

폐암 수술 전후의 합병증 관리

내과적 합병증 관리

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Appendix 1. Major Perioperative Morbidities As Defined by The Society of Thoracic Surgeons General Thoracic Database

Pulmonary

Atelectasis requiring bronchoscopy

Pneumonia

ARDS/respiratory failure

Bronchopleural fistula/empyema

Pulmonary embolus

Initial ventilator support >48 hours

Reintubation

Tracheostomy

Cardiovascular

Atrial arrhythmia requiring treatment

Ventricular arrhythmia requiring treatment

Myocardial infarction

Deep vein thrombosis requiring treatment

Infection

Surgical site infection, specify

Sepsis

Neurology

New central neurologic event

Miscellaneous

New renal failure per RIFLE criteria

Other events requiring operation with general anesthesia, specify

Mortality rate

- 1.6% ~ 2.3% after lobectomy
- 3.7% ~ 6.7% after pneumonectomy (STS or ESTS general thoracic surgery DB)

ARDS = acute respiratory distress syndrome; RIFLE = risk of renal dysfunction, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage kidney disease.

“The best treatment of postoperative complications is prevention.”

Contents

- Perioperative pulmonary pathophysiology
- Predisposing factors for respiratory complications
- Preoperative risk evaluation
- Issues
 - Venous thromboembolism
 - Pulmonary venous thrombosis
 - ILD exacerbation
 - Failure to rescue

Perioperative pulmonary pathophysiology

Diaphragm dysfunction

- Impaired force production and endurance capacity due to:
 - Altered chest wall/lung compliance with increased work of breathing
 - Impaired force due to prolonged mechanical ventilation
 - Direct injury to diaphragm or phrenic nerve
 - Reduced shortening fraction of the diaphragm
 - Reduced central drive (reflex; opioids)
 - Contiguous inflammatory process, etc.
- Can last several weeks
- Diaphragm dysfunction is similar with thoracotomy and with VATS, (recovery time is shorter with VATS)

Perioperative pulmonary pathophysiology

Abnormal lung function

- Pain and diaphragmatic dysfunction in the postoperative period
 - rapid shallow breaths w/o periodic deep breaths (sighs)
 - reducing functional residual capacity (FRC)
- FRC
 - the single most important lung volume measurement a/w the development of pulmonary complications
- As decreased FRC approaches closing volume (CV)
 - premature airway closure and atelectasis
 - V/Q mismatch (hypoxia), trapping of secretions (pneumonitis)
 - ★ CV is elevated in patients with underlying lung disease

