

Functional capacity throughout the lung cancer trajectory

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Background

Eastern Cooperative Oncology Group Performance Scale (ECOG PS)

Integral aspect of treatment selection, toxicity monitoring, and clinical trial eligibility.

Clinician based, subjective, with poor reliability and validity

Sørensen JB et al. 1993

Poor ECOG PS scores are strong predictors of prognosis.

West HJ et al. 2015

ECOG scores of 0, 1, or 2 provides essentially no additional prognostic information for patients with no obvious physical impairments.

Cheng S et al. 2017



Background

Recent comment in Journal of Clinical Oncology emphasizes that instead of the tolerability to treatment is based on the ***clinician's subjective estimate of patients' ability to perform ADL***, there is a need for an objective and dynamic evaluation of the patient's functional capacity.

Scott et al 2020

The 6-minute walk test (6MWT) is an essential measure for functional capacity, assessing prognosis and evaluating response to treatment across many respiratory diseases.

Holland et al 2014



Functional capacity

Functional capacity (6 minute walk distance < 400 m) before chemotherapy in patients with advanced stage lung cancer (n=64):

- **Higher disease progression**
- **Higher mortality**

Kasymjanova et al 2009

Functional capacity was an **independent predictor** of survival ($P = 0.003$) in patients with advanced stage lung cancer ($N=118$). **Each 50-m improvement** in 6MWD was associated with a 13% reduction in the risk of death.

Jones et al 2012



Aims and Hypotheses

Aim

The aim of this study is to investigate objective measures for functional capacity as predictors for survival and suitability to treatment.

Hypotheses

- Implementation of an objective measure for functional capacity (6MWT, sit-to-stand, hand-grip strength) pre-diagnosis is a sensitive predictor for 1-year survival
- An objective measure for functional capacity throughout the course of the treatment can reduce the risk of misclassification in suitability to treatment



Objectives

Objectives

To investigate the prognostic value in the following functional capacity tests in patients with lung cancer.

