21.5	21.5	−0.010	21.5	21.4	0.037	21.5	21.4	0.021	21.5	21.4	0.010	21.5	21.4	0.041
<18.5	17.2%	17.9%	−0.021	17.0%	16.5%	0.014	17.0%	16.2%	0.022	16.9%	16.3%	0.015	17.1%	16.3%	0.022
≥25	11.0%	13.5%	−0.075	11.1%	10.3%	0.026	11.1%	11.6%	−0.017	11.1%	11.1%	0.000	11.1%	10.8%	0.009
Brinkman Index	572.0	553.6	0.035	571.5	575.9	−0.008	571.5	570.3	0.002	573.9	595.2	−0.037	570.5	530.9	0.071
Barthel index	99.6	98.5	**0.167**	99.6	98.6	**0.153**	99.6	99.1	0.090	99.6	99.8	−0.071	99.6	99.8	−0.064
<100	2.1%	5.3%	**−0.166**	2.2%	3.5%	−0.081	2.2%	2.7%	−0.035	2.2%	1.9%	0.019	2.2%	1.9%	0.019
Charlson index	1.0	1.1	−0.067	1.0	0.9	0.038	1.0	0.8	**0.139**	1.0	1.0	−0.016	1.0	0.9	0.007
Elixhauser/van Walraven index	2.0	2.4	−0.085	2.0	1.6	**0.116**	2.0	1.5	**0.151**	2.0	1.5	**0.124**	2.0	2.1	−0.012
T≥3	39.7%	41.5%	−0.038	39.7%	38.9%	0.017	39.7%	41.4%	−0.033	39.6%	36.6%	0.063	39.8%	39.8%	0.000
N≥1	53.6%	50.3%	0.067	53.8%	55.4%	−0.033	53.8%	50.8%	0.060	53.5%	50.1%	0.067	53.9%	57.5%	−0.071
M=1	4.8%	2.7%	**0.113**	4.3%	5.4%	−0.050	4.3%	4.3%	0.000	4.7%	6.6%	−0.084	4.6%	4.1%	0.027
Preoperative respiratory rehabilitation	22.5%	16.5%	**0.152**	21.9%	20.3%	0.040	21.9%	20.3%	0.040	22.4%	24.4%	−0.046	21.7%	24.9%	−0.077
Mean Absolute SDif*			0.048			0.042			0.047			0.037			0.045

Values are presented as means, and percent.

SDif in bold indicates absolute standardized difference >0.1.

IPTW=inverse probability of treatment weighting, POM=preoperative oral management by dentists, PS=propensity score, SDif=standardized difference, SMRW=standardized mortality ratio weighting.

* The mean of absolute standardized differences of all variables in each matching; not the mean of standardized differences listed in this table. Complete lists of variables in each matching are presented in Supplemental Digital Content 2, http://links.lww.com/MD/C942.

Table 3

Standardized differences of the selected covariates of the preoperative oral management groups and control groups after weighting analyses.

