From Experts to Patients: Classifying People with Cancer Cachexia

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Introduction

A consensus on the definition and classification of cancer cachexia was recently published by an international panel of experts following the Delphi process.[1] A classification system dividing cancer cachexia into three categories was proposed: precachexia, cachexia and refractory cachexia.
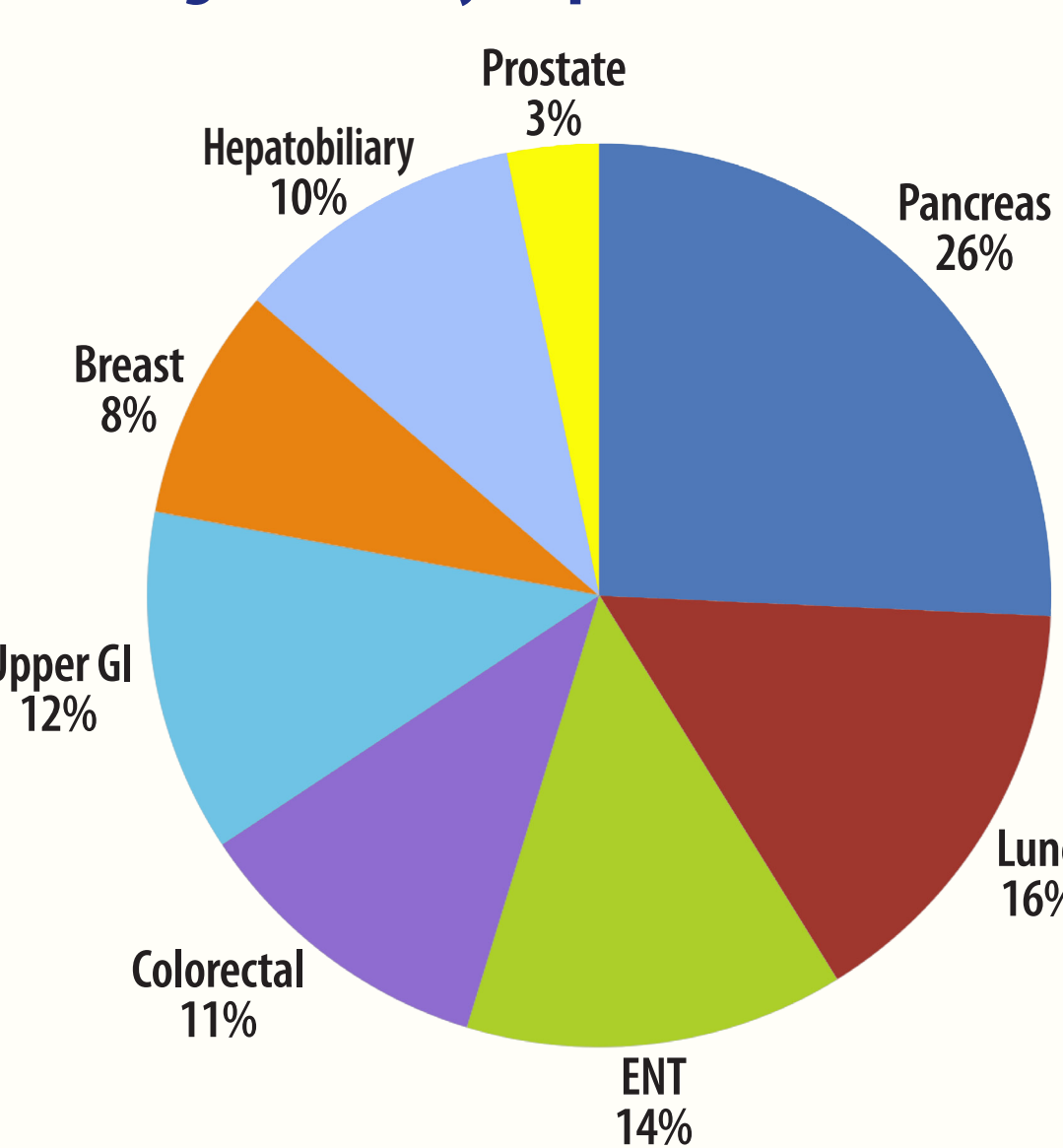
Objectives

1) To apply the published classification system to a population of patients recently diagnosed with an advanced cancer (Figure 1);

2) To determine if the primary tumor site influenced the proportions of patients with "precachexia" or "cachexia".

