

# Comparison of nutritional assessment with a new definition of cachexia in determining outcomes of advanced cancer patients

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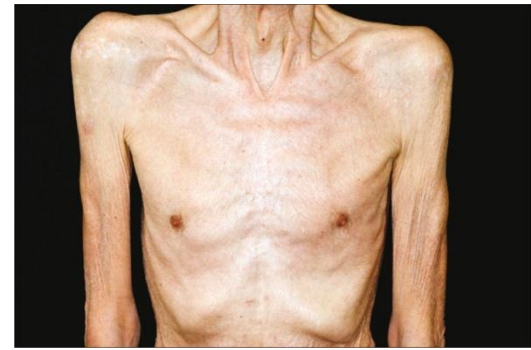
# Disclosure slide

- I have no Conflicts of Interest to declare related to this research.



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# Background



- Cancer cachexia syndrome (CCS) or cancer anorexia-cachexia syndrome is associated with many adverse clinical features and outcomes
  - weight loss, muscle wasting, loss of adipose tissue, anorexia, poor performance status, reduced QoL, reduced response to treatment and poor prognosis.
- Timely diagnosis and treatment has been difficult
- No standard therapies exist

# CCS

- Pathogenesis
  - Not fully understood, but probably multifactorial.
  - Large role of cytokines.
- Definition
  - Until recently there was a lack of uniform consensus about its definition or standardised diagnostic criteria.
  - Consensus statements have been proposed in the last few years ([115](#), [120](#), [121](#), [138-140](#)).

# International Consensus Statement in 2011

Cancer cachexia was defined as

*“a multifactorial syndrome characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment”*

(Fearon, et al 2011)

# Diagnostic Criteria

- *Weight loss of >5% over the previous 6 months (in the absence of simple starvation); **OR***
- *Body mass index (BMI) <20kg/m<sup>2</sup> and any degree of weight loss >2%; **OR***
- *Appendicular skeletal muscle index consistent with sarcopenia (male <7.26kg/m<sup>2</sup>; female <5.45kg/m<sup>2</sup>)\* and any degree of weight loss >2%.*

*\*Defined reference values (sex specific) and standardized body composition measurements are essential to undertake assessment of skeletal muscle depletion.*

*Although there is a paucity of reference values related to cancer-specific outcomes, a generally accepted rule is an absolute muscularity below the 5<sup>th</sup> percentile.*

# Patient Generated Subjective Global Assessment Tool (PG-SGA)

- The nutritional status is based on important risk factors such as:
  - weight loss (>5% of body weight over a short period of time);
  - inadequacy of nutrient intake over a month;
  - presence of clinical symptom(s) that affect patients' oral intake;
  - physical appearance (e.g. depletion of muscle and/or fat stores as a result of malnutrition);
  - presence of metabolic stress that leads to increased requirements (e.g. fever, steroids, etc).
  - performance status, stage of disease, age, and medical diagnosis
- 3 categories : A (well nourished), B (moderately malnourished) and C (Severely malnourished).
- Shown by us to correlate with inflammatory markers



# Study Aim

- To compare the relative prognostic utility of a new definition of CCS with nutritional status as defined by the Patient-Generated Subjective Global Assessment (PG-SGA) tool.

# Study Design for Cohort Study

- Prospective cohort study from Jan 2007 to Jan 2010 at the Sydney Cancer Centre, Concord Hospital.
- Sequential, newly diagnosed cancer patients
  - Medical Oncology Day Unit, Concord Hospital
- Eligibility Criteria
  - Patient > 18 years old with histological confirmation of cancer
  - ECOG Performance Status of 0-2
  - No prior systemic anti-cancer treatment for advanced disease
  - No surgery for 2 weeks prior to enrolment
  - Life expectancy > 3 months
- Exclusion Criteria
  - Physical or psychiatric illness that would affect patients' compliance and/or interfere with consent of follow up

# Data Collection

	<b>Baseline</b> <b>Before chemo</b>	<b>Day 1</b> <b>1<sup>st</sup> day of chemo</b>	<b>Day 7 to Day 10</b>	<b>On the day return for 2<sup>nd</sup> cycle chemo</b>	<b>Deaths up to the 7th of April 2011</b>
<b>Anthropometry</b>	<b>x</b>			<b>weight</b>	
<b>Functional assessment</b>	<b>x</b>				
<b>Nutritional assessment</b>	<b>x</b>				
<b>Bloods</b>	<b>X</b> <b>(either on the day of recruitment or day 1 before commencement of chemotherapy)</b>		<b>FBC</b>	<b>FBC + CRP + Alb</b>	
<b>Toxicities</b>				<b>X</b>	
<b>Survival</b>					<b>x</b>

# Hand Grip Strength

- Jamar Hydraulic Hand Dynamometer was used to measure the hand grip strength of both dominant and non-dominant hands.
- The best grip strength (kg) out of the three tests was used for data analysis



# Skeletal muscle mass



## Bioelectrical Impedance Analysis (BIA)

- A single frequency 50kHz BIA device (*ImpediMed DF 50*)
- Skeletal muscle mass (kg) =  $[(\text{height}^2 / \text{BIA-resistance} \times 0.401) + (\text{gender} \times 3.825) + (\text{age} \times -0.071)] + 5.102$   
(where height is in cm; BIA-resistance (R) is in ohms; gender (men = 1 and women = 0); and age is in years)
- The skeletal muscle mass (SM) was then divided into 5 percentile categories.