	IPTW using single-level PS			IPTW using fixed-effects PS			IPTW using random-effects PS			SMRW using single-level PS			SMRW using fixed-effects PS			SMRW using random-effects PS		
Open esophagectomy	POM (n=914)	Control (n=957)	SDif	POM (n=646)	Control (n=935)	SDif	POM (n=762)	Control (n=927)	SDif	POM (n=226)	Control (n=227)	SDif	POM (n=226)	Control (n=205)	SDif	POM (n=226)	Control (n=197)	SDif
Male	82.3%	82.2%	0.003	83.7%	82.0%	0.044	82.7%	82.3%	0.011	77.9%	79.2%	–0.032	77.9%	78.0%	–0.004	77.9%	78.9%	–0.026
Age (years)	66.7	66.8	–0.005	66.8	66.9	–0.002	66.9	66.8	0.009	66.4	66.3	0.012	66.4	66.5	–0.018	66.4	66.2	0.023
Body mass index	21.0	21.0	0.003	21.3	21.1	0.047	21.1	21.0	0.005	21.2	21.3	0.088	21.2	21.6	0.088	21.2	21.5	0.088
<18.5	18.6%	19.8%	–0.031	15.9%	19.7%	–0.099	18.2%	19.9%	–0.041	17.7%	15.8%	0.051	17.7%	14.6%	0.085	17.7%	15.3%	0.065
≥25	9.7%	9.8%	–0.006	10.2%	10.2%	–0.001	9.8%	10.0%	–0.006	11.5%	11.1%	0.012	11.5%	12.9%	–0.044	11.5%	12.0%	–0.015
Brinkman Index	561.8	592.9	–0.034	588.3	590.1	–0.002	561.5	593.3	–0.038	562.0	570.1	–0.019	562.0	554.8	0.016	562.0	568.3	–0.015
Barthel index	98.2	97.7	0.036	97.3	97.7	–0.022	97.7	97.7	0.001	98.0	98.3	–0.032	98.0	98.1	–0.003	98.0	98.1	–0.013
<100	6.5%	8.1%	–0.063	8.3%	8.6%	–0.012	7.4%	8.4%	–0.035	6.6%	6.0%	0.027	6.6%	8.2%	–0.058	6.6%	6.9%	–0.010
Charlson index	1.1	1.2	–0.016	1.1	1.2	–0.031	1.1	1.2	–0.025	1.2	1.2	0.014	1.2	1.2	0.024	1.2	1.1	0.050
Elixhauser/van Walraven index	2.4	2.7	–0.046	2.2	2.6	–0.064	2.2	2.6	–0.060	2.9	3.0	–0.019	2.9	2.8	0.027	2.9	2.8	0.035
T≥3	56.0%	56.3%	–0.006	58.6%	56.4%	0.045	56.2%	56.6%	–0.008	51.3%	50.2%	0.022	51.3%	49.7%	0.032	51.3%	50.8%	0.011
N≥1	63.5%	63.7%	–0.003	62.5%	63.5%	–0.021	62.2%	63.8%	–0.034	58.8%	59.8%	–0.019	58.8%	58.4%	0.009	58.8%	59.7%	–0.017
M=1	4.8%	4.5%	0.012	8.3%	5.0%	0.133	5.8%	4.8%	0.047	5.3%	5.5%	–0.007	5.3%	7.8%	–0.100	5.3%	6.7%	–0.059
Preoperative respiratory rehabilitation	19.3%	19.2%	0.003	24.0%	19.1%	0.120	22.1%	19.1%	0.074	26.5%	26.1%	0.009	26.5%	26.5%	0.002	26.5%	27.1%	–0.012
Mean absolute SDif*			0.023			0.044			0.030			0.016			0.032			0.018

