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ORIGINAL ARTICLE

Effect of combination of pre- and postoperative pulmonary rehabilitation on onset of postoperative pneumonia: a retrospective cohort study based on data from the diagnosis procedure combination database in Japan

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Abstract

Background To examine the effect of rehabilitation on postoperative pulmonary complication when it is conducted in combination of both before and after lung cancer surgery, as compared with either before or after surgery and no rehabilitation.

Methods A retrospective cohort study was conducted to examine the effect of rehabilitation before and after lung cancer surgery on the causes of postoperative pneumonia. Data were collected from the diagnosis procedure combination (DPC) database. Patients admitted who received operative treatment for a new primary (ICD codes: C34) were selected. The inclusion criteria were patients who had pneumonectomy, malignant tumor surgery for the lung (thoracotomy), or thoracoscopic surgery (endoscopic; treatment code: K511-00, K513-00~03, and K514-00, 02). The exclusion criteria were patients who had a lung transplantation (treatment code: K514-03~06), suspected diagnosis, and a pneumonia within 3 months before being diagnosed as having lung cancer. Main outcome was onset of postoperative pneumonia.

Results Among 76,739 lung cancer patients, 15,146 who underwent lung cancer surgery were included in the analysis. In the combination of pre- and postoperative group, as compared with the preoperative [odds ratio (OR), 95% confidence interval (CI) 2.8, 1.8–4.4], postoperative (1.9, 1.6–2.3), and no rehabilitation group (2.5, 2.1–2.8), the onset of pneumonia was less frequent.

Conclusions Combination of preoperative and postoperative rehabilitations significantly prevents postoperative pneumonia as compared with having preoperative, postoperative, or no rehabilitation.

Keywords Cancer rehabilitation · Postoperative complication · Lung cancer

Introduction

Malignant neoplasm is the leading cause of death in Japan [1]; lung cancer is the most frequent among them [2]. Although surgical operation is a typical approach for lung cancer, several researchers reported that the incidence of pulmonary complications involving pneumonia range from 7.5 to 20% postoperatively [3, 4], with a mortality rate of > 60% [5–7].

The effectiveness of rehabilitation has been examined for preventing pulmonary complications and protecting respiratory function after lung surgery [8–10]. Postoperative breathing training such as exhalation practice to stimulate expectorant and deep breaths in improving ventilation are performed with treadmill walking and ergometer exercise [11] to maintain motor function.

A study by Algar et al. [12] and a systematic review by Cavalhery [13] proved that preoperative rehabilitation decreases the risk of pulmonary complications. Its effectiveness for improving peak rate of oxygen consumption [14] and forced expiratory volume [15], and for shortening hospitalization duration [16] has been suggested. On the other hand, the effectiveness of postoperative rehabilitation

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in reducing the risk of postoperative complications was reported by Thomas et al. [17] and Hall et al. [18] Based on the existing evidence, rehabilitation before and after lung cancer surgery is recommended by cancer rehabilitation guideline [19–21].

However, the following three points are still unreported. First, it has not been examined the effect of combined rehabilitation both before and after surgery. Second, most prior studies are controlled trials that limited to experimental situations and rigorously conducted; therefore, the effect confirmed in the trials has not been verified in real-world situations. Third, the implementation status of rehabilitation in clinical practice is unknown.

The aim of this study was to examine the effect of rehabilitation on postoperative pulmonary complication when it is conducted both before and after lung cancer surgery, as compared with either before or after surgery and no rehabilitation practice. Moreover, we aimed to determine the implementation status of rehabilitation conducted before/after lung cancer surgery on the basis of large-scale administrative data in Japan.

Patients and methods

This report was based on the Reporting Studies Conducted Using Observational Routinely Collected Health Data (RECORD) Statement [22]. A retrospective cohort study was conducted to examine the effect of rehabilitation before and after lung cancer surgery on the causes of postoperative pneumonia. Data collected from the Diagnosis Procedure Combination (DPC) database and constructed from electronic prescriptions, and DPC data collected by Medical Data Vision Co., Ltd. (MDV), from an accumulated 18.2 million people, were used.

DPC is one of the medical claim databases that collect administrative data. DPC data are collected from target hospitals that subscribe to MDV [23]. Data include the basic attributes of the patients, detailed statement of medical practice, characteristics of the medical institution, existence of data related to medical care other than those provided by healthcare claims data [23].

