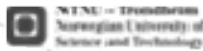


Associations between comorbidity and muscle measures in advanced non-small-cell lung cancer (NSCLC)

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Background

- Chemotherapy is the recommended palliative therapy for advanced NSCLC
- The survival benefit is limited and severe side-effects are common
- Many patients are old and suffer from other conditions
- Better methods for selecting those who benefit from, and tolerate such therapy are needed
- There are no established predictive factors/biomarkers. Treatment is based on an estimation of prognosis/PS.

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Comorbidity

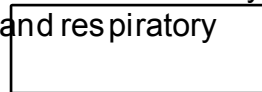
- Comorbidity has been identified as an independent prognostic factor for survival in several cancers
- The prognostic value appears to depend on expected survival time
- The prognostic importance is probably very limited in patients with a short survival time – such as in advanced NSCLC



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Muscle measures

- CT scans can be used to quantify skeletal muscle area and muscle attenuation
- Low muscle mass (sarcopenia) and muscle attenuation (fat-infiltration) are features of cancer cachexia and has been identified as independent prognostic factors for survival in several cancers
- Muscle depletion increases with age and can be caused by other conditions such as heart, vascular and respiratory diseases



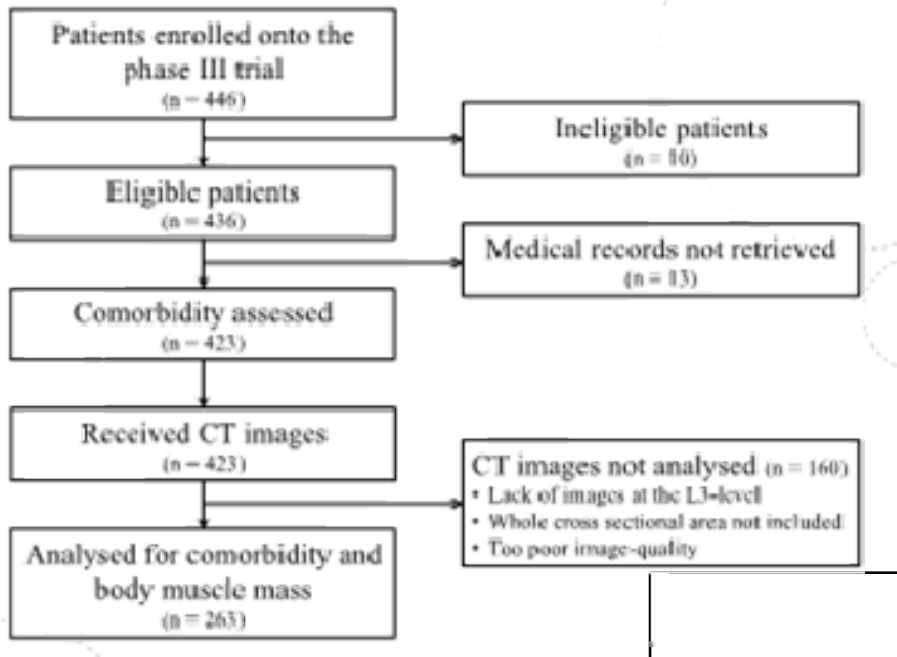
Research questions

- 1) Do patients with severe comorbidity have lower skeletal muscle index (SMI) than other patients?
- 1) Do patients with severe comorbidity have lower muscle attenuation (MA) than other patients?
- 1) Do patients with severe comorbidity have a shorter survival than other patients with similar SMI?
- 1) Do patients with severe comorbidity have a shorter survival than other patients with similar MA?

Patients

- Participants in a phase III study comparing pemetrexed/carboplatin versus gemcitabin/carboplatin as first-line chemotherapy in advanced NSCLC with available baseline CT scans
- Pemetrexed/carboplatin provided similar health-related quality of life (HRQoL) and survival with less hematologic toxicity

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The Cumulative Illness Rating Scale for Geriatrics (CIRS-G)

- The most comprehensive validated tool for assessment of comorbidity
- Comorbidity is rated 0 (*no comorbidity*) to 4 (*extremely severe comorbidity*) on 14 organ scales
- For this study, severe comorbidity was defined as any grade 3-4 comorbidity