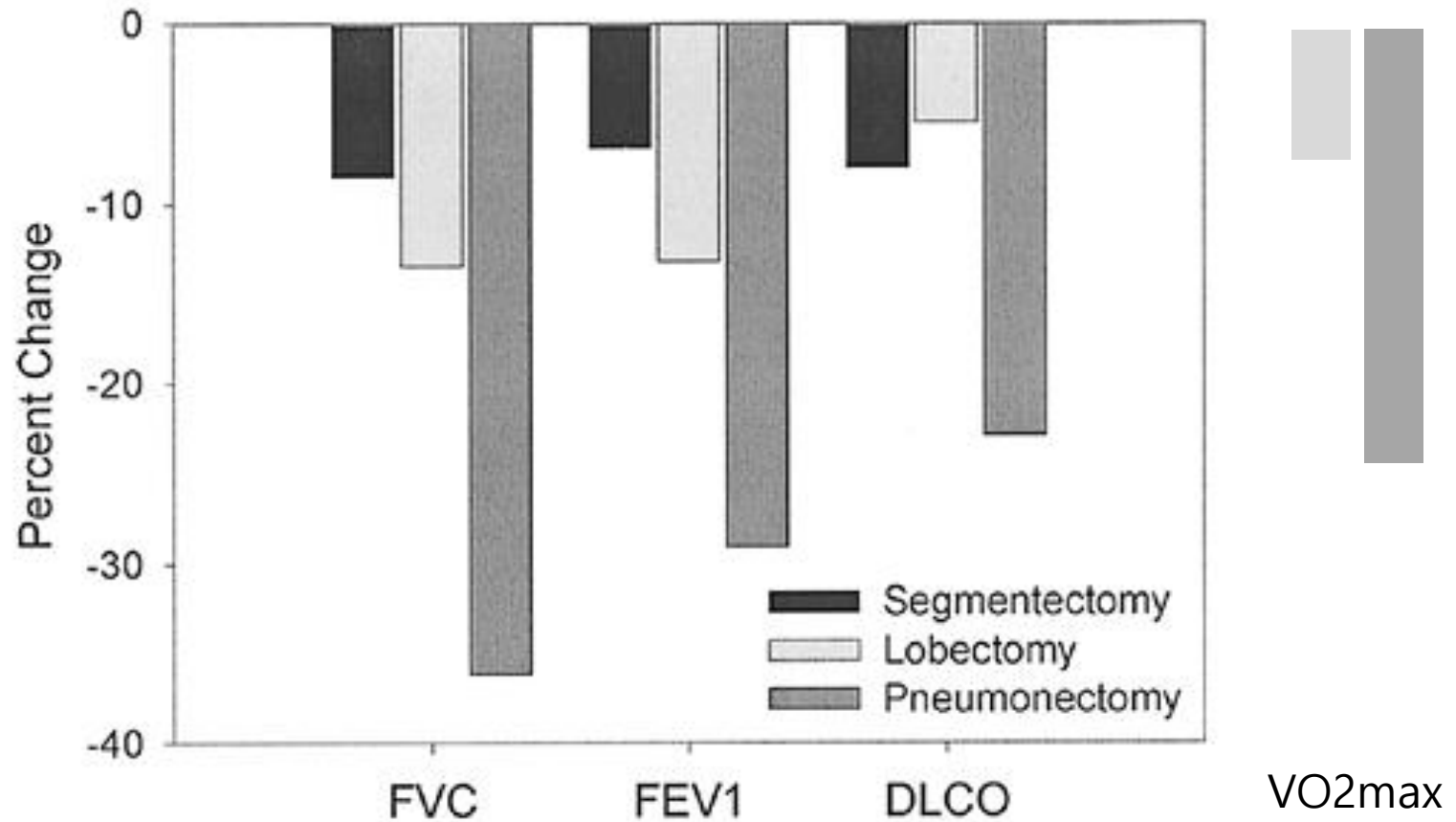
Perioperative pulmonary pathophysiology

- Reduction in inspiratory capacity and expiratory reserve volume
 - decline in the effectiveness of cough
 - increased difficulty in clearing of pulmonary secretions

Reduced lung volume d/t lung resection

- In early postoperative period, FEV1 and FVC reduces about 35%-50% below the predicted values (slightly greater decrement with thoracotomy than VATS)
 - By discharge, values approach 80% of predicted values.
 - Up to 3-4 months to approach postop pred. values.

Permanent changes in FVC, FEV₁, DL_{CO}, VO₂ max after lung resection



Perioperative pulmonary pathophysiology

Gas exchange

- Hypoxemia d/t microatelectasis a/w
 - reduction in lung volumes
 - abnormal mucociliary clearance
- Hypercapnia d/t
 - central respiratory depression (opiate analgesia, residual effects of anesthetic agents),
 - incomplete reversal of neuromuscular blockade
 - diaphragm dysfunction
 - splinting and abnormal rapid-shallow breathing pattern

Predisposing factors for respiratory complications - **preoperative**

- Old age
- Smoking history
- Insufficient pulmonary function
 - PPO FEV1<30%, or PPO DLCO<30%
 - VO2max<10ml/kg/min
- Underlying complex medical illness, i.e., ischemic heart disease
- Debilitated preoperative state (fatigue, anorexia, recent weight loss)
- Absence of preoperative teaching

Predisposing factors for respiratory complications - **intraoperative**

- Prolonged procedure, pooling of secretions, collection of operative debris
- Induced lung collapse
- Contusion of remaining parenchyma
- Loss of surfactant function from
 - High inspired FIO₂
 - Prolonged period of mechanical ventilation
- Overhydration
- Loss of ciliary function from effects of anesthesia

Predisposing factors for respiratory complications - **postoperative**

- Extent of parenchymal loss
- Inability or unwillingness of patient to cooperate with deep breathing/coughing exercises
- Hypoventilation secondary to anesthesia
- Decreased FRC
- Decreased chest wall compliance secondary to incision and pain response
- Damage to alveolar membrane secondary to aspiration
- Alveolar collapse secondary to vigorous endotracheal suctioning

Risk assessment for lung resection

Higher risk	Lower risk
FEV1 % < 60% DLCO % < 60%	FEV1 > 2L for pneumonectomy FEV1 > 1.5L for lobectomy, FEV1 > 0.6L for segmentectomy FEV1 > 80% pred
ppo FEV1 < 30-40% ppo DLCO < 30-40%	ppo FEV1 > 40-60% ppo DLCO > 40-60% ppo FEV1 > 800mL
VO2max < 10mL/kg/min Stair climbing < 12m Shuttle walk < 25 shuttles	VO2 max > 15-20mL/kg/min Stair climbing > 5flights for pneumonectomy, 3flights for lobectomy Cycle ergometry > 83 watts
pCO2 > 60mmHg pO2 < 45mmHg	pCO2 < 45mmHg pO2 > 60mmHg
Higher extent of resection (pneumonectomy > lobectomy > wedge resection)	Nonsmoker, smoking abstinence
Prolonged operation time	
Old Age, current smoking	



CHEST

Supplement

DIAGNOSIS AND MANAGEMENT OF LUNG CANCER, 3RD ED: ACCP GUIDELINES

Physiologic Evaluation of the Patient With Lung Cancer Being Considered for Resectional Surgery

**Diagnosis and Management of Lung Cancer,
3rd ed: American College of Chest Physicians
Evidence-Based Clinical Practice Guidelines**

*Alessandro Brunelli, MD, FCCP; Anthony W. Kim, MD, FCCP; Kenneth I. Berger, MD, FCCP;
and Doreen J. Addrizzo-Harris, MD, FCCP*

Preoperative assessment

AGE

- Although traditionally considered as a risk factor for perioperative complications, much of the additional risk from age results from comorbid factors.
- When studies control for comorbidities, patients are at mildly increased risk because of age.
- Current consensus is that **age alone, particularly in the presence of a good functional capacity, is not a contraindication to surgery.**