# Data Collection

- Survival
  - Defined as the time interval between date of baseline nutritional assessment conducted and the date of death from any cause.
  - Deaths up to the 7th of April 2011, which was the date that data were last updated.
  - 45% of entire cohort deceased at that time.

# Results – demographics

## 154 patients

Feature	
Median age	59 years
Age > 65 yrs	35%
Weight at baseline (mean)	70 kg (SD 15.1)
BMI baseline (mean)	25.1 (SD 5)
Male: Female	50:50
PGSGA A	63 (41%)
PGSGA B	68 (44%)
PGSGA C	23 (15%)
Mean PGSGA score	9.4 (SD 6.1)
PGSGA score ( $\geq 9$ )	50%

# Baseline demographic features

CRC	33%
Upper GI	18%
Thoracic	23%
Breast	21%
Others	5%
Advanced cancer	56%
NLR $\geq 5$	13%
mGPS 1 or 2	56%



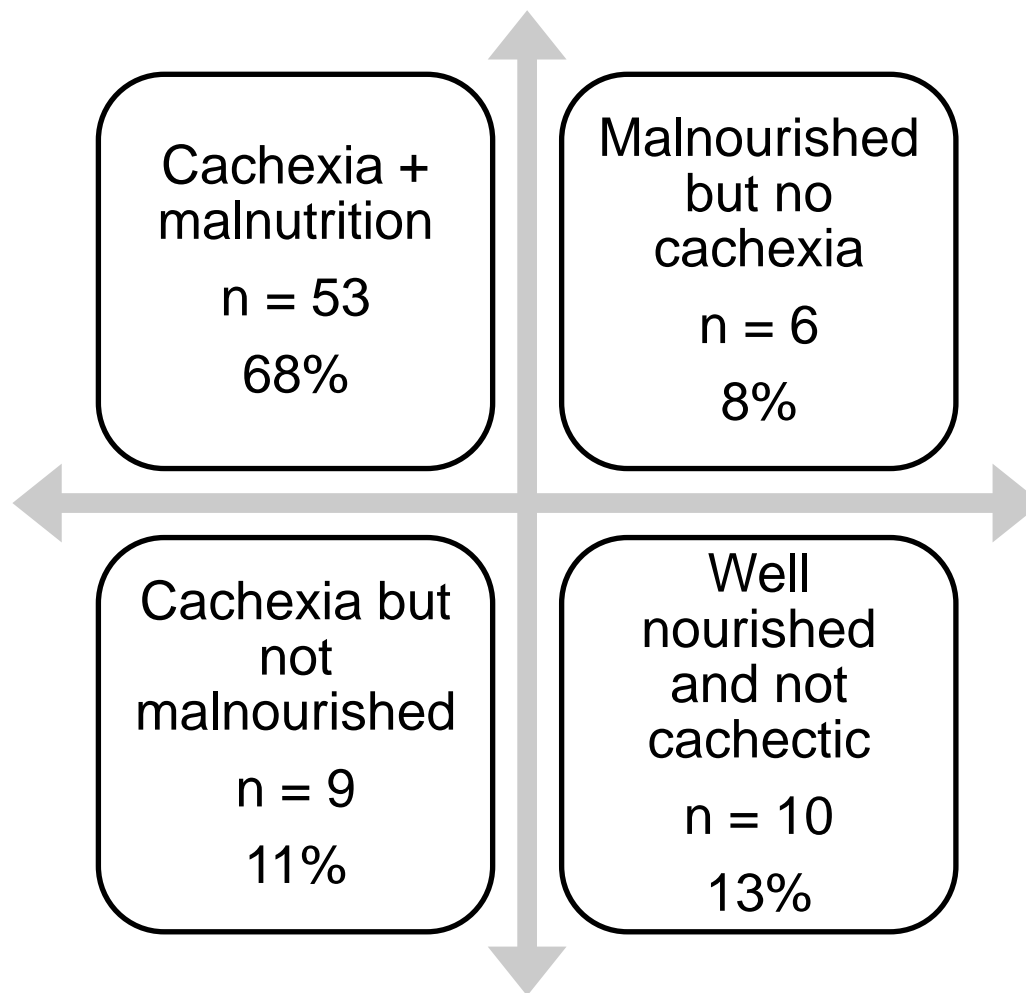
# Results

- 109 (46%) patients met  $\geq$  one criteria for CCS
- In patients with advanced cancer, 80% met  $\geq$  1 criteria for CCS (n= 62 of 78) – these are the focus for the survival studies
- Of these 58 (94%) met the first criteria and only four extra cases defined by one of the other two criteria

