

## Efficacy of Comprehensive Preoperative Pulmonary Rehabilitation Including Intensive Nutritional Support through an Interdisciplinary Team Approach

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Received date: October 17, 2016; Accepted date: October 28, 2016; Published date: November 03, 2016

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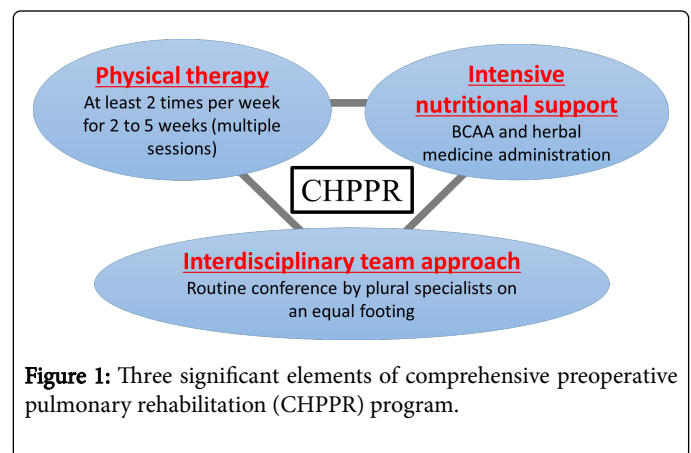
**Keywords:** Preoperative pulmonary rehabilitation; Postoperative complication; Lung cancer

### Introduction

Since surgical resection is the treatment of choice for localized lung cancer, developing an effective strategy to reduce the risk of postoperative complications caused by insufficient preoperative preparation is important; therefore, improving general and physical conditioning preoperatively should be considered essential for patients scheduled to undergo lung surgery [1,2]. Pulmonary rehabilitation has been demonstrated to be a beneficial intervention for improving pulmonary conditions; however, the duration of a standard program has generally been 6-12 weeks [3,4]. Thus, an effective, short-term, preoperative pulmonary rehabilitation program should be adopted, because patients with malignant disease should undergo surgery without delay. We had demonstrated that our specific preoperative rehabilitation protocol showed a beneficial effect; however, the assessment was conducted using the data including historical control [5]. Therefore, we carried out the reassessment of the efficacy of our specific preoperative pulmonary rehabilitation protocol using the prospectively collected data.

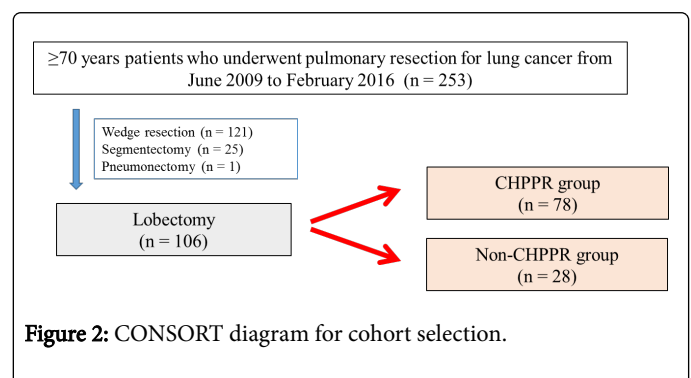
### Patients and Methods

Since June 2009, we have prospectively implemented a comprehensive preoperative pulmonary rehabilitation (CHPPR) program that includes 3 significant elements (Figure 1) [5]. The first element of the CHPPR program consists of multiple sessions of possibly high-intensity physical therapy and exercise (at least twice a week for 2-5 weeks), guided and assessed by physical therapists. The second element is intensive nutritional support with branched-chain amino acids (BCAA) and herbal medicine supplementation, guided and assessed by registered dietitians. Additionally, team conferences on an equal basis with all involved specialists, including doctors, physical therapists, dietitians, nurses, physiology laboratory technicians, and a clinical research coordinator, are held routinely to discuss efficient strategy for improving each patient's status; this interdisciplinary team approach is the third element of the CHPPR program.



**Figure 1:** Three significant elements of comprehensive preoperative pulmonary rehabilitation (CHPPR) program.

From June 2009 to February 2016, 253 patients aged over 70 years underwent surgical resection for lung cancer at our hospital, and 106 of them underwent standard lobectomy (Figure 2). Of the 106, 78 underwent lobectomy after participating in the CHPPR program (CHPPR group); 28 patients declined to participate (non-CHPPR group). The assignment of patients was mainly based on their preference; therefore, this was not a randomized study.



**Figure 2:** CONSORT diagram for cohort selection.

We defined morbidity as the ratio of patients who developed postoperative complications with grade 2 or higher in the Clavien-Dindo classification [6]. The difference in characteristics and postoperative complication rate (morbidity) between 2 groups (CHPPR vs. non-CHPPR) was determined using Fisher's exact test.

Univariate and multivariate logistic regression analyses for the postoperative complication were also conducted.

## Results

Table 1 shows the patient characteristics, perioperative conditions, and morbidity rate in 2 groups. There was no significant difference in patient characteristics between the CHPPR group and the non-CHPPR group.

