

FUNCTIONAL CAPACITY THROUGHOUT THE LUNG CANCER TRAJECTORY

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Purpose of study

Identify an objective measure for functional status

Evaluate treatment-related functional decline



Reduce the risk of misclassification to tolerability to treatment



Why is functional status important?

- A measurement for continuous evaluation and planning of treatment and rehabilitation
- Low functional status yields a higher mortality

RS. Braithwaite et al, 2003 on hip fractures:

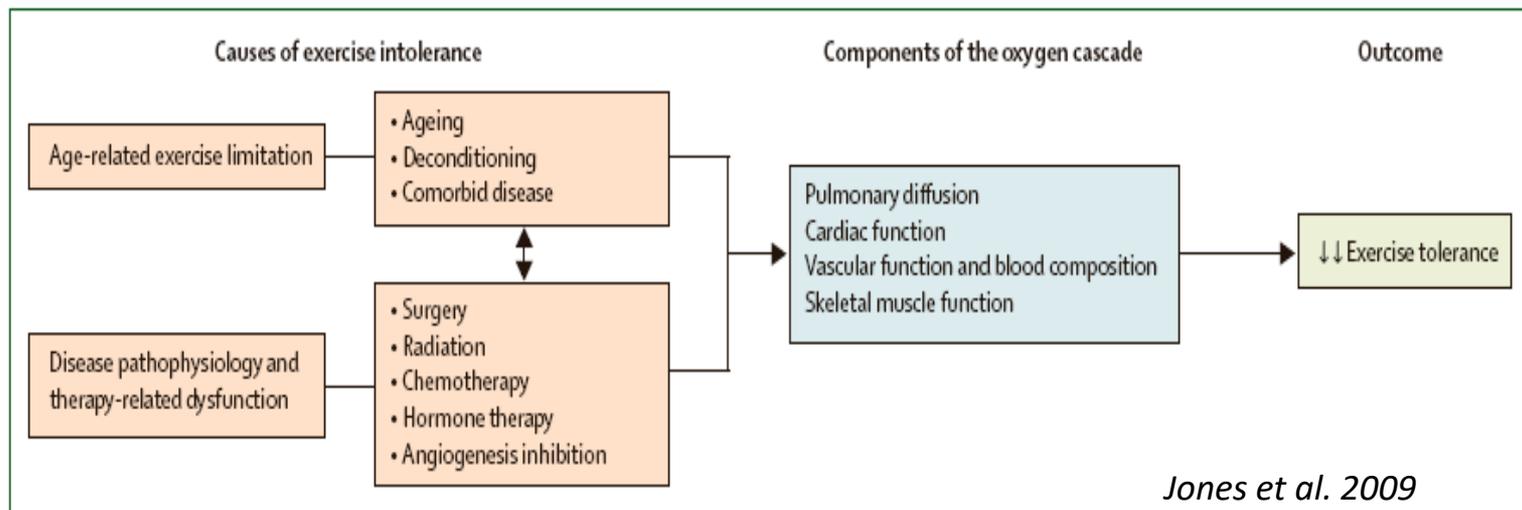
- Reduced life expectancy of 1.8 years or 25 %
- Substantial morbidity, mortality and costs



Why is functional status important?

Patients with lung cancer at diagnosis:

- Above 67 years of age
- Current or former smoker
- Not meeting the general recommendations of physical activity
- Deconditioned



Why is functional status important?



Avoidance of symptom triggers (namely physical activity) **promotes a vicious cycle of inactivity and functional decline**



Why is functional status important?

Main concerns for patients with lung cancer (n=660):

- fear of losing **independence**
- being a **burden** on their caregivers
- not being able to **perform daily activities**
- fear of losing **function**

Gralla et al 2014



Why is functional status important?

