

Physical Function at the Time of Diagnosis: the Role of Cancer Cachexia





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Background

Cachexia is a multifactorial process of skeletal muscle and adipose tissue atrophy resulting in progressive weight loss. Inconsistencies in the definition of cachexia have limited the characterisation of the condition and its use clinically. We have recently applied the international consensus classification system for cancer cachexia (Fearon et al., 2011) on people with advanced cancer. It enabled us to classify patients as normal, with precachexia, or with cachexia.

Cachexia has been associated with poor quality of life and particularly with poor physical function. Physical function has been identified as being an important domain of Health-Related Quality of Life that may be strongly influenced by nutritional and possibly by cachexic status (Fearon et al., 2006).

Results and Conclusion



Comfortable

Gait Speed

Mean (SD)

1.25 (0.26)

1.07 (0.27)

1.07 (0.30)

0.11

Two Minute

Walk Test

Mean (SD)

130.88 (32.03)

113.59 (41.15)

0.18

10.21 (3.84) 119.76 (43.60)

Our main objective was to determine whether cachexic state, as defined by the consensus classification, predicted physical function at the time of diagnosis. A second aim was to verify the role of systemic inflammation in predicting physical function.

Methods

198 persons with a recent diagnosis of advanced cancer of various origins from the McGill University Health Center (MUHC) and the Jewish General Hospital (JGH) in Montréal, Canada, were evaluated prior to the initiation of their cancer treatments. Patients were determined as having cachexia if they had a recalled weight loss of 5% or more in the past 6 months, if they had a recalled weight loss of 2 to 5% in the past 6 months and a BMI below 20, and if they had a recalled weight loss of 2 to 5% in the past 6 months and Sarcopenia (Janssen et al, 2002). Patients were initially determined as having precachexia if they had a recalled weight loss of no more than 5% in the past 6 months and self-reported Anorexia or abnormally high CRP levels ($\geq 10 \text{ mg/L}$). Physical function was measured by the distance walked during 2 minute-walk test (2MWT), the Timed-Up and Go (TUG), comfortable gait speed over 5 meters, and by the self-reported physical function subscale of the SF-36 (PFI). Serum C-reactive protein (CRP) levels were collected and measured. Multiple linear regressions were used to analyze the relationship between the variables, controlling for age, gender, and primary tumour origin.

	Cachexia	Precachexia	Normal	
9	82 (53.3%)	46 (29.8%)	26 (16.9%)	

 Table 2: Mean Physical Function by Cachexia Status

Tua*

Mean (SD)

9.02 (2.12)

10.0 (3.59)

0.36

N (%)

26 (16.9)

46 (29.9)

82 (53.3)

	Variables	N (SD) or N (%)			
	Cachexic State				
	Normal	26 (16.9)			
	Precachexia	46 (29.9)			
	Cachexia	82 (53.3)			
	Physical Function				
Physical	Timed-Up and Go (TUG) (s)	9.9 (3.5)			
Functioning	2 Minute Walk-Test (2MWT) (m)	118.5 (40.7)			
Mean (SD)	Comfortable gait speed (m/s)	1.1 (0.3)			
84.00 (19.58)	Physical Function Subscale	69.1 (26.0)			
67.33 (27.36)	Systemic Inflammation (C	C-Reactive Protein)			
65.44 (25.56)	< 10 mg/L	39 (34.5)			
0.07	≥10 mg/L	52 (46.0)			
0.06	Missing	41			

*Higher means worse

Statistically Significant Means (p-value)

Normal

Precachexia

Cachexia

Cachexia Status

Table 3: Multiple Regression with Timed Up and Go as the Outcome

Timed Up and Go (s)					
Predictors	Categories (for categorical predictors)	Unstan Coeff	dardized ficients	Standardized coefficients	
		Beta	Standard Error		
	Normal (Ref)	-	-	-	
Cachexic State	Precachexia	-0.41	1.05	-0.06	
	Cachexia	-0.42	1.04	-0.06	
Systemic	< 10 mg/L	-	-	-	
(C-Reative Protein)	≥10 mg/L	1.89*	0.69	0.29*	
Confounding Variables					
Age (per 10 years)		0.6*	0.3	2.4*	
Sex	Female (Ref)	-	-	-	
	Male	-0.34	0.68	-0.05	
Overall Model					
Total R-Square		0.21			