Medical doctors input basic attributes of the patients, such as sex, birthdate, date of hospitalization, main illness, the disease that triggered the admission, the disease that caused the most consumption of medical resources, preoperative comorbidities, and complications after admission. It is a distinctive feature of DPC data that diagnosis names are recorded both on admission and after hospitalization [24]. Individual medical practice details (e.g., surgery, anesthesia, rehabilitation, and medication history), along with the date of operation, number of practice, quantity used, and reference unit, are recorded. Institutional data include the number of hospitals, number of hospital beds, and the basic charge for admission. Information on "how much medical practice of how many medical remuneration points were carried out" could be obtained for claims data. We have guaranteed an opportunity to refuse to participate in this research by directly notifying all research participants from each facility; additionally, information on the usage in the research was released on the facility's internet homepage or its notice board. Moreover, data used in the present study have been converted into unlinkable anonymization by the MDV. This prevents the researcher from handling the correspondence table, thereby making the data used in this study impossible to link to the personal information of the patients.

Participants and data extraction

The target disease name was selected according to the code of the International Statistical Classification of Diseases and Related Health Problems Version 10 [25] (ICD code) and the Medical intervention classification master code [26] (treatment code).

Using the ICD codes of a previous study [27] as reference, hospitalized patients who received operative treatment for a new primary lung cancer (ICD codes: C34) were selected. The inclusion criteria were patients who had pneumonectomy, malignant tumor surgery for the lung (thoracotomy), or thoracoscopic surgery (endoscopic; treatment code: K511-00, K513-00~03, and K514-00, 02). The exclusion criteria included death from lung cancer before the surgery, a lung transplantation (treatment code: K514-03~06), suspected diagnosis, and a pneumonia within 3 months before being diagnosed with lung cancer. Respiratory disease was defined as pneumonia.

Data from January 2018 to March 2018 that were anonymized by the MDV were accessed. Data that can potentially identify individual patients were not verified. A single database, which was not linked with external data, was used for this study.

Measurement variable

The cofounding variables, effect modifier, and prognostic factor of the relevance between having both preoperative and postoperative rehabilitations and onset of pneumonia were extracted. The extracted items were sex, age, smoking index, respiratory function on admission (Hugh–Jones classification), height, weight, cancer stage classification (TNM staging), comorbidities on admission (chronic respiratory illness, interstitial pneumonia, chronic cardiac failure, hepatic disorder, chronic renal failure, and cerebrovascular accident), performance in activities of daily living on admission (Barthel Index), operative procedure (endoscopic or thoracotomy), and number of days and units of rehabilitation. Lung cancer patients with comorbid chronic respiratory disease have a higher rate of postoperative pneumonia than those who do not [28]. Also, interstitial pneumonia co-morbid with lung cancer is likely to exacerbate postoperatively [29]. In addition, patients with chronic cardiac failure [30], hepatic disorder [31], chronic renal failure [32], and cerebrovascular accident [33] have a higher risk of pneumonia than those who do not; thus, co-morbidity status of these three diseases were included.

The implementation pattern of pre- and postoperative rehabilitation was classified into four groups as follows: combination of both preoperative and postoperative rehabilitation groups (combination group), preoperative rehabilitation group (preoperative group), postoperative rehabilitation group (postoperative group), and no rehabilitation group.

Preoperative period was defined as (1) 7 days before surgery, when medical remuneration points for respiratory rehabilitation as a preoperative rehabilitation was obtainable; (2) patients were hospitalized for cancer treatment, because patient's rehabilitation fee could be assessed. Postoperative rehabilitation is defined on the day of surgery and after surgery. In the previous study, as postoperative pneumonia occurs immediately after surgery [34], rehabilitation after the onset of pneumonia was omitted from the postoperative rehabilitation. Cancer stage was sorted according to seven levels based on the TNM staging as follows: stage IA, IB, IIA, IIB, IIIA, IIIB, and IV [4]. The Hugh–Jones classification [35] was used to sort respiratory function on admission in I–V stage levels.

Outcome

Primary outcome was determined on the basis of postoperative onset of pneumonia. Postoperative is defined as from the day of surgery to the day of discharge. Pneumonia is a representative disease for which the effect of rehabilitation could be anticipated in the attempt of preventing postoperative pulmonary complications [36].

Statistical analysis

Descriptive statistics

First, the implementation rates of rehabilitation in the combination, preoperative, postoperative, and no rehabilitation groups were determined. Second, the implementation patterns of rehabilitation and operative procedure were sorted, and then the incidence rate of pneumonia was determined.