Population

Between March 2009 and July 2011, 198 adult patients with a recent diagnosis of advanced cancer with an ECOG performance status ≥ 3 and a survival estimate > 3 months, were recruited from the McGill University Health Centre and the Jewish General Hospital, Montreal, Canada. Subjects were evaluated prior to treatment and followed prospectively. Self-reported weight loss over the preceding 6 months was available for 154 patients.

Figure 1: Distributions of Cancer Types among the Study Population

Pancreas 26%, Lung 16%, ENT 14%, Colorectal 11%, Upper GI 12%, Breast 8%, Hepatobiliary 10%, Prostate 3%

Methods

Assessment and definition of Anorexia

To define anorexia we used two questions from the Functional Assessment of Anorexia/Cachexia Therapy additional concerns section (FAACT)[2] and one dimension of the Edmonton Symptom Assessment Scale (ESAS)[3]:

Anorexia was deemed to be present if patients experienced at least one symptom of "anorexia" based on the following criteria:

• To the item "I have good appetite" (FAACT c6), the patient answered "Not at all " or "A little bit";

• To the item "When I eat I seem to get full quickly" (FAACT act10), the patient answered "Somewhat", "Quite a bit" or "Very Much";

• To the ESAS VAS item (Best appetite to Worst possible appetite), two cut-off points were used for the definition:
  ○ Strict definition of anorexia: ≥ 6,
  ○ More inclusive definition of anorexia: ≥ 4.

Anthropometric measurements and biomarker

• Body weight and height were recorded;

• Body Mass Index (BMI) was calculated;

• Bioelectrical Impedance Analysis (BIA) was performed
  ○ Patients were classified as normal or with Sarcopenia (of any kind) according to published guidelines (Janssen et al, 2002); [4]

• Blood samples were collected and serum C-reactive protein (CRP) levels were measured.
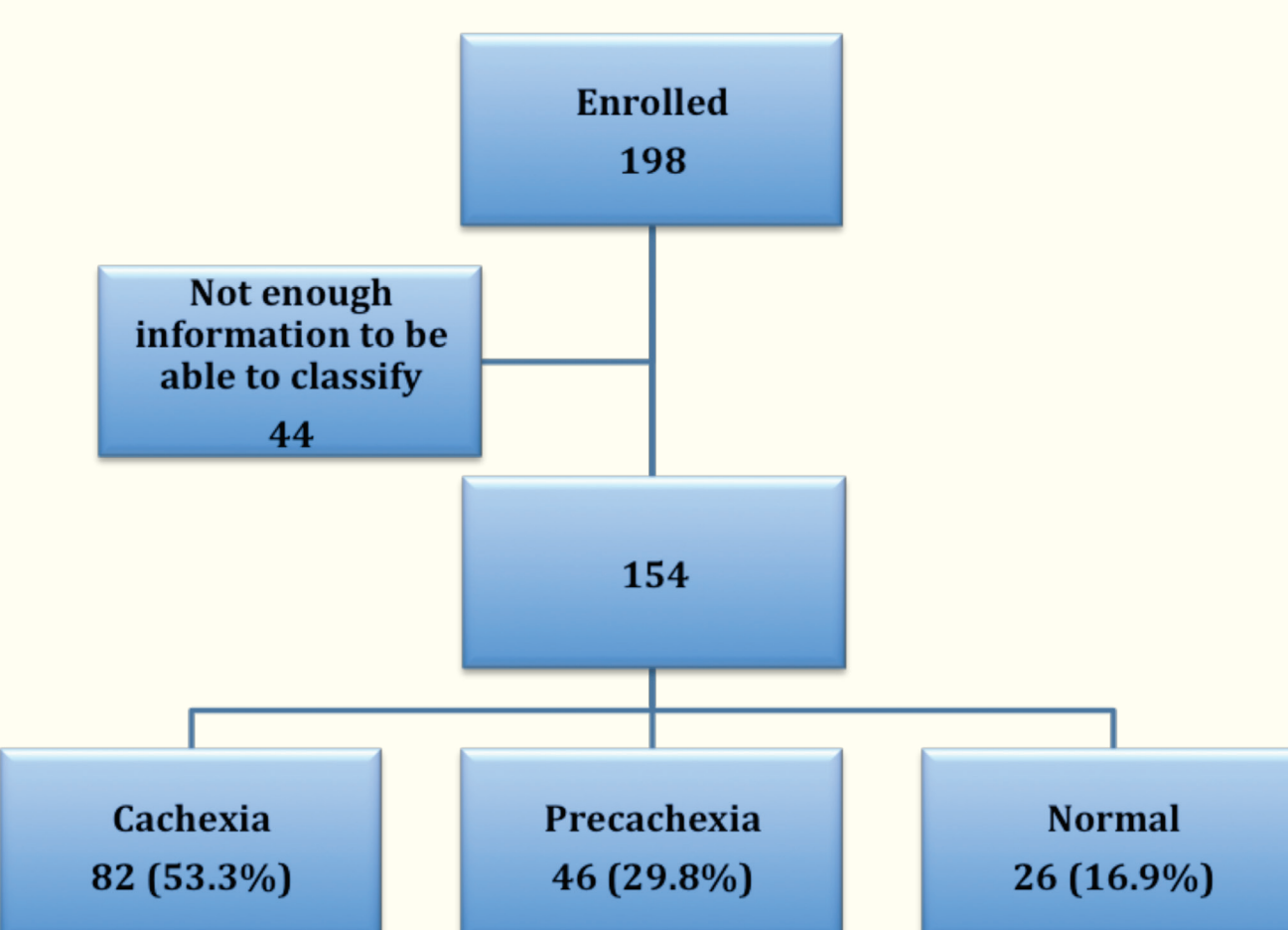
Classification of Cachexia