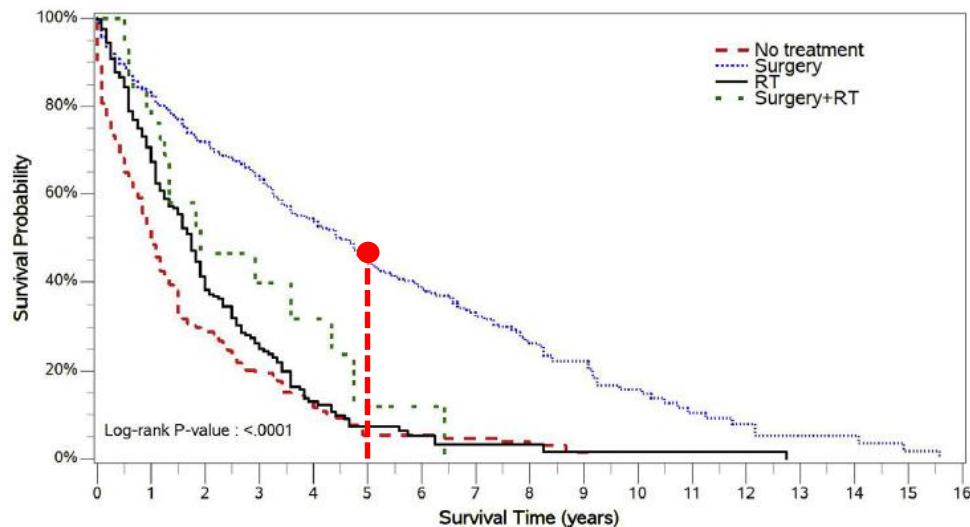
2.6.2. In elderly patients with lung cancer who are potential candidates for curative surgical resection it is recommended that they be fully evaluated regardless of age (Grade 1C).

Octogenarians

- By the SEER database, 50% of lung cancer are diagnosed in > 70 yo, and 15% in > 80 yo. And 18% of > 75 yo present with localized ds.
- Life expectancy
 - Average people in their 80's: >5-9 yrs
 - Untreated/palliative care-only patients with lung cancer: 1.5 yrs
- Elderly patients are more likely to develop toxicity from other Tx.
- Surgical resection is associated with long-term survival in a substantial proportion of octogenarians with early stage lung cancer.
 - 5-year survival in stage I varies between 50% and 60%
- Nowadays restriction of potentially curative surgery on the basis of age alone is no longer an appropriate option.

Early Stage NSCLC in Octogenarian and Older Patients : A SEER Database Analysis

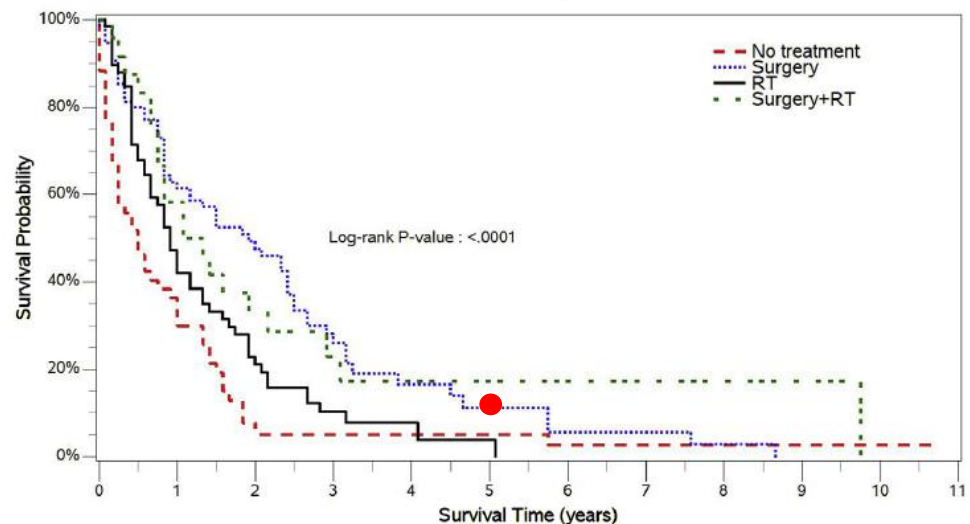
- Between 1988 and 2007
- 1338 NSCLC octogenarians
- Surgery : 44.4% (inc. trend)
- PS or comorbidity: NA – bias?



Stage I (n=1116)

Median Survival (95% CI; yrs)

Surgery Only (n=518)	4.4 (3.7-5)
RT Only (n=276)	1.9 (1.3-4.3)
Surgery + RT (n=31)	1.8 (1.5-1.9)
No Treatment (n=291)	1 (0.8-1.2)



Stage II (n=222)

Median Survival (95% CI; yrs)

Surgery Only (n=76)	1.9 (1-2.4)
RT Only (n=70)	1.2 (0.8-2.2)
Surgery + RT (n=24)	0.9 (0.7-1.3)
No Treatment (n=52)	0.5 (0.3-0.9)

❖ Life expectancy of octog.: 8.4yrs

Median overall survival (all): 3.8 yrs

Clinical Lung Cancer, 2015;17:285-91

Smoking and increasing frequency of pul. Cx : suppressive effect of smoking on innate immune system

Smoking impairs

- Mucociliary escalator
 - Normalisation after smoking cessation requires 15 days
- Antimicrobial/proinflammatory fx of alveolar macrophages
 - Normalisation after smoking cessation requires
 - 3 months for phagocytic function
 - 6 months for proinflammatory function

Is the incidence of major pulmonary morbidity after lung resection associated with the timing of smoking cessation?

