ORIGINAL ARTICLE

Influence of nutritional status and frailty phenotype on health-related quality of life of patients with bladder or kidney cancer

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Abstract

Purpose This research aimed to assess the impact of nutritional status and frailty in the health-related quality of life (HRQoL) of patients with bladder or kidney cancer.

Methods This was a cross-sectional study with individuals aged 20 years or older. Frailty phenotype was defined using the criteria of Fried et al. (2001). Patient-Generated Subjective Global Assessment (PG-SGA) classified nutritional status. The European Organization for Research and Treatment of Cancer Quality of life questionnaire Core-30 third version (EORTC QLQ-C30) assessed HRQoL.

Results Forty-four patients with bladder and 44 with kidney cancer, mostly male, with a mean age of 65.9 and 58.6 years, respectively, were evaluated. Presence of frailty was not different between young and older adults. More than 80% of the robust subjects were well-nourished, while there was a predominance of frail with some degree of malnutrition ($p < 0.05$). The summary score of HRQoL was worse among the frails than pre-frails and robusts, both in bladder (68.5 vs 86.8 vs 89.5; $p = 0.002$) and in kidney cancer (54.9 vs 82.9 vs 91.4; $p < 0.001$), as well as in malnourished compared to well-nourished with bladder (72.9 vs 90.3; $p = 0.003$) and kidney cancer (69.4 vs 88.3; $p = 0.001$). After adjusted, frailty and malnutrition continued associated with poor summary score ($p < 0.05$).

Conclusion These findings indicate that frailty and malnutrition negatively affect HRQoL of patients with bladder or kidney cancer in several aspects.

Keywords Bladder cancer · Kidney cancer · Frailty · Malnutrition · Quality of life

Introduction

Cancer is expected to rank as the leading cause of death and the single most important barrier to increasing life expectancy in every country of the world in the 21st century. According to GLOBOCAN estimates of cancer incidence and mortality there would be about 18.1 million new cancer cases and 9.6 million cancer deaths in 2018 [1]. In Brazil, it is estimated for the 2020–2022 triennium 625,000 new cases of cancer each year, of which 7,590 cases of bladder cancer in men, ranking seventh among the most incidents, and 3,050 in women, corresponding to the 14th most common [2]. On the other hand, kidney cancer is not among the most common types of cancer in Brazil [2]; its incidence rises globally with the highest rates in developed countries and accounts for 2% of the global cancer burden [3, 4].

Cancer and its treatment are severely debilitating and are associated with health-related quality of life (HRQoL); thereby it is well accepted to consider its impact when making patient management or treatment decisions [5, 6]. Quality of life is defined as a subjective multidimensional construct representing functional status, psychosocial well-being, health

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perceptions, and disease/treatment-related symptoms [7]. Then individual characteristics among cancer patients such as functional impairment, co-morbidity, and psychosocial disabilities have predictive value for HRQoL [6].

Malnutrition is an independent factor for the deterioration of the HRQoL, and a low HRQoL is associated with nutrition-related symptoms and weight loss [8]. Its prevalence in patients with cancer has been reported to range from about 20% to more than 70% due to many factors, as impaired food intake, increased energy and protein needs, decreased anabolic stimuli, and altered metabolism in different organs or tissues [9].

Frailty is considered as a biological syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, and causing vulnerability to adverse outcomes [10]. The relationship between malnutrition and frailty in older adults has been established, with a considerable overlap between both conditions. With the presence of chronic disease, such as cancer, rates of frailty increase significantly [11]. Furthermore, being frail is associated with worse HRQoL in the cancer population [6, 12].

Thus, cancer may simultaneously influence patient's nutritional status, HRQoL, and frailty, suggesting that there may be interrelations among these factors. Nonetheless, it is unknown about these interrelationships in patients with bladder and kidney cancer. Therefore, the aim of this study was to assess the impact of frailty and nutritional status in the HRQoL of patients with bladder or kidney cancer.

Methods

Study design and participants

This was a cross-sectional study performed at a referral cancer hospital in Rio de Janeiro, Brazil. A convenience sample of individuals were recruited from January to December 2018. Eligibility criteria were patients aged 20 years or older, registered with histologically confirmed bladder or kidney cancer from January 2016 to December 2017.

Exclusion criteria were patients in palliative care, referred for treatment at another hospital unit or started treatment at another hospital, those who did not return for beginning treatment, with a history of cancer in the last five years, dementia or other mental or clinical conditions that make it impossible to answer the questionnaires, and who did not agree to sign the consent form.

The National Cancer Institute Jose Alencar Gomes da Silva Committee of Ethics on Research approved this study (protocol number 54778216.7.0000.5274). All participants of the study gave their written informed consent.

Data collection

A trained nutritionist performed all measurements and questionnaires on the same day, with participants who were in any stage or type of curative treatment, in outpatient clinics or during hospitalization.

Sociodemographic and health characteristics

Individuals answered a questionnaire with sociodemographic information. Clinical data were collected from medical records, as well as information about the first type of cancer treatment and the performance of any other associated therapy, within 3 months. Cancer stage system followed the American Joint Committee on Cancer (AJCC) [13].