- 6MWT

Endpoints

- Complications to treatment
- Overall survival

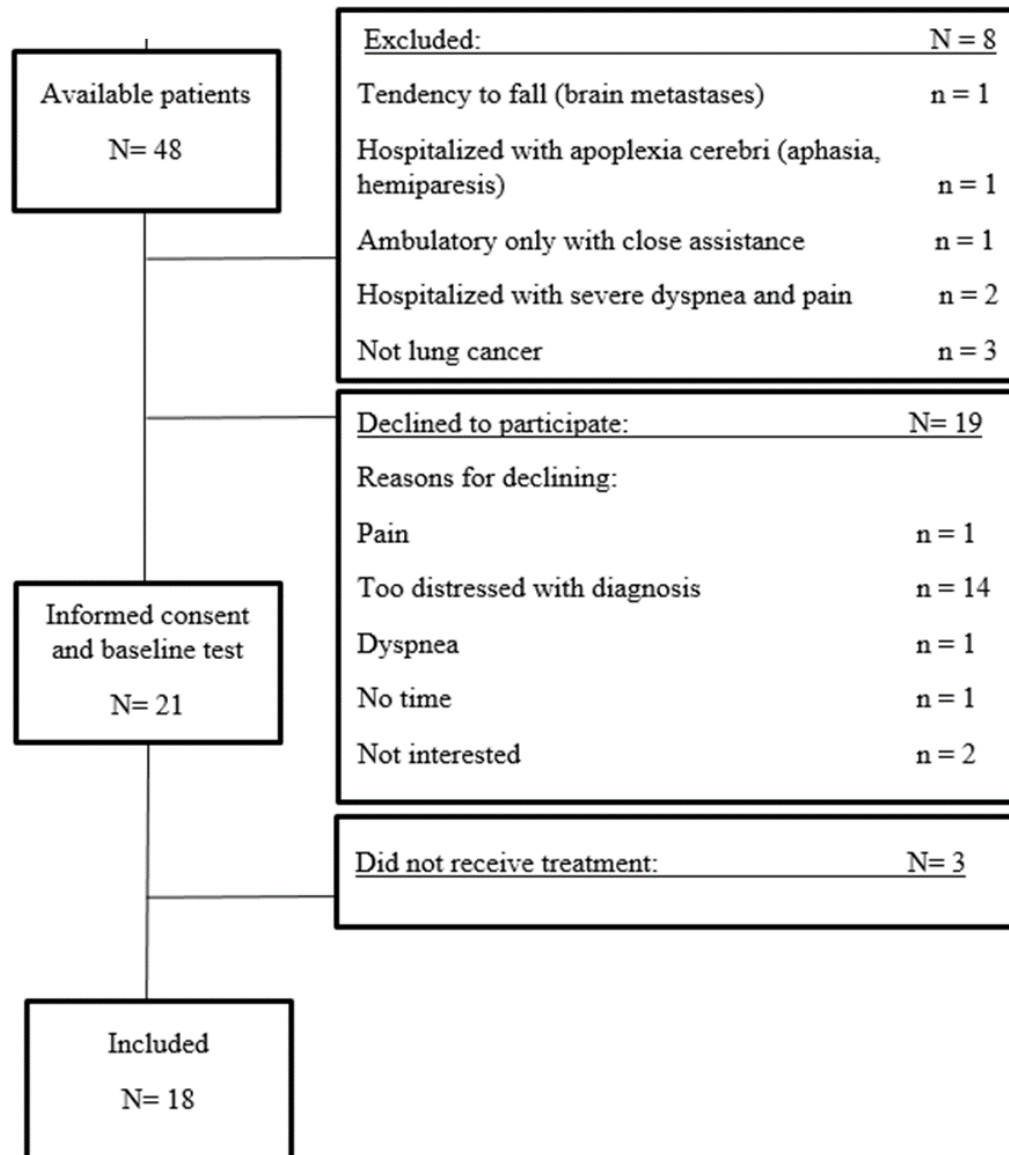


The 6-Minute Walk Test as a pre-treatment predictor for adverse events to first line treatment in patients with stage I-IV lung cancer: A descriptive, feasibility study

Domain	Definition	Measure	Criteria for determining success
Acceptance	Interest and willingness to participate	Percent of patients approached who enrolled	>30 %
Practicality	The extent to which a program can be carried out with intended participants using existing means, resources and circumstances	Availability of necessary structural resources	Ability to execute in hospital settings (undisturbed corridor of 20-50 m)
Demand	The extent to which a new intervention is likely to be used	Percentage of the available patients physically able to perform the 6MWT	>80 %
		Percentage of eligible patients excluded due to safety criteria prior to the 6MWT	<10%



Flow chart



Clinical characteristics	Total
Cancer diagnosis	
NSCLC	18
<i>Squamous cell carcinoma</i>	5
<i>Adenocarcinoma</i>	12
<i>Large cell carcinoma</i>	1
Cancer stage	
Ia/Ib	3
IIa/IIb	2
IIIa	3
IIIb	6
IV	4

First line treatment	
Surgery (VATS)	4
<i>Lobectomy</i>	4
<i>LLL n=2, RML n=1, LUL n=1</i>	
Radiation and chemotherapy	8
<i>Cisplatin + vinorelbine + radiation</i> <i>(LU026 2gy x 33, 5 f/w)</i>	5
<i>Cisplatin + vinorelbine + radiation</i> <i>(LU026 2gy x 33, 5 f/w)</i>	3
Chemotherapy only	3
<i>Cisplatin + Vinorelbine</i>	2
<i>Carboplatin + pemetrexed</i>	1
Radiation only	2
<i>3 gy x 10, 5 f/w</i>	1
<i>15 gy x 3, 3 f/w</i>	1
Immunotherapy	1
<i>Pembrolizumab</i>	1
ECOG-PS	
0	15
1	2
2	1
Lung function**	
FEV1 (%)	70 (20,56)
FEV1/FVC (%)	68,53 (8,22)
Blood parameters**	
Hemoglobin	7,97 (1,27)
C-Reactive Protein	28,7 (50,02)
*LLL = Left lower lobe, LUL= Left upper lobe, RML= Right middle lobe	
**Values are expressed as means and standard deviations	