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Score	0	1	2	3	4
Heart		x			
Vascular			x		
Haematopoietic	x				
Respiratory				x	
Eyes, ears, nose, throat and larynx	x				
Upper gastro-intestinal tractus	x				
Lower gastro-intestinal tractus	x				
Liver	x				
Renal	x				
Genitourinary	x				
Musculoskeletal/integument	x				
Neurological	x				
Endocrine/metabolic and breast	x				
Psychiatric illness	x				

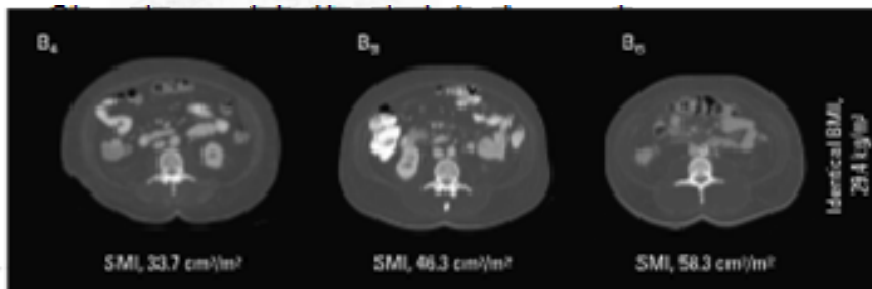
Total number of categories endorsed	3
Total score	6
Severity index (total score/total number of categories endorsed)	2
Number of categories at level 3	1
Number of categories at level 4	0

Linn et al, J Am Geriatr Soc 1968

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Assessment of muscle mass

- Skeletal muscle index (cm²/m²) and muscle attenuation (HU) were assessed at the 3rd lumbar level on CT scans obtained before chemotherapy



Martin et al, JCO 2013

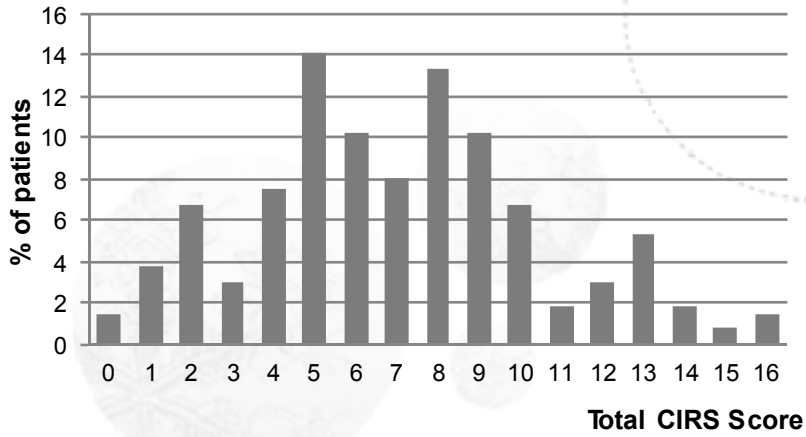
Definition of sarcopenia and low MA

BMI category (kg/m ²)	SMI (cm ² /m ²)		MA (HU)	
	Men	Women	Men	Women
Underweight (< 20.0)	< 43	< 41	< 41	< 41
Normal weight (20.0 to 24.9)	< 43	< 41	< 41	< 41
Overweight (25.0 to 29.9)	< 53	< 41	< 33	< 33
Obese (≥ 30.0)	< 53	< 41	< 33	< 33