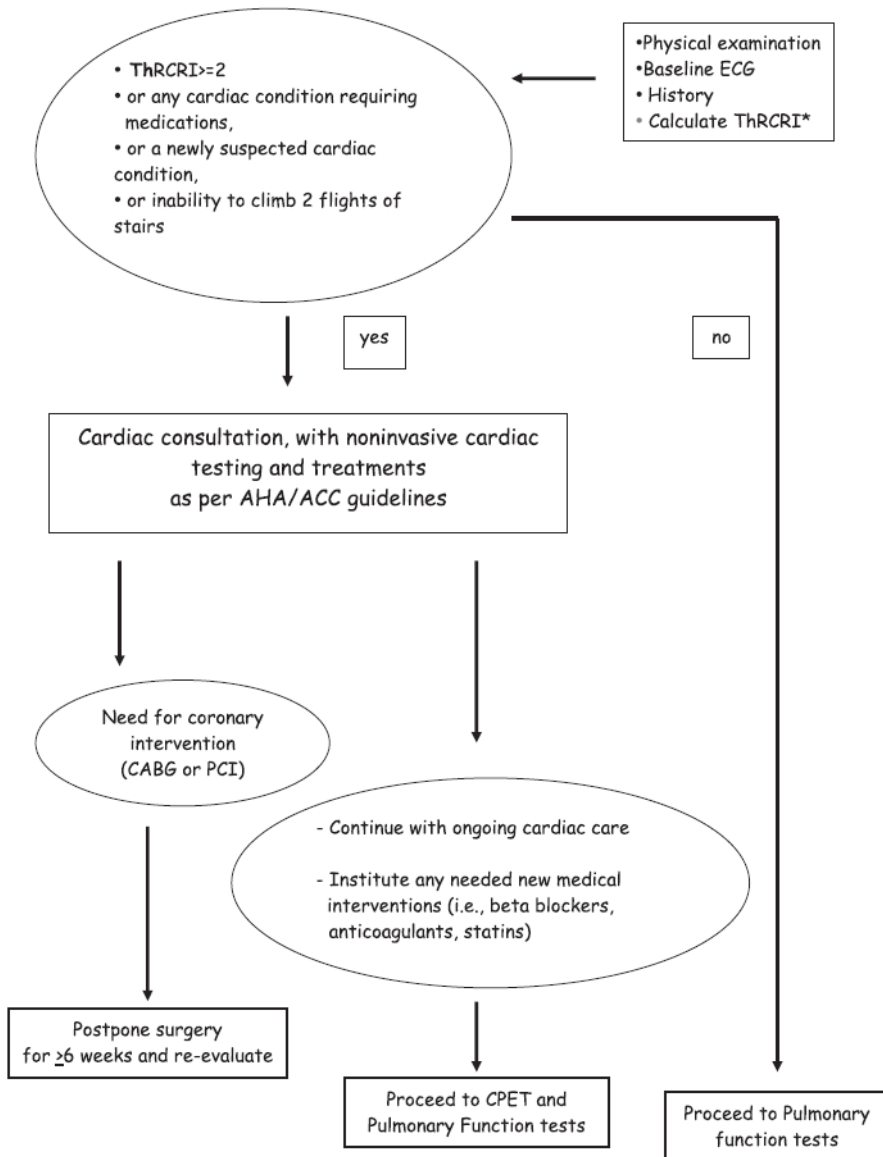
- Medline search 1950~2011, reviewed 49 papers, 7 with best evidence (level 2b)
- In most studies, smoking abstinence was shown to reduce the incidence of post-operative pulmonary complications (PPCs).
- The timing of cessation is not clearly identified, although there is some evidence showing reduction in risk of PPCs with increasing interval since cessation.
 - Smoking abstinence for ≥ 4 wks before surgery was necessary to reduce the incidence of major pulmonary events. (2 studies)
 - Pre-operative smoke-free period of >10 weeks produced complication rates similar to those of patients who had never smoked. (1 study)

7.4.2. In all patients with lung cancer being considered for surgery who are actively smoking, tobacco dependence treatment is recommended (Grade 1C).

Cardiovascular risk

- Patients with lung cancer are predisposed to atherosclerotic cardiovascular disease because of cigarette smoking.
- The prevalence of underlying coronary artery disease: 11%~17%
- The risk of major postoperative cardiac complications: 2%~3%
 - myocardial ischemia, pulmonary edema, ventricular fibrillation or primary cardiac arrest, complete heart block, and cardiac-related death
- Preoperative cardiovascular risk assessment should be performed.

Physiologic evaluation cardiac algorithm



Thoracic Revised Cardiac Risk Index (ThRCRI)