Multiple logistic regression analysis

To determine the independent effect of rehabilitation patterns, a multiple logistic regression analysis was conducted. The following predictor variables were selected: lung cancer stages (seven levels), sex, age, height, weight, number of days of rehabilitation, Barthel Index, co-morbidities on admission (chronic respiratory illness, interstitial pneumonia, chronic cardiac failure, hepatic disorder, chronic renal failure, and cerebrovascular accident), respiratory function on admission (Hugh–Jones classification), smoking index, and whether rehabilitation fee was assessed. Following this, the relevance between the implementation pattern of preoperative and postoperative rehabilitations and onset of pneumonia was analyzed.

The variance inflation factor (VIF) was used to admit multicollinearity when VIF was $\geqq 10$. The analysis was performed for all the subjects and adopted for each surgical procedure group, namely the endoscopic and thoracotomy groups.

For missing values, the situation and pattern of the missing data were confirmed. Among the subjects included in the analysis, $\geqq 5\%$ had missing values. Multiple logistic regression analysis using the multiple imputation method was performed [37].

For the variables subjected to the multiple imputation method, even the condition of normal distribution has not been met or be in the case of categorical variables, the effect on the analysis was reported to be small [38]. Therefore, variables with the assumption of normal distribution were equally treated. Even if the substituted value of the categorical variable did not collide with the category of a particular variable, the assigned value was not rounded on the basis of the study of Alison [38]. Twenty sets of substitute models were generated, and then integrated using Rubin's rules [39].

In this study, onset of pneumonia was defined as an outcome and was considered to be that rehabilitation prevented pneumonia when the odds ratio was > 1. For the data processing, Stata 15 (StataCorp LCC., USA) and JMPpro.ver13 (SAS Institute Inc., USA) were used.

This study was conducted with the approval of the ethics committee of Kyoto University Graduate School and Faculty of Medicine, Kyoto University Hospital (Authorization no. R1376).

Results

Patient attribution

Among 76,739 lung cancer patients, 15,146 who underwent lung cancer surgery and free from pneumonia 3 months prior to the development of cancer were included in the analysis (Fig. 1).

The patients' attributes are shown in Tables 1, 2 and 3. Of the patients, 8724 (57.6%) were male and 6622 (42.4%) were female, with a mean (standard deviation SD) age of

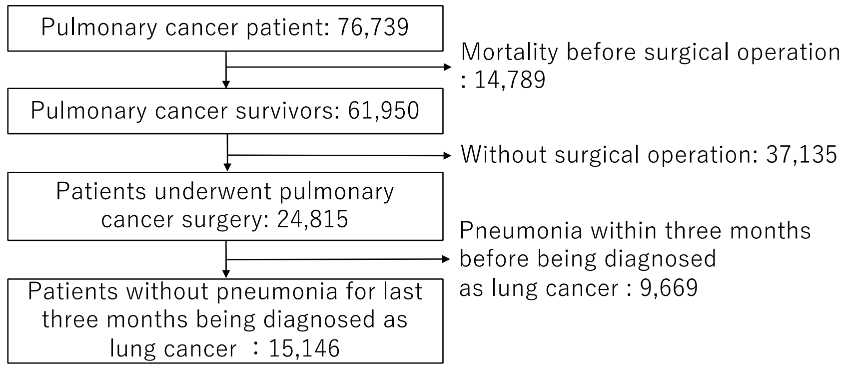

Fig. 1 Patient inclusion

69.1 (9.4) years. For the operative procedure, 12,505 patients (82.6%) underwent endoscopic surgery and 2771 (18.3%) had a thoracotomy. Of these patients, 2483 (16.4%) developed pneumonia. As comorbidities, chronic respiratory illness, interstitial pneumonia, and hepatic disorder were found in 4455 (29.4%), 3646 (24.0%), and 2188 patients (14.4%), respectively. The mean (SD) Barthel Index score on admission was 96.1 (18.0). The cancer stages were as follows: IA, 7113 patients (46.9%); IB, 2298 (15.2%); IIA, 801 (5.3%); IIB, 448 (3.0%); IIIA, 792 (5.2%); IIIB, 31 (0.2%); and IV, 303 (2.0%). No significant difference was found between other attributes such as operative procedure and each intervention group.

