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Effects of perioperative oral care on prevention of postoperative pneumonia after lung resection: Multicenter retrospective study with propensity score matching analysis

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ABSTRACT

Background: Postoperative pneumonia can be a fatal complication that may occur after lung resection in cancer patients. Some reports have shown that the incidence of postoperative pneumonia is decreased after esophageal surgery by perioperative oral care; however, there exist no data to suggest that a lack of perioperative oral care can be a risk factor for postoperative pneumonia after lung resection. To investigate the association between the preventive effect of oral care and postoperative pneumonia, we conducted a multicenter, retrospective study of lung cancer patients who underwent lung resection.

Methods: Between January 2014 and December 2016, a total of 721 patients underwent lung resections at 1 of the 6 hospitals included in our study. Among 721 patients, 280 (38.8%) received perioperative oral care, and the remaining 441 (61.2%) did not receive any such care. Propensity score matching was performed to minimize selection biases associated with the comparison of retrospective data between the oral care and control groups.

Results: Of the 721 patients, 54 (7.5%) experienced postoperative pneumonia involving 13 of the 280 patients (4.6%) in the oral care group and 41 of the 441 patients (9.3%) in the control group ($P = .02$). On propensity score analysis, a significant difference was also found between oral care intervention and incidence of postoperative pneumonia ($P = .002$).

Conclusion: Our results suggest that perioperative oral care is an effective method to decrease the occurrence of postoperative pneumonia in patients who have undergone lung resection.

Introduction

Lung cancer is a leading cause of death worldwide.[1] Patients undergoing lung resection are more prone to postoperative pulmonary and infectious complications, subsequently leading to high morbidity.[2] Among postoperative complications, postoperative pneumonia is the most serious infection that occurs after lung resection. Thus, preventing the occurrence of postoperative pneumonia is critical for better survival outcomes in these patients.

Some studies have shown that the incidence of postoperative pneumonia after esophageal cancer surgery is decreased after oral care intervention,[3,4] but no studies have reported the lack of perioperative oral care as a risk factor for postoperative pneumonia after lung cancer surgery. We conducted this retrospective study to investigate the preventive effect of oral care on postoperative

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pneumonia among patients with lung cancer who underwent lung resection.

Patients and Methods

Patients

A total of 721 patients with lung cancer underwent lung resection between January 2014 and December 2016 at one of the following six university hospitals in Japan: Kobe University, Nagasaki University, Shinshu University, Nagoya City University, Osaka City University, and Kagoshima University. Of these 721 patients, 280 (38.8%) requested perioperative oral care from their chief physicians in the hospital, and the remaining 441 (61.2%) patients had not made any such request. We designated the patients receiving oral care as the "oral care group" and those who did not receive oral care as the "control group." The design of this study was approved by the institutional review board of Kobe University Hospital (Authorization number: 160015).

Oral care

Each patient in the oral care group received care from a dentist and dental hygienist. This care was provided a few days presurgery and postsurgery, and the care plan included oral health maintenance, removal of dental calculus, removal of tongue coating with a toothbrush, and extraction of teeth with severe periodontitis.

Variables

The objective variable was the occurrence of postoperative pneumonia. Postoperative pneumonia was diagnosed comprehensively by the respiratory surgeons after degrees Centigrade, evaluating for the degree of body temperature above 37°C, laboratory data such as white blood count (WBC) and C-reactive protein (CRP), and diagnostic images such as chest X-ray or chest computed tomography (CT). The following variables were reviewed retrospectively from the medical records and analyzed: (1) patient factors—age, sex, performance status (PS), drinking of alcohol, Brinkman index, diabetes mellitus, cerebrovascular disease, and body mass index (BMI); (2) preoperative data—forced expiratory volume (FEV) 1.0%, serum albumin and cholesterol concentrations, leukocyte count; (3) perioperative treatment or care—neoadjuvant chemotherapy and perioperative oral care; (4) pathologic stage (P stage); (5) operative factors—type of resection (wedge, segmental, lobectomy, or lung resection), operative approach (thoracoscopic or open surgery), operation time, blood loss, and transfusion. P stage was classified according to the tumor, node, metastasis (TNM) classification system for lung cancer, published by the Union for International Cancer Control (UICC).