Patient-Generated Subjective Global Assessment (PG-SGA)

PG-SGA was assessed by the Portuguese version, validated for use in Brazil by Gonzalez et al. (2010) [14]. It consists of a questionnaire, developed from the method created by Ottery (1994) [15], specifically to meet the characteristics of adult cancer patients. It includes questions about symptoms of nutritional impact present in cancer patients; history of weight loss and food intake; function capacity; disease; age; metabolic stress and physical examination (deficit of subcutaneous fat mass or muscle and presence of edema or ascites). It provides a score (higher score indicates higher malnutrition risk), and categorizes patients into three distinct classes of nutritional status: A—well nourished or anabolic, B—moderately malnourished or suspected of being malnourished, and C—severely malnourished [14].

Anthropometrics measures

Weight was taken with participants wearing light clothes and barefoot or with socks (digital scale Filizola®, with maximum capacity of 150 kg), and height through the stadiometer attached to the scale. Body mass index (BMI) was calculated as body weight in kilograms divided by squared height in meters (kg/m^2).

Frailty

Frailty was assessed with the Frailty Phenotype defined by Fried et al. (2001) [10] and adapted to the Brazilian population [16], as the presence of at least 3 of the following criteria: (1) unintentional weight loss (5% of body weight in prior year); (2) low hand grip strength, measured with Jamar Hydraulic Hand Dynamometer (Sammons Preston TM, Canada) thrice in each hand alternately, obtaining the highest strength value (cut-off point was the lowest 20%, adjusted for sex and BMI); (3) self-report of exhaustion, identified by two questions from

the Center for Epidemiological Studies Depression scale, in the validated version translated to Portuguese by Silveira and Jorge (2000) [17]; (4) slow walking speed, where subjects walked 4.6 m straight path, with no obstacles, at their usual speed [18] (cut-off point was the slowest 20%, adjusted for sex and height); and (5) low physical activity level, assessed by a short version of the International Physical Activity Questionnaire, translated and validated for the Brazilian population [19] (the cut-off point was the lowest quintile of physical activity according to sex). Individuals with none of these characteristics were robust, whereas those with one or two were classified as pre-frail.

Health-related quality of life (HRQoL)

The European Organization for Research and Treatment of Cancer Quality of life questionnaire Core-30 third version (EORTC QLQ-C30), specific for oncology, validated and translated to Portuguese [20], was used to assess HRQoL.

The QLQ-C30 is a multidimensional questionnaire composed of five multi-item function scales, three multi-item symptom scales, five single-item symptom scales, one item that assesses the financial impact of the treatment, and a two-item global quality of life scale. For the functional scales and global health status, a higher score indicates better health, whereas a higher score in symptoms indicates a higher level of symptom burden. All scales, except global health status and financial difficulties, were summarized into summary score, using the model of Giesinger et al. (2016) [21].

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 20.0 (SPSS, Inc., Chicago, IL, USA).

The Kolgomorov-Smirnov test was applied to verify the normality of the distributions. The Student's t test was used to compare two continuous variables with normal distributions and ANOVA with post hoc Bonferroni test for three variables, whereas for not normal distribution the nonparametric Mann-Whitney or Kruskal-Wallis tests were performed. To compare categorical variables, the chi-square test or Fisher's exact test was used. Spearman's correlation tested the association between phenotype frailty and PG-SGA score, and Pearson correlation the association between frailty and age.

For the scales of the QLQ-C30 that were statistically different between the phenotypes of frailty and PG-SGA classifications, a regression model was applied to form the strength of the association between HRQoL and frailty or malnutrition. Multiple linear regression analysis was performed by the *Enter* method, considering the 95% confidence interval (CI), adjusting for confounders. The cofounders tested were age, sex, presence of metastasis, ongoing oncologic treatment

(radiotherapy, chemotherapy, or surgery in the last 30 days), presence of comorbidities, and performance status. Those with $p < 0.25$ in the univariate analysis, for each quality of life constructed scale and tumor location, were used for adjustments in the multivariate model. Homoscedasticity and possible biases of the model were analyzed by residual analysis and all assumptions were observed. To identify the explanatory power of the model, the coefficient of determination was calculated. The significance level of 5% probability was adopted in all cases ($p < 0.05$).

Results

Patients included and population characteristics

A total of 88 patients, 67% of those eligible for participation, were included in this study (Fig. 1), 44 with bladder and 44 with kidney cancer. Most of the population was male and the mean age were 65.9 and 58.6 years, respectively, for patients with bladder and kidney cancer. Surgery was the first treatment for both cancer sites, and the majority of the individuals did not have metastasis. Patients whose first treatment was surgical ($n = 80$), 11.3% ($n = 9$) also underwent chemotherapy within 3 months after surgery, and 2.5% ($n = 2$) chemotherapy and radiotherapy. Differences in sociodemographic and health characteristics of kidney and bladder cancer patients in smoking, years of education, and cancer staging were observed (Table 1).

Frailty phenotype and nutritional status

There was no difference between patients with bladder and kidney cancer regarding BMI, PG-SGA, gait speed, and grip strength, as described in Table 1. Most individuals were well-nourished; 29.5% and 43.3%, respectively, of the bladder and kidney cancer patients had some degree of malnutrition, according to PG-SGA.

Frailty prevalence was not statistically different in patients with bladder and kidney cancer (18.2% vs 20.5%, respectively). The majority of the individuals were pre-frail (47.7% in bladder cancer and 45.4% in kidney cancer) and 34.1% were robust for both cancer sites. Presence of frailty was not different between young adults (20 to 60 years old, 37.5% of the sample) and older people (> 60 years, 62.5% of the sample) with bladder ($r = 0.224$, $p = 0.14$) or kidney ($r = -0.101$, $p = 0.512$) cancer.

