2018
28-30 JUNE
VIENNA, AUSTRIA
SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE

Cachexia and Nutrition SG

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Definition of Cancer Cachexia

- Multi-factorial syndrome
  - Characterized by ongoing loss of skeletal muscle mass ± loss of fat mass
  - Cannot be reversed fully by conventional nutritional support
  - Leads to progressive functional impairment

Weight loss >5% over 6 mo that cannot be attributed to simple starvation

or

BMI <20 + weight loss >2%

or

Appendicular skeletal muscle mass index consistent with **sarcopenia + weight loss >2%**

- **BMI,** body mass index.

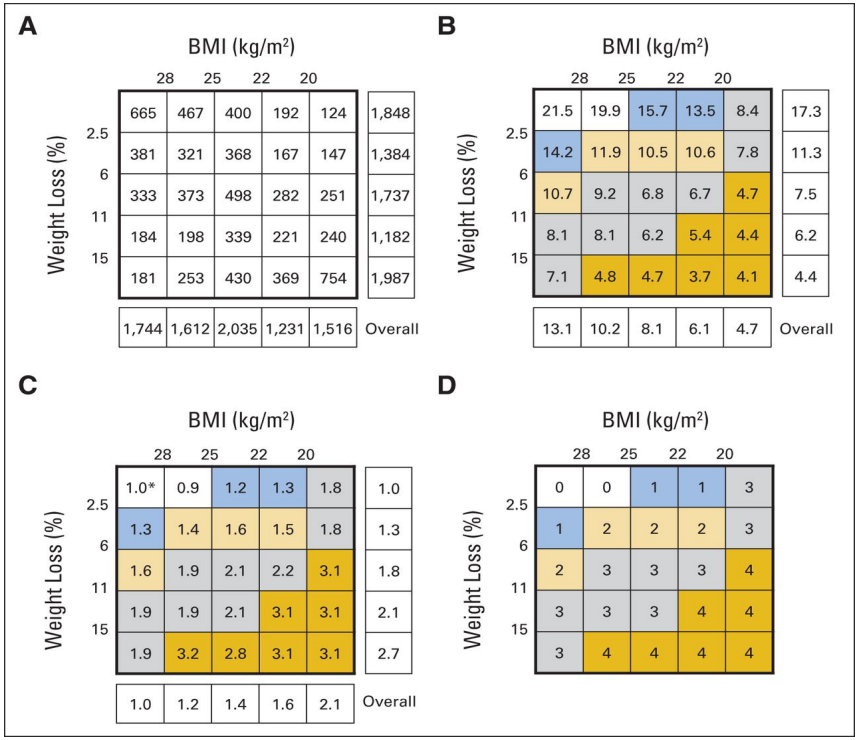
Fearon K, et al. *Lancet Oncol*. 2011;12:489-495 .

Prognostic value of Anorexia-Cachexia

Relationship between Prognosis

- Weight
- Appetite
- Nutritional Impact Symptoms
- Body Composition
- Multiple Domains of cachexia

Reduced survival = a function of body mass index & percent weight loss



A

BMI (kg/m²)

Weight Loss (%)	28	25	22	20	
2.5	665	467	400	192	124	1,848
6	381	321	368	167	147	1,384
11	333	373	498	282	251	1,737
15	184	198	339	221	240	1,182
	181	253	430	369	754	1,987
	1,744	1,612	2,035	1,231	1,516	Overall

B

BMI (kg/m²)

Weight Loss (%)	28	25	22	20	
2.5	21.5	19.9	15.7	13.5	8.4	17.3
6	14.2	11.9	10.5	10.6	7.8	11.3
11	10.7	9.2	6.8	6.7	4.7	7.5
15	8.1	8.1	6.2	5.4	4.4	6.2
	7.1	4.8	4.7	3.7	4.1	4.4
	13.1	10.2	8.1	6.1	4.7	Overall

C

BMI (kg/m²)

Weight Loss (%)	28	25	22	20	
2.5	1.0*	0.9	1.2	1.3	1.8	1.0
6	1.3	1.4	1.6	1.5	1.8	1.3
11	1.6	1.9	2.1	2.2	3.1	1.8
15	1.9	1.9	2.1	3.1	3.1	2.1
	1.9	3.2	2.8	3.1	3.1	2.7
	1.0	1.2	1.4	1.6	2.1	Overall

D

BMI (kg/m²)

Weight Loss (%)	28	25	22	20	
2.5	0	0	1	1	3
6	1	2	2	2	3
11	2	3	3	3	4
15	3	3	3	4	4
	3	4	4	4	4

