Symbiosis

www.symbiosisonline.org
www.symbiosisonlinepublishing.com
ISSN Online: 2372-0980

Research article | Journal of Nutritional Health & Food Science | Open Access

Identification of Sarcopenia Risk in Oncology Outpatients using the SARC-F Method

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Received: June 08, 2018; Accepted: August 03, 2018; Published: August 7, 2018

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Abstract

Introduction: Sarcopenia is a common syndrome of highly catabolic diseases like cancer. Maintaining adequate body composition is fundamental for oncology patients' best prognosis. Existing tools to help in early identification of sarcopenia are limited and impractical in outpatient care. The SARC-F questionnaire, validated by Malmstrom et al, in order to screen the risk of sarcopenia can help on the early diagnosis and intervention. The objective of this study was to evaluate the sarcopenia risk in oncology outpatients by SARC-F tool, and to analyze its relationship with the Body Mass Index (BMI) and treatment toxicity.

Method: A prospective study was carried out to 52 elderly oncology outpatients of a tertiary hospital clinic in São Paulo, Brazil. The patients' risk of sarcopenia was assessed by SARC-F questionnaire, through direct interview, at the time of radiotherapy or chemotherapy. The demographic data collected were sex, age, diagnosis, weight, presence of toxicity and BMI, (classified according to SABE PAHO, 2003). Toxicity classification was performed according to the Common Toxicity Criteria of the National Cancer Institute.

Results: In the study, most patients were males (n=32, 61.53%), mean age was 72 years-old (± 8.4), weight showed mean of 72.9 kg (± 12.9) and BMI of 25, 65 kg/m^2 (±3, 85), classifying as eutrophic 55.7% (n=29), 19.2% underweight (n=10) and 25% overweight (n=13). Of the patients, 34 were undergoing to chemotherapy (65.38%) and 18 to radiotherapy (34.19%). The most frequent neoplasms were: prostate (n=8, 15, 38%), breast (n = 7, 13, 46%), lung (n=7, 13, 46% 62%) and others (n=25; 48.08%). Toxicity was presented in 55.76% of patients (n=29), being the most common inappetence (n=9; 31.03%); nausea (n=5; 17.24%) and diarrhea (n=5; 17.24%). Among the patients who presented a risk for sarcopenia (n=6; 11.53%), according to SARC-F, the majority were female (n=4; 66.6%) aged 80 to 90 years-old (n=3; 50.0%). Of patients at sarcopenia risk, 33.3% were underweight, 50.0% were eutrophic and 16.6% were overweight according to the BMI classification. Regarding toxicity, 66.6% (n=4) of the sarcopenia risk patients presented toxicity, 50.0% with inappetence (n=2) and 50.0% with nausea or diarrhea (n=2).

Conclusion: There was a risk of sarcopenia in 11.53% of the patients (n=6), but it was not related to BMI. As for toxicity, the tool revealed a positive relation regarding sensitivity but without statistical relevance. SARC-F is a quick and simple screening method for sarcopenia, which can be applied by any healthcare professional. However, further studies are needed for application in clinical oncology area.

Keywords: Sarcopenia; Oncology; Outpatients

Introduction

Sarcopenia is a syndrome characterized by a gradual and generalized process of lean mass loss and strength reduction, associated to functionality decrease [1]. The syndrome has primary origin when triggered by mechanisms primarily correlated with age, involving hormones, apoptosis and mitochondrial dysfunctions. While its secondary origin is the result of organic failure, inflammatory, malignant or endocrine diseases. A prevalence of 50% sarcopenia is estimated in the elderly over 80 years-old [1, 2].

Cancer is characterized by uncontrolled cell growth. Metabolic changes such as exacerbated energy expenditure, inflammation, anorexia and the tumor mass metabolism contribute to the quick nutritional status deterioration due to inflammatory mediators and adverse effects of treatment [1, 3, 5, 6].

The metabolic disturbances caused by the tumor mass that contribute to patient's malnutrition and sarcopenia include:

- Increased production of inflammatory cytokines, such as TNF-α and IL-6. In excess, these cytokines trigger the release of myofibrillar proteins that inhibit AKT / mTOR pathway signaling, thus contributing to muscle atrophy. In parallel to this, occurs MuRF-1 (muscle RING finger-containing protein 1) and MAFbx (atrogin) protein activation, both of which potentiate muscle loss and functionality reduction. Inflammatory cytokines further reduce appetite, contributing to food inappetence [5, 6].