Creatinine >2 mg/dl: 1 point

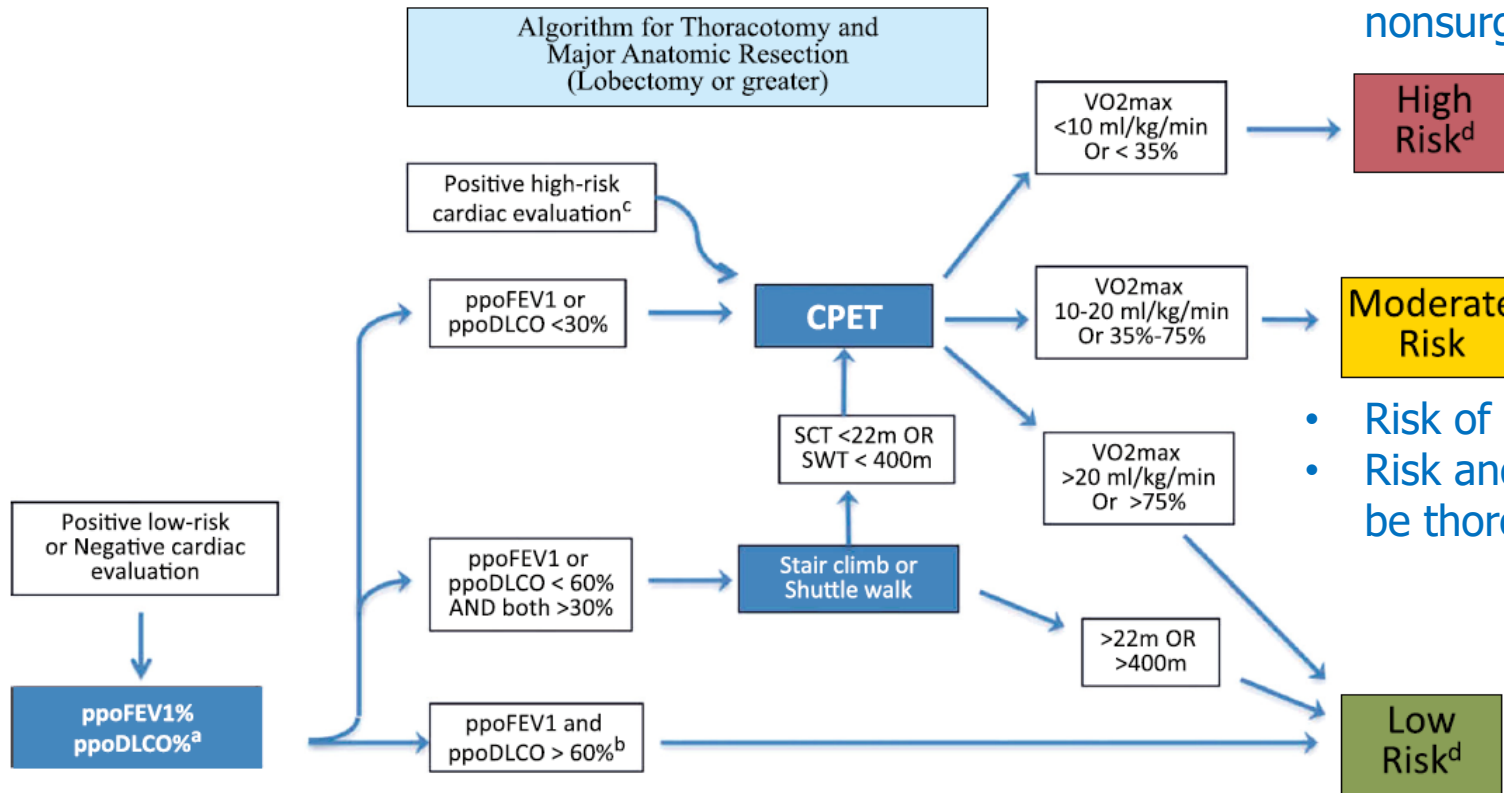
Previous stroke or TIA: 1.5 points

Previous ischemic heart disease: 1.5 points

Pneumonectomy: 1.5 points

- ✓ Aggressive cardiac interventions should be reserved only for patients who need them irrespective of surgery, but interventions specifically for surgery are of limited benefit.

Physiologic evaluation resection algorithm



- Risk of mortality > 10%
- Sublobar resection or nonsurgical options

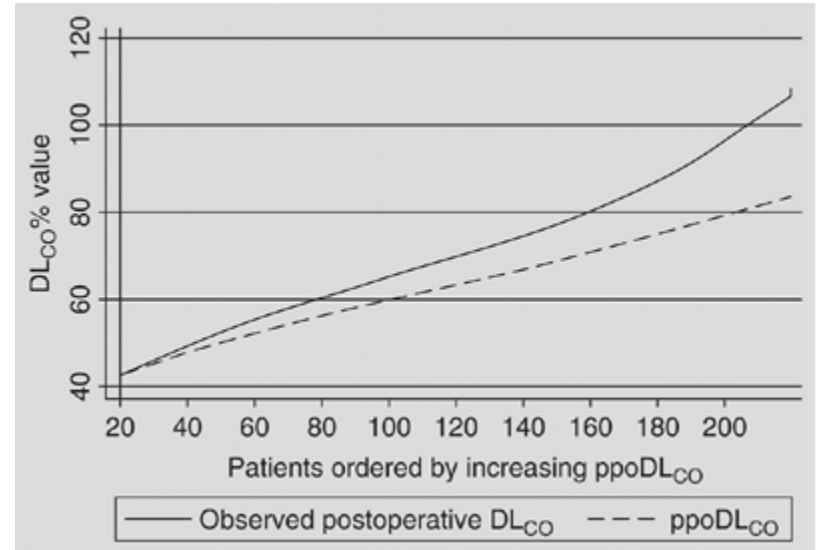
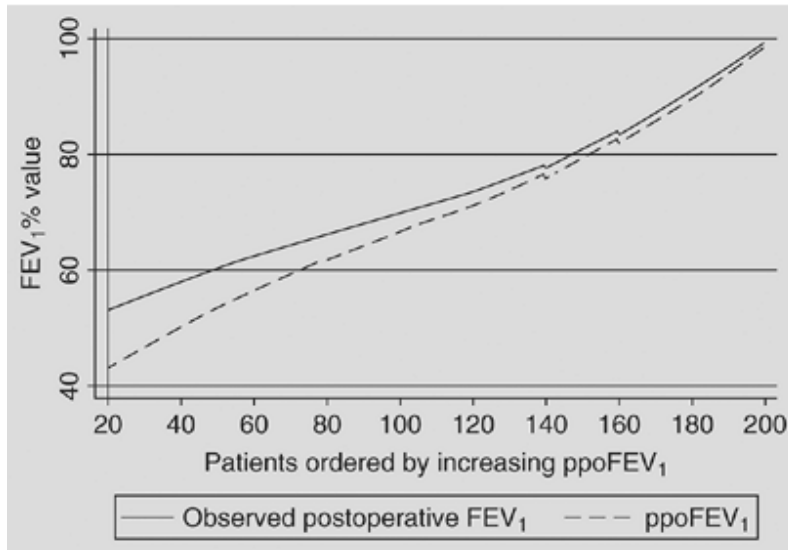
- Risk of mortality 1~10%
- Risk and benefit should be thoroughly discussed.