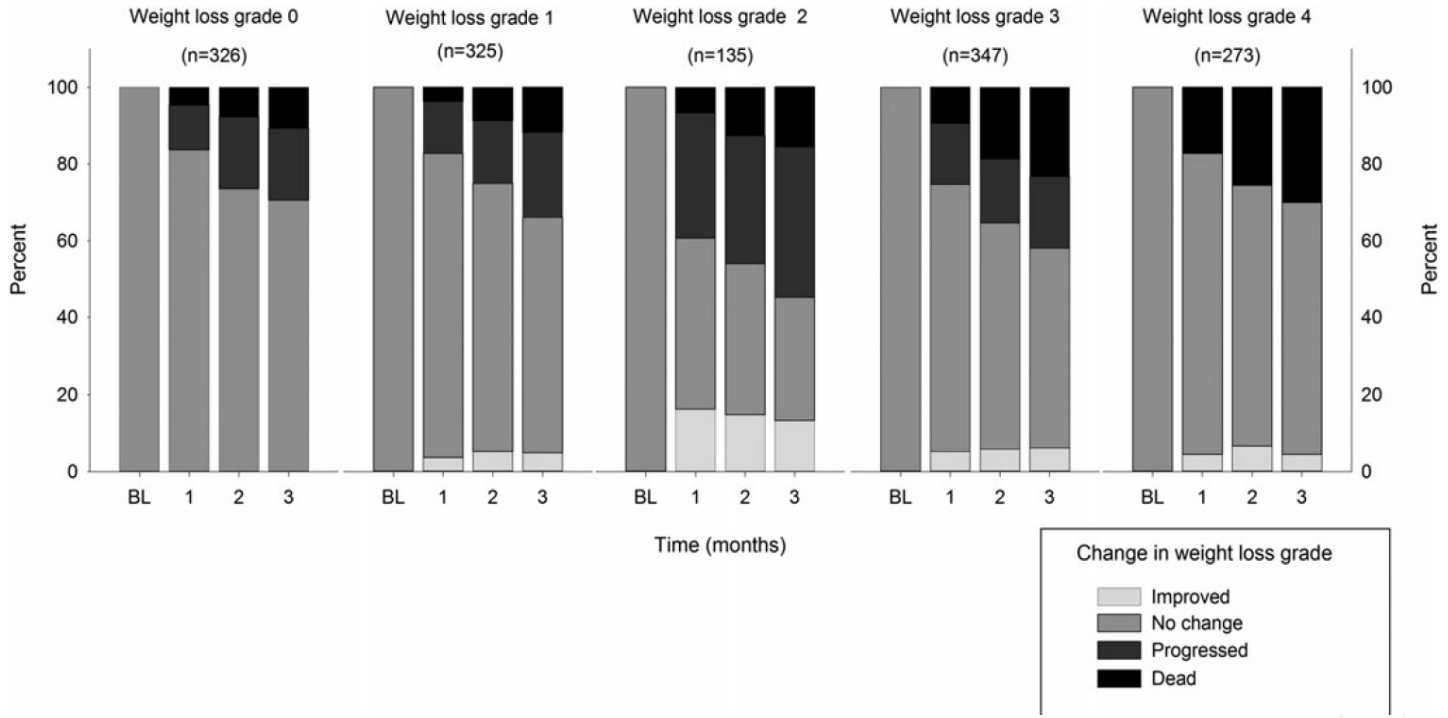
Median survival by grade
0=20.9 months
1=14.6
2=10.8
3=7.6
4=4.3

Panels A to C represent a 5 × 5 matrix analysis of the five categories of BMI and five categories of %WL for a total of 25 possible combinations. The (A) sample size, (B) median overall survival (months), and (C) unadjusted estimated hazard ratios (HRs; HR, 1.0) are presented for each cell. (*) Reference categories are BMI ≥ 28.0 kg/m2 and weight stable ± 2.4%. Different colors represent significant differences (P < .05) in median overall survival and HRs within and between cells of the matrix. Panel D represents the BMI-adjusted WL grading system (grades 0 to 4)

Lisa Martin; Pierre Senesse; Ioannis Gioulbasanis; Sami Antoun; Federico Bozzetti; Chris Deans; Florian Strasser; Lene Thoresen; R. Thomas Jagoe; Martin Chasen; Kent Lundholm; Ingvar Bosaeus; Kenneth H. Fearon; Vickie E. Baracos; *JCO* **2015,** 33, 90-99.