Frailty phenotype was associated with nutritional status according to PG-SGA. Most robust patients were classified as well-nourished (86.7% of those with bladder cancer and 80% with kidney cancer). While 75% and 88.9% of the frail, respectively, for bladder and kidney cancer, had suspected malnutrition or moderate and severe malnutrition. In addition,

Table 1 Study population characteristics

Variables	Patients with bladder cancer ($n = 44$)	Patients with kidney cancer ($n = 44$)	p value
Age (years)	65.9 (± 10.9)[e]	58.6 (± 13.1)[e]	0.006[a]
Sex			
Male (%)	70.5	54.5	0.12[b]
Female (%)	29.5	45.5	
Smoking			
Yes (%)	36.4	15.9	0.03[b]
No (%)	63.6	84.1	
Alcoholism			
Yes (%)	18.2	20.5	0.79[b]
No (%)	81.8	79.5	
Marital status			
Single (%)	2.3	11.4	
Married (%)	77.3	63.6	0.30[b]
Widower (%)	11.4	11.4	
Divorced (%)	9.1	13.6	
Income (basic salary)[g]			
< 1	2.3	6.8	
1 to < 3	67.4	50.0	0.92[c]
3 to < 5	25.6	29.5	
5 or +	0	11.4	
Undeclared	4.7	2.3	
Education (years)			
< 9	50	29.5	
9–12	25	50	0.04[b]
> 12	25	20.5	
Comorbidities			
No (%)	38.6	29.6	
Hypertension (%)	36.4	63.6	0.15[c]
Diabetes (%)	11.4	0	
Hypertension and diabetes (%)	9.0	6.8	
Others (%)	4.6	0	
Performance status			
0 (%)	61.4	56.8	0.87[c]
1 (%)	25.0	22.7	
2 (%)	9.1	15.9	
3 (%)	4.5	4.5	
Tumor histological type (%)			
Renal cell carcinoma			
Clear cell		74.4	
Papillary		4.7	
Chromophobe		9.3	
Low-grade urothelial carcinoma	36.4		
High-grade urothelial carcinoma	54.5		
Adenocarcinoma	4.6		
Others	4.5	11.6	
Cancer stage			
Unavailable data (%)	43.2	20.5	
Stage I (%)	25	22.7	
Stage II (%)	11.4	18.2	0.02[b]

Table 1 (continued)

Variables	Patients with bladder cancer ($n = 44$)	Patients with kidney cancer ($n = 44$)	p value
Stage III (%)	11.4	4.5	
Stage IV (%)	9.1	34.1	
Presence of metastasis			
Yes (%)	9.1	36.4	0.002[b]
No (%)	90.9	63.6	
Treatment phase			
Pretreatment (%)	9.1	25	0.06[c]
Ongoing treatment (%)	47.7	27.3	
Post treatment (%)	43.2	47.7	
First cancer treatment			
Surgery (%)	90.9	90.9	
Chemotherapy (%)	6.8	6.8	1.00[c]
Radiotherapy (%)	2.3	0	
Other (%)	0	2.3	
Current weight (kg)	72 (48.3–122.5)[f]	79 (54–108)[f]	0.14[d]
Usual weight (kg)	72 (53–150)[f]	78 (56–115)[f]	0.16[d]
Height (m)	1.66 (± 0.9)[e]	1.65 (± 0.11)[e]	0.54[a]
BMI (kg/m^2)	27.08 (± 5.2)[e]	28.9 (± 3.8)[e]	0.65[a]
PG-SGA, score	2.5 (1–15)[f]	3.0 (1–24)[f]	1.83[d]
PG-SGA, classification			
A (%)	70.5	56.8	0.44[c]
B (%)	27.3	38.6	
C (%)	2.2	4.6	
Grip strength (kg)	29.9 (± 10.1)[e]	30.0 (± 10.6)[e]	0.7[a]
Gait speed (s)	4.4 (2.6–9.8)[f]	4.1 (3–9.3)[f]	0.35[d]

SD standard deviation, *min* minimum, *max* maximum, *BMI* body mass index, *PG-SGA* Patient-Generated Subjective Global Assessment

[a] Student's *t*-test

[b] Pearson chi-square test

[c] Fisher's exact test

[d] Mann-Whitney test

[e] Mean (± standard deviation)

[f] Median (minimum–maximum)

[g] Basic salary in Brazil in 2018 was R$ 954.00

it was found that PG-SGA score was significantly higher among frail individuals (Fig. 2). No significant difference was observed between the patients' nutritional status and frailty, according to the treatment phase in both cancers sites, bladder ($p = 0.257$) or kidney ($p = 0.369$).

The impact of frailty and nutritional status on HRQoL

There was no significant difference in HRQoL outcomes of patients with bladder and kidney cancer according to global health status, functional scales, and summary score. Subjects classified as frail (Table 2) and malnourished (Table 3) had worse physical functioning, role functioning, and summary score ($p < 0.05$). While in relation to the symptom scale, there was a higher occurrence of fatigue and pain in both cancer sites.

After adjusted, at both tumor locations being frail or malnourished continued to be associated with poor role functioning and summary score of HRQoL, and reduced physical functioning was associated with frailty (Table 4).