Statistical analyses

All statistical analyses were performed using the SPSS software (v 24.0, Japan IBM Co, Tokyo, Japan). The association of each variable with postoperative pneumonia was analyzed by Fisher exact test or the χ^2 test for categorical variables, one-way ANOVA for parametric ratio scale, and Mann-Whitney *U* test for nonparametric ratio scale, followed by multivariate analysis with logistic regression analysis. A probability value (*P* value) of less than .05 was accepted as significant.

To minimize selection biases associated with the comparison of retrospective data analysis, a propensity score matching was performed between oral care and control groups. For each patient, a propensity score for oral care intervention was calculated by logistic regression analysis of all predictive variables. Later, the

Table I
Background factors of the original 721 patients

Variable	Category	Control group	Oral care group	*P* value
Age (years)		65–76 (70)	63–75 (70)	.356
Sex	Male	268	178	.479
	Female	173	102	
PS	PS0	409	238	.001*
	PS1-3	32	42	
Drinking	(−)	200	127	1.000
	(+)	241	153	
Brinkman index		0–1,000 (600)	0–955 (533)	.417
Diabetes mellitus	(−)	375	238	1.000
	(+)	66	42	
Cerebrovascular disease	(−)	401	254	1.000
	(+)	40	26	
BMI (kg/m^2)		19.8–24.4 (22.1)	19.9–24.7 (22.4)	.473
FEV (%)		68.0–81.8 (74.7)	67.7–80.9 (74.7)	.983
Albumin (g/dL)		4.0–4.5 (4.2)	3.9–4.5 (4.2)	.583
Leukocyte (/μL)		4,485–6,700 (5,500)	650–7,000 (5,770)	.095
Cholesterol (mg/dl)		199 ± 37.9	197 ± 38.3	.629
Neoadjuvant chemotherapy	(−)	428	270	.668
	(+)	13	10	
Stage	stage 1	298	173	.127
	stage 2-4	143	107	
Type of Resection	Wedge or segmental resection	94	49	.215
	Lobectomy or lung resection	347	231	
Operative approach	Thoracoscopic surgery	400	191	< .001*
	Open surgery	41	89	
Operation time (minutes)		141–253 (194)	164–291 (223)	.018*
Blood loss (g)		6.3–110 (50)	20–197 (80)	< .001*
Transfusion	(−)	425	259	.025*
	(+)	16	21	

Note: Values are expressed as the mean ± standard deviation in a parametric ratio scale, 25%–75% teil in a nonparametric ratio scale, or number of patients in a nominal scale.

* Significant.

Table II
Correlations between each variable and postoperative pneumonia in original 721 patients (univariate analysis)

Variable	Category	Pneumonia (−)	Pneumonia (+)	*P* value
Age (years)		64–75 (70)	65.8–76 (71)	.700
Sex	Male	406	40	.059
	Female	261	14	
PS	PS0	602	45	.107
	PS1-3	65	9	
Drinking	(−)	309	18	.087
	(+)	358	36	
Brinkman index		0–1,000 (540)	400–1,133 (790)	.016*
Diabetes mellitus	(−)	566	47	.843
	(+)	101	7	
Cerebrovascular disease	(−)	608	47	.323
	(+)	59	7	
BMI (kg/m^2)		19.8–24.5 (22.3)	18.8–23.9 (22.1)	.486
FEV (%)		68.0–81.6 (74.8)	66.3–77.4 (73.0)	.138
Albumin (g/dL)		4.0–4.5 (4.3)	3.9–4.3 (4.1)	.011*
Leukocyte (/μL)		4,000–6,800 (5,560)	5,000–7,925 (5,850)	.180
Cholesterol (mg/dl)		198 ± 38.0	196 ± 38.6	.717
Neoadjuvant chemotherapy	(−)	646	52	.688
	(+)	21	2	
Stage	stage 1	441	30	.137
	stage 2-4	226	24	
Type of resection	Wedge or segmental resection	134	9	.722
	Lobectomy or lung resection	533	45	
Operative approach	Thoracoscopic surgery	552	39	.065
	Open surgery	115	15	
Operation time (minutes)		145–264 (201)	193–296 (232)	.006*
Blood loss (g)		10–150 (50)	13.8–298 (100)	.070
Transfusion	(−)	636	48	.050
	(+)	31	6	
Oral care intervention	(−)	400	41	.020*

Note: Values are expressed as the mean ± standard deviation in a parametric ratio scale, 25%–75% teil in a nonparametric ratio scale, or number of patients in a nominal scale.
* Significant.

propensity score–matched cases (450 patients) were evaluated by univariate analysis.