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



Measuring functional status

ECOG-Performance Status

- First published in 1982 – applied since 1960
- Physician rated subjective score
- Assess the disease impact on patient's daily living abilities
- Track changes in a patient's level of functioning
- Eligibility for clinical trials
- Determine suitability for treatment



Measuring functional status

Reliability of the ECOG-PS is fair but with higher agreement in patients with good performance status (PS 0-2) than in more affected patients (PS 3-4)

J.B. Sørensen et al, 1993

Performance status assessment in cancer patients. An inter-observer variability study

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Summary The ECOG Scale of Performance Status (PS) is widely used to quantify the functional status of cancer patients, and is an important factor determining prognosis in a number of malignant conditions. The PS describes the status of symptoms and functions with respect to ambulatory status and need for care. PS 0 means no symptoms and functions with respect to ambulatory status and need for care. PS 1 means some symptoms, but still near fully ambulatory. PS 2 means less than 50% and PS 3 means more than 50% of daytime in bed, while PS 4 means completely bedridden. An inter-observer variability study of PS assessment has been carried out to evaluate the non-chance agreement among three oncologists rating 100 consecutive cancer patients. Total consistency was observed in 40 cases, agreement between two observers in 53 cases, and total disagreement in seven cases. Kappa statistics reveal the ability of the observers compared to chance alone and were used to evaluate inter-observer agreement. Overall Kappas was 0.44, (95% confidence limits 0.38-0.51). The Kappas for PS 0 was 0.55 (0.44-0.67), while those for PS 1, 2, 3 and 4 were 0.48 (0.37-0.60), 0.31 (0.19-0.42), 0.43 (0.22-0.55), and 0.37 (0.17-0.47), respectively. If one observer allocated patients to PS 0-2, then another randomly selected observer placed the patients in the same category with a probability of 0.92. For patients with PS 3-4 the probability that the same category would be chosen was 0.62. Overall, the non-chance agreement between observers was only moderate, when all ECOG Performance Status groups were considered. However, agreement with regard to allocation of patients to PS 0-2 versus 3-4 was high. This is of interest because this cut-off is often used in clinical studies.

Performance status (PS) is an assessment of the patients' actual level of function and capability of self-care. It has repeatedly been demonstrated that PS is an important prognostic factor for survival in several major cancer forms, e.g. breast cancer (Swenerton *et al.*, 1979), ovarian cancer (Lund *et al.*, 1990), small cell lung cancer (Østerlind & Andersen, 1986), and non-small cell lung cancer (Sørensen *et al.*, 1989). Accordingly, PS must be taken into consideration in the planning and evaluation of clinical trials of cancer treatment. It has also been suggested that PS might be used as part of the assessment of the patient's quality of life (Cazaz *et al.*, 1988).

Several scales for measuring PS have been suggested, among which the most widely used are Karnofsky's Scale of Performance Status (Karnofsky *et al.*, 1948), and ECOG Scale of Performance Status (Zubrod *et al.*, 1960). In spite of their common use there is only limited information about the validity and reliability of these scales.

The validity relates to whether the scale actually measures the intended subject, while reliability deals with the degree of confidence we have in the individual measurements, and is often described as intra- and inter-observer variability.

Only few previous trials have evaluated the validity of Karnofsky Performance Status Scale (Mor *et al.*, 1984; Wood *et al.*, 1981; Schag *et al.*, 1984), and studies on the ECOG Scale are even more sparse.

No intra-observer variability analysis has been reported for any of the PS scales. In contrast, three previous papers report on the inter-observer variability in the use of Karnofsky Performance Status Scale (Schag *et al.*, 1984; Yates *et al.*, 1980; Hutchinson *et al.*, 1979). No other scales have been extensively evaluated, though Conill *et al.* reported on the use of the ECOG Scale of Performance Status in a group of ambulatory patients (Conill *et al.*, 1990).

Yates *et al.* (Yates *et al.*, 1980) evaluated the Karnofsky Scale with respect to inter-observer variability between nurses and social workers and found a correlation coefficient of 0.89. Poor correlation among PS assessment by doctors was reported by Hutchinson *et al.* (Hutchinson *et al.*, 1979), who

included patients requiring hemodialysis or patients admitted to the emergency room. This might influence the results, as the Karnofsky Scale was originally designed for use in cancer patients.