	IPTW using single-level PS			IPTW using fixed-effects PS			IPTW using random-effects PS			SMRW using single-level PS			SMRW using fixed-effects PS			SMRW using random-effects PS		
Thoracoscopic esophagectomy	POM (n=1636)	Control (n=1644)	SDif	POM (n=1186)	Control (n=1629)	SDif	POM (n=1325)	Control (n=1605)	SDif	POM (n=373)	Control (n=373)	SDif	POM (n=373)	Control (n=358)	SDif	POM (n=373)	Control (n=334)	SDif
Male	81.9%	81.6%	0.006	83.0%	81.6%	0.036	82.5%	81.6%	0.024	84.5%	84.5%	–0.002	84.5%	84.3%	0.004	84.5%	84.5%	–0.001
Age (yrs)	67.1	66.9	0.015	66.5	66.9	–0.033	66.9	66.9	–0.003	67.0	67.2	–0.023	67.0	67.3	–0.043	67.0	67.1	–0.018
Body mass index	21.5	21.5	0.002	21.7	21.5	0.035	21.6	21.5	0.015	21.5	21.5	0.001	21.5	21.5	0.001	21.5	21.5	0.010
<18.5	16.8%	17.7%	–0.022	16.9%	17.4%	–0.015	17.3%	17.7%	–0.012	17.2%	16.7%	0.013	17.2%	15.7%	0.040	17.2%	16.8%	0.009
≥25	12.9%	12.9%	0.000	14.4%	13.1%	0.039	13.8%	13.0%	0.022	11.0%	11.1%	–0.002	11.0%	11.8%	–0.026	11.0%	11.4%	–0.013
Brinkman Index	571.1	557.7	0.015	527.4	552.8	–0.032	545.1	555.4	–0.012	572.0	571.7	0.001	572.0	549.8	0.052	572.0	562.3	0.023
Barthel index	99.2	98.7	0.045	99.2	98.7	0.059	99.3	98.7	0.066	99.6	99.4	0.074	99.6	99.3	0.090	99.6	99.4	0.076
<100	5.0%	4.6%	0.021	5.3%	4.6%	0.031	4.9%	4.7%	0.010	2.1%	2.2%	–0.005	2.1%	2.4%	–0.019	2.1%	2.3%	–0.010
Charlson index	1.0	1.0	–0.026	1.0	1.0	–0.036	0.9	1.0	–0.036	1.0	1.0	0.002	1.0	0.9	0.030	1.0	0.9	0.026
Elixhauser/van Walraven index	2.1	2.3	–0.034	1.8	2.3	–0.078	1.9	2.3	–0.068	2.0	2.0	0.014	2.0	1.8	0.067	2.0	1.9	0.049
T≥3	40.6%	41.0%	–0.010	43.3%	40.9%	0.047	42.0%	41.2%	0.017	39.7%	39.3%	0.007	39.7%	38.8%	0.018	39.7%	39.7%	0.000
N≥1	52.0%	51.1%	0.017	53.0%	50.6%	0.047	52.3%	51.0%	0.025	53.6%	53.9%	–0.006	53.6%	51.9%	0.035	53.6%	53.7%	–0.002
M=1	3.1%	3.1%	–0.004	3.8%	3.2%	0.030	3.4%	3.2%	0.009	4.8%	4.7%	0.005	4.8%	5.1%	–0.011	4.8%	5.3%	–0.020
Preoperative respiratory rehabilitation	17.7%	17.8%	–0.004	21.2%	17.8%	0.085	20.1%	18.0%	0.053	22.5%	22.3%	0.005	22.5%	22.4%	0.002	22.5%	23.5%	–0.024
Mean absolute SDif*			0.017			0.044			0.026			0.005			0.017			0.011

Values are presented as means, and percent.

IPTW=inverse probability of treatment weighting, POM=preoperative oral management by dentists, PS=propensity score, SDif=standardized difference, SMRW=standardized mortality ratio weighting.

* The mean of absolute SDifs of all variables in each weighting analysis; not the mean of listed SDifs in this table. Complete lists of variables in each weightings are presented in Supplemental Digital Content 2 , http://links.lww.com/MD/C942.

Table 4

Comparison of the postoperative outcomes between the preoperative oral management groups and control groups at baseline and after matching.

Open esophagectomy	Baseline			Single-level Matching			Preferential within-cluster matching			Fixed-effects matching			Random-effects matching		
	POM (n=226)	Control (n=730)	(R)D	POM (n=225)	Control (n=225)	(R)D	POM (n=225)	Control (n=225)	(R)D	POM (n=205)	Control (n=205)	(R)D	POM (n=224)	Control (n=224)	(R)D
All PPCs	10.6%	16.4%	**−5.8%**	10.7%	11.6%	−0.9%	10.7%	16.0%	−5.3%	11.2%	18.0%	**−6.8%**	10.3%	12.1%	−1.8%
Aspiration pneumonia	2.2%	4.5%	−2.3%	2.2%	3.6%	−1.3%	2.2%	2.7%	−0.4%	2.4%	2.0%	0.5%	2.2%	1.3%	0.9%
Postoperative LOS	37.2	36.4	0.8	37.3	34.9	2.4	37.3	32.2	5.1	37.6	33.0	4.6	36.6	36.4	0.2
Medical costs (100 JPY)	42,865	42,172	693	42,923	40,855	2068	42,923	39,935	2988	42,703	40,870	1833	42,274	43,313	−1039
Duration of antibiotics adm.	11.6	11.6	0.0	11.6	11.9	−0.3	11.6	10.9	0.7	11.4	10.3	1.1	11.5	10.7	0.8

