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Prospective randomized controlled study on the effects of **vagus nerve pulmonary branch preservation** during video-assisted thoracic surgery lobectomy in non-small cell lung cancer: whether it can **decrease postoperative cough** and **pulmonary complications**

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# Objective/Background

- **Postoperative cough after lobectomy is observed in**
  - Postoperative 1 year : **60% of patients**
  - Postoperative 5 years: **24.7 – 50% of patients**
- Mediastinal LN dissection increase postoperative cough
- Female patients are at higher risk of postoperative cough
  
- **Does preservation of the vagus nerve during mediastinal LN dissection**
  1. **Reduce the rate of postoperative chronic cough and pulmonary complications?**
  2. **Can be done oncologically safely and completely?**

Patients with clinical stage T1-3/N0-1/M0 lung cancer from July 1<sup>st</sup> 2021 – June 30<sup>th</sup> 2023

## Inclusion

1. Informed consent
2. 80 ≥ Age ≥ 18
3. Clinically suspicious or diagnosed with NSCLC
4. Preoperative **clinical T1-3/N0-1/M0**
5. Preoperative ECOG 0 or 1
6. Preoperative ASA class I-III
7. Preoperative PFT: **FEV1 ≥ 60%, DLCO ≥ 60%**
8. Patients **eligible R0** (complete resection) with simple lobectomy with MLND

## Exclusion

1. Smoking within 2 weeks prior to operation
2. Preop antipertussive medications within 2 weeks prior to operation
3. Pregnant or breast feeding patients
4. Psychological illness
5. Severe lung adhesion
6. Open thoracotomy
7. History of other malignancies <2 years prior to operation
8. **Preoperative RTx or Chemotherapy <6 months** prior to operation
9. **Clinical N2** or patients who received **neoadjuvant therapy**
10. Patient diagnosed with other **cough-related disease**: COPD, asthma, ILD, GERD

**Group 0 (Control)**  
N=99

**Primary Outcomes: analysis of postoperative cough and its impact on daily life**

*Postoperative 1month / 2month/ 6month / 12month*

1. Cough Visual Analog Scale (VAS)
2. Korean version of Leicester Cough Questionnaire (LCQ)

**Group 1 (Vagus preservation)**  
N= 93

**Secondary Outcomes:**

1. Postoperative pulmonary function test
2. Postoperative pulmonary complication incidence, length of hospital stay, other complications
3. Oncologic safeness: total number of resected LNs, nodal upstaging frequency
4. Measurement of vagus nerve injury by quantification of serum level bradykinin, PGE2

# Results: Clinical Characteristics in Control vs. Vagus Groups

	Group 0 (Control) N=99	Group 1 (Vagus preservation) N= 93	P value
Operated Lung Right Left	61 (61.6) 38 (38.4)	62 (65.3) 33 (34.7)	0.600
Nodal upstaging	13 (13.1)	8 (8.6)	0.317
Postop airleak	2 (2)	2 (2.1)	0.958
Postop bleeding	1 (1)	1 (1.1)	0.971
Postop chylothorax	2 (2)	1 (1.1)	0.594
Postop RTx	2 (2)	4 (4.3)	0.374
Postop ChemoTx	<b>30 (30.7)</b>	<b>17 (18.1)</b>	<b>0.048</b>
Recurrence	3 (3)	0	0.247
LN dissected	<b>21.61±8.03</b>	<b>18.6±7.5</b>	0.090
Sex			
Male	40 (40.8)	42 (43.7)	
Female	58 (59.2)	54 (56.3)	

Vagus nerve preservation was **equally oncologically safe and feasible**, without statistical significant difference from control group.

# Results: Changes in Pulmonary Function Test

	Group 0 (Control) N=98	Group 1 (Vagus preservation) N= 93	P value
PreFEV1	2.53±0.57	2.63±0.63	0.269
PreFEV1/FVC	77.2±7.13	76.3±6.53	0.344
PreDLCO	102.21±17.0	99.2±15.3	0.238
1moFEV1	2.00±0.52	2.12±0.53	0.144
1moFEV1/FVC	74.2±9.22	74.35±7.56	0.916
1moDLCO	81.25±15.9	84.3±12.18	0.492
3moFEV1	2.10±0.55	2.18±0.54	0.303
3moFEV1/FVC	74.73±8.39	73.81±8.23	0.416
3moDLCO	87.57±16.11	84.11±14.26	0.212
6moFEV1	2.19±0.57	2.26±0.56	0.34
6moFEV1/FVC	74.76±8.21	73.68±7.64	0.35
6moDLCO	86.98±18.11	84.71±16.31	0.392
12moFEV1	2.23±0.55	2.28±0.54	0.545
12moFEV1/FVC	73.71±7.86	72.94±8.56	0.516
12moDLCO	90.1±18.49	88.05±15.28	0.429
<b>Change in year</b>			
FEV1	-12.29±13.39	-13.77±13.11	0.437
FEV1/FVC	-5.28±13.01	-5.21±13.42	0.971
DLCO	-0.16±0.25	-0.14±0.23	0.72

