Original Article

What are the risk factors for postoperative home oxygen therapy in patients with lung cancer?

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Background: Home oxygen therapy (HOT) is used to treat chronic respiratory diseases and is sometimes required in patients with lung cancer after radical surgery. We aimed to identify the risk factors for postoperative home-based oxygen therapy in patients with lung cancer.

Methods: Patients who underwent surgery for primary lung cancer at Chiba University Hospital between January 2019 and March 2021 were included. Patients who did not undergo complete resection, died in hospital after surgery, or used oxygen therapy preoperatively were excluded. Eligible patients were divided into HOT and non-HOT groups. They were retrospectively analyzed for risk factors for postoperative HOT using medical records in a multivariate analysis.

Results: A total of 410 patients were included in this study, 24 (5.9%) of whom required HOT after surgery. The HOT group comprised significantly more men, heavy smokers, and patients with pulmonary comorbidities, low percent forced expiratory volume, percent forced vital capacity, predicted postoperative forced expiratory volume in 1 s, and postoperative pulmonary complications on univariate analysis. In a multivariate analysis, independent risk factors for postoperative HOT were pulmonary comorbidities [odds ratio (OR): 5.94; 95% confidence interval (CI): 1.64–21.5; P=0.002) and postoperative pulmonary complications (OR: 5.39; 95% CI: 2.14–13.5; P<0.001). The postoperative HOT application rate was calculated according to a formula developed for this purpose.

Conclusions: Comorbid pulmonary diseases and postoperative pulmonary complications were significantly associated with postoperative HOT in patients with lung cancer.

Keywords: Home oxygen therapy (HOT); lung cancer; lung resection

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Introduction

Home oxygen therapy (HOT) is required for a number of chronic respiratory diseases. The American Thoracic Society guidelines recommend prescribing long-term continuous oxygen therapy for at least 15 hours per day for adults with chronic obstructive pulmonary disease (COPD) or interstitial lung disease (ILD) with severe chronic resting room air hypoxemia (1). In a previous study, long-term continuous oxygen therapy improved the survival of patients with COPD and severe hypoxemia. However, no studies have shown that HOT can improve survival in patients with other chronic lung diseases (2,3).

Although patients with COPD and/or ILD often require HOT, they are more likely to develop primary lung cancer than those without chronic pulmonary diseases. Exposure to toxic gases and particulates, particularly cigarette smoke, can cause these diseases. Patients with COPD and ILD are three to four times and two to four times more likely to develop lung cancer, respectively, than those without COPD or ILD (4-8).

Patients with lung cancer and comorbid pulmonary diseases may have an increased risk of deteriorating pulmonary function after radical surgery for lung cancer and are also likely to require HOT after surgery. In a previous study, 15% of patients with lung cancer required postoperative HOT, had a poor prognosis, and had a reduced quality of life (9).

Identifying the risk factors for HOT after surgery in patients with lung cancer is beneficial for clinicians during decision-making and for obtaining informed consent from high-risk patients. This study aimed to identify risk factors for postoperative HOT in patients with primary lung cancer. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1539/rc).

Highlight box

Key findings
- The risk factors for postoperative home oxygen therapy (HOT) in patients with lung cancer were comorbid pulmonary diseases and the development of postoperative pulmonary complications.

What is known and what is new?
- Only a few studies have reported risk factors (high body mass index and low diffusing capacity of the lungs for carbon monoxide) for postoperative HOT in patients with lung cancer.
- Our study revealed new risk factors: (I) comorbid pulmonary diseases and (II) postoperative pulmonary complications. We developed the following formula for HOT application rates: HOT (%) = $1/1 + e^{-y}$ ($y = 0.32 + x_1 + x_2 + x_3 + x_4 + x_5 + x_6$).

What is the implication, and what should change now?
- Lung cancer patients with pulmonary comorbidities require careful consideration of surgical indications and adequate postoperative management. Especially, the combination of pre- and postoperative complications lead to a high risk of HOT administration. Close attention to postoperative pulmonary complications could lead to more patients being discharged without HOT.

Methods

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Committee of Chiba University Graduate School of Medicine approved this study on February 17, 2022 (No. M10232). Individual consent for this retrospective analysis was waived.