- Risk of mortality < 1%
- Pneumonectomy safe

Major lung resection for patients at the lower limits of lung function

- Curative lung resection surgery can be performed in patients with PPO lung function as low as 30% predicted, provided the patient demonstrates an acceptable exercise capacity.
- Compared to patients with normal lung function, patients with more severe obstructive lung disease experience less percentage loss of lung function as measured by spirometry.
 - Frequent improvement in measured lung function and respiratory symptoms postoperatively
 - Don't use absolute limits for determining which patients should be excluded from consideration for major lung resection.

ppo FEV₁ and ppo DL_{CO} values relative to those observed at 3 months



- Relative inaccuracy of PPO lung function in higher-risk patients
- “lung volume reduction” effect in COPD (improvement in respiratory mechanics and elastic recoil)
- Distention of remaining alveoli, leading to recruitment of capillary surface area and blood volume
- Be careful to use of DL_{CO} cutoff values to eliminate patients from consideration for major lung resection.

Risk reduction

- Correction of comorbid conditions including cardiovascular and pulmonary disease
- Preoperative pulmonary toilet instruction
- Smoking cessation (Grade 1C)
- Cardiopulmonary rehabilitation (Grade 1C)
- Combined Lung volume reduction surgery and lung cancer resection (Grade 2C)
- Sublobar resection in high risk patients
- Minimal invasive surgery
- Chest physiotherapy, pain control, ambulation, incentive spirometry for atelectasis

VTE After Lung Cancer Resection

- Patients with lung cancer undergoing resection have a higher risk of VTE compared with those with other solid organ cancers.
- Risk factors for VTE in lung cancer
 - age, obesity, smoking, and race, as well as cancer-related factors including tumor biology, histologic features, and stage of disease
- Increased risk for perioperative VTE
 - extended periods of bed rest, reduced postoperative ambulation, and higher levels of discomfort associated with chest incisions, performance of thoracotomy and extent of resection
- VTE after lung resection: 0.2% ~ 20%
 - Majority of VTE occurs in the initial postoperative period
 - Risk lasts up to 30 days after resection (persists after discharge)
- About 1/3 of postoperative VTEs occur after discharge

Prevention of VTE in Nonorthopedic Surgical Patients

ACCP guideline

5.4.1. For thoracic surgery patients at moderate risk for VTE who are not at high risk for perioperative bleeding, we suggest LDUH (Grade 2B), LMWH (Grade 2B), or mechanical prophylaxis with optimally applied IPC (Grade 2C) over no prophylaxis.

Remarks: Three of the seven authors favored a strong (Grade 1B) recommendation in favor of LMWH or LDUH over no prophylaxis in this group.

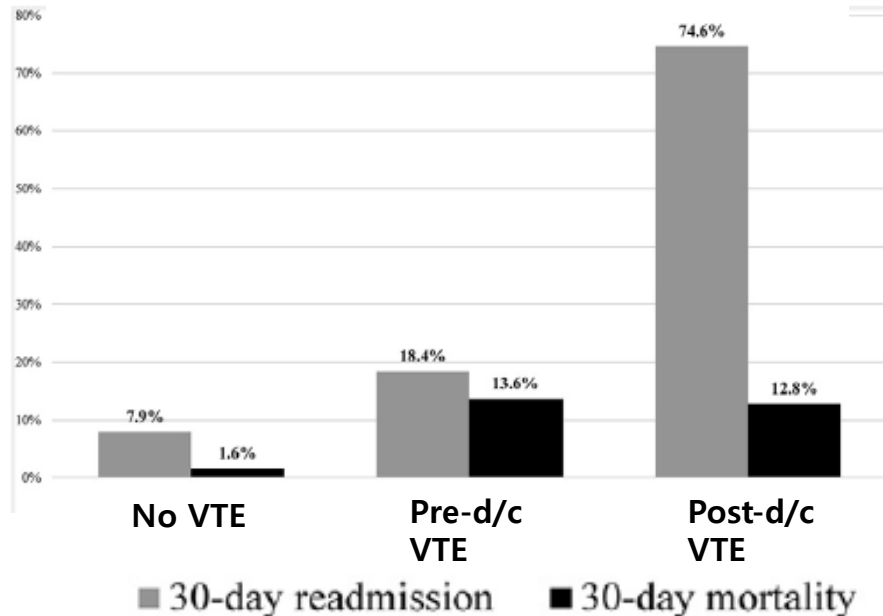
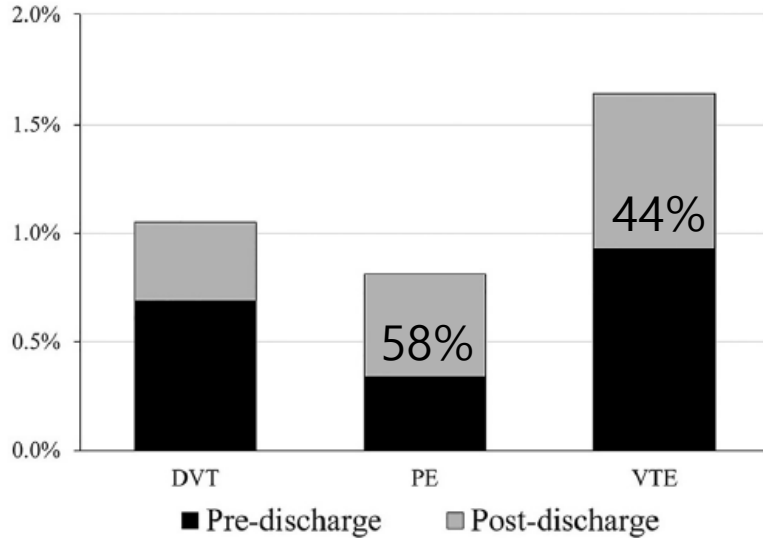
5.4.2. For thoracic surgery patients at high risk for VTE who are not at high risk for perioperative bleeding, we suggest LDUH (Grade 1B) or LMWH (Grade 1B) over no prophylaxis. In addition, we suggest that mechanical prophylaxis with ES or IPC should be added to pharmacologic prophylaxis (Grade 2C).