Descriptive statistics

The implementation pattern for rehabilitation in the combination, preoperative, postoperative, and no rehabilitation groups was as follows: 4729 (33.4%), 269 (1.8%), 2105 (13.9%), and 8043 (53.1%), respectively (Table 4). Postoperative pneumonia occurred in 478 (10.0%), 61 (22.3%), 366 (17.2%), and 1621 patients (19.8%) in the combination, preoperative, postoperative, and no rehabilitation groups, respectively. According to operational procedure, in the order of endoscopy and thoracotomy, pneumonia was found in 402 (10.7%) and 76 (7.6%), 55 (22.2%) and 6 (25.0%), 300 (17.1%) and 66 (18.3%), and 1291 (19.2%) and 330 patients (23.9%), respectively.

Multiple logistic regression analysis

The results of the analysis are shown in Table 5. VIF did not exceed ≧ 10 in any model.

In the combination group, as compared with the preoperative [odds ratio (OR), 95% confidence interval (CI) 2.8, 1.8–4.4], postoperative (1.9, 1.6–2.3), and no rehabilitation (2.5, 2.1–2.8) group, the onset of pneumonia was less frequent. The postoperative group had a significantly lower incidence of pneumonia than the no rehabilitation group (OR 1.3, 95% CI 1.1–1.5). No significant difference in the onset of pneumonia was found between the preoperative and no rehabilitation groups, and between the postoperative and preoperative groups.

Among the patients who underwent endoscopic surgery, those in the combination group had a lower incidence of pneumonia than the preoperative (OR, 95% CI 2.8, 1.8–4.4), postoperative (1.9, 1.6–2.2), and no rehabilitation (2.5, 2.1–2.8) group. The postoperative group had a significantly lower incidence of pneumonia than the no rehabilitation group (OR 1.3, 95% CI 1.1–1.5). No significant difference was found between the preoperative and no rehabilitation groups, and between the postoperative and preoperative groups.

Among the patients who underwent thoracotomy, those in the combination group had a lower incidence of pneumonia than the preoperative (OR, 95% CI 4.2, 2.9–6.3), postoperative (1.9, 1.6–2.3), and no rehabilitation (2.4, 2.1–2.7) groups. The postoperative group had significantly less onset of pneumonia than the preoperative (OR, 95% CI 2.2, 1.5–3.3) and no rehabilitation (OR: 1.2, 95% CI 1.1–1.4) groups. No significant difference in the onset of pneumonia was found between the preoperative and no rehabilitation groups.

With the multiple imputation, the analysis results remained the same (refer to Supplement).

Discussion

From the claims data of 15,146 postoperative lung cancer patients, the combination of both preoperative and postoperative rehabilitations decreased the risk of postoperative pneumonia compared with preoperative alone, postoperative alone, and no rehabilitation. Comparing with no rehabilitation group, postoperative rehabilitation alone was significantly related to less postoperative pneumonia. It should be emphasized that, despite such an effectiveness, rehabilitation was not prescribed for more than half of the study patients.

Analysis of the administrative data, which reflect real-world practice, has shown that combination of preoperative

Table 1 Patient attribution (all patients)