Thoracoscopic esophagectomy	Baseline			Single-level Matching			Preferential within-cluster matching			Fixed-effects matching			Random-effects matching		
	POM (n=373)	Control (n=1271)	(R)D	POM (n=370)	Control (n=370)	(R)D	POM (n=370)	Control (n=370)	(R)D	POM (n=361)	Control (n=361)	(R)D	POM (n=369)	Control (n=369)	(R)D
All PPCs	12.6%	14.3%	−1.7%	12.7%	14.6%	−1.9%	12.7%	12.7%	0.0%	12.2%	13.3%	−1.1%	12.5%	10.0%	2.4%
Aspiration pneumonia	3.2%	4.9%	−1.7%	3.2%	3.2%	0.0%	3.2%	2.7%	0.5%	3.0%	3.6%	−0.6%	3.3%	3.3%	0.0%
Postoperative LOS	29.1	31.2	−2.2	28.9	29.1	−0.2	28.9	27.0	1.9	28.9	30.8	−2.0	29.0	29.0	0.0
Medical costs (100 JPY)	34,390	36,847	−2457	34,365	35,595	−1229	34,365	33,832	533	34,402	36,931	−2529	34,349	36,862	−2513
Duration of antibiotics adm.	8.8	9.7	−0.9	8.8	8.9	−0.1	8.8	7.9	0.9	8.8	9.7	−0.8	8.8	9.6	−0.8

Values are presented as percent, and days, unless otherwise indicated.

(R)D=(risk) difference, adm=administration, JPY=Japanese Yen, LOS=length of hospital stay, POM=preoperative oral management by dentists, PPC=postoperative pulmonary complication.

Risk difference in bold indicates $P<.05$.

Details including the number of cases, median, 1st and 3rd quartiles, and P values are provided in Supplemental Digital Content 3, http://links.lww.com/MD/C942.

Table 5

Comparison of the postoperative outcomes between the preoperative oral management groups and control groups in IPTW analyses.

Open esophagectomy	IPTW using single-level propensity scores					IPTW using fixed-effects propensity scores					IPTW using random-effects propensity scores				
	POM (n=914)	Control (n=957)	(R)D	95% CI		POM (n=646)	Control (n=935)	(R)D	95% CI		POM (n=762)	Control (n=927)	(R)D	95% CI	
All PPCs	12.8%	16.0%	−3.2%	−9.1	2.7	10.9%	16.1%	−5.1%	−10.9	0.6	11.8%	15.9%	−4.1%	−9.8	1.6
Aspiration pneumonia	2.1%	4.2%	−2.0%	−4.4	0.4	1.5%	4.0%	**−2.5%**	−4.4	−0.6	1.6%	4.1%	**−2.5%**	−4.5	−0.5
Postoperative LOS	36.6	36.1	0.6	−3.9	5.0	36.6	35.8	0.8	−4.2	5.7	36.5	36.1	0.4	−4.1	5.0
Medical costs (100 JPY)	42,008	41,909	99	−3563	3760	41,495	41,826	−332	−4528	3865	42,088	41,948	139	−3766	4,044
Duration of antibiotics adm.	11.4	11.5	−0.1	−1.9	1.6	11.0	11.5	−0.6	−2.5	1.4	11.1	11.5	−0.5	−2.3	1.3

Thoracoscopic esophagectomy	IPTW using single-level propensity scores					IPTW using fixed-effects propensity scores					IPTW using random-effects propensity scores				
	POM (n=1636)	Control (n=1644)	(R)D	95% CI		POM (n=1186)	Control (n=1629)	(R)D	95% CI		POM (n=1325)	Control (n=1605)	(R)D	95% CI	
All PPCs	11.5%	14.3%	−2.8%	−6.6	1.0	12.2%	13.7%	−1.5%	−6.5	3.4	12.4%			−5.8	3.1
Aspiration pneumonia	2.8%	4.8%	**−2.1%**	−4.1	−0.1	2.4%	4.5%	**−2.1%**	−4.0	−0.2	2.6%	4.6%	**−2.0%**	−3.9	−0.1
Postoperative LOS	29.2	31.2	−1.9	−4.6	0.8	28.9	30.8	−1.9	−4.5	0.7	29.5	30.8	−1.4	−4.2	1.4
Medical costs (100 JPY)	34,418	36,765	**−2347**	−4398	−296	34,121	36,652	**−2531**	−4412	−651	34,488	36,700	**−2212**	−4227	−198
Duration of antibiotics adm.	9.0	9.7	−0.8	−2.2	0.7	8.8	9.6	−0.8	−2.0	0.4	9.0	9.6	−0.6	−2.1	0.8

Values are presented as percent, and days, unless otherwise indicated.