5.4.3. For thoracic surgery patients who are at high risk for major bleeding, we suggest use of mechanical prophylaxis, preferably with optimally applied IPC, over no prophylaxis until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade 2C).

- Very low risk for VTE (< 0.5%; Caprini score, 0)
 - Low risk for VTE (~1.5%; Caprini score, 1-2)
 - Moderate risk for VTE (~3.0%; Caprini score, 3-4)
 - High risk for VTE (~6.0%; Caprini score, ≥5)
 - Duration of prophylaxis?
 - Extended prophylaxis beyond hospital discharge?
- cf. abdominal and pelvis surgery

Timing and Risk Factors Associated With VTE After Lung Cancer Resection

- ACS NSQIP dataset: 14,308 patients \geq lobectomy, VTE w/i 30 days of operation
- PFT, smoking history, PS not available



Factors for postdischarge VTE

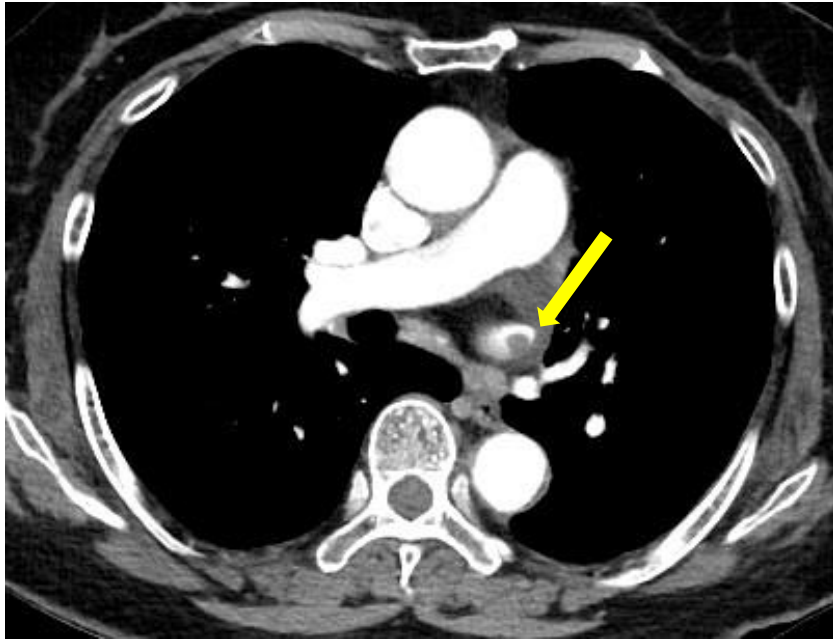
Age > 65, Men, ASA class 4, severe COPD, pneumonectomy, thoracotomy, prolonged OP time, extended LOS, pre-discharge complication

Table 3. Multivariable Regression Analysis Identifying Demographic and Perioperative Characteristics Associated With Postdischarge Venous Thromboembolism

Variable	OR	95% CI		p Value
Age (y)				
<65s	1.0	Ref		Ref
65–80	2.2	1.4	3.5	<0.01
>80	2.6	1.3	5.2	0.01
Body mass index				
Underweight	1.6	0.5	5.5	0.40
Normal	1.0	Ref		Ref
Overweight	1.1	0.6	1.8	0.81
Obese	2.0	1.2	3.3	<0.01
Surgical approach				
Lobectomy	1.0	Ref		Ref
Pneumonectomy	3.4	2.0	5.9	<0.01
Operative time				
\leq 75th percentile	1.0	Ref		Ref
Extended	1.5	1.0	2.3	0.05

➤ Post-d/c prophylaxis should be considered in patients at high risk for VTE

Pulmonary vein stump thrombosis



F/72

AC, LUL, pT2aN0M0, stage IB
- LULobectomy 2018.5.10
- adjuvant NP CTx #4

- Long (Lt. sup.) PV stump after LULobectomy may cause blood stasis, predisposing to thrombus formation.
- 4-13% after LULobectomy
- May cause arterial embolization of vital organs, including cerebral infarction.
- Time of onset of the embolic event or the time of thrombus detection: days ~ months after surgery
- Generally treated in the same manner as LA appendage thrombus with anticoagulant therapy

Postoperative AE of ILD

- Postoperative AE of interstitial pneumonia in lung cancer is frequent (10%-20%) and is associated with mortality rates of 33.3%~100%.
- Definition of AE caused by pulmonary resection
 - 1) onset within 30 days after pulmonary resection
 - 2) intensified dyspnea
 - 3) increase in the interstitial shadow on chest x-ray and chest CT scan
 - 4) decrease in arterial O₂ tension of > 10mmHg under similar conditions
 - 5) no evidence of pulmonary infection
 - 6) exclusion of alternative causes, such as cardiac failure, pulmonary embolism, or other identifiable causes of lung injury
- Factors that lead to endothelial stress and AEILD
 - Fluid overload, 1-lung ventilation, positive pressure ventilation, high conc. O₂ exposure, large lung volume resection, reduced vascular bed...