Bladder cancer

Frail patients had worse HRQoL in physical and role functioning, fatigue, and summary score than pre-frails and robust, as well as malnourished compared to well nourished.
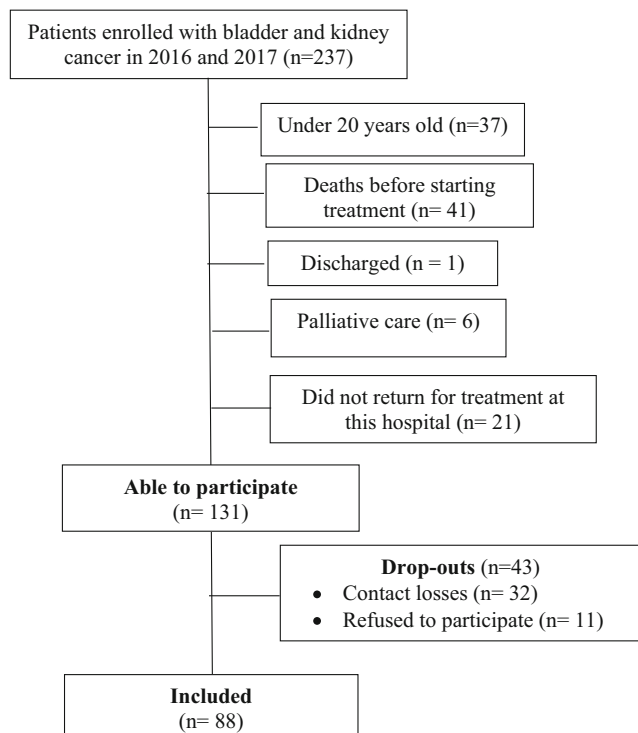
Fig. 1 Flowchart of the inclusion and exclusion process of the study

Moreover, pain was greater in frails and malnourished than in the robust or well nourished.

Frailty accounted for a reduction of 41% on physical functioning, 33% in role functioning, and 13% in summary score. Malnutrition diminished 25% of role functioning and 14% of summary score.

Regarding symptoms, being malnourished increased pain by 41%, while frailty predicted 26% of appetite loss. Insomnia was higher in those patients classified as moderately or severely malnourished. However, in multiple linear regression analysis adjusted for sex, *performance status*, and ongoing treatment, it was not significant ($p = 0.181$)

Kidney cancer

Patients with kidney cancer when frail or malnourished worsened global health status (GHS); physical, role, and emotional functioning; fatigue; nausea and vomiting; pain; and summary score than pre-frails and robust or well-nourished. Appetite loss was associated with frailty but not to nutritional status in both tumor sites.

After adjusting, patients with kidney cancer when frail or malnourished kept a worse GHS, even as role functioning. They also had worse emotional and cognitive functioning ($p < 0.05$); nevertheless, these did not remain after adjustment.

Being frail predicted 32% of nausea and vomiting, 44% of pain, and 24% of appetite loss. While malnutrition increased pain by 24%.

Discussion

To our knowledge, this is the first study to indicate the impact of frailty and nutritional status on HRQoL of patients with bladder or kidney cancer. An impaired summary score was observed in those individuals with frailty and/or malnutrition.

Frailty phenotype and PG-SGA have correspondence in their constructs, like weight loss, functional capacity, and gastrointestinal tract symptoms [10, 14, 15]; thereby, these conditions overlap in their occurrence. Because of these, we analyzed the impact of frailty and nutritional status in HRQoL apart in the multivariate models. The association between malnutrition and frailty was confirmed in the present study, as seen before [11, 22].
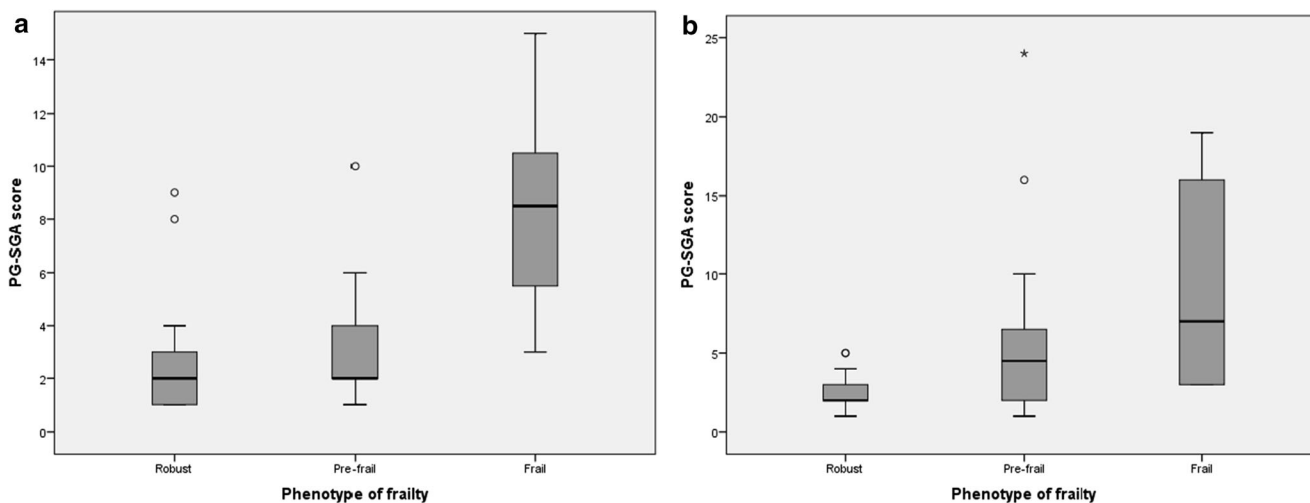