- Lipolysis induction by the adrenergic metabolic pathway

that activates and stimulates protein kinase A, Adipose Tissue Triglyceride Lipase (ATGL) and Hormone-Sensitive Lipase (HSL), which release into the plasma free-chain fatty acid to be used as energy supply [6].

For these reasons, attention to patient' nutritional status is essential for treatment good prognosis and quality of life recovery. Uncontrolled levels of protein depletion may impair or even discontinue anticancer treatments, since chemotherapeutics agents are metabolized in muscle tissue and its dosage is calculated according to muscle mass at the treatment beginning [5, 6]. Approximately 20% of cancer patient deaths are secondary to malnutrition. Patients with muscle mass depletion present a greater risk of treatment toxicity, lower survival and worse clinical outcome [7, 8].

Treatment toxicity is measured by gastrointestinal symptoms, and classification is performed based on the extent to which they manifest themselves. According to the Brazilian Institute of Oncology Nutrition (IBNO), the most common toxicities are anorexia (26%), nausea and vomiting (33%), xerostomia (19%), odynophagia (11%) and diarrhea (16%) [5, 9].

Early identification of patients at risk of malnutrition and sarcopenia is essential to enable appropriate intervention and improve nutritional status. Therefore, the aim of the present study was to evaluate the sarcopenia risk in oncological outpatient population using the SARC-F questionnaire; and to analyze if there is an association between SARC-F and Body Mass Index (BMI) classification and with the SARC-F and toxicity symptoms during the anticancer treatment.

Methods

A prospective, descriptive study carried out in a private hospital of São Paulo, Brazil, from April to May 2017. Were included elderly oncology outpatients (≥ 60 years-old). Exclusion criteria were physical and/or mental incapacity to perform the requested questionnaire.

The questionnaire used in this study was the SARC-F in the validated version for Portuguese language, indicated for screening the risk of sarcopenia. It is composed of five objective questions, self-reported by the patient in direct interview mode that was applied during oncology treatment (chemotherapy and radiotherapy). SARC-F questionnaire includes five components: strength, assistance walking, rise from a chair, climb stairs, and falls. The scale scoring range from 0 to 10 (i.e. 0–2 points for each component; 0 = best performance to 10 = worst performance) and classify the patient as symptomatic (≥ 4 points) or healthy (0 to 3 points) (Chart 1) [10].

The data collected were sex, age, weight, height, body mass index (BMI), diagnosis, type of treatment, presence and symptom of toxicity.

Component	Question	Scoring
Strength	How much difficulty do you have in lifting and carrying 10 pounds?	None = 0 Some = 1 A lot or unable = 2
Assistance in walking	How much difficulty do you have walking across a room?	None = 0 Some = 1 A lot, use aids, or unable = 2
Rise from a chair	How much difficulty do you have transferring from a chair or bed?	None = 0 Some = 1 A lot or unable without help = 2
Climb stairs	How much difficulty do you have climbing a flight of 10 stairs?	None = 0 Some = 1 A lot or unable = 2
Falls	How many times have you fallen in the past year?	None = 0 1–3 falls = 1 4 or more falls = 2

Chart 1: SARC-F screening for sarcopenia. Adapted from Malmstrom et al (2013)

The BMI results for elderly patients (≥ 60 years-old) were classified by using the SABE/OPAS (Survey on Health, Welfare and Aging by Pan American Health Organization) classification of 2003. Toxicity classification was performed according to the Common Toxicity Criteria of the National Cancer Institute (version 2.0) [5, 11, 12, 13].

Mean, median and standard deviation were calculated for the quantitative variables and absolute frequencies or percentages for the qualitative variables as appropriate. Pearson' qui-square test was applied for the categorical variables, with p-value lower or equal to 0.05 considered as statistically significant. Simple

linear regression was used to establish possible associations between variables and SARC-F. Data were analyzed by using Microsoft Office Excel 2010 version.

The uniterms utilized were sarcopenia, oncology, oncology outpatient.