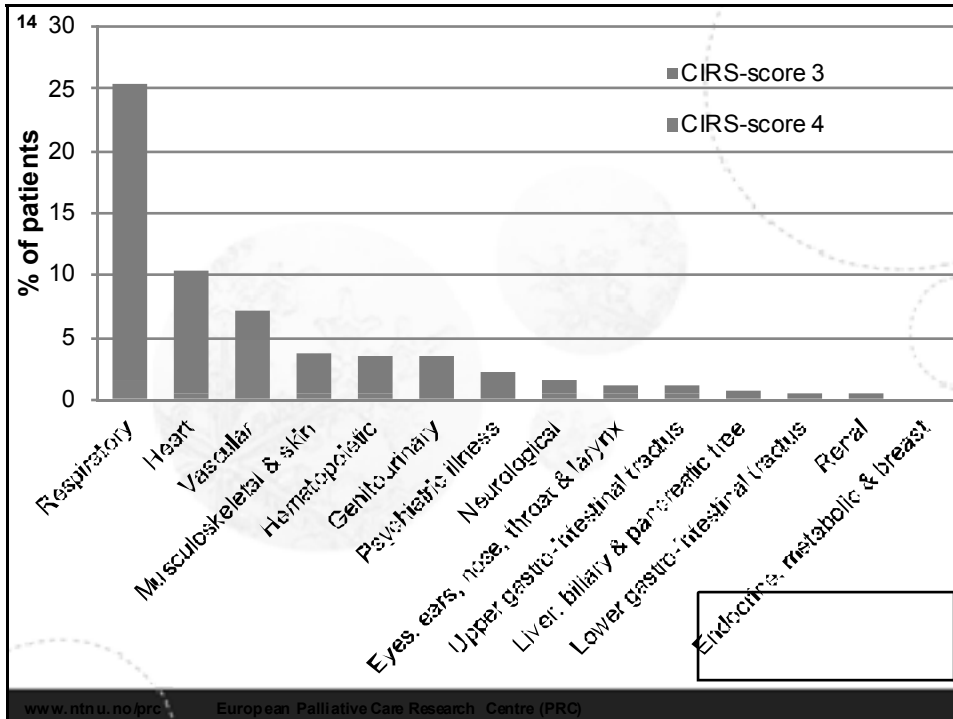
Patient characteristics

Patient characteristics		All patients (n =263)
		%
<i>Age, years</i>	Mean (range)	66 (37-90)
	≥ 75 years	21%
<i>Gender</i>	Male	57%
	Female	43%
<i>Performance status</i>	0-1	79%
	2	21%
<i>Extent of disease</i>	Stage IIIB	26%
	Stage IV	74%
<i>Study treatment</i>	Pemetrexed/carboplatin	50%
	Gemcitabin/carboplatin	50%
<i>Loss of appetite</i>	Yes	53%
	No	46%
<i>Height</i>	Mean (range)	171 (150-200)
<i>Body weight, kg</i>	Mean (range)	69 (37-107)

Comorbidity



Any grade 3 or 4	48.0 %
Any grade 4 or ≥ 2 grade 3	14.4 %
Any grade 4 or ≥ 3 grade 3	8.7 %



Body composition

BMI (kg/m²)