**No significant  
difference in PFT**

# Results: Change in Cough VAS in Control vs. Preservation Groups

	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=99	0	1.6±1.4	2.9±2.1	2.4±1.9	1.9±1.9	1.3±1.6
Preserving group n=95	0.05±0.33	1.3±1.5	2±1.71	1.4±1.2	0.9±0.9	0.6±0.9

VAS: 0 – 10

**Lower cough VAS in preservation group since postop 1month**

# Results: Change in Physical Domain in Control vs. Preservation Groups

	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=99	52.7±3.6	48.42±6.3	44.3±7.4	46.8±6.8	47.8±6.3	49.8±9.4
Preserving group n=95	51.9±3.5	48.1±7.3	47.8±8.5	48.5±4.7	51.1±8.1	50.6±4.5

**Higher Physical Domain LCS in preservation group**  
**Therefore, better physical status including less cough**

Physical domain: 56  
Social domain: 28  
Psychological domain: 49

# Results: Change in Social Domain in Control vs. Preservation Groups

	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=99	27.6±1.3	25.8±3.3	23.7±5.0	24.8±4.5	25.7±3.8	26.0±3.9
Preserving group n=95	27.5±1.4	25.9±3.6	25.5±3.0	26.1±2.3	27.1±1.4	27.2±1.8

**Higher Social Domain LCS in preservation group**

Physical domain: 56  
Social domain: 28  
Psychological domain: 49

# Results: Change in Psychologic Domain in Control vs. Preservation Groups

	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=99	43.4±2.1	40.9±5.0	38.9±6.9	40.3±6.5	41.5±5.8	42.2±9.6
Preserving group n=95	43.3±2.0	41.7±5.5	41.7±6.8	41.6±4.7	43.6±8.0	43.0±3.1

**Higher Psychological Domain LCS in preservation group**

Physical domain: 56

Social domain: 28

Psychological domain: 49

# Results

- Vagus nerve preservation LN dissection is oncologically safe and feasible, without pulmonary complications
- Preservation group has lower postoperative cough VAS since postop 1 month
- Preservation group has better physical, social, and psychological well-being since postop 1 month

# Results: Change in Cough VAS in Male / Female Subgroups

## Table 1. Change in Cough VAS in Male Control vs. Preservation Groups

Male N=81	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=40	0	1.7±1.5	2.17±2.1	1.38±1.3	1.5±1.9	1.15±1.4
Preserving group n=41	0.05±0.218	1.32±1.5	1.93±1.7	1.37±1.5	0.85±0.91	0.51±0.71
P value	<i>0.004</i>	<i>0.625</i>	<i>0.203</i>	<i>0.955</i>	<b><i>0.016</i></b>	<b><i>0.009</i></b>

## Table#. Change in Cough VAS in Female Control vs. Preservation Groups

Female N=113	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=59	0	1.54±1.3	3.42±1.97	3.05±1.96	2.1±1.9	1.37±1.7
Preserving group n=54	0.06±0.4	1.22±1.5	2.06±1.75	1.44±1.04	0.96±0.93	0.7±0.9
P value	<i>0.035</i>	<i>0.322</i>	<i>0.512</i>	<b><i>0.001</i></b>	<b><i>0.001</i></b>	<b><i>0.002</i></b>

**Lower Cough VAS** in female preservation group from postop 2<sup>nd</sup> month to 1 year

# Results: Change in Physical Domain in Male and Female Subgroups

**Table1. Change in Physical Domain in Male Control vs. Preservation Groups**

Male N=81	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=40	53.03±3.75	49±5.51	47.28±5.18	49.3±5.2	48.5±6.2	50.03±6.3
Preserving group n=41	51.73±3.45	47.6±7.47	47.02±5.6	58.2±5.1	52.59±11.3	50.95±3.02
P value	<i>0.552</i>	<i>0.115</i>	<i>0.924</i>	<i>0.685</i>	<i>0.858</i>	<i>0.008</i>

**Table2. Change in Physical Domain in Female Control vs. Preservation Groups**

Female N=113	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=59	52.53±3.6	48.03±6.8	42.32±8.15	45.08±7.2	47.39±6.4	49.58±11
Preserving group n=54	52.09±3.5	48.54±7.14	48.39±10.2	48.7±4.4	50. ±4.04	50.3±5.4
P value	<i>0.580</i>	<i>0.382</i>	<i>0.841</i>	<b><i>0.001</i></b>	<b><i>0.001</i></b>	<b><i>0.033</i></b>