Risk factors for postop AE of ILD

Patient-related	Surgery-related
Age >75 years	>4-hour-long operations
IPF versus other ILDs	high preoperative O2 conc.
honeycomb pattern on CT	parenchyma resection extent
fibrosis in the non-operated lung	Intraoperative fluid overload
functional limitation	
low FVC	
elevated KL6 or CRP levels	
preoperative steroid use in IPF	

Impact and predictors of acute exacerbation of interstitial lung diseases after pulmonary resection for lung cancer

- Retrospective cohort study, 64 institutions, 41,742 lung cancer pts, 1763 cases with ILDs analyzed
- AE in 164/1763 patients (9.3%; 95% CI=8.0-10.8), POD 7d (0-29)
- Side of AE: OP side 14.2%, Contralateral 25.2%, Bilateral 60.6%
- Mortality rate of 43.9%: top cause of 30-day mortality (71.7%)
- Independent risk factors of AE
 - surgical procedures, male sex, history of exacerbation, preoperative steroid use, elevated KL-6, UIP>non-UIP on CT, reduced % pred. VC
- Surgical procedures: strongest association with AE ($P<0.001$)
 - wedge resection as the reference
 - lobectomy or segmentectomy: OR=3.83 (95% CI=1.94-7.57)
 - bi-lobectomy or pneumonectomy: OR=5.70 (95% CI=2.38-13.7)
 - Anatomic resection requires longer OP time, increased hilar vascular procedures and node dissection which may hinder the lymphatic flow
- Perioperative prophylactics (steroids, sivelestat) showed no positive effect on AE prevention

Japanese guideline for the treatment of idiopathic pulmonary fibrosis

- Based on the evidence outlined above, the guideline formulation committee recommends that lung cancer patients with comorbid IPF or other IPs should not be given preventive drug administration against post-surgical acute exacerbation (apart from antifibrotic drugs) (strength of recommendation 1, quality of evidence C).

Ministry of Health, Labour and Welfare, the Study Group on Diffuse Pulmonary Disorders, Scientific Research/Research on Intractable Diseases, and Japanese Respiratory Society

Prevention of complication vs. decreasing failure-to-rescue

- It is proposed that higher mortality rates may be associated with higher complication rates at poor-performing hospitals and that LMHs are more proficient at using practices that prevent complications.
 - Efforts should be aimed at improving surgeons' technical proficiency
- Another hypothesis may be that LMHs are better at recognizing and managing complications effectively once they have occurred or decreasing "failure-to-rescue" rates.
 - Efforts should focus on systems aimed at early recognition and management of complications.

Lung Cancer Resection at Hospitals With High vs Low Mortality Rates

- Retrospective cohort study
- 645 lung resections in 18 LMHs and 25 HMHs among 1279 hospitals in NCDB

Mortality rates (1.8% in LMH vs 8.1% in HMH; $P < .001$)

- Significant difference in adherence to evidence-based practices aimed at preventing complications (intraoperative monitoring, VTE prophylaxis,...)

Table 3. Incidence of Complications and Case Fatality Rates at LMHs and HMHs

Complication	Incidence of Complication			Case Fatality Rate		
	LMH, % ^a	HMH, % ^a	OR of Complication (95% CI)	LMH, % ^a	HMH, % ^a	OR of Mortality (95% CI)
Any	15.6	23.3	1.79 (0.99-3.21)	8.7	25.9	6.55 (1.44-29.88)
Any surgical	3.7	2.8	0.73 (0.26-2.00)	22.9	15.0	NA ^b
Any medical ^c	13.7	21.8	1.92 (1.00-3.66)	9.7	26.3	5.95 (1.12-31.39)
Cardiopulmonary event	9.1	10.7	1.23 (0.70-2.16)	14.6	34.5	8.61 (0.77-95.48)
Thromboembolic event ^d	0.2	0.9	4.77 (0.28-79.10)	NA ^e	NA ^e	NA ^e
Other	6.6	14.3	2.60 (1.07-6.33)	4.5	23.6	15.39 (1.52-155.67)

- No significant (marginal) increases in complications associated with variation in adherence to these practices. Differences in morbidity do not explain the large differences in mortality rates.
- Our results suggest that differences in mortality rates are not d/t variations in perioperative practices but rather differences in failure to rescue.
- The importance of recognizing and managing a complication effectively once it has occurred

Conclusion

- Assess each potential risk factor for each patient.
- Do not ignore warning signs of increased risk. There is rarely a need for urgent surgery precluding a formal and careful evaluation of risk factors.
- However, don't use absolute limits for determining which patients should be excluded from consideration for major lung resection.
- The medical team should know how to forecast possible complications, how to prevent them, how to diagnose them early, and how to treat them efficiently, so that a minor event does not progress to a major morbidity.
- Close cooperation among multidisciplinary team is warranted and the role of pulmonologists is crucial.

Thank
you