	Operative procedure	All patients				
	Rehabilitation patterns	All patients	Combination group	Preoperative group	Postoperative group	No rehabilitation group
N		15,146	4729	269	2105	8043
Sex, *N* (%)	Male	8724 (57.6)	2686 (56.8)	153 (56.9)	1247 (59.2)	4638 (57.7)
	Female	6622 (42.4)	2043 (43.2)	116 (43.1)	858 (40.8)	3405 (42.3)
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Age (mean ± SD)		69.1 ± 9.4	69.4 ± 9.3	70.3 ± 9.4	70.0 ± 9.2	68.6 ± 9.6
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
BMI (kg/m^2) (mean ± SD)		22.7 ± 4.2	22.8 ± 3.7	22.4 ± 4.4	22.8 ± 3.6	22.6 ± 4.6
	Missing; *N* (%)	137 (0.9)	25 (0.2)	4 (0.02)	7 (0.05)	101 (0.6)
Onset of pneumonia	*N* (%)	2483 (16.4)	473 (10.0)	60 (22.3)	361 (17.2)	1589 (19.8)
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Comorbidities on admission, *N* (%)	Chronic respiratory illness	4455 (29.4)	1269 (26.8)	136 (50.6)	540 (25.7)	2510 (31.2)
	Interstitial pneumonia	3646 (24.0)	1244 (26.3)	35 (13.0)	651 (30.9)	1716 (21.3)
	Chronic cardiac failure	1620 (10.7)	611 (13.0)	26 (9.7)	162 (7.7)	821 (10.2)
	Hepatic disorder	2188 (14.4)	745 (15.8)	43 (16.0)	293 (13.9)	1107 (13.8)
	Chronic renal failure	867 (5.7)	271 (5.7)	21 (7.8)	147 (7.0)	428 (5.3)
	Cerebrovascular accident	402 (2.7)	144 (3.0)	13 (4.8)	56 (2.7)	189 (2.4)
BI (mean ± SD)		96.1 ± 18.0	98.7 ± 8.0	99.2 ± 6.3	98.1 ± 10.3	94.0 ± 23.1
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cancer stage, *N* (%)	IA	7113 (46.9)	2084 (44.1)	75 (27.9)	928 (44.1)	4026 (50.1)
	IB	2298 (15.2)	746 (15.8)	25 (9.3)	395 (18.8)	1132 (14.1)
	IIA	801 (5.3)	249 (5.3)	8 (3.0)	120 (5.7)	424 (5.3)
	IIB	448 (3.0)	126 (2.7)	9 (3.3)	100 (4.8)	213 (2.6)
	IIIA	792 (5.2)	239 (5.1)	10 (3.7)	143 (6.8)	400 (5.0)
	IIIB	31 (0.2)	6 (0.1)	0 (0)	5 (0.2)	20 (0.2)
	IV	303 (2.0)	81 (1.7)	4 (1.5)	38 (1.8)	180 (2.2)
	Missing; *N* (%)	3360 (22.2)	1198 (25.3)	138 (51.3)	376 (17.9)	1648 (20.5)
Hugh–Jones classification, *N* (%)	I	11,867 (78.4)	3479 (73.6)	216 (80.3)	1681 (80.1)	6491 (80.9)
	II	2044 (13.5)	780 (16.5)	29 (10.8)	233 (11.0)	1002 (12.5)
	III	510 (3.4)	200 (4.2)	10 (3.7)	98 (4.8)	202 (2.5)
	IV	157 (1.0)	55 (1.1)	5 (1.8)	28 (1.3)	69 (0.9)
	V	60 (0.4)	40 (0.8)	1 (0.3)	4 (0.2)	15 (0.1)
	Missing; *N* (%)	508 (3.4)	175 (3.7)	8 (3.0)	61 (2.9)	264 (3.3)
Number of units of rehabilitation in hospital (mean ± SD)		3.6 ± 9.2	8.0 ± 10.5	2.1 ± 9.9	7.7 ± 15.2	0.0 ± 0.0
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Number of days of rehabilitation in hospital (mean ± SD)		3.4 ± 8.9	7.2 ± 9.7	1.8 ± 9.8	7.9 ± 15.3	0.0 ± 0.0
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Comorbidities on admission is calculated total number

$N = 15{,}146$

BMI body mass index, *BI* Barthel Index

Table 2 Patient attribution (endoscopic)