Results

The random and non-probabilistic sample consisted of 52 elderly individuals, with 32 male (61.5%), mean age of 72 years (± 8.4), mean weight of 72,9 kg (± 12.9) and mean BMI of 25.65 kg/m^2 (±3.85). According to BMI, there was 10 underweight (19.2%), 29 eutrophic (55.8%) and 13 overweight (25%) patients.

Toxicities were related by 55.8% of patients. The adverse events most frequently reported by patients were appetite loss (31.03%), nausea (17.24%), diarrhea (24%).

In the study, 34patients were undergoing to chemotherapy (65.4%) and 18 to radiotherapy (34.6%). The type of neoplasia presented a prevalence of 15.4% to prostate (n=8), 13.5% to breast (n=7), 13.5% to lung (n=7), 9.6% to rectum (n=5) and 48.1% to other types (n=25; 48, 1%) Table 1.

Table 1: Characteristics of patients

Variables	n=52	%
Sex		
Female	20	38,5
Male	32	61,5
Age (years)		
60 to 69	23	44,2
70 to 79	17	32,7
80 to 89	11	21,2
90 to 100	1	1,9
Type of tumor		
Adenoneuroendocrine	1	1,9
Esophagus	1	1,9
Gastric	1	1,9
Glioblastoma	3	5,8
Liver	1	1,9
Lymphoma	1	1,9
Follicularlymphoma	2	3,8
Hodgkin's lymphoma	1	1,9
Non Hodgkin's lymphoma	2	3,8
Tongue	1	1,9
Breast	7	13,6
Myelodysplasia	2	3,8
Myeloma	2	3,8
Ovarian tumor	1	1,9
Pancreas	2	3,8
Peritoneum	1	1,9
Prostate	8	15,5
Lung	7	13,6
Rectum	5	9,7
Soft tissue sarcoma	2	3,8
Brain	1	1,9
Treatment type		
Chemotherapy	34	65,4
Radiotherapy	18	34,6
SARC-F		
Sarcopenia risk (6-10 points)	6	11,5
No sarcopenia risk (0-5 points)	46	88,5
Body Mass Index (BMI)		
≤ 23 –Underweight	10	19,2
23,0 to 28,99 – Eutrophia	29	55,8
≥29.0 – Overweight	13	25,0
Toxicity		
No	24	46,2
Yes	28	53,8
Adverse symptoms		
Inappetence	9	17,3
Diarrhea	5	9,6
Nausea	5	9,6
Constipation	4	7,7
Abdominal colic	1	1,9
Dysphagia	1	1,9
Tastedisorders	1	1,9
Vomiting	2	3,8

According to SARC-F, 6 patients (11, 5%) were at sarcopenia risk, of these 66, 6% were female and most aged 80 to 90 years (n=3; 50, 0%) Table 2. The BMI classification was compared to sarcopenia (n = 6): 2 (33.3%) underweight, 3 (50.0%) eutrophic, 1 (16.6%) overweight Table 3 (Graphic 1).

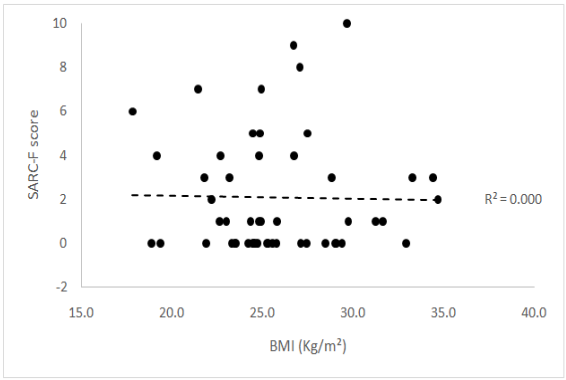
According to BMI, 57.14% of the patients were eutrophic. Patients presenting toxicity were 53.8% and the most common of them was inappetence (43.8%). Of the 28 patients who presented toxicity, only 7 (25%) were classified at nutritional risk by BMI (underweight), of these the most common symptoms were constipation and inappetence (28.57%) Table 4 (Graphic 2).