**Higher Physical Domain** in female preservation group from postop 2<sup>nd</sup> month to 1 year

# Results: Change in Social Domain in Male/ Female Sugroups

**Table1. Change in Social Domain in Male Control vs. Preservation Groups**

Male N=81	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=40	27.48±1.52	26.15±3.06	25.65±3.17	26.7±2.26	26.1±3.46	26.75±2.43
Preserving group n=41	27.51±1.52	25.34±4.34	25.46±2.47	25.83±2.74	27.32±1.01	27.46±1.5
P value	<i>0.972</i>	<i>0.095</i>	<i>0.175</i>	<i>0.441</i>	<b><i>0.001</i></b>	<b><i>0.001</i></b>

**Table2. Change in Social Domain in Female Control vs. Preservation Groups**

Female N=113	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=59	27.7±1.03	25.54±3.39	22.4±5.53	23.4±5.09	25.4±3.97	25.54±4.73
Preserving group n=54	27.4±1.25	26.3±2.79	25.5±3.4	26.37±1.86	27±1.59	27±2.03
P value	<i>0.013</i>	<i>0.38</i>	<i>0.002</i>	<b><i>0.001</i></b>	<b><i>0.001</i></b>	<b><i>0.002</i></b>

**Higher Social Domain** in female preservation group from postop 2<sup>nd</sup> month to 1 year

# Results: Change in Psychologic Domain in Male / Female Subgroups

**Table1. Change in Psychologic Domain in Male Control vs. Preservation Groups**

Male N=81	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=40	43.05±1.65	41.03±5.14	41.9±5.2	43.03±3.7	41.6±6.11	42.13±5.5
Preserving group n=41	43.34±1.92	41±5.69	40.9±4.3	41.05±5.45	44.2±11.75	42.8±2.4
P value	<i>0.187</i>	<i>0.634</i>	<i>0.69</i>	<i>0.138</i>	<i>0.868</i>	<i>0.066</i>

**Table2. Change in Psychologic Domain in Female Control vs. Preservation Groups**

Female N=113	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=59	43.68±2.36	40.9±5.0	36.92±7.15	38.4±7.28	41.39±5.7	42.32±11.7
Preserving group n=54	43.19±2.16	42.26±5.37	42.24±8.21	42.0±4.06	43.2±3.2	43.15±3.6
P value	<i>0.809</i>	<i>0.719</i>	<i>0.403</i>	<b><i>0.001</i></b>	<b><i>0.002</i></b>	<i>0.063</i>

**Higher Psychological Domain in female preservation group from postop 2<sup>nd</sup> month to 1 year**

# Results: Change in Cough VAS in Right vs. Left Lung

## Table1. Change in Cough VAS in Right Lobe Control vs. Preservation Groups

Right N=124	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=62	0	1.53±1.28	2.65±1.9	1.97±1.85	1.74±1.93	1.05±1.29
Preserving group n=62	0.03±1.78	1.27±1.62	1.9±1.6	1.32±1.21	0.82±0.95	0.63±0.95
P value	<i>0.004</i>	<i>0.0335</i>	<i>0.116</i>	<b><i>0.006</i></b>	<b><i>0.001</i></b>	<b><i>0.090</i></b>

## Table2. Change in Cough VAS in Left Lobe Control vs. Preservation Groups

Left N=70	Pre op (before op)	Post op (before discharge)	1month	2month	6month	12month
Control group n=37	0	1.73±1.56	3.38±1.2	3.05±1.86	2.05±1.9	1.68±1.93
Preserving group n=33	0.09±0.52	1.24±1.2	2.18±1.85	1.58±1.28	1.09±0.84	0.61±0.66
P value	<i>0.032</i>	<i>0.375</i>	<i>0.299</i>	<b><i>0.017</i></b>	<b><i>0.004</i></b>	<b><i>0.001</i></b>

**Left Lung has lower cough VAS at POD 2 Months**

# Results

- Vagus nerve preservation LN dissection is oncologically safe and feasible
  - Pulmonary complication does not increase with vagus nerve preservation
  - Vagus nerve preservation does not impact PFT postoperatively
  - But shows lower cough VAS and higher physical, social, and psychological well-being since postop 2month
  - Preservation group has lower cough VAS in left pulmonary resection than right side
- Preservation may have better impact on female patients undergoing left lung surgery especially 2months after surgery
- Clinically postoperative cough decreases after 2 months

# Conclusion

- Female Preservation group has
    - 1) lower postoperative cough VAS since postop 1month, with clinically significant lower cough VAS from postop 2month
    - 2) better physical, social, and psychological well-being since postop 2month
  - Preservation group has lower cough VAS in left pulmonary resection than right side
- ➔ Preservation may have better impact on female patients undergoing left lung surgery especially 2months after surgery**