



Malnutrition in patients who underwent surgery for spinal metastases

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Background: Malnutrition is common among cancer patients and has been associated with increased morbidity and mortality. The primary objective of this study was to evaluate the nutritional status of patients who underwent surgical treatment for spinal metastases. In addition, the association between nutritional status and length of stay, health related quality of life (HRQOL), the occurrence of adverse events and survival was investigated.

Methods: A single center prospective observational cohort study including patients with spinal metastases who underwent surgical treatment was performed. Demographic, diagnostic, treatment, and HRQOL (SOSGOQ2.0 and EQ-5D-3L) data were prospectively collected at baseline and 12 weeks post-treatment. Nutritional status was evaluated with the Patient-Generated Subjective Global Assessment (PG-SGA).

Results: A total of 39 patients were included. Malnutrition as determined by the PG-SGA was present in 36 (92%) of the patients, of whom 32 (82%) were moderately malnourished and 4 (10%) were severely malnourished. Malnourishment was associated with lower baseline SOSGOQ2.0 total scores, SOSGOQ2.0 physical function, mental health and social functioning scores, EQ-5D total scores and EQ-5D mobility scores. No association between malnutrition and survival could be determined.

Conclusions: The prevalence of malnutrition among surgically treated patients with spinal metastases is high. Malnutrition demonstrated to be associated with lower baseline HRQOL scores. Future larger studies are needed to further investigate the prognostic significance of malnutrition.

Keywords: Spine; tumor; spinal neoplasm; malnutrition

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Introduction

The spine is the most common site for bony metastases, with up to 70% of the patients with advanced cancer developing spinal metastases (1). Metastatic spine disease can result in debilitating pain and increases the risk for pathological fracture, neurological deficits, spinal cord compression and spinal instability. Proper management of metastatic spinal disease is therefore essential. Radiotherapy has been the standard of care for the treatment of uncomplicated

painful spinal metastases with surgery generally reserved for patients with pain caused by mechanical instability and/or symptomatic spinal cord compression (2). Although surgery has shown to result in significant improvements in health-related quality of life (HRQOL), it has also been associated with potential high rates of adverse events (3-6). Due to the palliative nature of the procedures, the benefits of surgery should outweigh the risks; accurate prediction of survival and associated surgical risks are therefore important as it may assist in determining the type and extent of treatment

offered. In order to optimize treatment selection, we need to identify prognostic factors that are ideally easy to assess, reliable and modifiable.

Nutritional status as a prognostic factor has been gaining attention in the oncology literature (7-10). Malnutrition has been reported in 40% to 80% of the cancer patients, and has been associated with profound consequences such as increased morbidity, mortality, risk of complications, length of stay and decreased patient reported treatment outcomes (11-14). Malnutrition in a cancer patient is complex and is influenced by different factors including physical symptoms, nutritional intake, caloric need, systemic inflammation, muscle mass depletion and treatment-related side effects (9), which are not simply managed by increasing caloric intake. Historically, nutritional status has been assessed using laboratory values, anthropometric measurements and various scoring systems, reflecting the lack of consensus for a gold standard for assessing nutritional status and defining malnutrition. More recently, the Patient-Generated Subjective Global Assessment (PG-SGA) is increasingly being used to assess patients' nutritional status and has been validated in the oncology population (13,15).

To date there is a paucity of literature regarding the nutritional status of patients with spinal metastases and its potential prognostic significance. The primary objective of this study was, therefore, to evaluate the nutritional status of patients who underwent surgical treatment for spinal metastases. In addition, the association between the pre-operative nutritional status and length of stay, HRQOL, the occurrence of adverse events and survival was explored.

Methods

A single center (University Medical Center Utrecht, The Netherlands) prospective observational cohort study of patients with spinal metastases who were over the age of 18 and underwent surgical stabilization with or without postoperative radiotherapy for spinal metastases was performed. Patients were not eligible for inclusion if they were diagnosed with a primary spinal bone tumor or a primary central nervous system tumor, or were unable to complete the nutritional assessment. The local institutional review board approved the research protocol and all patients provided written informed consent.

Data regarding demographics, primary tumor diagnosis, surgical and/or radiotherapy treatment, neurological status [American Spinal Injury Association (ASIA) score] (16), Karnofsky performance (17) status, adverse events and

survival were prospectively collected. Governmental databases were accessed to retrieve information regarding survival. Quality of life was evaluated at baseline, 6- and 12-week follow-up using the Spine Oncology Study Group Outcomes Questionnaire (SOSGOQ2.0) and the Euroqol five dimensions (EQ-5D-3L). The SOSGOQ2.0 is a spine oncologic specific HRQOL measure, which includes 20 items divided in five domains including physical functioning, mental health, pain, neurological function and social functioning (18,19). A higher score on the SOSGOQ and the EQ-5D-3L represents a better quality of life. The EQ-5D is a generic HRQOL measure based on the evaluation of five HRQOL dimensions.