	Operative procedure	Endoscopic				
	Rehabilitation patterns	All patients	Combination group	Preoperative group	Postoperative group	No rehabilitation group
N		12,505	3760	248	1756	6741
Sex, *N* (%)	Male	6966 (55.7)	2032 (54.0)	139 (56.0)	1000 (57.0)	3795 (56.3)
	Female	5539 (44.3)	1728 (46.0)	109 (44.0)	756 (43.0)	2946 (43.7)
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Age (mean ± SD)		69.3 ± 9.5	69.7 ± 9.2	70.2 ± 9.6	70.0 ± 9.2	68.7 ± 9.7
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
BMI (kg/m^2) (mean ± SD)		22.7 ± 4.3	22.9 ± 3.7	22.4 ± 4.5	22.8 ± 3.6	22.6 ± 4.7
	Missing; *N* (%)	20 (0.16)	7 (0.2)	0 (0)	2 (0.1)	11 (0.2)
Onset of pneumonia	*N* (%)	2048 (16.4)	402 (10.7)	55 (22.2)	300 (17.1)	1291 (19.2)
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Comorbidities on admission, *N* (%)	Chronic respiratory illness	3560 (28.5)	969 (25.8)	129 (52.0)	435 (24.8)	2027 (30.1)
	Interstitial pneumonia	2967 (23.7)	920 (24.5)	29 (11.7)	567 (32.3)	1451 (21.5)
	Chronic cardiac failure	1335 (10.7)	519 (13.8)	23 (9.3)	123 (7.0)	670 (9.9)
	Hepatic disorder	1819 (14.5)	583 (15.5)	41 (16.5)	244 (13.9)	951 (14.1)
	Chronic renal failure	738 (5.9)	221 (5.9)	20 (8.1)	128 (7.3)	369 (5.5)
	Cerebrovascular accident	344 (2.6)	117 (3.1)	12 (4.8)	46 (2.6)	169 (2.5)
BI (mean ± SD)		96.2 ± 17.9	98.7 ± 8.1	99.0 ± 6.6	98.3 ± 10.1	94.1 ± 22.8
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cancer stage, *N* (%)	IA	6370 (50.9)	1872 (49.8)	67 (27.0)	839 (47.8)	3636 (53.9)
	IB	1877 (15.0)	621 (16.5)	23 (9.3)	367 (20.9)	906 (13.4)
	IIA	521 (4.2)	153 (4.1)	6 (2.4)	91 (5.2)	281 (4.2)
	IIB	274 (2.2)	76 (2.0)	8 (3.2)	67 (3.8)	128 (1.9)
	IIIA	456 (3.6)	110 (2.9)	4 (1.6)	100 (5.7)	252 (3.7)
	IIIB	16 (0.1)	2 (0.1)	0 (0)	3 (0.2)	11 (0.2)
	IV	239 (1.9)	71 (1.9)	4 (1.6)	33 (1.9)	147 (2.2)
	Missing; *N* (%)	2752 (22.0)	936 (24.9)	136 (54.8)	300 (17.1)	1380 (20.5)
Hugh–Jones classification, *N* (%)	I	9853 (78.8)	2801 (74.5)	201 (81.0)	1422 (81.0)	5429 (80.5)
	II	1644 (13.1)	583 (15.5)	28 (11.3)	185 (10.5)	848 (12.6)
	III	416 (3.3)	156 (4.1)	9 (3.6)	75 (4.3)	176 (2.6)
	IV	123 (1.0)	39 (1.0)	5 (2.0)	20 (1.1)	59 (0.9)
	V	59 (0.4)	35 (0.5)	0 (0)	2 (0.1)	13 (0.2)
	Missing; *N* (%)	419 (3.4)	146 (3.9)	5 (2.0)	52 (3.0)	216 (3.2)
Number of units of rehabilitation in hospital (mean ± SD)		3.3 ± 7.4	7.5 ± 10.1	1.2 ± 5.0	7.2 ± 8.4	0.0 ± 0.0
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Number of days of rehabilitation in hospital (mean ± SD)		3.1 ± 7.7	6.7 ± 8.6	1.3 ± 9.3	7.4 ± 13.6	0.0 ± 0.0
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Comorbidities on admission is calculated total number

N = 15,146

BMI body mass index, *BI* Barthel Index

Table 3 Patient attribution (thoracotomy)