# Results: Baseline - advanced

	Non-cachexia (Did not meet criteria) n=16	Cachexia (Met $\geq 1$ criteria) n=62	P value
Age, years (median, IQR)	62 (IQR 17)	63 (IQR 14)	
65 years and above, n	4 (25%)	27 (44%)	0.254
Tumour group, n			0.207
Thoracic	10 (62.5%)	18 (29%)	
Colorectal (CRC)	4 (25%)	21 (34%)	
Upper Gastrointestinal (UGI)	2 (12.5%)	22 (35%)	
Others	0 (0)	1 (2%)	
Male, n	12 (75%)	39 (63%)	0.557
BMI at baseline, kg/m <sup>2</sup> (mean $\pm$ SD)	26.2 (SD 5.2)	24.0 (SD 4.7)	0.106
Underweight (BMI <18.5 kg/m <sup>2</sup> )	0 (0%)	6 (9%)	0.334
Obese (BMI $\geq 30.0$ kg/m <sup>2</sup> )	3 (19%)	6 (9%)	0.383

	Non-cachexia (Did not meet criteria) n=16	Cachexia (Met ≥1 criteria) n=62	P value
Nutritional Status, n (%)			
Malnourished (PG-SGA B or C)	6 (38%)	53 (86%)	<0.001
Nutritional risk score (mean ± SD)	8 (SD 6.3)	13 (SD 5.9)	0.006
Scored risk score ≥9, n (%)	6 (38%)	47 (77%)	0.005
Best handgrip strength, kg (mean ± SD)	34.6 (SD 8.8)	35.0 (SD 8.7)	0.887
Male	37.3 (SD 9.1)	38.8 (SD 7.1)	0.619
Female	29.3 (SD 5.6)	25.5 (SD 3.7)	0.162
% of patients with <10 <sup>th</sup> percentile (sex specific)	2 (17%)	3 (9%)	0.590
Skeletal mass, kg (mean ± SD)	26.5 (SD 5.3)	23.7 (SD 5.2)	0.101
Male	28.7 (SD 3.9)	27.1 (SD 2.6)	0.182
Female	19.8 (SD 2.1)	17.7 (SD 2.2)	0.122

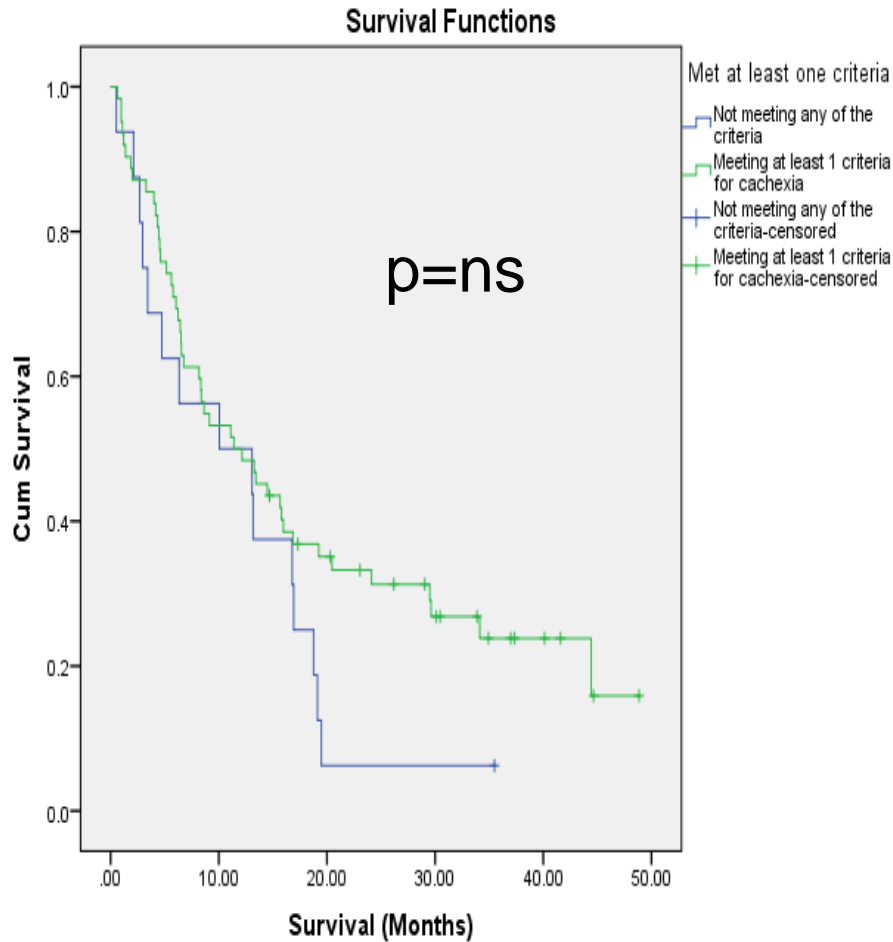


**Figure 1:** Classification of advanced cancer patients who were malnourished and met the criteria for cancer cachexia (total n=78).