(R)D=(risk) difference, adm=administration, CI=confidence interval, IPTW=inverse probability of treatment weighting, JPY=Japanese Yen, LOS=length of hospital stay, POM=preoperative oral management by dentists, PPC=postoperative pulmonary complication.

(Risk) difference in bold indicates $P<.05$.

P values, estimated by generalized linear models, are provided in Supplemental Digital Content 4, http://links.lww.com/MD/C942.

the fee schedule as of 2016, these costs would be offset based on the IPTW analyses results of further reduction in the medical costs (221,200 to 253,100 JPY, equivalent to about $2000 to $2200, for thoracoscopic esophagectomy). The 2012 Japanese guidelines of esophageal carcinoma recommended preoperative oral care before esophagectomy.[20] However, this recommendation has been deleted in the newest guidelines published in 2018,[21] possibly since the levels of evidence supporting the effectiveness of POM on postoperative complications were not high enough.[22] Risk factors of PPC with good evidence including congestive heart failure, ASA class of 2 or more, advanced age, chronic obstructive pulmonary disease, functional dependence, prolonged surgery, and lower preoperative serum albumin level were reported.[23] The relationship between POM by dentists and PPC following esophagectomy is not supported by reports with high-level evidence. However, recently, a multicenter study (n=539) demonstrated that POM by dentists could reduce postoperative pneumonia following esophageal cancer surgery,[23] and a study using a large-scale national administrative claims database (n=16,177 for esophageal cancer, among n=509,179 for 6 cancers) showed that POM by dentists reduced PPCs of major cancer surgery.[24] Nevertheless, the current guidelines of esophagectomy including Japanese guidelines of esophageal carcinoma[21] and enhanced recovery for esophagectomy,[25] do not recommend POM by dentists as routine perioperative care. In our study, we showed that POM by dentists could prevent postoperative aspiration pneumonia following both open and thoracoscopic esophagectomy, and save the medical costs of thoracoscopic esophagectomy based on IPTW analyses which estimated ATE. These results suggested that POM by dentists should be recommended as routine perioperative care for all patients undergoing esophagectomy, regardless of the surgery type.

To analyze data with clustered structure, multilevel regression models are used frequently. Despite the increasing use of PS analyses in medical and healthcare studies, few studies have performed PS analyses considering clustered data structure.[12,16] With regard to both PS matching and weighting analyses, the results of simulation studies showed that by ignoring clustered structures there was biased estimation of the treatment effects.[12,16] To the best of our knowledge, our study is the first PS analyses of Japanese DPC data as clustered data from multiple hospitals; so far, only a few studies incorporated hospital volume as a variable in their PS models. We conducted PS analyses with and without considering the clustered structure and showed that the results obtained using the 2 approaches could be different. An earlier report indicated that hospital volume, one of the cluster-level confounders, influenced mortality rates following esophagectomy in Japan,[26] as in other countries. In our study, PS weighting analyses revealed that by incorporating the variables representing hospital volume into the PS models, the estimates of analyses using single-level PSs fluctuated more than those of analyses using multilevel PSs (Supplemental Digital Content 4, http://links.lww.com/MD/C942), which implies that analyses that do not consider the clustered structure of data are not robust enough, consistent with the simulation studies. Moreover, hospital volume is not the only cluster-level confounder; the institutional heterogeneity of esophagectomy was previously reported to persist even among high-volume hospitals in Japan.[27] Researchers should consider the unmeasured cluster-level confounders in PS analyses of data with clustered structure.