Fig. 2 PG-SGA score and phenotype of frailty. *PG-SGA* Patient-Generated Subjective Global Assessment. (a) Patients with bladder cancer ($n = 44$)—Spearman's correlation: $r = 0.491$, $p = 0.001$. (b) Patients with kidney cancer ($n = 44$)—Spearman's correlation: $r = 0.519$, $p < 0.001$

Table 2 Quality of life and frailty phenotype of patients with bladder and kidney cancer

Quality of life constructed scales	Bladder cancer				Kidney cancer			
	Robust ($n = 15$) Mean ($\pm$ SD)	Pre-frail ($n = 21$) Mean ($\pm$ SD)	Frail ($n = 8$) Mean ($\pm$ SD)	p value[a]	Robust ($n = 15$) Mean ($\pm$ SD)	Pre-frail ($n = 20$) Mean ($\pm$ SD)	Frail ($n = 9$) Mean ($\pm$ SD)	p value[a]
Global health status	74.4 ($\pm$ 17.9)	79.0 ($\pm$ 24.8)	63.5 ($\pm$ 19.4)	0.245	85.5 ($\pm$ 14.9)[b]	79.6 ($\pm$ 21.5)[c]	50.9 ($\pm$ 24.8)[b, c]	0.001
Physical functioning	92.9 ($\pm$ 11.9)[b]	89.2 ($\pm$ 16.2)[c]	45.8 ($\pm$ 29.4)[b, c]	0.000	93.3 ($\pm$ 11.5)[b]	81.7 ($\pm$ 20.4)[c]	39.2 ($\pm$ 29.3)[b, c]	0.000
Role functioning	96.7 ($\pm$ 12.9)[b]	88.9 ($\pm$ 23.8)[c]	52.1 ($\pm$ 42.2)[b, c]	0.001	98.9 ($\pm$ 4.3)[b]	77.5 ($\pm$ 32.5)[b, c]	12.9 ($\pm$ 23.2)[b, c]	0.000
Emotional functioning	60 ($\pm$ 33.5)	66.7 ($\pm$ 37.8)	51.0 ($\pm$ 33.7)	0.567	73.3 ($\pm$ 15.8)[b]	59.2 ($\pm$ 36.2)[c]	21.3 ($\pm$ 31.7)[b, c]	0.001
Cognitive functioning	83.3 ($\pm$ 16.7)	77.8 ($\pm$ 28)	93.7 ($\pm$ 8.6)	0.231	91.1 ($\pm$ 12.4)[b]	71.7 ($\pm$ 27.6)	61.1 ($\pm$ 26.3)[b]	0.009
Social functioning	90.0 ($\pm$ 18.7)	87.3 ($\pm$ 25.8)[c]	77.1 ($\pm$ 28.1)	0.463	92.2 ($\pm$ 10.7)[b]	83.3 ($\pm$ 22.9)	59.2 ($\pm$ 39.2)[b]	0.009
Fatigue	8.1 ($\pm$ 11.5)[b]	19.6 ($\pm$ 32.6)[c]	54.2 ($\pm$ 43.4)[b, c]	0.004	8.1 ($\pm$ 13.6)[b]	20.5 ($\pm$ 23.9)[c]	48.1 ($\pm$ 36.8)[b, c]	0.002
Nausea and vomiting	0	0.8 ($\pm$ 3.6)	0	0.589	0[b]	2.5 ($\pm$ 8.1)[c]	33.3 ($\pm$ 36.3)[b, c]	0.000
Pain	8.9 ($\pm$ 12.4)[b]	21.4 ($\pm$ 36.7)	54.2 ($\pm$ 44.3)[b]	0.010	12.2 ($\pm$ 23.1)[b]	23.2 ($\pm$ 29.8)[c]	83.3 ($\pm$ 33.3)[b, c]	0.000
Dyspnea	4.4 ($\pm$ 11.7)	6.3 ($\pm$ 22.6)	25.0 ($\pm$ 38.8)	0.117	2.2 ($\pm$ 8.6)	5.0 ($\pm$ 12.2)	3.7 ($\pm$ 11.1)	0.758
Insomnia	24.2 ($\pm$ 32)	23.8 ($\pm$ 30)	45.8 ($\pm$ 50.2)	0.292	24.2 ($\pm$ 36.6)	25.0 ($\pm$ 33.9)	44.4 ($\pm$ 21.5)	0.343
Appetite loss	2.2 ($\pm$ 8.6)[b]	1.6 ($\pm$ 7.2)[c]	33.3 ($\pm$ 47)[b, c]	0.002	2.2 ($\pm$ 8.6)[b]	1.7 ($\pm$ 7.4)[c]	29.6 ($\pm$ 42.3)[b, c]	0.003
Constipation	6.7 ($\pm$ 18.7)	3.2 ($\pm$ 10)	16.7 ($\pm$ 35.6)	0.266	11.1 ($\pm$ 30)	16.7 ($\pm$ 33.3)	18.5 ($\pm$ 24.2)	0.812
Diarrhea	4.4 ($\pm$ 11.7)	4.8 ($\pm$ 11.9)	0	0.551	0[b]	0[c]	18.5 ($\pm$ 37.7)[b, c]	0.018
Financial difficulties	26.7 ($\pm$ 38.2)	14.3 ($\pm$ 29)	12.5 ($\pm$ 24.8)	0.449	6.7 ($\pm$ 13.8)	31.7 ($\pm$ 45.2)	44.4 ($\pm$ 47.1)	0.050
Summary score	89.5 ($\pm$ 7.6)[b]	86.8 ($\pm$ 14.5)[c]	68.5 ($\pm$ 17)[b, c]	0.002	91.4 ($\pm$ 6.9)[b]	82.9 ($\pm$ 13.7)[c]	54.9 ($\pm$ 16.7)[b, c]	0.000