Results

Background factors of the 721 patients included in this study are presented in Table I. A comparison between the control and oral care groups revealed significant differences in the following variables: PS, operative approach, operation time, blood loss, and transfusion.

Of the 721 patients, 54 (7.5%) experienced postoperative pneumonia, involving 13 of the 280 patients (4.6%) in the oral care group and 41 of the 441 patients (9.3%) in the control group ($P = .02$) (Table II). Based on the results of the univariate analysis, Brinkman index, serum albumin, operation time, and oral care intervention were found to be significantly correlated with the development of postoperative pneumonia (Table II). Further, multivariate analysis showed the following variables to be significantly correlated with postoperative pneumonia : FEV1% (odds ratio [OR]: 0.975, 95% confidence interval [CI]: 0.953–0.997), open surgery (OR: 2.158, 95% CI: 1.068–4.358), lesser serum albumin concentration (OR: 0.520, 95% CI: 0.284–0.952), greater operation time (OR: 1.002, 95% CI: 1.000–1.004), and lack of oral care intervention (OR: 2.946. 95% CI: 1.476–5.883).

To minimize selection biases associated with the comparison of retrospective data analysis, propensity score analysis resulted in the identification of 225 matched pairs (ie, 450 patients) out of the 721 subjects (Table III). A concordance index (c-index) of 0.685 was obtained, allowing us to differentiate relatively distinctively between patients undergoing nonoperative care and operative treatments. The Hosmer-Lemeshow test detected an insignificant degree ($P = .684$) of miscalibration. The propensity score predicts the probability of a patient receiving operative l treatment, and we achieved a score in the range of 0.03510–0.86153 and 0.03937–0.86647 for the control and oral care groups, respectively. Univariate analysis revealed significant differences between oral care intervention and postoperative pneumonia ($P = .002$).

Discussion

Postoperative pneumonia is one of the most common complications in lung cancer patients who have undergone lung resection.[5,6] In particular, postoperative pneumonia is associated with high mortality.[7] Studies have reported that the incidence rate of postoperative pneumonia after lung resection ranges 2.9%–10.7%.[8–12] In the present study, postoperative pneumonia occurred in 7.5% of our patients (54 out of 721 participants), consistent with the incidence rate of other reports.

In an attempt to determine a preventive measure for postoperative pneumonia, many clinical studies have examined the risk factors associated with this condition.[13–15] Factors, such as smoking and operation time, have been associated commonly with the incidence of postoperative pneumonia in patients with lung cancer.[16–19] In the present study, univariate analysis revealed Brinkman index, serum albumin concentration, operation time, and perioperative oral care to be associated with occurrence of postoperative pneumonia. Because serum albumin concentration is an index of nutritional condition, nutritionally deprived patients undergoing lung resection might be at greater risk of developing infections than others. A multivariable analysis of our 721 patients identified a lesser degree of lung function (%FEV1), open thoracotomy (versus thoracoscopic resection), lesser serum albumin concentration, a greater operation time, and lack of perioperative oral care as the risk factors associated with the occurrence of