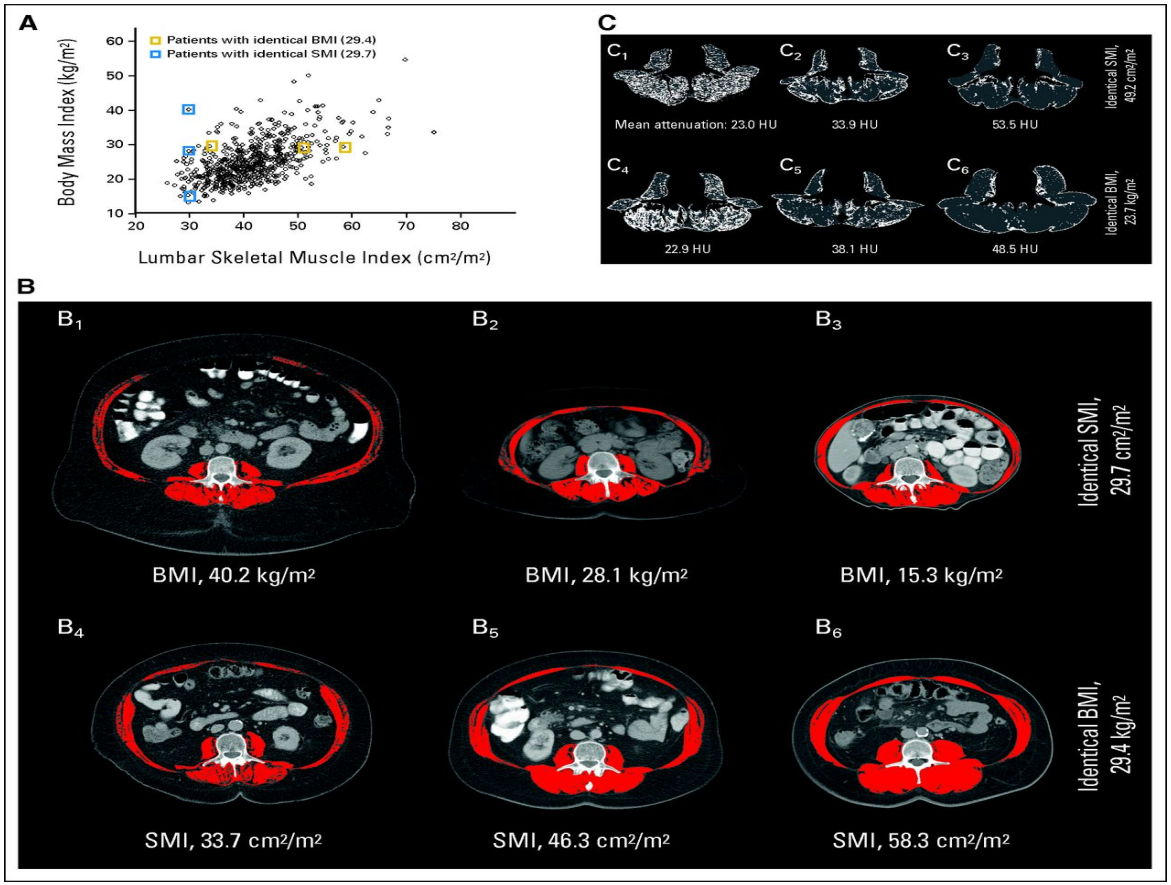
Identifying progression or reversibility

Figure 4 Bar charts for each baseline weight loss grade (0–4) showing the likelihood of improvement to preceding or progress to subsequent grades or death at 1, 2, and 3 months of follow-up.



Variation between skeletal muscle index (SMI) and body mass index (BMI)

for females (n = 645)

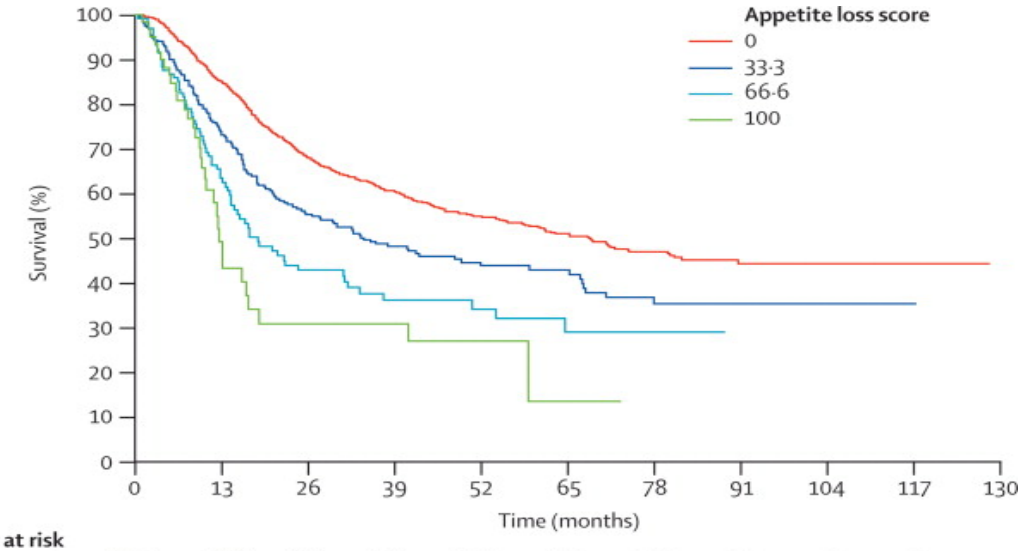


Martin L et al. JCO 2013;31:1539-1547

Patients with cancer cachexia by the conventional criterion (involuntary weight loss) and by two additional criteria (muscle depletion and low muscle attenuation) share a poor prognosis, regardless of overall body weight

JOURNAL OF CLINICAL ONCOLOGY

Baseline quality of life as prognostic indicator of survival Meta-analysis of individual patient data EORTC clinical trials



Number at risk										
0	1314	984	686	486	310	195	128	46	9	1
33·3	348	205	132	90	60	42	27	12	4	1
66·6	133	65	37	22	17	10	6	0	0	0
100	63	17	9	8	5	1	0	0	0	0