SD standard deviation

[a] ANOVA

[b, c] Post hoc test Bonferroni = $p < 0.05$

Table 3 Quality of life according to nutritional status of patients with bladder and kidney cancer

Quality of life constructed scales	Bladder cancer			Kidney cancer		
	PG-SGA classification			PG-SGA classification		
	A (n = 29) Mean (± SD)	B + C (n = 15) Mean (± SD)	p value[a]	A (n = 25) Mean (± SD)	B + C (n = 19) Mean (± SD)	p value[a]
Global health status	78.2 (± 19.3)	67.8 (± 25.7)	0.140	86.7 (± 17.5)	61.4 (± 23.4)	0.000
Physical functioning	89.2 (± 18.1)	69.8 (± 31.3)	0.039	88.5 (± 16.7)	61.7 (± 32.9)	0.003
Role functioning	94.8 (± 14.2)	65.5 (± 40.6)	0.016	90.7 (± 24.6)	46.5 (± 42.2)	0.000
Emotional functioning	69 (± 31.7)	47.2 (± 38.7)	0.052	67.0 (± 30)	42.1 (± 36.3)	0.017
Cognitive functioning	85.1 (± 16.9)	77.8 (± 30.7)	0.313	83.3 (± 19.2)	66.7 (± 30)	0.043
Social functioning	90.8 (± 17.6)	77.8 (± 31.9)	0.158	86.7 (± 22)	74.6 (± 30.6)	0.135
Fatigue	11.5 (± 17.7)	42.2 (± 38.7)	0.023	12.4 (± 21.1)	34.5 (± 31.2)	0.008
Nausea and vomiting	0	1.1 (± 4.3)	0.334	1.3 (± 6.7)	16.7 (± 29.4)	0.038
Pain	6.3 (± 11.2)	55.5 (± 43)	0.001	14.7 (± 26.5)	54.4 (± 41.1)	0.001
Dyspnea	6.9(± 20.7)	13.3 (± 30.3)	0.410	1.3 (± 6.7)	7.0 (± 14)	0.114
Insomnia	18.4 (± 27.6)	46.7 (± 41.4)	0.027	21.3 (± 31.7)	38.6 (± 38.9)	0.113
Appetite loss	2.3 (± 8.6)	17.8 (± 37.5)	0.136	1.3 (± 6.7)	15.8 (± 32.1)	0.069
Constipation	4.6 (± 14.7)	11.1 (± 27.2)	0.306	16.0 (± 34.8)	14.0 (± 23.1)	0.833
Diarrhea	4.6 (± 11.7)	2.2 (± 8.6)	0.492	0	8.8 (± 26.8)	0.172
Financial difficulties	14.9(± 30.3)	24.4 (± 34.4)	0.352	14.7 (± 30.6)	40.3 (± 46.6)	0.046
Summary score	90.3 (± 8.2)	72.9 (± 18.3)	0.003	88.3 (± 11.7)	69.4 (± 19.9)	0.001

SD standard deviation, *PG-SGA* Patient-Generated Subjective Global Assessment

[a] Student's *t*-test

We observed that among 18% to 20% of our patients were frail, similar to other studies that showed yet associations between frailty and cancer [6, 12, 23–27], but these were in the older population. In the present study, presence of frailty was not different between young and older adults, reinforcing that dealing with a cancer diagnosis, independently of the age, is associated with frailty and worse quality of life [6]. Kumar et al. have also concluded that frailty was independent of chronologic age [25]. Even more importantly, our results showed that frailty negatively influenced physical and role functioning and summary score of HRQoL in bladder or kidney cancer patients. As well as Arruda et al. had demonstrated that being frail were strongly associated with poor HRQoL in Global Health Status and in the summary score of elderly women with epithelial ovarian cancer, so as age was not a significant determinant of HRQoL [12]. Cancer and its therapeutic interventions are significant stressors that have the potential to challenge physiological reserve, resulting poor outcomes, as short-term surgical morbidity, surgical mortality, less likely initiate chemotherapy, shorter overall survival, and worse HRQoL [6, 12, 25, 26], even as frailty is independently associated with lower patient-reported quality of life [6, 28].