Patients

Patients who underwent lung resection for primary lung cancer at our institution between January 2019 and March 2021 were included. Lobectomy with curative intention was performed, except for patients with low pulmonary function or severe comorbidity who underwent sublobar resection. Patients who did not undergo complete resection, died postoperatively, or received oxygen therapy before surgery were excluded. Patient characteristics such as age, sex, smoking index, body mass index (BMI), comorbidities, preoperative spirometry test results, surgical procedure, predicted postoperative lung function, and postoperative complications were retrospectively obtained from medical records. To examine the risk factors for postoperative oxygen therapy, patients were divided into two groups, with (HOT group) and without HOT (non-HOT group), and patient characteristics and postoperative complications were compared between the two groups. Patients received respiratory rehabilitation for at least one week postoperatively. Despite the rehabilitation, patients with percutaneous oxygen saturation (SpO_2) <90% at rest or on exertion were considered for HOT at discharge. The predicted postoperative lung function of percent forced vital capacity (FVC) (ppo%FVC) and percent forced expiratory volume in 1 s (FEV1) (ppo%FEV1) were calculated as follows: ppo%FVC (or %FEV1) = preoperative %FVC (or %FEV1) × (42 subsegments − the number of subsegments to be resected)/42 (10). In cases in which wedge resection was performed, ppo%FVC and ppoFEV1 were defined as the preoperative values of %FVC and %FEV1, respectively. Postoperative complications were considered significant if they were grade 3 or higher according to the Clavien-Dindo classification.

Statistical analysis

Fisher's exact test was used to compare the HOT and non-

Table 1 Patient characteristics in HOT and non-HOT groups

Characteristics	HOT (n=24)	Non-HOT (n=386)	P value
Male	23 (96%)	238 (62%)	<0.001
Age ≥75 years	11 (46%)	136 (35%)	0.380
BMI ≥25 kg/m^2	7 (29%)	103 (27%)	0.813
Smoking index ≥400	22 (92%)	210 (54%)	<0.001
Comorbidities			
Pulmonary	21 (88%)	149 (39%)	<0.001
Cardiovascular	16 (67%)	210 (54%)	0.293
Diabetes	5 (21%)	57 (15%)	0.387
Preoperative spirometry			
%FVC <80%	2 (8%)	22 (6%)	0.870
%FEV1 <80%	12 (50%)	100 (26%)	0.016
FEV1.0/FVC <70	15 (63%)	123 (32%)	0.003
Surgical procedure			0.325
Wedge resection	3 (13%)	32 (8%)	
Segmentectomy	3 (13%)	98 (25%)	
Lobectomy	18 (75%)	256 (66%)	
Postoperative lung function			
ppo%FVC <80%	10 (42%)	144 (37%)	0.669
ppo%FEV1 <80%	20 (83%)	221 (57%)	0.017
Postoperative complications			
Pulmonary	16 (67%)	83 (22%)	<0.001
Pneumonia	10 (42%)	31 (8%)	<0.001
Prolonged air leakage	9 (38%)	54 (14%)	0.001
Other	2 (8%)	10 (3%)	0.151
Cardiovascular	1 (4%)	7 (2%)	0.385
Other	2 (8%)	14 (4%)	0.239

HOT, home oxygen therapy; BMI, body mass index; ppo%FVC, predicted postoperative percent forced vital capacity; ppo%FEV1, predicted postoperative percent forced expiratory volume in 1 s.

HOT groups for each patient characteristic such as sex, age, BMI, smoking index, comorbidities, spirometry test results, surgical procedure, predicted postoperative lung function, and postoperative complications. The cutoff values for %FEV1 and ppo%FEV1 were set at 80%, which is the borderline between moderate and severe COPD. Multivariate analysis was performed for patients in whom significant differences were detected in univariate analysis. From these data, we derived an equation that indicates the probability of postoperative HOT. The significance level was set at P values <0.05. All statistical analyses were performed using JMP software (version 16.0; SAS Institute Inc., Cary, NC, USA).

Results

A total of 410 patients were included in this study. Patient characteristics are listed in *Table 1*. HOT was required for

Table 2 Multivariate analysis for HOT application after lung resection

Factor	Odds ratio	95% CI	P value
Male	4.05	0.46–35.5	0.144
Smoking index ≥400	2.22	0.43–11.3	0.301
Pulmonary comorbidities (+)	5.94	1.64–21.5	0.002
ppo%FEV1 <80%	1.37	0.41–4.51	0.598
Pulmonary complications (+)	5.39	2.14–13.5	<0.001

HOT, home oxygen therapy; CI, confidence interval; ppo%FEV1, predicted postoperative percent forced expiratory volume in 1 s.

Table 3 Coefficients in the formula of HOT application

Factor	Yes	No
Preoperative factors		
x_1: COPD	+0.66	–0.66
x_2: ILD	+1.31	–1.31
x_3: asthma	+0.07	–0.07
Postoperative factors		
x_4: pneumonia	+0.90	–0.90
x_5: prolonged air leakage	+0.80	–0.80
x_6: AE-IP	+1.13	–1.13

HOT, home oxygen therapy; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; AE-IP, acute exacerbation of interstitial pneumonia.