Finally, patients were classified as normal, precachectic or cachectic according to the published consensus by Fearon et al.[1]

• Patients were classified as cachectic if (one of the following):
  ○ Recalled weight ≥ 5% in the past 6 months,
  ○ Recalled weight ≥ 2% and < 5% in the past 6 months and a BMI < 20 kg/m2,
  ○ Recalled weight ≥ 2% and < 5% in the past 6 months and Sarcopenia.

• Patients were classified as precachectic (**"strict" definition**) if:
  ○ Recalled weight loss ≥ 2% and < 5% in the past 6 months *AND* self-reported anorexia (which included the FAACT items and the ESAS Appetite score ≥ 6) *AND* CRP ≥10 mg/L.

• Patients were classified as precachectic (**"all inclusive" definition**) if:
  ○ Recalled weight change < 5% in the past 6 months *AND* anorexia (which included the FAACT items and the ESAS appetite score ≥ 4) *OR* CRP ≥10 mg/L.

RESULTS

Figure 2: Flow Diagram of Subject Inclusion

Enrolled 198 → Not enough information to be able to classify 44 → 154 → Cachexia 82 (53.3%), Precachexia 46 (29.8%), Normal 26 (16.9%)

*Applying the above "strict" definition of precachexia to our population, lead to the identification of only 4 patients.

Table 2: Cachectic Status by Cancer Type

		Cachexia %	Precachexia %	Normal %	CRP ≥ 10 mg/L % [†]
Colorectal	(n: 17)	70.6	29.4	0.0	71.4
Pancreatic	(n: 40)	69.2	23.1	7.7	26.7
Prostate	(n: 5)	60.0	20.0	20.0	0.0
Upper GI	(n: 19)	57.9	31.6	10.5	64.3
Lung	(n: 24)	45.8	33.3	20.8	57.1
Hepatobiliary	(n: 16)	43.8	25.0	31.3	54.6
Breast	(n: 13)	38.5	30.8	30.8	37.5
ENT	(n: 21)	28.6	42.9	28.6	33.3

*precachexia: (weight <5% and anorexia or CRP>10 mg/L) [†] Missing: 41

Cachexia was highly prevalent at diagnosis in advanced colorectal, pancreatic and upper gastro-intestinal cancers.

"All inclusive" precachexia was also prevalent in most cancer types.