	Operative procedure	Thoracotomy				
	Rehabilitation patterns	All patients	Combination group	Preoperative group	Postoperative group	No rehabilitation group
N		2771	1006	24	360	1381
Sex, *N* (%)	Male	1848 (66.7)	680 (67.6)	17 (70.8)	253 (70.3)	898 (65.0)
	Female	923 (33.3)	326 (32.4)	7 (29.2)	107 (29.7)	483 (35.0)
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Age (mean ± SD)		68.5 ± 9.2	68.4 ± 9.6	70.8 ± 7.7	70.3 ± 9.1	68.1 ± 8.9
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
BMI (kg/m^2) (mean ± SD)		22.7 ± 3.8	22.8 ± 3.8	22.7 ± 3.0	22.7 ± 3.8	22.6 ± 3.9
	Missing; *N* (%)	20 (0.7)	7 (0.1)	0 (0)	2 (0.5)	11 (0.8)
Onset of pneumonia	*N* (%)	478 (17.3)	76 (7.6)	6 (25.0)	66 (18.3)	330 (23.9)
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Comorbidities on admission, *N* (%)	Chronic respiratory illness	933 (33.7)	310 (30.8)	8 (33.3)	107 (29.7)	508 (36.8)
	Interstitial pneumonia	702 (25.3)	332 (33.0)	7 (29.2)	86 (23.9)	277 (20.1)
	Chronic cardiac failure	303 (10.9)	97 (9.6)	3 (12.5)	39 (10.8)	164 (11.9)
	Hepatic disorder	384 (14.1)	169 (16.8)	2 (8.3)	51 (14.2)	162 (11.7)
	Chronic renal failure	135 (4.8)	52 (5.2)	2 (8.3)	20 (5.6)	61 (4.4)
	Cerebrovascular accident	60 (2.2)	28 (2.8)	1 (4.2)	10 (2.8)	21 (1.5)
BI (mean ± SD)		95.4 ± 19.5	98.7 ± 7.7	100.0 ± 0.0	97.6 ± 10.8	92.4 ± 25.9
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cancer stage, *N* (%)	IA	790 (28.5)	272 (27.0)	8 (33.3)	92 (25.6)	418 (30.3)
	IB	449 (16.2)	149 (14.8)	2 (8.3)	53 (14.7)	245 (17.7)
	IIA	293 (10.6)	102 (10.1)	3 (12.5)	36 (10.0)	152 (11.0)
	IIB	178 (6.4)	55 (5.5)	1 (4.2)	34 (9.4)	88 (6.4)
	IIIA	346 (12.5)	135 (13.4)	6 (25.0)	50 (13.9)	155 (11.2)
	IIIB	15 (0.5)	4 (0.4)	0 (0)	2 (0.6)	9 (0.7)
	IV	67 (2.4)	20 (2.0)	1 (4.2)	12 (3.3)	34 (2.5)
	Missing; *N* (%)	633 (22.8)	269 (26.7)	3 (12.5)	81 (22.5)	280 (20.3)
Hugh–Jones classification, *N* (%)	I	2108 (76.1)	702 (69.8)	17 (70.8)	265 (73.6)	1124 (81.4)
	II	424 (15.3)	208 (20.7)	1 (4.2)	50 (13.9)	165 (11.9)
	III	98 (3.5)	45 (4.5)	1 (4.2)	24 (6.7)	28 (2.0)
	IV	38 (1.4)	16 (1.6)	1 (4.2)	9 (2.5)	12 (0.9)
	V	10 (0.4)	5 (0.5)	1 (4.2)	2 (0.6)	2 (0.1)
	Missing; *N* (%)	93 (3.4)	30 (3.0)	3 (12.5)	10 (2.8)	50 (3.6)
Number of units of rehabilitation in hospital (mean ± SD)		5.1 ± 14.7	9.8 ± 11.7	11.1 ± 27.8	10.6 ± 31.5	0.0 ± 0.0
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Number of days of rehabilitation in hospital (mean ± SD)		4.9 ± 13.2	9.0 ± 12.6	6.4 ± 12.9	10.9 ± 24.3	0.0 ± 0.0
	Missing; *N* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Comorbidities on admission is calculated total number

N = 15,146

BMI body mass index, *BI* Barthel Index

Table 4 The implementation pattern for rehabilitation and onset pneumonia

	All patients				Endoscopic				Thoracotomy			
	Onset		Offset		Onset		Offset		Onset		Offset	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Combination group ($n=4729$)	478	10.0	4256	90.0	402	10.7	3358	89.3	76	7.6	930	92.5
Preoperative group ($n=269$)	61	22.3	209	77.7	55	22.2	193	77.8	6	25.0	18	75.0
Postoperative group ($n=2105$)	366	17.2	1744	82.9	300	17.1	1456	82.9	66	18.3	294	81.7
No rehabilitation group ($n=8043$)	1621	19.8	6454	80.2	1291	19.2	5450	80.9	330	23.9	1051	76.1

n (%)

$N=15{,}146$

and postoperative pulmonary rehabilitations were the most effective in preventing postoperative pneumonia. For the effect of preoperative rehabilitation, the following have been reported: improvements in postoperative respiration function [40, 41], motor function [42], and gait durability [43], and shortened length of hospital stay [44, 45]. In addition, the effect of postoperative rehabilitation includes improvement of 1-s forced expiratory volume, which represents respiratory function [46, 47], and improvement of quality of life [48]. As pulmonary complications including pneumonia is caused by retained respiratory secretion invoked by a decreased postoperative ventilation [49], both preoperative and postoperative rehabilitations may prevent pneumonia through improvement of postoperative respiratory function. Compared with preoperative rehabilitation, the direct effect of postoperative rehabilitation toward limited range of motion due to the pain of operative wounds [50] and decrease in pulmonary blood flow in the resected region [51, 52] on the prevention of postoperative complication looks promising.

The present study did not confirm the effect of preoperative rehabilitation supported by previous studies. This can be explained by the difference in features between real-world and experimental research data. In randomized controlled trials (RCTs), the subjects are strictly selected and detailed rules on intervention are established [53], whereas in real-world clinical situations, the subjects and methods of intervention are diverse. For example, in a RCT that verified the effects of respiratory rehabilitation on patients with chronic obstructive pulmonary disease (COPD) [54], the rehabilitation group had a lower re-hospitalization rate than the control group. On the other hand, the retrospective cohort study [55] that used data from a database showed no significant difference between the two groups. In addition, it was reported that in a RCT that targeted COPD patients, the inclusion criteria only fit 20% of the actual patients [56]. As with differences in subjects, differences in methods of intervention between real-world and experimental research data are pointed out too. In the field of rehabilitation, the method of intervention is usually difficult to control, especially that only a small number of patients undergo preoperative rehabilitation. Considering the variation in subjects and intervention method, like the difference between the experimental study and the real world, the difference in the effect was observed between this research and the previous studies.