Table 2: SARC-F's performance for sarcopenia screening

	Risk for sarcopenia (n=6)				No risk for sarcopenia (n=46)			
	Female (n= 4)		Male (n= 2)		Female (n= 16)		Male (n=30)	
Age	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
60 to 69	1	25,0	0	-	9	56,3	13	43,3
70 to 79	2	50,0	0	-	6	37,5	9	30,0
80 to 89	1	25,0	2	100,0	1	6,3	7	23,3
90 to 100	0	-	0	-	0	-	1	3,3
TOTAL	4	100,0	2	100,0	16	100,0	30	100,0

Table 3: Description of BMI and SARC-F classification (n=52)

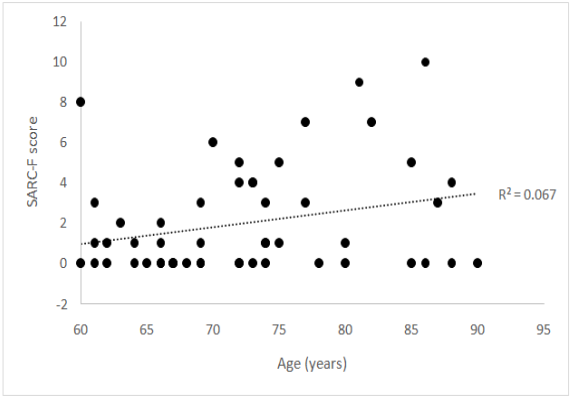
	Sarcopenia risk	No sarcopenia risk
Underweight	2(4%)	8 (15%)
Eutrophia	3 (6%)	26 (50%)
Overweight	1 (2%)	12 (23%)



Graphic 1: Scatterplot of SARC-f versus BMI

Table 4: Correlation between the presence of toxicity and SARC-F classification (n=52)

	Sarcopenia risk	No sarcopenia risk	*p-value*
Toxicity presence	2	22	0,50
No toxicity	4	24	



Graphic 2: Scatterplot of SARC-f versus Age

Discussion

Barbosa et, al. (2016) reported low sensitivity but high specificity to identify sarcopenia risk by the SARC-F questionnaire in its isolate application. The factors that contribute to this fact are related to the questions that mainly evaluate the performance, creating a gap regarding the evaluation of the lean mass loss, given that these are the two main strands for the sarcopenia characterization, according to The European Group of Sarcopenia in Elderly (EWGSOP) [1, 4]. The group proposed a possibility to make SARC-F more sensitive, by using calf circumference (cut-off point: 33 cm for women and 34 cm for men), which is considered gold standard for the elderly. However, in oncology patients anthropometric measurements may be influenced by non-nutritional factors, such as edema due to, for example, drugs administered during treatment [4, 8].

The EWGSOP offers other options for muscle mass measure like computed tomography, considered a gold standard method, electric bioimpedance and others [1]. Some of these technologies to analyze body composition are not financially feasible to identify sarcopenia [5, 11].

Dynamometry is an effective measure for all age groups and provides support for both, isolated muscle mass and muscle performance, being an extremely valuable aid to the SARC-F questionnaire. In addition, completing the questionnaire with these instruments helps to reduce the subjectivity of self-reporting [4].

Regarding the results obtained in the study (11.5% of the sample with risk of sarcopenia), it is worth to mentioning that the tumors with the highest incidence were: prostate, breast and lung. It is known that neoplasias with the highest nutritional risk are those located in gastrointestinal tract, which is a possible justification for the low prevalence of the risk of sarcopenia [9].

Concerning to toxicity, the study showed SARC-F pre disposition for specificity of toxicity. It suggests that SARC-F may be assertive about the risk of sarcopenia, since sarcopenia patients have a greater chance of presenting adverse effects to treatment.

In addition, it is important to emphasize that BMI is a pattern of population analysis, widely used in the clinical practice. However, it may not to be a sensitive parameter, especially in the elderly oncologic population where the height used is usually the one reported and the weight is altered due to anticancer treatments [1, 2].

The study presented biases, as the small sample with great heterogeneity, the different types of neoplasias presented and the non-control of the number of treatment sessions that the patients underwent at the time of collection. Justifying the intention of the study, to portray the heterogeneity in daily care reality of an oncological clinic.

Conclusion

The risk of sarcopenia was present in 11.53% of the sample (n = 6), but it did not demonstrated relation with BMI or toxicity. SARC-F is a quick and simple screening method for sarcopenia, which can be applied by any healthcare professional. However, further studies are needed for application in clinical oncology area. Studies with SARC-F associated with tools to measure muscle mass and strength, such as Handgrip or thumb adductor muscle thickness (EMAP), are suggested.

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