Agreement between oncologists on the one hand and psychologists or psychiatrists on the other was evaluated by Schag *et al.* (Schag *et al.*, 1984) in 75 cancer patients. They found a correlation coefficient of 0.89. The question of agreement among oncologists was not evaluated. This issue has been addressed in one study (Conill *et al.*, 1990), though not with the use of Kappa statistics for the evaluation of non-chance agreement. The purpose of the present study was to evaluate the reliability of the ECOG Scale of Performance Status by measuring the non-chance agreement between three oncologists.

Materials and methods

The three observers were oncologists working in the clinic who otherwise had no specific training for the actual project.

The patient population was 100 consecutive in-patients at the clinic seen on randomly selected days during the 3-month study period. The patients were included, after informed consent had been obtained. Each observer interviewed the patient on the same day, usually within a 3-h period, and scored the patient according to the ECOG Scale of Performance Status (Table 1). Each observer was blinded for the rating of the other observers and did not see the hospital records before rating.

Table 1 Eastern Cooperative Oncology Group (ECOG) scale of performance status

Value	Description
0	Normal activity
1	Symptoms, but nearly fully ambulatory
2	Some bed time, but needs to be in bed less than 50% of normal daytime
3	Needs to be in bed greater than 50% of normal daytime
4	Unable to get out of bed

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Increased risk of misclassification of suitability to treatment

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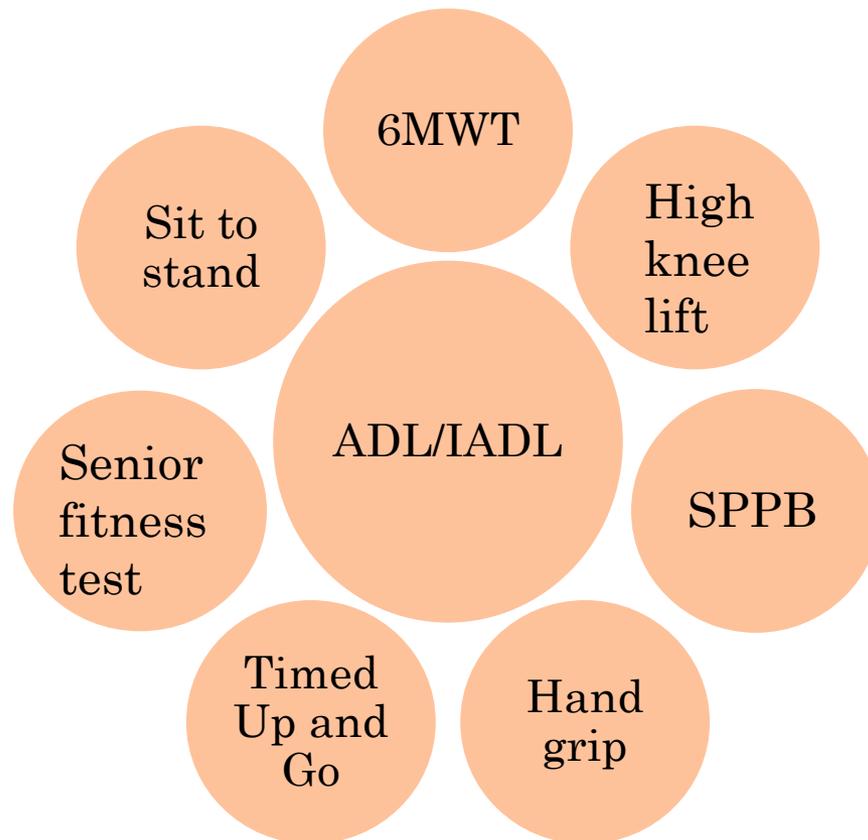
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Identifying an objective measure for functional status



Assessment of sensitivity to 1-year survival and tolerability to treatment

- Prospective observational study
- N=164

Inclusion:

- Historically confirmed NSCLC (stage I-IV), SCLC
- Any type of oncological treatment

Exclusion:

- Surgical patients
 - Other malignancies
- 

Assessment of sensitivity to 1-year survival and tolerability to treatment

- Endpoints
 - Functional status (follow-up)
 - Complications to treatment (follow-up)
 - 1-year survival



In summary...

- Identify objective measure for functional status that is sensitive to complications to treatment and 1-year survival
- Create a tool for targeted aims for maintenance of functional status



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THANK YOU