The present results showed that approximately 30% of the study patients underwent combination of both preoperative and postoperative rehabilitations, and approximately 14% underwent postoperative rehabilitation alone. The previous study investigating the evidence practice gap (EPG) in the field of Japanese rehabilitation reported that, among indicative patients, only 23.7% inpatients and 4.2% outpatients received cardiac rehabilitation [57]. Although the implementation rates were slightly higher in this study, the recommended treatment by the Japanese cancer rehabilitation guideline [19] was only implemented for 1 of 3 patients who require the treatment. These gaps may be due to that clinicians are not fully aware of the guideline recommendations [58] or there are barriers for clinicians to implement evidence-based practice [59, 60]. There are also the patient-related factor (comorbidity status [57, 58]) and the environmental factor. In addition, effect of rehabilitation, particularly pulmonary rehabilitation that is examined in the present study, has been undermined and not been recognized well among clinicians in general. To conduct a pulmonary rehabilitation in Japan, the cancer or respiratory rehabilitation fee is part of the medical fee system. Only 384 facilities [61] in Japan could conduct cancer rehabilitation under medical insurance, which met the facility criteria and charge cancer rehabilitation fee. Masako et al. [62] reported that there is a wide gap between hospitals that perform cancer rehabilitation 100% and hospitals that do not perform it at all.

This study has some limitations. First, because it is a retrospective cohort study based on a database, available data were limited. For example, medical practice (a surgical volume and experience of rehabilitation), institutional data (the size of hospital and medical remuneration points) and patients' medical conditions, and socioeconomic

Table 5 Multiple logistic regression analysis (complete case)

	All patients				Endoscopic				Thoracotomy			
	OR	*p* value	95% CI lower	95% CI upper	OR	*p* value	95% CI lower	95% CI upper	OR	*p* value	95% CI lower	95% CI upper
Combination group												
vs preoperative group	2.8	<0.0001*	1.8	4.4	2.8	<0.0001*	1.8	4.4	4.2	<0.0001*	2.9	6.3
vs postoperative group	1.9	<0.0001*	1.6	2.3	1.9	<0.0001*	1.6	2.2	1.9	<0.0001*	1.6	2.3
vs no rehabilitation group	2.5	<0.0001*	2.1	2.8	2.5	<0.0001*	2.1	2.8	2.4	<0.0001*	2.1	2.7
Postoperative group												
vs preoperative group	1.5	0.08	1.0	2.3	1.5	0.08	1.0	2.4	2.2	<0.0001*	1.5	3.3
vs no rehabilitation group	1.3	0.0015*	1.1	1.5	1.3	0.0011*	1.1	1.5	1.2	0.0025*	1.1	1.4
Preoperative group												
vs no rehabilitation group	0.9	0.52	0.6	1.3	0.9	0.53	0.6	1.3	0.6	0.0035*	0.4	0.8

OR odds ratio, *CI* confidence interval

factors. Therefore, the confounding factors, apart from the data acquired in the present study, could not be adjusted. Second, this study did not include outpatient rehabilitation before admission. As the aim of this study was to examine the effect of rehabilitation conducted in combination of both before and after lung cancer surgery on postoperative pulmonary complication, the analysis was limited to patients hospitalized to meet the criteria for charging the cancer patient rehabilitation fee. Therefore, those who received rehabilitation before admission were not included in the preoperative rehabilitation group; thus, the effect on the prevention of the complication in the preoperative rehabilitation group may have been relatively underestimated. Third, the DPC data used in this study represent a part of all hospitals in Japan. DPC data used in this study are Japan's large-scale administrative data. It is unlikely that the data are seriously biased on a certain portion of hospital; however, generalization should be made with caution. Fourth, factor on a facility level could not be taken into account since IDs for each hospital were unknown.

In conclusion, the combination of both preoperative and postoperative rehabilitations decreased the risk of postoperative pneumonia compared with preoperative alone, postoperative alone, and no rehabilitation. However, cancer rehabilitation was prescribed to only one-third of the patients in need.

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Compliance with ethical standards

Conflict of interest There are no companies in COI relationship that should be disclosed.

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