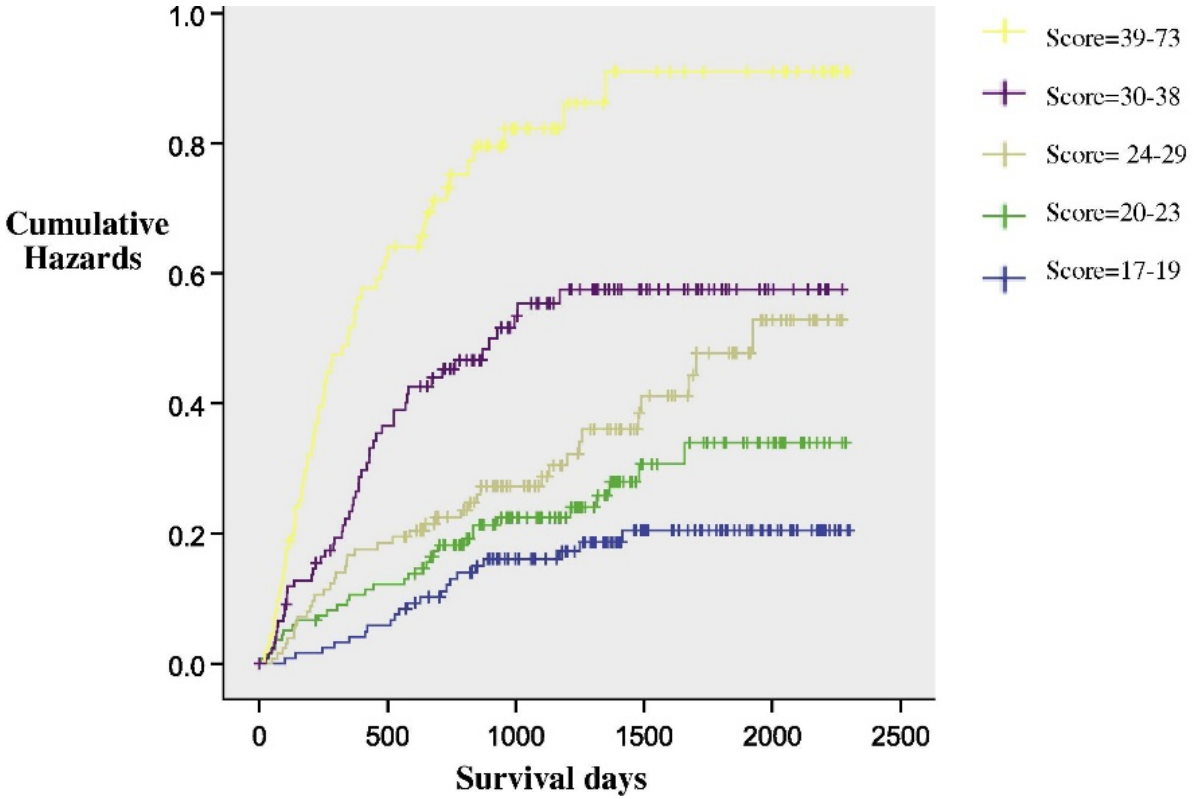
Appetite loss score	Median survival (months; 95% CI)	1-year survival (%; 95% CI)
0	68·86 (58·38–81·12)	86·11 (83·88–87·80)
33·3	35·35 (26·68–59·37)	76·50 (71·38–80·82)
66·6	17·28 (14·39–31·47)	66·19 (56·81–74·00)
100	12·65 (10·64–18·69)	57·94 (42·57–70·63)

Overall survival curves stratified by QLQ-C30 appetite loss scoreQLQ-C30=the European Organisation for Research and Treatment of Cancer quality-of-life core questionnaire

Chantal Quinten, Corneel Coens, Murielle Mauer, Sylvie Comte, Mirjam AG Sprangers, Charles Cleeland, David Osoba, Kristin Bjordal, Andrew Bottomley