Factors		CHPPR	Non-CHPPR	p Value
n		78	28	
Age		75.9 ± 0.5	75.5 ± 0.8	0.661
Gender	(female/male)	32/46	12/16	0.867
VC (L)		2.77 ± 0.22	3.00 ± 0.41	0.645
FEV1.0 (L)		2.09 ± 0.15	1.90 ± 0.30	0.513
Approach	(VATS/open)	69/9	26/1	0.513
Operative time (min)		213 ± 8	230 ± 14	0.307
Blood loss (g)		148 ± 12	185 ± 38	0.394
Smoking history	(current, ever/never)	48/30	17/11	1
Diabetes mellitus	(yes/no)	17/61	3/25	0.199
PRS in E-PASS		0.44 ± 0.02	0.39 ± 0.03	0.219
CRS in E-PASS		0.24 ± 0.22	0.17 ± 0.04	0.116
Morbidity rate		14.1%	35.7%	0.014

**Table 1:** Patient characteristics, perioperative conditions, and morbidity rate; CHPPR: Comprehensive Preoperative Pulmonary Rehabilitation; VC: Vital Capacity; FEV1.0: Forced Expiratory Volume in One Second; VATS: Video-Assisted Thoracic Surgery; PRS:

Preoperative Risk Score; CRS: Comprehensive Risk Score; E-PASS: Estimation of Physiologic Ability and Surgical Stress.

Complication		CHPPR	Non-CHPPR
Type	Grade		
Respiratory	2	7 (9.0%)	4 (14.3%)
	3-5	3 (3.8%)	2 (7.1%)
Cardiovascular	2	0	1 (3.6%)
	3-5	0	0
Others	2	1 (1.3%)	2 (7.1%)
	3-5	0	1 (3.6%)
Total	2	8 (10.3%)	7 (25.0%)
	3-5	3 (3.8%)	3 (10.7%)

**Table 2:** Type and grade of postoperative complication.

The differences in the preoperative risk score (PRS) and comprehensive risk score (CRS) of Estimation of Physiologic Ability and Surgical Stress (E-PASS) [7] between 2 groups were not statistically significant. However, the morbidity rates in the CHPPR group and in the non-CHPPR group were 14.1% and 35.7%, respectively ( $p=0.014$ ). Severe postoperative complications occurred predominantly in the non-CHPPR group. Tables 2 and 3 shows the results of univariate and multivariate logistic regression analysis of risk factors for morbidity. Univariate analysis showed that operative approach, operative time, amount of blood loss, smoking history, and CHPPR participation were statistically significant factors associated with morbidity ( $p=0.006$ ,  $p=0.024$ ,  $p=0.042$ ,  $p=0.032$ , and  $p=0.018$ , respectively). Multivariate analysis revealed that CHPPR participation was an independent beneficial factor for reducing the morbidity ( $p=0.005$ ).

Factors		Univariate analyses			Multivariate analyses		
		Odds ratio	95% CI	P Value	Odds ratio	95% CI	P Value
Age		1.08	0.97-1.22	0.165	1.06	0.91-1.24	0.444
Gender	(female/male)	2.02	0.74-6.13	0.172	1.80	0.22-14.98	0.579
VC (L)		0.74	0.36-1.45	0.385	0.49	0.07-3.03	0.447
FEV1.0 (L)		0.54	0.22-1.28	0.167	0.62	0.08-5.86	0.667
Approach	(VATS/open)	0.16	0.04-0.58	0.006	0.26	0.04-1.48	0.129
Operative time (min)		1.01	1.00-1.01	0.024	1.01	1.00-1.02	0.200
Blood loss (g)		1.00	1.00-1.00	0.042	1.00	1.00-1.00	0.544
Smoking history	(current, ever/never)	3.28	1.10-12.12	0.032	2.86	0.39-26.23	0.310
Diabetes mellitus	(yes/no)	0.67	0.15-2.27	0.538	0.89	0.16-3.86	0.614
CHPPR	(yes/no)	0.30	0.11-0.81	0.018	0.18	0.05-0.59	0.005

**Table 3:** Logistic regression analyses of risk factors for morbidity; CI: Confidence Interval; VC: Vital Capacity; FEV1.0: Forced Expiratory Volume in One Second; VATS: Video-Assisted Thoracic Surgery; CHPPR: Comprehensive Preoperative Pulmonary Rehabilitation.

## Conclusion

In conclusion, although this was not a randomized control study and the sample number was limited, the relatively short-term CHPPR protocol, which comprised 3 fundamental elements, appeared to have beneficial effects for elderly (over 70 years old) patients scheduled to undergo standard lobectomy for lung cancer.

There is growing evidence that preoperative interventions based on moderate-intense aerobic exercise in patients undergoing lung resection for lung cancer improve functional capacity and reduce postoperative mortality [8-10]; however, to establish an enforceable beneficial program of relatively short-term preoperative pulmonary rehabilitation for outpatients is still important issue. More comprehensive and sophisticated management strategies for lung cancer patients planning to undergo pulmonary resection need to be clearly investigated.

## Acknowledgement

We thank Makiko Kubota for her contribution as a medical assistant, and Yoko Sumitani for her contribution as a clinical research coordinator.

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