Definition of minor and major complications registered

Minor complications

Grade 1

- Subcutaneous emphysema (no intervention)
- Prolonged airleak (no intervention)
- Small pneumothorax (no intervention)
- Hyperthyreose (no intervention)
- Constipation (stool softener)
- Radiation induced pneumonitis (radiographic changes but asymptomatic or symptoms not requiring steroids)
- Leukopenia (total WBC: $\geq 2.0 - < 3.0 \times 10^9 /L$)
- Orthostatic hypotension (no intervention)
- Hypokalemia (3,5-3 mmol/L)



Grade 2

Tinnitus (not interfering with ADL)

Subcutaneous emphysema (drainage)

Dyspnea (by exertion)

Anemia (Hgb 4.9-6.2)

Leukopenia (total WBC: $\geq 1.0 - < 2.0 \times 10^9 /L$)

Pneumonia (radiographic changes, requiring steroids)

Radiation induced pneumonitis (radiographic changes, requiring steroids)

Major complications

Grade 3

Pneumothorax (Requiring surgical, endoscopic or radiological intervention)

Arrhythmia (symptomatic and requiring treatment)

Renal affection (eGFR $< 25 \%$)

Pneumonia (requiring oxygen)

Anemia (Hgb 4,9-4 mmol/L, requiring blood transfusion)

Pleural effusion (tube drainage, thoracenteses)

*WBC= White Blood Cells, ADL=Activities of Daily Living, Hgb=Hemoglobin,
eGFR=Estimated Glomerular Filtration Rate,



Overview of complications to first line treatment

	No complications	Minor complications	Major complications	<i>p</i>
n/N	4/18	8/18	6/18	
6MWD, m (mean + SD)	530 + 68	436 ± 62	360 + 136	0.043
<i>Type of treatment</i>				
Surgery	1	2	1	0.212
Chemo + Radiation	2	4	2	
Chemotherapy only	1	1	1	
Radiation therapy only	0	0	2	
Immunotherapy	0	1	0	
<i>Clinical parameters</i>				
CRP, mg/L	9 ± 9	15 ± 23	17 ± 19	0.836
FEV1/FVC	72.50 ± 4.31	67.45 ± 9.37	72.45 ± 8.65	0.195
Hgb, mmol/L	9 ± 1	8 ± 1	7 ± 1	0.117
BMI	24 ± 5	27 ± 4	24 ± 3	0.166

*PS=Performance Status, CRP=C-reactive Protein, FEV1/FVC= forced expiratory volume in first second to forced vital capacity ratio, Hgb=hemoglobin, BMI=Body Mass Index



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PS1	0	1	1	
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Conclusion

The 6MWT as a predictor for adverse events to antineoplastic treatment in lung cancer needs to be investigated prospectively in a larger population of selected patients.



Patients under suspicion for lung cancer. (N=300)

Intervention

- 6MWT as a supplement to the physician's clinical evaluation.

Control

- Physician's clinical evaluation as usual.

Allocation to **surgery, oncologic treatment**, (Chemotherapy and/or radiotherapy/immunotherapy) and **no treatment** based on guidelines and the physician's clinical evaluation.

Intervention

- 6MWT every 3rd month as a supplement to the physician's clinical evaluation.

Control

- Physician's clinical evaluation as usual.

Outcomes

Survival (months) from the time of diagnosis and **complications** to treatment. End of **follow-up is 24** months after diagnosis or until **death**



Status

Collaboration:

All departments involving patients with lung cancer in Capital region of Copenhagen.

- Dept. of Medicine, Section of Pulmonary Medicine, Herlev-Gentofte Hospital and Bispebjerg Hospital
- Dept. of Oncology, Herlev-Gentofte Hospital and Rigshospitalet.
- Dept. of Cardiothoracic Surgery, Rigshospitalet
- Dept. of Physiotherapy, Herlev-Gentofte Hospital, Bispebjerg Hospital and Rigshospitalet.



Status