Lancet Oncol Volume 10, Issue 9, 2009, 865–871

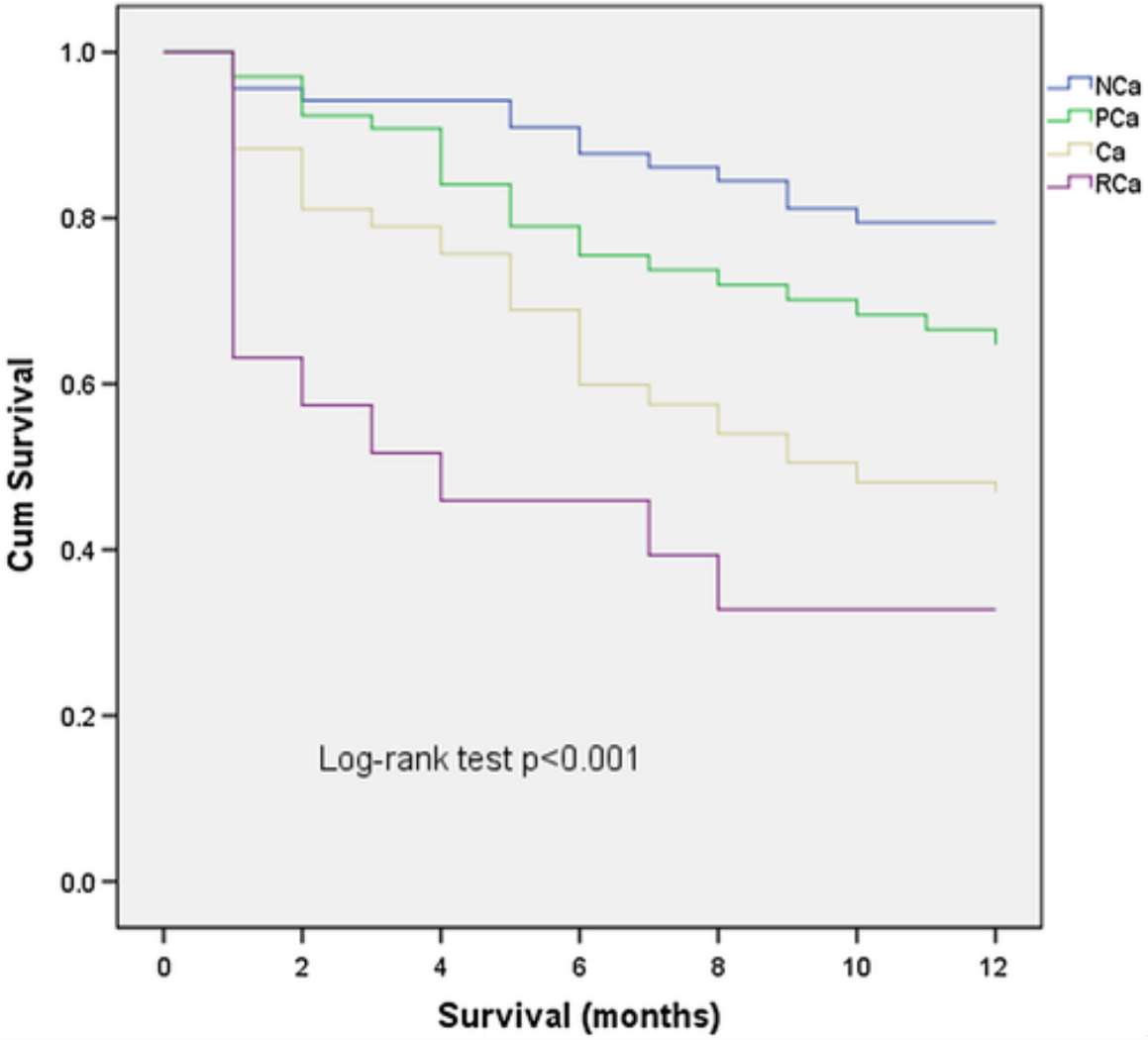
Nutrition impact symptoms in a population cohort of head & neck cancer patients: Multivariate regression analysis of symptoms on oral intake, weight loss and survival



Cumulative hazard plots of survival (days) for total symptom score quintiles.

Arazm Farhangfar, Marcin Makarewicz, Sunita Ghosh, Naresh Jha, Rufus Scrimger, Leah Gramlich, Vickie Baracos
Oral Oncology, Volume 50, Issue 9, 2014, 877–883

Development and validation of a clinically applicable score to classify cachexia stages in advanced cancer patients



Zhou T.J Cachexia Sarcopenia Muscle. 2018

Pharmacological Management of Nutritional Impact Symptoms

Nutritional Impact Symptom	Pharmacological Intervention
Early satiety; bloating; GERD	Metoclopramide 10mg qid to q4h po
Constipation	Laxatives e.g. polyethylene glycol, senna
Nausea/Vomiting	Metoclopramide for non-CINV Olanzapine 5mg qhs if possibly CINV, depression Mirtazapine 15mg qhs if depression, insomnia, anxiety
Depressed mood or anxiety	Mirtazapine first choice Duloxetine if neuropathic pain
Dysgeusia	Zinc supplement trial for 2 weeks
Fatigue	Testosterone replacement in males Vitamin D replacement
Severe pain e.g. Mucositis	Opioid, topical mouthwash

CINV = chemotherapy-induced nausea or vomiting

Goals	•Identify those at increased risk •Identify patients early •Monitor relevant outcomes •Incorporate a multidisciplinary approach
Assessment Tool	•Symptom severity assessment including appetite (e.g. ESAS) •Checklist of nutritional impact factors and weight loss • abbreviated PG-SGA,ESAS or other •Physical performance (e.g. SPPB, handgrip) dynamometer
Multidisciplinary* Management	•Physician = Pharmacological symptom management, education •Dietitian = Nutritional counseling, protein and calorie goal •Physical Therapist = resistance and aerobic exercise, fall prevention •Psychologist = reframing eating, conscious control, body image •Nurse = education, reinforcement of management plan, phone contact
Monitor Key Outcomes	•Weight change, BMI •Appetite •Fatigue, Nutritional impact symptoms and overall symptom burden •Physical performance •Body composition


2019
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Weight-Related Outcomes in Patients with Cancer