Appetite disorders, like anorexia, may be a common problem among oncologic patients. The causes of lack of appetite are diverse: systemic inflammatory response, cancer treatment, anatomic changes after surgery, nutrient deficiency, and psychological symptoms like anxiety and depression [29]. In a Brazilian multicenter study with 4783 cancer patients, loss of appetite was an independent factor associated with malnutrition (OR 1.93, 95% CI 1.64–2.28) [30]. It may affect not only nutritional status but also quality of life [31]. Nevertheless, in the present study, the negative impact of appetite loss on HRQoL of malnourished patients was not seen, probably because it is already part of PG-SGA construct, used to evaluate nutritional status. On the other hand, frailty contributed about 25% of the loss of appetite, adversely affecting the quality of life.

The use of objective parameters (anthropometric, chemical, and immunological) to assess nutritional status has been questioned, as they are affected by many factors, not only by nutritional features. Therefore, PG-SGA seems to be more sensitive, because it detects early stages of malnutrition [14]. The present research, using PG-SGA, showed that around 29 and 41% of the bladder and kidney cancer patients had some degree of malnutrition. Other studies with bladder neoplasm had reported a range from about 16–33% [32, 33]. While few data exist on the prevalence of malnourishment on kidney cancer, Morgan et al. had described that 23% of their sample of patients with renal cell carcinoma had nutritional deficiency [34]. The presence of a tumor and its treatment impact on a number of factors, such as metabolic alterations and reduced food

Table 4 Impact of frailty and nutritional status in quality of life constructed scales and summary score of patients with bladder and kidney cancer

Variables	Bladder cancer (n = 44)						Kidney cancer (n = 44)					
	Models	B	95% CI	β	AR²	p value	Models	B	95% CI	β	AR²	p value
Global health status	Univariate						Univariate					
	Frail	−44.907	−59.0 to −30.8	−0.703	0.483	<0.001	Frail	−31.217	−46.5 to −16.0	−0.538	0.272	<0.001
	PG-SGA (B+C)	−21.937	−36.9 to −6.9	−0.415	0.152	0.005	PG-SGA (B+C)	−25.263	−37.7 to −12.8	−0.534	0.268	<0.001
	Multivariate[a,c,d,f]						Multivariate[a,b,c,d]					
							Frail	−27.710	−49.5 to −5.9	−0.477	0.255	0.014
							PG-SGA (B+C)	−22.219	−36.4 to −8.0	−0.470	0.307	0.003
Physical functioning	Univariate						Univariate					
	Frail	−40.959	−57.7 to −24.2	−0.641	0.449	<0.001	Frail	−47.407	−69.9 to −31.9	−0.689	0.462	<0.001
	PG-SGA (B+C)	−15.605	−32.2 to 1.0	−0.295	0.172	0.065	PG-SGA (B+C)	−26.779	−42.1 to −11.4	−0.478	0.210	0.001
	Multivariate[a,d,f]						Multivariate[b,c,d,e,f]					
							Frail	−33.182	−52.2 to −14.1	−0.482	0.593	0.001
							PG-SGA (B+C)	−11.004	−25.5 to 3.5	−0.196	0.489	0.132
Role functioning	Univariate						Univariate					
	Frail	−40.046	−59.9 to −20.2	−0.532	0.266	<0.001	Frail	−73.704	−93.4 to −54.0	−0.759	0.566	<0.001
	PG-SGA (B+C)	−31.905	−48.6 to −15.2	−0.512	0.244	<0.001	PG-SGA (B+C)	−44.175	−64.6 to −23.7	−0.558	0.296	<0.001
	Multivariate[a,d,f]						Multivariate[a,b,c,d,e]					
	Frail	−32.845	−55.6 to −10.1	−0.436	0.253	0.006	Frail	−43.793	−65.8 to −21.8	−0.451	0.731	<0.001
	PG-SGA (B+C)	−25.575	−44.2 to −6.9	−0.410	0.239	0.009	PG-SGA (B+C)	−21.995	−38.2 to −5.7	−0.278	0.677	0.009
Fatigue	Univariate						Univariate					
	Frail	39.352	15.8 to 62.9	0.462	0.195	0.002	Frail	32.910	14.2 to 51.6	0.481	0.213	0.001
	PG-SGA (B+C)	34.127	14.9 to 53.3	0.484	0.216	0.001	PG-SGA (B+C)	22.058	6.1 to 38.0	0.396	0.137	0.008
	Multivariate[a,d,f]						Multivariate[a,b,c,e]					
							Frail	15.503	−9.0 to 40.0	0.227	0.324	0.208
							PG-SGA (B+C)	12.731	−3.7 to 29.1	0.229	0.338	0.124
Nausea and vomiting	Univariate						Univariate					
	Frail	17.912	−37.8 to 61.9	0.210	0.401	0.125	Frail	31.905	19.2 to 44.6	0.617	0.366	<0.001
	PG-SGA (B+C)	18.382	−0.02 to 36.8	0.261	0.423	0.050	PG-SGA (B+C)	15.333	3.1 to 27.5	0.364	0.112	0.015
							Multivariate[a,b,c,d]					
							Frail	32.459	15.2 to 49.7	0.627	0.411	<0.001
							PG-SGA (B+C)	10.178	3.1 to 23.5	0.242	0.234	0.130
Pain	Univariate						Univariate					
	Frail	37.963	12.4 to 63.5	0.420	0.157	0.005	Frail	64.762	43.2 to 86.3	0.683	0.454	<0.001
	PG-SGA (B+C)	51.667	34.8 to 68.5	0.690	0.464	<0.001	PG-SGA (B+C)	39.719	19.1 to 60.3	0.514	0.247	<0.001
	Multivariate[d,e,f]						Multivariate[a,b,c,d]					