Table 4 Multivariate analysis of pulmonary comorbidities and postoperative complications for HOT after lung resection

Factor	Odds ratio	95% CI	P value
COPD	3.75	1.35–10.4	0.009
ILD	13.9	3.28–59.0	0.001
Asthma	1.15	0.13–10.3	0.902
Pneumonia	6.01	2.08–17.4	0.002
Prolonged air leakage	4.93	1.72–14.1	0.004
AE-IP	9.69	0.82–114	0.101

HOT, home oxygen therapy; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; AE-IP, acute exacerbation of interstitial pneumonia.

24 patients (5.9%) at discharge. Compared to the non-HOT group, the HOT group was predominantly male and had more patients with a smoking index of ≥400, lung comorbidities, low %FEV1, low FEV1/FVC, low ppo%FEV1, and postoperative pulmonary complications such as pneumonia and prolonged air leakage. More patients with low pulmonary function were included in the HOT group. Nevertheless, there was no difference in the choice of procedure between the two groups, and postoperative lung function was predicted to be lower in the HOT group than in the non-HOT group. Age, BMI, non-pulmonary comorbidities, %FVC, surgical procedure, ppo%FVC, and postoperative non-pulmonary complications were not significantly different between the groups. The most common pulmonary comorbidity was COPD (n=88). ppo%FEV1 was a more substantial reflection of postoperative lung function than preoperative %FEV1 since ppoFEV1 also calculated the lung loss due to the surgery. Multivariate analyses were performed on the datasets for sex, smoking index, lung comorbidities, ppoFEV1, and postoperative pulmonary complications (*Table 2*). Pulmonary comorbidities [odds ratio (OR): 5.94; 95% confidence interval (CI): 1.64–21.5; P=0.002] and postoperative pulmonary complications (OR: 5.39; 95% CI: 2.14–13.5; P<0.001) were revealed as independent risk factors for postoperative HOT. The major comorbidities in this cohort were COPD (76%), ILD (19%), and asthma (5%). The postoperative pulmonary complications included pneumonia (42%), prolonged air leakage (38%), and acute exacerbation of interstitial pneumonia (10%). The following formula was developed to calculate the postoperative HOT rate using regression analysis based on quantification theory with respect to pulmonary comorbidities and postoperative pulmonary complications that were identified as risk factors for HOT in multivariate analysis: HOT (%) = $1/1 + e^{-y}$ ($y = 0.32 + x_1 + x_2 + x_3 + x_4 + x_5 + x_6$). Coefficients x_1–x_6 are listed in *Table 3*. Based on this formula, the postoperative HOT rate was 1% in patients who had neither pulmonary comorbidity nor postoperative pulmonary complications and 6% in those who experienced postoperative pneumonia. Furthermore, multivariate analysis was performed on the datasets of COPD, ILD, and asthma, the major comorbidities in this cohort, as well as pneumonia, prolonged air leakage, and acute exacerbation of interstitial pneumonia, the major postoperative pulmonary complications (*Table 4*). COPD (OR: 3.75; 95% CI: 1.35–10.4; P=0.009) and ILD (OR: 13.9; 95% CI: 3.28–59.0; P=0.001) were independent risk factors in pulmonary comorbidities. Pneumonia (OR: 6.01; 95% CI: 2.08–17.4; P=0.002) and prolonged air leakage (OR: 4.93; 95% CI: 1.72–14.1; P=0.004) were postoperative

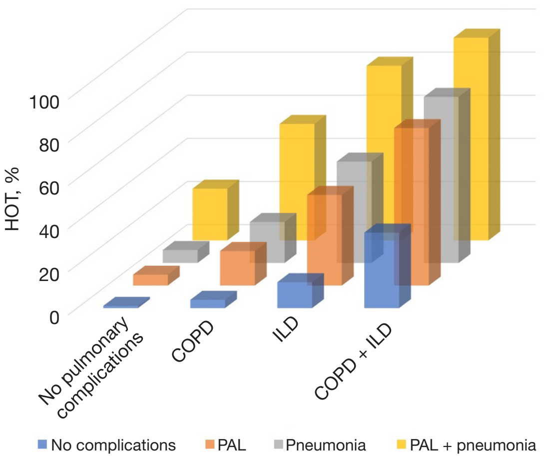

Figure 1 Probability of HOT application for each factor. COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; HOT, home oxygen therapy; PAL, prolonged air leakage.

complications that were independent risk factors for HOT. *Figure 1* shows a bar chart based on the postoperative HOT rate calculated with and without pulmonary comorbidities and complications.