Among previous studies to determine the risk factors of complications following esophagectomy in the Japanese population, some studies used databases,[26,28] such as the National Clinical Database (NCD) and the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB).[24] The NCD contains variables that are almost the same as those of the American College of Surgeons' National Surgical Quality Improvement Program,[29] and the NDB contains all electric health insurance claims of Japan. The NCD has various clinical variables such as the values of preoperative laboratory tests, and intraoperative blood loss, which are not included in the claims database. The DPC used in our study comprises a mixture of claims and discharge summaries. Since these databases cannot be linked currently, the DPC is the most popular database for various healthcare studies due to its mixed nature. The DPC data contains some diagnosis-specific variables such as the TNM classification for cancer patients, and information of both PDPS and FFS-based medical services at admission. Using the DPC data to investigate the effects of POM by dentists, we determined multiple outcomes including the incidence of PPCs and the total medical costs, with adjusting for various patient-level confounders.

Our study has some limitations. First, the DPC data does not contains clinical data except for some diagnosis-specific variables. Some of the known risk factors, such as the results of laboratory tests, are not available, which may cause insufficient adjustment of the risk factors for various outcomes. Doctors may consider referring patients with high risk of PPC based on results of preoperative laboratory tests to a dentist for POM. However, this would lead to underestimating the effects of POM,[24] so the result of reduced rate of postoperative aspiration pneumonia in our study should be consistent. Second, we only had information of each admission period, but not that of before and after admission. We assigned cases with claims of additional fees for surgery preceded by POM as the POM group, not with claims of treatment fees for perioperative oral management by dentists. It is possible that the additional fees were not input by the hospital at which surgery was performed, nevertheless POM had been administered by dentists before surgery. However, this would also lead to underestimating the effects of POM, if some cases with POM accidentally assigned to the control group. Preoperative chemotherapy, which is regarded as standard procedure for resectable esophageal cancer cases in Japan,[21] could not be reviewed in our study if conducted before admission for surgery. Nishino et al[30] reported that oral care may be provided to patients who received chemotherapy since oral mucositis is a frequent adverse effect following chemotherapy, which could reduce the incidence of postoperative pneumonia. However, a previous multicenter study incorporating various risk factors including POM by dentists and neoadjuvant chemotherapy reported that neoadjuvant chemotherapy was not related to the incidence of postoperative pneumonia.[22] We were unable to conduct patient follow-up after discharge, and so, could not determine the LOS in patients with transfer from the hospital at which esophagectomy was performed to another hospital after discharge. The DPC data has the variable of destination after discharge including the home, another hospital, and the nursing home. We were unable to determine the overall LOS if a patient did not return home after esophagectomy, but could check the balance of this variable instead. The absolute standardized differences of the 3 postmatching populations and 2 weighted populations were >0.1; more patients in the POM groups through fixed- and random-effects matching, and SMRW analyses using fixed- and random-effects PSs of open esophagectomy were transferred to other hospitals, whereas less patients in the POM groups through random-effects matching of thoracoscopic esophagectomy were transferred. The absolute standardized differences in all of the IPTW analyses were ≤ 0.1, suggesting that the effects of transfer were minimal.

5. Conclusion

Our results suggested that POM by dentists for all patients undergoing open or thoracoscopic esophagectomy could reduce the incidence of postoperative aspiration pneumonia. It also could reduce the total medical costs of thoracoscopic esophagectomy. Thus, POM by dentists can be considered as routine perioperative care for all patients undergoing esophagectomy, regardless of the expected risk for PPC.

Author contributions

Conceptualization: Jung-ho Shin, Susumu Kunisawa, Yuichi Imanaka.
Data curation: Kiyohide Fushimi.
Formal analysis: Jung-ho Shin.
Funding acquisition: Yuichi Imanaka.
Methodology: Jung-ho Shin, Yuichi Imanaka.
Project administration: Susumu Kunisawa.
Resources: Susumu Kunisawa, Kiyohide Fushimi.
Supervision: Yuichi Imanaka.
Writing – original draft: Jung-ho Shin.
Writing – review & editing: Susumu Kunisawa, Kiyohide Fushimi, Yuichi Imanaka.