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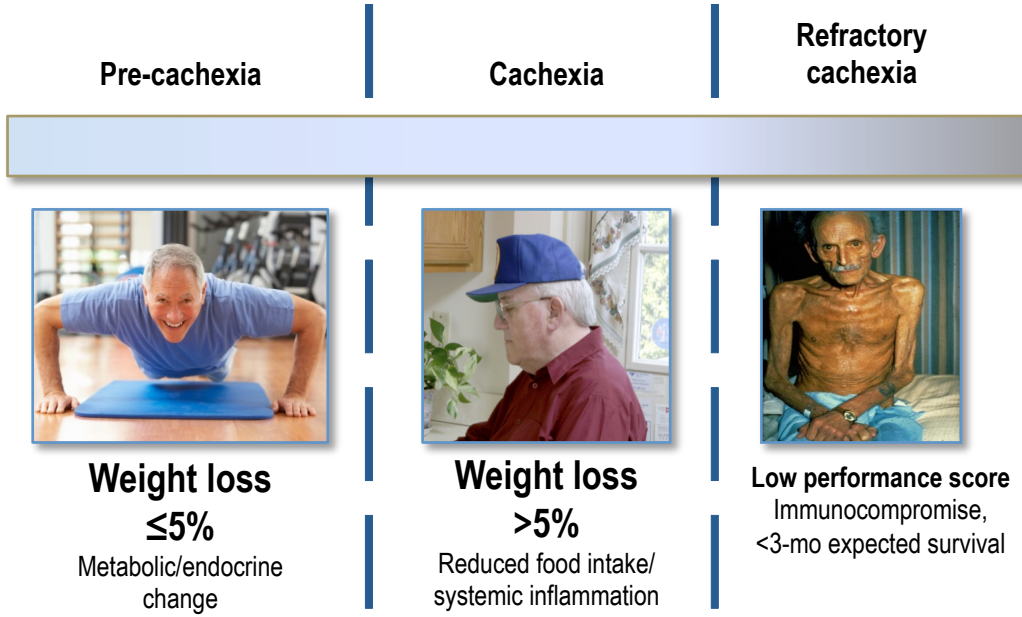
- Increased risk for complications, death[1]
- Decreased treatment response [2]
- Greater failure to complete cycles of therapy[2,6]
- Increased toxicity[3]
- Increased fatigue[4]
- Lower QoL[5,8]
- Decreased Performance status
- Low testsoterone

1. DeWys WB, et al. *Am J Med*. 1980;69:491-497; 2. Ross PJ, et al. *Br J Cancer*. 2004;90:1905-1911; 3. Kazemi-Bajestani SM. *Semin cell Dev 2016*; 4. Parmar MP, et al. *Support Care Cancer*. 2013;21:2049-2057; 5. Mariani L, et al. *Support Care Cancer*. 2012;20:301-309; 6 *Andreyev Eur J Cancer 1998;7 Chlebowski,8. Thoresen Eur J Cancer Care 2012*

Stages of Cancer Cachexia



"In the beginning of the malady it is easy to cure but difficult to detect, but in the course of time, not having been either detected or treated in the beginning, it becomes easy to detect but difficult to cure."

Niccolo Machiavelli

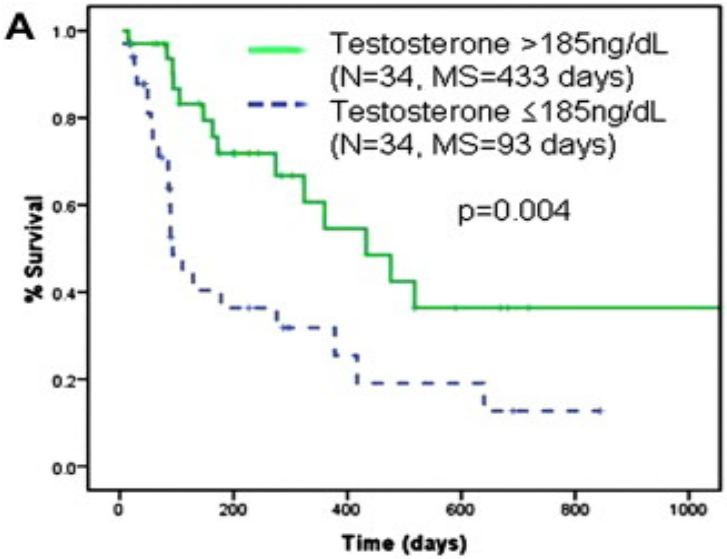
Fearon K, et al. *Lancet Oncol*. 2011;12:489-495.