Table III
Background factors of the 450 patients after propensity score matching

Variable	Category	Control group	Oral care group	*P* value
Age (years)		64–75 (70)	63.5–75 (70)	.637
Sex	Male	135	139	.772
	Female	90	86	
PS	PS0	196	200	.664
	PS1-3	29	25	
Drinking	(−)	104	102	.925
	(+)	121	123	
Brinkman index		0–980 (600)	0–1,000 (495)	.637
Diabetes mellitus	(−)	196	191	.587
	(+)	29	34	
Cerebrovascular disease	(−)	202	201	1.000
	(+)	23	24	
BMI (kg/m^2)		19.8–24.2 (22.1)	19.9–24.7 (22.5)	.451
FEV (%)		67.4–80.9 (74.7)	67.8–80.9 (74.8)	.925
Albmin (g/dL)		4.0–4.4 (4.2)	3.9–4.5 (4.2)	.850
Leukocyte (/μL)		4,600–6,775 (5,500)	4,480–6,925 (5,590)	.760
Cholesterol (mg/dl)		197 ± 37.6	198 ± 38.9	.794
Neoadjuvant chemotherapy	(−)	216	217	1.000
	(+)	9	8	
Stage	stage 1	139	141	.923
	stage 2-4	86	84	
Type of resection	Wedge or segmental resection	40	38	.901
	Lobectomy or lung resection	185	187	
Operative approach	Thoracoscopic surgery	184	182	.904
	Open surgery	41	43	
Operation time (minutes)		151–275 (209)	159–224 (209)	.925
Blood loss (g)		10–150 (60)	10–170 (60)	.925
Transfusion	(−)	214	211	.681
	(+)	11	14	

Note: Values are expressed as the mean ± standard deviation in a parametric ratio scale, 25%–75% teil in a nonparametric ratio scale, or number of patients in a nominal scale.

pneumonia. Many studies have shown that lesser lung function is associated with postoperative complications including pneumonia.[20–22] Jeon et al[23] reported that video-assisted thoracoscopic surgery (VATS) is associated with a lesser incidence of pulmonary complications compared with open thoracotomy. In general, malnutrition or a greater operation have an even greater risk of a patient developing infection postoperatively.

It is well known that silent aspiration plays an important role in the incidence of pneumonia. Lung cancer is observed more frequently in elderly patients who subsequently develop pneumonia, presumably attributable to the silent aspiration associated with age-related impairment of coughing and swallowing reflexes. Hoshikawa et al[24] reported that elderly patients show suppressed swallowing reflex in general; however, postoperatively, this effect is further pronounced along with transient attenuation of the cough reflex. These investigators also reported that it is necessary to develop an effective system to provide preoperative, dentist-assisted, professional oral care, especially for elderly and high-risk patients under consideration for lung resection. Akutsu et al[25] reported that pathogens in preoperative dental plaque are risk factors for postoperative pneumonia. Therefore, we believe that perioperative oral care can decrease bacteria in patients' oropharyngeal region of the bronchi and prevent pneumonia.

Since 2012, oral care has been covered by the medical insurance system in Japan and, at the present, most Japanese patients receive perioperative oral care before. In fact, some studies have reported that the incidence of postoperative pneumonia has decreased because of the institution of perioperative oral care, [3,4] but there has been no evidence to confirm oral care as a risk factor for postoperative pneumonia after lung resection. In the present study, logistic regression analysis of the propensity score–matched patients (450) revealed the lack of oral care intervention to be a significant contributor to the overall burden of postoperative pneumonia.

This study has some weaknesses. First, biases were decreased as much as possible using an analysis of propensity score matching; despite this approach, removing all biases may be difficult, because of the retrospective nature of this study. Second, the six hospitals do not have a unified oral care protocol. Third, there was a difference in the operative approach between the two groups (thoracoscopic surgery or open surgery). However, in Japan, most hospitals treat patients according to predefined guidelines, such as the *Clinical Guidelines for Lung Cancer*.[26]

In the future, we aim to study the effects of perioperative oral care in the prevention of postoperative pneumonia after lung resection, using a prospective study design, with the presence or absence of postoperative pneumonia as the primary end point. We also plan to develop a unified protocol of perioperative oral care management. In the prospective study, all patients will receive a unified protocol of perioperative oral management, including extraction of teeth, and oral care that we will develop. In addition, we aim to further discuss the method of oral care intervention, as well as the effective timing and frequency.

In conclusion, this is the first study to report the lack of oral care as a risk factor of postoperative pneumonia in cancer patients after lung resection. Our study has applicability and generalizability because we analyzed a large number of participants in a multicenter analysis. In addition, to minimize selection biases associated with the comparison of retrospective data analysis, we evaluated propensity score–matched patients. We believe that perioperative oral care may serve as an effective method to prevent the occurrence of postoperative pneumonia in patients who have undergone lung resection.

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