Table 4 (continued)

	Bladder cancer (n = 44)					Kidney cancer (n = 44)				
	B	95% CI	β	AR^2	p	B	95% CI	β	AR^2	p
Appetite loss										
Univariate										
Frail	22.181	− 3.9 to 48.3	0.245	0.330	0.094	43.777	15.8 to 71.7	0.462	0.539	0.003
PG-SGA (B + C)	41.644	22.4 to 60.9	0.557	0.517	< 0.001	24.174	4.4 to 43.9	0.313	0.498	0.018
Multivariate (Bladder [c, d]; Kidney [b, c, d])										
Frail	31.481	15.3 to 47.6	0.518	0.251	< 0.001	27.725	12.8 to 42.6	0.501	0.233	0.001
PG-SGA (B + C)	25.910	7.4 to 44.4	0.427	0.247	0.007	24.417	2.9 to 45.9	0.441	0.185	0.027
Summary score										
Univariate										
Frail	− 19.418	− 29.6 to − 9.2	− 0.509	0.241	< 0.001	− 31.650	− 41.5 to − 21.8	− 0.709	0.490	< 0.001
PG-SGA (B + C)	− 18.375	− 26.4 to − 10.4	− 0.581	0.322	< 0.001	− 18.919	− 28.6 to − 9.2	− 0.520	0.253	< 0.001
Multivariate (Bladder [d, f]; Kidney [a, b, c, d, e])										
Frail	− 13.233	− 24.3 to − 2.1	− 0.347	0.305	0.021	− 21.690	− 32.9 to − 10.4	− 0.486	0.667	< 0.001
PG-SGA (B + C)	− 14.111	− 22.6 to − 5.6	− 0.446	0.380	0.002	− 10.844	− 19.1 to − 2.5	− 0.298	0.604	0.012

Multiple linear regression analysis was performed when the predictors tested (to be frail or classification B or C for PG-SGA) were significant according to the univariate analysis. The cofounders presented in the multivariate models were those with $p < 0.25$ when tested alone for each dependent variable

PG-SGA (B + C) classification B or C for Patient-Generated Subjective Global Assessment, CI confidence interval, B unstandardized coefficients, β standardized coefficients, AR^2 adjusted R^2

Cofounders tested:

[a] Age

[b] Presence of metastasis

[c] Ongoing treatment

[d] Performance status

[e] Sex

[f] Presence of comorbidities

intake, that determine nutritional status and contribute to impairment of physical, psychological, and social conditions, simultaneously influencing HRQoL [8, 35]. We also demonstrated that malnutrition was a significant independent predictor of diminished HRQoL with a reduction of role function and summary score and an increase of pain in patients with bladder cancer. Furthermore, an impairment of summary score, GHS, physical and role function, and rise of pain in kidney cancer. Other study of HRQoL in patients with lung cancer had demonstrated that the well-nourished respondents evaluated their quality of life better in all functional scales and presented less intensive symptoms in general [36]. These findings are consistent with Nourissat et al., which observed that the scores for physical, emotional, cognitive, and social functions were significantly higher for those patients who had not lost weight. For these patients the symptom scores were lower, compared with patients who had lost more than 10% of weight [37].

The strength of this research is to be the first study reporting frailty and malnutrition in patients with bladder or kidney cancer and their impact in HRQoL. Moreover, data collection for frailty, malnutrition, and HRQoL were based on widely used and well-validated instruments. Nonetheless, we noted limitations as the reduced sample, because of the high number of deaths before the start of the study and loss of contact with patients during the study recruitment; the study population was not at the same treatment point, and since this was an observational cross-sectional study, a causal effect between frailty, malnutrition, and HRQoL could not be established. The results found in this study represent the population of a reference center for the treatment of urological cancer in Brazil. However, due to the sample size, we cannot confirm that these results are representative for all patients with bladder and kidney cancer. Further well-designed studies, with a larger number of patients, need to be carried out to confirm these data.

Conclusion

The present study, with bladder and kidney cancer patients, demonstrated that frailty occurs regardless of older ages, and there was a high prevalence of pre-frailty. In addition, we observed a strong association between frailty phenotype and nutritional status, by PG-PGSGA, which share some common determinants. Moreover, frailty and malnutrition negatively influenced HRQoL in several aspects, especially summary score. These findings are important for future nutrition interventions. By improving or preventing frailty and

malnourishment, we could enrich quality of life of these populations at any time during oncologic treatment.

Author contributions Patrícia Fonseca dos Reis: 1. design, acquisition, analysis, and interpretation of data; 2. drafting the article and critical revision of important intellectual content; 3. final approval of the version to be submitted; 4. agreement to be accountable for all aspects of the work.

Patrícia Sousa de França: 1. acquisition of data; 2. critical revision of important intellectual content; 3. final approval of the version to be submitted; 4. agreement to be accountable for all aspects of the work.

Mylena Pinto dos Santos: 1. acquisition of data; 2. critical revision of important intellectual content; 3. final approval of the version to be submitted; 4. agreement to be accountable for all aspects of the work.

Renata Brum Martucci: 1. substantial contributions to the conception or design of the work; 2. critical revision of important intellectual content; 3. final approval of the version to be submitted; 4. agreement to be accountable for all aspects of the work.

Declarations

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