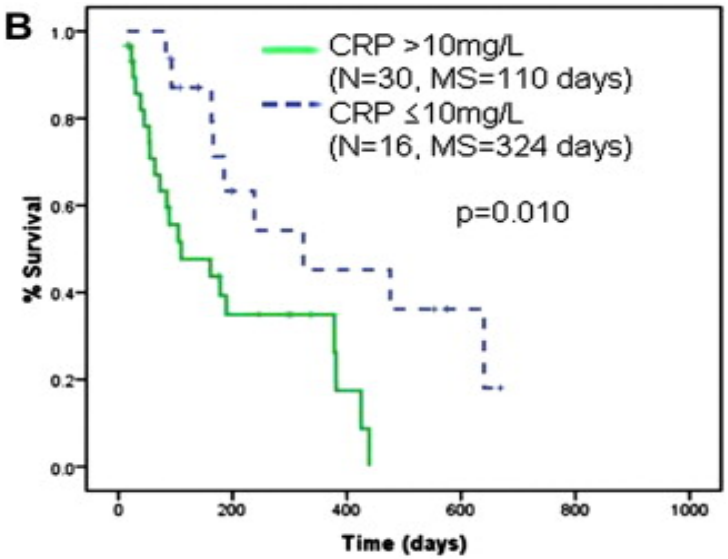
Summary

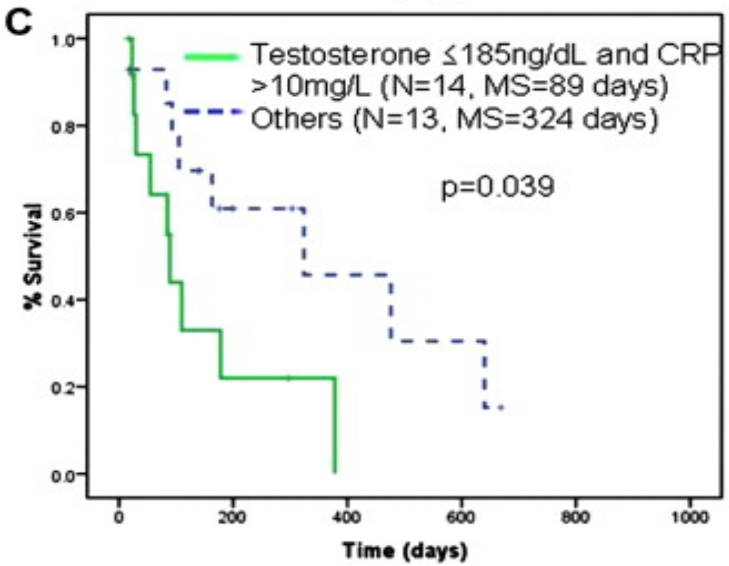
- Consensus Cancer Cachexia definition updated
- Core criterion =weight loss

  Weight loss criteria modified by initial BMI
- Validated by large study resulting in grading system 0-4
- Additional domains may enhance the system
- Importance of appetite and NIS
- Body composition throughout trajectory
- Identify patients in clinical practice,

  prognosticate, design and inclusion of subjects in clinical trials







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Survival analyses (Kaplan-Meier) with comparisons of curves . Survival of male patients with testosterone levels ≤185 ng/dL (blue) was decreased.

Associations Among Hypogonadism, C-Reactive Protein, and Survival in Male Cancer Patients with Cachexia

Egidio Del Fabbro, David Hui, Zohra I. Nooruddin, Shalini Dalal, Rony Dev, Gina Freer, Lynn Roberts, J. Lynn Palmer, Eduardo Bruera

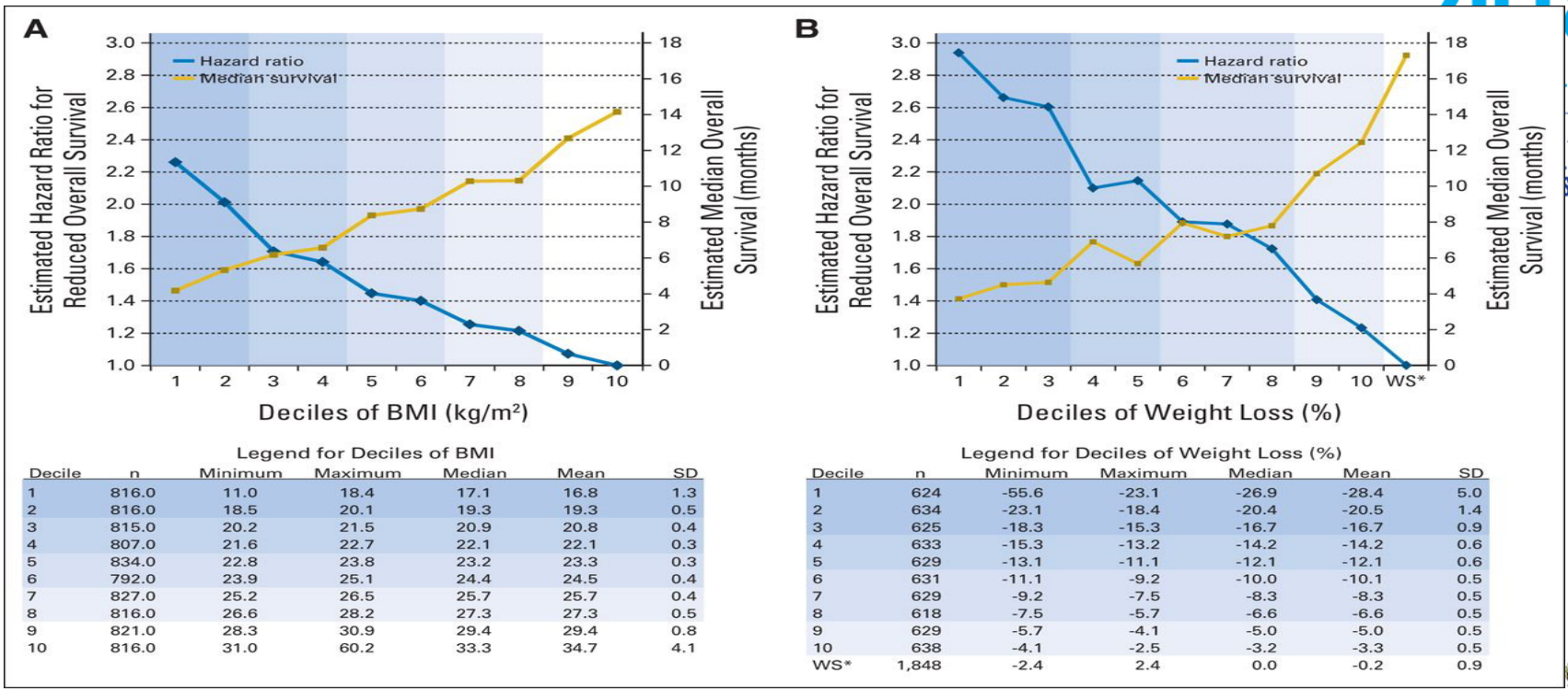
www.mascc.org/meeting
Journal of Pain and Symptom Management, Volume 39, Issue 6, 2010, 1016–1024

Nutritional Impact Symptoms and treatment

In a Cancer Cachexia Clinic

Del Fabbro ,Hui ,Dalal ,Dev ,Bruera et al. *J Pall Med*. 2011;14:1004-1008.