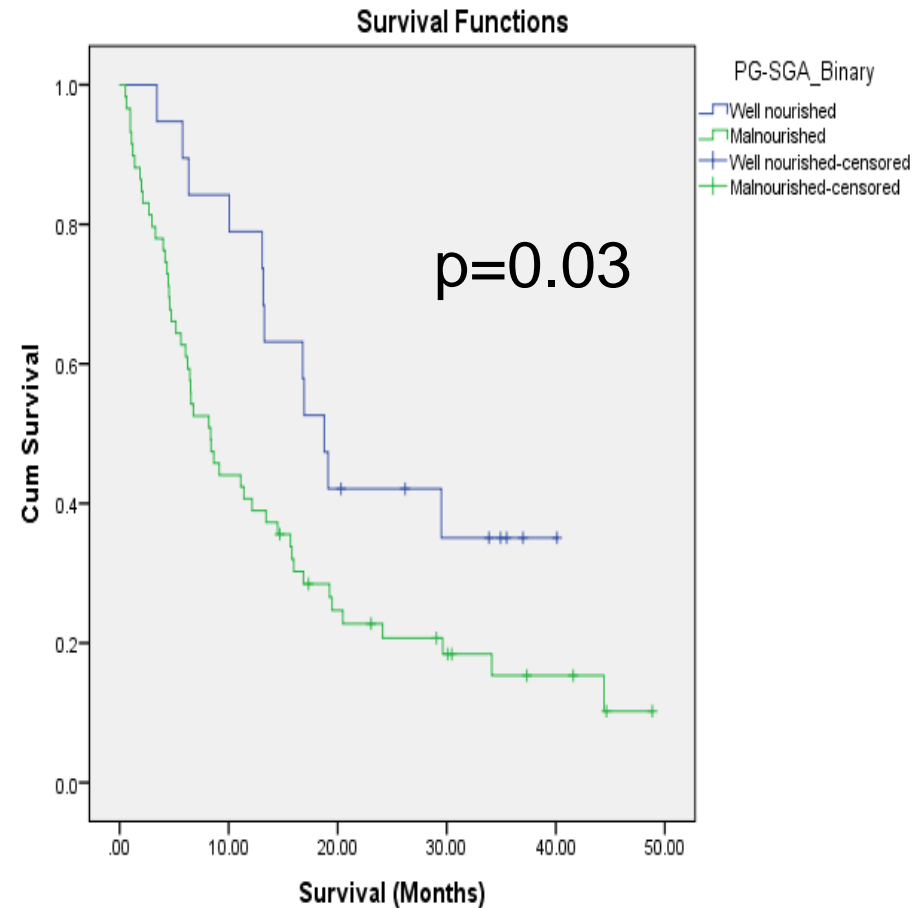
# Overall Survival

	Cachexia (Met $\geq 1$ criteria)	Malnourished (PG-SGA B or C)
Estimated overall survival, mths, median (95% CI)	11.4 (5.5 – 17.3)	8.3 (5.5 – 11.1)
Log rank test (Chi-square)	2.24	4.7

# Overall Survival (months) – advanced pts



Cachexia vs non-cachexia



Malnourished vs well-nourished

# Discussion

- Preliminary data, need confirmation in larger studies
- Criteria for cachexia did not identify clinically useful prognostic groups
- PGSGA provided a stronger prediction of survival
- Should we use the PG-SGA tool alone, or with/without inflammatory markers to identify patients that are appropriate for interventions or clinical studies.

# Limitations

- Potential sampling bias
  - Not initially intended to be used to validate the diagnostic criteria from the latest international consensus
  - Heterogeneous group
- Selection bias
  - Patients who were fit for chemotherapy.
  - This may have contributed to the low numbers of patients who presented with severe muscle wasting and physical functional impairment compared to other study populations that included patients who were not fit for chemotherapy.
  - However interventions probably need to happen in conjunction with chemotherapy



# Conclusion

- The optimal tool to identify potential patients with cachexia or pre-cachexia for future trials deserves further investigation
- Nutritional analysis tools such as the PGSGA may be useful in this process.