References

[1] Fitzmaurice C, Dicker D, Pain A, et al. Global Burden of Disease Cancer CollaborationThe Global Burden of Cancer 2013. JAMA Oncol 2015;1:505–27.
[2] Baba Y, Yoshida N, Shigaki H, et al. Prognostic impact of postoperative complications in 502 patients with surgically resected esophageal squamous cell carcinoma: a retrospective single-institution study. Ann Surg 2016;264:305–11.
[3] Yang CK, Teng A, Lee DY, et al. Pulmonary complications after major abdominal surgery: National Surgical Quality Improvement Program analysis. J Surg Res 2015;198:441–9.
[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;25:93–7.
[5] Marino PJ, Wise MP, Smith A, et al. Community analysis of dental plaque and endotracheal tube biofilms from mechanically ventilated patients. J Crit Care 2017;39:149–55.
[6] Ministry of Health, Labour and Welfare. [Fee schedule revision, fiscal year 2012]. Available at: http://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/iryouhoken/iryouhoken15/. Accessed November 16, 2018. Japanese.
[7] Ministry of Health, Labour and Welfare. [Fee schedule revision, fiscal year 2014]. Available at: http://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000032996.html. Accessed November 16, 2018. Japanese.
[8] DPC Research Group. [Study on proper evaluation of function and resource requirement of healthcare based on sustained refinement of diagnostic group classification]. Available at: http://www.dpcsg.jp/about.html. Accessed November 16, 2018. Japanese.
[9] Choi J, Dekkers OM, le Cessie S. A comparison of different methods to handle missing data in the context of propensity score analysis. Eur J Epidemiol 2019;34:23–36.
[10] Gagne JJ, Glynn RJ, Avorn J, et al. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol 2011;64:749–59.
[11] Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care.* 2005;43:1130–1139.
[12] Arpino B, Mealli F. The specification of the propensity score in multilevel observational studies. Comput Stat Data Anal 2011;55:1770–80.
[13] Arpino B, Cannas M. Propensity score matching with clustered data. An application to the estimation of the impact of caesarean section on the Apgar score. Stat Med 2016;35:2074–91.
[14] Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. Pharm Stat 2011;10:150–61.
[15] Sato T, Matsuyama Y. Marginal structural models as a tool for standardization. Epidemiology 2003;14:680–6.
[16] Li F, Zaslavsky AM, Landrum MB. Propensity score weighting with multilevel data. Stat Med 2013;32:3373–87.
[17] Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 2009;28:3083–107.
[18] Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. Stat Med 2015;34:3661–79.
[19] van Walraven C, Austin PC, Jennings A, et al. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. Med Care 2009;47:626–33.
[20] Kuwano H, Nishimura Y, Oyama T, et al. Guidelines for diagnosis and treatment of carcinoma of the esophagus April 2012 edited by the Japan Esophageal Society. Esophagus 2015;12:1–30.
[21] Kitagawa Y, Uno T, Oyama T, et al. Esophageal cancer practice guidelines 2017 edited by the Japan esophageal society: part 2. Esophagus 2018;16:25–43.
[22] 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.
[23] Gallart L, Canet J. Post-operative pulmonary complications: understanding definitions and risk assessment. Best Pract Res Clin Anaesthesiol 2015;29:315–30.
[24] Ishimaru M, Matsui H, Ono S, et al. Preoperative oral care and effect on postoperative complications after major cancer surgery. Br J Surg 2018;105:1688–96.
[25] Findlay JM, Gillies RS, Millo J, et al. Enhanced recovery for esophagectomy: a systematic review and evidence-based guidelines. Ann Surg 2014;259:413–31.
[26] Nishigori T, Miyata H, Okabe H, et al. Impact of hospital volume on risk-adjusted mortality following oesophagectomy in Japan. Br J Surg 2016;103:1880–6.
[27] Kataoka K, Nakamura K, Mizusawa J, et al. Variations in survival and perioperative complications between hospitals based on data from two phase III clinical trials for oesophageal cancer. Br J Surg 2015;102:1088–96.
[28] Takeuchi H, Miyata H, Gotoh M, et al. A risk model for esophagectomy using data of 5354 patients included in a Japanese nationwide web-based database. Ann Surg 2014;260:259–66.
[29] Gotoh M, Miyata H, Hashimoto H, et al. National Clinical Database feedback implementation for quality improvement of cancer treatment in Japan: from good to great through transparency. Surg Today 2016;46:38–47.
[30] Nishino T, Takizawa H, Yoshida T, et al. [Current status and effectiveness of perioperative oral health care management for lung cancer and esophageal cancer patients]. Kyobu Geka 2016;69: 30–4.