Nutrition Impact Symptoms	Number Affected (%)	Corresponding Intervention	Number Treated Among Affected (%)
Early satiety	94 (62)	Metoclopramide	74 (79)
Constipation	78 (52)	Laxative	68 (87)
Nausea/vomiting	67 (44)	Antiemetic (metoclopramide)	54 (81)
Depressed mood	63 (42)	Antidepressant (mirtazapine)	51 (81)
Dysgeusia	42 (28)	Zinc supplement	20 (48)
Dysphagia	21 (14)	G I/speech therapy	5 (24)
Dry mouth	14 (9)	Artificial saliva	2 (14)
Mucositis pain	11 (7)	Opioid, topical mouthwash	3 (27)
Dental issues	8 (5)	Dental referral	2 (25)



Legend for Deciles of BMI

Decile	n	Minimum	Maximum	Median	Mean	SD
1	816.0	11.0	18.4	17.1	16.8	1.3
2	816.0	18.5	20.1	19.3	19.3	0.5
3	815.0	20.2	21.5	20.9	20.8	0.4
4	807.0	21.6	22.7	22.1	22.1	0.3
5	834.0	22.8	23.8	23.2	23.3	0.3
6	792.0	23.9	25.1	24.4	24.5	0.4
7	827.0	25.2	26.5	25.7	25.7	0.4
8	816.0	26.6	28.2	27.3	27.3	0.5
9	821.0	28.3	30.9	29.4	29.4	0.8
10	816.0	31.0	60.2	33.3	34.7	4.1

Legend for Deciles of Weight Loss (%)

Decile	n	Minimum	Maximum	Median	Mean	SD
1	624	-55.6	-23.1	-26.9	-28.4	5.0
2	634	-23.1	-18.4	-20.4	-20.5	1.4
3	625	-18.3	-15.3	-16.7	-16.7	0.9
4	633	-15.3	-13.2	-14.2	-14.2	0.6
5	629	-13.1	-11.1	-12.1	-12.1	0.6
6	631	-11.1	-9.2	-10.0	-10.1	0.5
7	629	-9.2	-7.5	-8.3	-8.3	0.5
8	618	-7.5	-5.7	-6.6	-6.6	0.5
9	629	-5.7	-4.1	-5.0	-5.0	0.5
10	638	-4.1	-2.5	-3.2	-3.3	0.5
WS*	1,848	-2.4	2.4	0.0	-0.2	0.9

Fig 1. Line graphs representing the relationships between deciles of (A) body mass index (BMI) and (B) percent weight loss (%WL) to overall survival. Decile 1 represents (A) the lowest BMI and (B) the highest %WL. Decile 10 represents (A) the highest BMI and (B) the lowest %WL. Blue lines represent unadjusted estimated hazard ratios (HRs) associated with reduced overall survival. Reference categories are BMI decile 10 (BMI > 30.9 kg/m2; HR, 1.0) and weight stable (WS; ± 2.4%; HR, 1.0). Risk of reduced survival increases with decreasing BMI and increasing %WL. Gold lines represent the estimated median overall survival in months. Median survival decreases with decreasing BMI and increasing %WL. Different shades of blue in the figure indicate significant differences (P < .05) in median survival between deciles. (*) WS is ± 2.4%.

Published in: Lisa Martin; Pierre Senesse; Ioannis Gioulbasanis; Sami Antoun; Federico Bozzetti; Chris Deans; Florian Strasser; Lene Thoresen; R. Thomas Jagoe; Martin Chasen; Kent Lundholm; Ingvar Bosaeus; Kenneth H. Fearon; Vickie E. Baracos; *JCO* **2015,** 33, 90-99.

Weight loss in Cancer, present-day

- Obesity increasing worldwide
- Classification of Weight loss should be based on contemporary data
- European and Canadian study of 8160 patients
- Prognostic significance of **Weight loss** in patients

who initially have a low, intermediate, or high **BMI**

Published in: Lisa Martin; Pierre Senesse; Ioannis Gioulbasanis; Sami Antoun; Federico Bozzetti; Chris Deans; Florian Strasser; Lene Thoresen; R. Thomas Jagoe; Martin Chasen; Kent Lundholm; Ingvar Bosaeus; Kenneth H. Fearon; Vickie E. Baracos; *JCO* **2015,** 33, 90-99.

Additional domains

- Body composition[1]
- Patient reported outcomes

  Appetite[2]

  Nutrition Impact symptoms [3,4]

  Fatigue and function[5]
- Dietary intake[6]
- Physical Function[7]
- Chronic inflammation[8]
- Other- chemo & endocrine dysfunction[9]

1.Prado .Proc nutr Soc 2016 Quinten Lancet Oncology 2011. 2. Farhangfar 2010 Oral Onc. 3.Zhou JPSM 2017 4.Del Fabbro JPM 2010 6. Nasrah Clin Nutr. 2016 9.Burney JCEM2012