Sex differences in functional capacity influence surgical selection and outcomes in lung cancer surgery

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Objectives

Sex differences in postoperative outcomes after lung cancer surgery are well documented. However, the role of preoperative functional capacity in surgical selection and postoperative risk remains unclear. This study examined sex differences in preoperative cardiopulmonary exercise testing (CPET) performance in patients excluded from surgery due to functional limitations and in those accepted for surgery. We further assessed whether sex independently predicts major pulmonary complications (MPC) or 30-day mortality after adjustment for CPET-derived variables.

Methods

In 498 patients referred for CPET (2008–2020), reasons for non-surgical management were reviewed. CPET variables included weight-indexed VO_2peak, percent-predicted VO_2peak, and VE/VCO_2 slope. Logistic regression evaluated associations between sex and outcome in patients who underwent lobectomy, with sequential adjustment for surgical extent, comorbidities, and CPET results.

Results

Of 498 evaluated patients, 224 underwent resection (52 sub lobar, 149 lobectomies, 23 pneumonectomies). Patients denied surgery for functional limitations (n=91) had markedly lower VO_2peak and percent-predicted VO_2peak than operated patients (table 1). Women excluded from surgery had preserved functional capacity (80% predicted VO_2peak and VE/VCO_2 slope 35.8), comparable to men who underwent lobectomy (78%, VE/VCO_2 slope 35.1). Male sex was associated with increased postoperative risk (OR 3.15, 95% CI 1.39–7.16), persisting after adjustment for comorbidities and surgical extent (OR 2.69, 95% CI 1.11–6.50) but abolished after inclusion of percent-predicted VO_2peak (OR 1.39, 95% CI 0.51–3.77).

Conclusions

The excess postoperative risk observed in men after lung cancer lobectomy appears largely mediated by poorer relative aerobic capacity (% predicted VO_2peak). Women excluded from surgery had similar physical capacity as men who underwent major pulmonary resection. Using percent-predicted VO_2peak or VE/VCO_2 slope rather than weight-indexed VO_2peak may offer more sex-equal risk stratification.

Table 1. Functional data and comorbidities for patients evaluated due to suspected or confirmed lung cancer.

	CPET due to suspected lung cancer, n=498					Not operated. decision based on functional data, n=91					Patients selected for lobectomy, n=149				
	Men		Women			Men		Women			Men		Women		
CPET measures	N	Mean	N	Mean	P	N	Mean	N	Mean	P	N	Mean	N	Mean	P
VO2peak. ml/min	250	1384	248	1104	**<0.001**	49	1174	42	896	**<0.001**	66	1478	83	1159	**<0.001**
VO2peak. ml/kg/min	250	17.3	248	16.3	**0.008**	49	14.5	42	13.3	0.07	66	18.2	83	16.7	**0.01**
% VO2peak	250	74	248	95	**<0.001**	49	64	42	80	**<0.001**	66	78	83	99	**<0.001**
VE/VCO2 slope	228	35.6	221	33.6	**0.005**	43	37.6	37	35.8	0.34	58	35.1	80	33.3	0.1
FEV1, L/min	250	2.3	248	1.7	**<0.001**	49	2.0	42	1.3	**<0.001**	66	2.5	83	1.8	**<0.001**
% FEV1	250	73	248	72	0.7	49	63	42	59	0.30	66	77	83	77	0.91
DLCO, mmol/kPa/min	213	5.7	218	4.4	**<0.001**	39	4.9	39	3.4	**<0.001**	57	6.2	70	4.9	**<0.001**
% DLCO	213	70	218	74	0.05	39	60	39	58	1	57	77	70	79	0.48
Comorbidities	N	%	N	%	P	N	%	N	%	P	N	%	N	%	P
COPD	113	45	114	46	0.83	27	55	32	76	**0.04**	32	49	31	37	0.17
Heart failure	49	20	22	9	**<0.001**	14	29	6	14	0.10	14	21	5	6	**0.006**
Diabetes mellitus	70	28	32	13	**<0.001**	17	35	6	14	**0.03**	23	35	7	8	**<0.001**
Obesity	19	8	18	7	0.88	6	12	6	14	0.77	5	8	3	4	0.29
Hyperlipidaemia	55	22	47	19	0.40	11	22	12	29	0.50	19	29	12	15	**0.03**
Hypertension	136	55	125	50	0.37	29	59	23	55	0.67	40	61	36	43	**0.04**
Ischemic heart disease	83	33	49	20	**<0.001**	21	43	10	24	0.06	25	38	13	16	**0.002**
Previous myocardial infarction	38	15	28	11	0.2	10	20.4	6	14.3	0.44	12	18	7	8	0.076

CPET – Cardiopulmonary Exercise Testing
VO_2peak – Peak oxygen uptake
ml/kg/min – Milliliters of oxygen per kilogram body weight per minute
% VO_2peak – Percent-predicted peak oxygen uptake (adjusted for age, sex, and body size)
VE/VCO_2 slope – Ventilatory efficiency (minute ventilation/carbon dioxide output slope)
FEV_1 – Forced Expiratory Volume in 1 second
DLCO – Diffusing capacity for carbon monoxide
COPD – Chronic Obstructive Pulmonary Disease