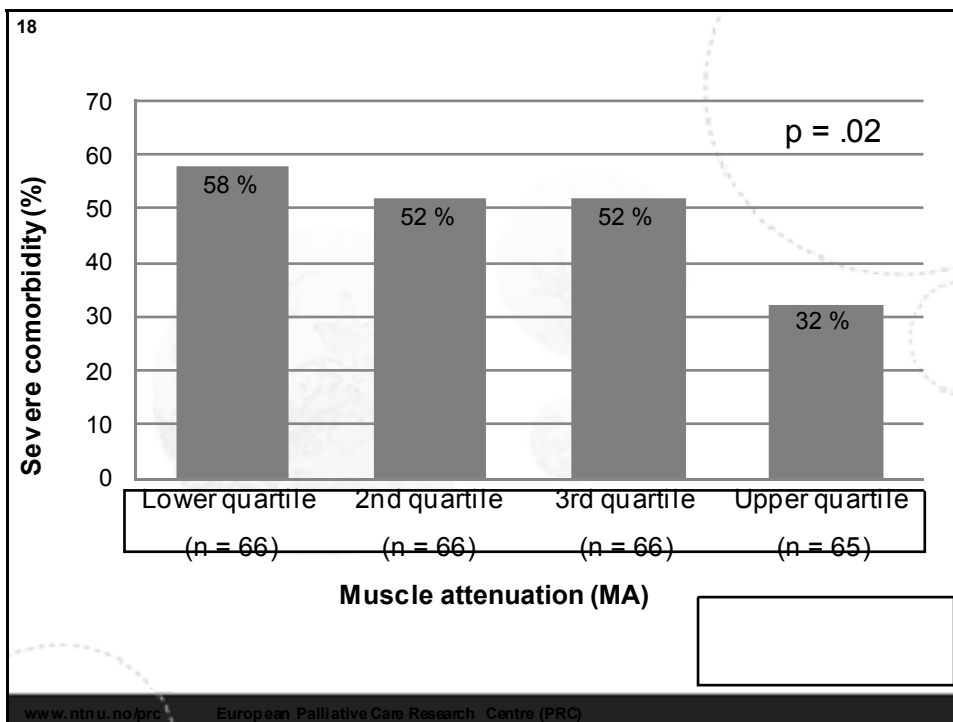
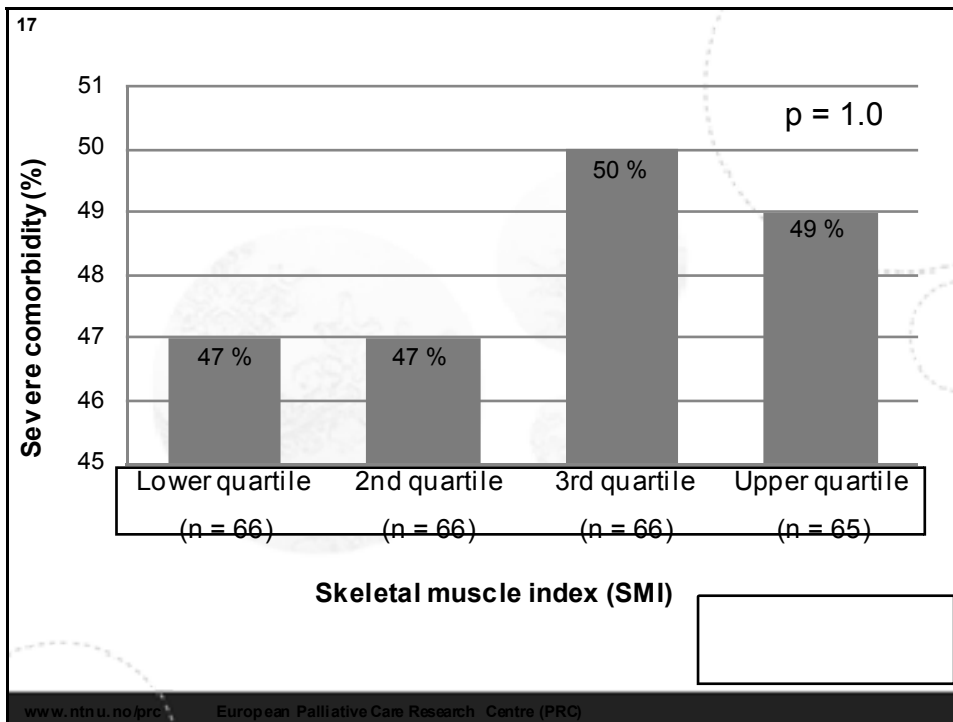
Underweight (< 20.0)	16 %
Normal weight (20 to 24.9)	51 %
Overweight (25 to 29.9)	30 %
Obese (≥ 30.0)	4 %

Median SMI (cm²/m²) 44 (27-71)

Median MA (HU) 37 (16-60)

Muscle measures and comorbidity

	Median SMI (cm ² /m ²)	Median MA (HU)
Severe comorbidity	44.5	35.6
No severe comorbidity	44.1	39.1
<i>p-value</i>	.7	.001



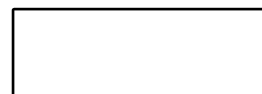
Established prognostic factors

Gender (male vs. female)	6.7 vs 9.2 months	p = .3
PS (0/1 vs. 2)	7.7 vs 5.9 months	p = .01
Extent of disease (IIIB vs. IV)	6.9 vs 9.1 months	p = .04
Loss of appetite (yes vs. no)	6.5 vs 9.2 months	p = .004



New prognostic factors?

Severe comorbidity (yes vs. no)	6.7 vs 7.9 months	p = .3
Sarcopenia (yes vs. no)	8.6 vs 7.2 months	p = .2
Low MA (yes vs. no)	7.7 vs 6.7 months	p = .4



Skeletal muscle index (SMI)

	CIRS 3-4	CIRS < 3	p
Lower quartile (n = 66)	5.1 months	7.7 months	.6
2nd quartile (n = 66)	10.3 months	7.1 months	.5
3rd quartile (n = 66)	12.9 months	7.3 months	.2
Upper quartile (n = 65)	6.0 months	6.9 months	.9

Muscle attenuation (MA)

	CIRS 3-4	CIRS < 3	p
Lower quartile (n = 66)	5.1 months	9.3 months	.8
2nd quartile (n = 66)	10.3 months	7.9 months	.6
3rd quartile (n = 66)	12.9 months	6.3 months	.5
Upper quartile (n = 65)	6.0 months	6.7 months	.9

Conclusion

- Patients with severe comorbidity had lower MA than other patients
- There were no other significant associations between comorbidity and muscle measures – or overall survival