Table 4: Multiple Regression with 2 Minute Walk Test as the Outcome

2 Minute Walk Test (m)					
Predictors	Categories (for categorical predictors)	Unstandardized Coefficients Beta Standard Error		Standardized coefficients	
	Normal (Ref)	-	_	-	
Cachexic State	Precachexia	-10.5	14.2	-0.11	
	Cachexia	-16.4	14.0	-0.20	
Systemic	< 10 mg/L	-	-	-	
(C-Reative Protein)	≥10 mg/L	17.74*	9.46	-0.21*	
Confounding Variable					
Age (per 10 years)		-7.1*	3.6	-2.2*	
Sex	Female (Ref) Male	- -0.15	- 9.17	-0.001	
Overall Model					
Total R-Square		0.22	2		



Table 5: Multiple Regression with Comfortable Gait **Speed as the Outcome**

Comfortable Gait Speed (m/s)				
Predictors	Categories	Unstan Coef	dardized ficients	Standardized coefficients
. real clore	predictors)	Beta	Standard Error	
	Normal (Ref)	-	-	-
Cachexic State	Precachexia	-0.07	0.08	-0.12
	Cachexia	-0.11	0.08	-0.20
Systemic Influence	< 10 mg/L	-	-	-
(C-Reative Protein)	≥10 mg/L	-0.14*	0.05	0.26*
Confounding Variable	es			
Age (per 10 years)		-0.08	0.02	-3.5
Sov	Female (Ref)	-	-	-
	Male	0.03	0.05	0.06
Overall Model				
Total R-Square	0.32			

Standardized coefficient = Beta $x \mid 1$ Standard Deviation Ref: Reference Category (for categorical variables) *: p < 0.05

Table 6: Multiple Regression with Physical Function Subscale as the Outcome

Physical Functioning Subscale (SF-36)					
Predictors	Categories (for categorical predictors)	Unstan Coeff	dardized icients	Standardized coefficients	
		Beta	Standard Error		
	Normal (Ref)	-	-	-	
Cachexic State	Precachexia	1.15	8.37	0.02	
	Cachexia	-4.87	8.28	-0.10	
Systemic	< 10 mg/L	_	-	-	
(C-Reative Protein)	≥10 mg/L	13.11*	5.42	-0.26*	
Confounding Variable	S				
Age (per 10 years)		-5.0	2.1	-0.2	
Sov	Female (Ref)	-	-	-	
JCA	Male	10.03*	5.30	0.20*	
Overall Model					
Total R-Square		0.28	3		



References

Fearon K, Strasser F, Anker SD. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 2011; 12: 489-495

Janssen I, Heymsfi eld SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons associated with functional impairment and physical disability. J Am Geriatric Soc 2002; 50: 889-96.

Fearon KC, Voss AC, Hustead DS. Definition of cancer cachexia: effect of weight loss, reduced food intake, and systemic inflammation on functional status and prognosis. American Journal of Clinical Nutrition. 2006;83(6):1345-1350

26%

At the time of diagnosis, systemic inflammation as measured by CRP seems to be an important predictor of physical function, as it was a statistically significant predictor for all 4 outcomes of physical function. As is to be expected, age was also a statistically significant predictor of physical function for 3 measures of physical function. Gender was significant for the patientreported measure of physical function. Surprisingly, cachexic state, as well as primary tumour origin, did not seem to have a statistically significant effect on physical function.

Although physical function was on average lower in patients with precachexia and cachexia than in normal

patients, cachexic state in itself does not seem to be a significant predictor of physical function at the time of advanced cancer diagnosis.

Recalled weight loss might be an imprecise measure of weight loss which could affect the determination of cachexic state in this patient population.

Longitudinal analyses of physical function levels during the disease progression, as affected by recorded weight loss and cachexic state determination, however might still be influenced by the presence of cancer cachexia.