Discussion

This study evaluated the risk factors of HOT after primary lung cancer surgery. According to the univariate analysis, male sex, a smoking index ≥400, pulmonary comorbidities, ppo%FEV1, and postoperative pulmonary complications were significant risk factors for postoperative HOT in patients with primary lung cancer. According to multivariate analysis, only pulmonary comorbidities and postoperative pulmonary complications remained independent risk factors for postoperative HOT. Comorbidities included COPD, ILD, and asthma, whereas postoperative pulmonary complications included pneumonia, prolonged air leakage, and acute exacerbation of interstitial pneumonia. Based on these results, the probability of HOT after surgery was expressed as a formula. A previous study in the United States reported that BMI and low diffusing capacity of the lungs for carbon monoxide (DLCO) were independent risk factors for postoperative HOT in patients with lung cancer (11). However, BMI was not a significant factor in our study, which may be due to the low obesity rate among Japanese patients in this study. Preoperative DLCO was not tested in a sufficient number of patients and was therefore not included in the analysis, which is a major limitation of this study. Low ppo%DLCO has been reported in past research as an independent risk factor for postoperative complications (12). Therefore, if possible, future studies on the risk factors for postoperative HOT should include DLCO data.

Our study revealed that the risk of postoperative HOT increased significantly when postoperative pulmonary complications occurred in patients with respiratory diseases. Previous studies have reported that patients with lung cancer with respiratory illness experience postoperative pulmonary complications such as pneumonia or air leakage more frequently than those without respiratory illness (13-17). Therefore, when operating on patients with lung cancer and pulmonary comorbidities, it is extremely important to prevent postoperative respiratory complications to avoid HOT. While pulmonary comorbidities and postoperative pulmonary complications were both risk factors for HOT, pulmonary comorbidities were directly a risk factor for pulmonary complications. Therefore, postoperative management of lung cancer patients with pulmonary comorbidities should be very cautious.

Previous studies indicated preoperative rehabilitation decreased postoperative pulmonary complications and hospital stay. The rehabilitation included muscle training, aerobic exercise, and lower extremity endurance training, which continued for roughly 2 to 4 weeks, at least a week (18-21). In the other report, pulmonary rehabilitation for at least four weeks has been reported to increase the 6-minute walking distance and improve shortness of breath in patients with COPD (22); therefore, preoperative rehabilitation can be expected to prevent postoperative pneumonia, HOT, and deterioration of quality of life. In addition, a recent study showed that patients with lung cancer in the enhanced recovery after surgery (ERAS) program had fewer postoperative pulmonary complications (23). Perioperative management, including such as ERAS program, rather than preoperative rehabilitation only, might be important to reduce respiratory complications. Adequate perioperative management would play a key role in preventing postoperative HOT.

However, although several studies have been conducted, no such effect of the administration of antibiotics to prevent pneumonia after lung resection has been reported (24,25). Various techniques that aim to minimize postoperative air leakage were reported, such as fibrin glue spread during operation, using a stapler with the polyglycolic acid sheet, or postoperative drain management using water seals and digital drainage systems. The combination usage of these devices/techniques potentially reduces postoperative air leakage and, as a result of HOT (26-29).

The present study also suggests that surgical indications are vital factors in the risk of HOT. In a previous report, patients who started HOT decreased their quality of life, which was a problem (1). It is still under argument that whether or not surgery should be avoided, and other treatment options chosen if the HOT high-risk patients. However, at the least, we should esteem patient willingness and inform multiple treatment options and their complications to the patient. Other therapeutic modalities, such as radiation or chemotherapy, especially immunotherapy, could be alternatives for high-risk patients (30-32).

This study had several limitations. First, this was a single-institution retrospective study and the number of patients was small. Additional data on preoperative arterial blood gas and DLCO, which are considered to reflect pulmonary function, were lacking in our database. Multicenter prospective clinical trials involving a sufficient number of patients are required to clarify the risk factors of postoperative HOT in primary lung cancers. Second, there was a lack of postoperative follow-up in patients who underwent postoperative HOT. In the real world, the follow-up sequence and timing of HOT cessation are not defined globally and depend only on physician discretion. Future studies should clarify whether HOT is temporary or permanent following lung cancer resection.

Conclusions

This study revealed risk factors for postoperative HOT in patients with primary lung cancer. Significant risk factors were comorbid pulmonary diseases such as COPD and ILD and the development of postoperative pulmonary complications such as pneumonia and air leakage. Furthermore, the combination of comorbidities and complications can lead to a high rate of postoperative HOT. Patients with pulmonary comorbidities require careful consideration of surgical indications and adequate postoperative management. Increased attention on postoperative pulmonary complications may result in patients being discharged without HOT.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1539/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1539/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Committee of Chiba University Graduate School of Medicine approved this study (No. M10232) on February 17, 2022. Individual consent for this retrospective analysis was waived.

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