Table 1: Patient Characteristics

Variables		Descriptive Statistics (N: 154) N(%)
Gender	Male	90 (58.4 %)
	Female	64 (41.6 %)
Age Distribution	20 to 35 years	4 (2.6 %)
	36 to 50 years	16 (10.4 %)
	51 to 65 years	60 (39.0 %)
	> 65 years	74 (48.4 %)
	Mean Age (SD)	63.3 (± 12.3)
Weight loss	No weight loss	64 (41.6)
	>2% to <5%	17 (11.0)
	≥ 5%	73 (47.4)
BMI	<20	22 (14.3)
	≥20	110 (71.4)
	Missing	22 (14.3)
Sarcopenia	No	55 (35.7)
	Yes	77 (50.0)
	Missing	22 (14.3)
**Anorexia **	No	51 (33.1)
	Yes	102 (66.2)
	Missing	1 (0.65)
Systemic Inflammation	CRP: 2-10 mg/L	39 (25.3)
	CRP: ≥10 mg/L	52 (33.8)
	Missing	41 (26.62)

*(Includes anorexia (esas≥4) or feeling full (faact_c6) or appetite loss (faact_act10)

Table 3: Patient Weight Change and Mortality at Three Months and Overall Survival Status by Cachectic State

Status at study entry N (%)		Further Weight loss at Three Months N (%)		Median survival Months (95% CI[†])
Normal	26 (16.9)	<2%	20 (76.9)	NA*
		≥ 2 - <5%	3 (11.5)	
		≥ 5%	0 (0.0)	
		Missing	3 (11.5)	
		Dead	0 (0.0)	
Precachexia	46 (29.9)	<2%	32 (69.6)	17.5 [9.17, NA*]
		≥ 2 - <5%	2 (4.3)	
		≥ 5%	3 (6.5)	
		Missing	2 (4.43)	
		Dead	7 (15.2)	
Cachexia	82 (53.3)	<2%	44 (53.7)	12.2 [8.03, 14.6]
		≥ 2 - <5%	13 (15.9)	
		≥ 5%	9 (11.0)	
		Missing	6 (7.3)	
		Dead	10 (12.2)	

*Insufficient events to calculate median survival [†] Confidence Interval: 95%

At 3 months, patients considered normal presented the same level of weight loss as patients with "all inclusive" precachexia. Death was observed in the precachexia and cachexia groups.

Patients with precachexia had an overall shorter median survival than patients within the normal group.

Twenty-four patients with cachexia presented further weight loss at 3 months. This group of patients had the same overall survival as the precachexia group.

DISCUSSION

In our sample, cachexia is present in a large proportion of patients with a variety of advanced cancer types. However, this may be due to a bias in referrals to the study.

The definition of cachexia was readily applicable to our patient population.

Quantitative definitions of anorexia, inflammation and the specificity of metabolic change have not been proposed by the panel of experts.[2] We propose that the expert panel consider developing quantitative measures for anorexia, metabolic change and inflammation.

In this study, we operationally defined precachexia in regard to anorexia (based on three patient reported outcomes of anorexia) and inflammatory status (based on a specific CRP level), in patients who lost <5% of their body weight. By doing so, the group of patients identified as "precachectic" differed in 3 month survival as compared to patients without precachexia.

Our recruitment process excluded patients with a survival estimate of < 3 months; however, 17 died before this time point. This may be due to the fact that we included patients with an ECOG of 3.

Patients with symptoms of anorexia and the evidence of an inflammatory state (as defined by an increased CRP), regardless of minor weight loss, form a special group and should therefore receive a complete envelope of care combining conventional anticancer treatment with an approach addressing anorexia and chronic inflammation.

This approach should involve drug therapy, nutritional counseling, exercise and consideration of other symptoms which contribute to anorexia: mouth problems, dysphagia, pain, psychological distress, etc.

The program described above crosses nutritional therapeutic boarders. It has the characteristics of a palliative care program and may be looked upon as an example of palliative care applied early in the course of a predictably fatal disorder. Thus the work of Fearon's group may further the cause of nutrition and palliative care uniting in common purpose.

Conclusion

Many patients with an advanced cancer presented signs of precachexia and cachexia at diagnosis. Based on these findings, the definition of cachexia as outlined in Fearon et al.[1] could readily be applied. However, the definition of precachexia deserves further reflection with respect to further quantification of anorexia, chronic inflammation and metabolic changes contributing to cachexia. The identification of weight loss, anorexia and chronic inflammation should lead to the early referral of patients with advanced cancer to a comprehensive palliative care cancer nutrition-rehabilitation program.

References

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