Nutritional status was evaluated at baseline using the short-form of the PG-SGA (13). The short form of the PG-SGA is completed by the patient and includes an assessment of weight, weight change, nutritional intake, physical symptoms and performance status. The sum of the different assessments results in a numeric risk score, with a higher score denoting a greater risk for malnutrition and a need for dietary consultation. A score of 9 or above denotes a critical need for a nutritional intervention. In addition to the numeric score, patients were assigned a PG-SGA global score based on the short form assessments (13,15). Three PG-SGA global scores can be distinguished indicating: (I) a well-nourished patient, (II) suspected malnutrition and (III) malnutrition.

Statistics

Demographic and HRQOL data were summarized using descriptive statistics (mean and standard deviation (SD) or median and range for continuous variables; absolute number and frequency for categorical variables). The independent samples *t*-test, Wilcoxon rank sum test and one-way ANOVA were used to compare differences in continuous data; Chi-square and Fisher's exact tests were used for categorical data. The SOSGOQ2.0 and EQ-5D-3L scores were analyzed by their total scores and by their subdomains respectively. Univariate logistic regression and linear regression were used to determine the association between nutritional status and the occurrence of complications, length of stay, EQ-5D scores and SOSGOQ2.0 scores and survival. Kaplan-Meier survival curves were drawn and patients who did not reach the 12 weeks follow-up time point were censored. The log-rank test was used to compare survival between the three PG-SGA categories. Cox proportional hazards analyses were used to assess the

Table 1 Baseline characteristics

Characteristics	Value
Age at surgery, mean (SD) (years)	62.2 (10.5) (N=39)
Gender, n [%]	N=39
Female	19 [49]
Male	20 [51]
Weight, mean (SD) (kg)	75.2 (12.4) (N=39)
BMI, mean (SD) (kg/m ²)	26.1 (3.9) (N=39)
Karnofsky performance status, n [%]	N=39
40	3 [8]
50	8 [21]
60	3 [8]
70	14 [36]
80	6 [15]
90	5 [13]
Site of the primary cancer, n [%]	N=39
Breast	10 [26]
Lung	7 [18]
Prostate	3 [8]
Kidney	7 [18]
Other	12 [31]
ASIA Impairment Scale, n [%]	N=39
A–C	0 [0]
D	8 [33]
E	31 [67]
Tomita classification, n [%]	N=38
2–3	3 [8]
4–5	18 [47]
6–7	17 [45]
8–10	0 [0]
Tokuhashi classification, n [%]	N=38
0–8	10 [26]
9–11	21 [55]
12–15	7 [18]
Subjective Global Assessment, n [%]	N=39
Well-nourished (A)	3 [8]
Malnourished	36 [92]
Moderately malnourished (B)	32 [82]
Severely malnourished (C)	4 [10]

correlation between the numerical PGSGA risk scores and survival. Given the descriptive and explorative nature of the study no ante hoc sample size calculation was performed. All statistical analyses were performed using IBM SPSS statistics for Macintosh, version 24.0 (Armonk, NY: IBM Corp). The significance level was set at $P < 0.05$.

Results

Demographics

A total of 39 patients were included in the final analysis; 19 patients were male (49%) and the mean age was 62.2 years (SD 10.5). The most common primary tumor was breast cancer (N=10) followed by renal cell cancer (N=7) and lung cancer (N=7). Pre-operatively, 31 patients presented neurologically intact (ASIA E), eight patients presented with ASIA D and none of patients presented with ASIA A–C. Baseline characteristics of the study population are displayed in *Table 1*.

Surgical details

A posterior surgical approach was used in all operations. Five or more vertebral bodies were instrumented in 14 patients (36%), four vertebral bodies in three patients (8%), and three vertebral bodies in 21 patients (54%). One patient underwent cement augmentation of a single vertebral body (3%). The median operating time was 120 minutes (range, 60–180 minutes); median blood loss was 100 mL (range, 50–1,400 mL). Fourteen patients received post-operative adjuvant radiotherapy; the most common fractionation schedule was 10×3 Gy in nine patients, followed by 1×8 Gy in three patients, and 5×4 Gy in one patient.

Nutritional status

According to the PG-SGA short form assessment, 11 of 39 patients did not require a dietary intervention (score 0–3), 28 required a dietary intervention of which in 10 patients a critical need for an intervention was indicated (score of 9 or higher). Based on the PG-SGA global scores, only 3 of 39 patients were well-nourished (global score A) and 36 (92%) were malnourished. Of the malnourished patients, 32 (82%) patients were moderately or suspected of being malnourished (global score B) and 4 (10%) patients were severely malnourished (global score C). Nutritional intake problems (e.g., less than usual or liquid food) were reported by 74% of the patients; 50% of the patients who had no

Table 2 Unadjusted HRQOL scores over time by Subjective Global Assessment (SGA) category

Variables	N	SGA A, mean (95% CI)	SGA B, mean (95% CI)	SGA C, mean (95% CI)	P value
SOSGOQ2.0 overall					
Baseline	39	68.3 (55.6–81.0)	51.4 (48.0–54.9)	51.3 (28.4–74.0)	0.015
12 weeks	25	67.4 (52.1–82.7)	63.2 (57.7–68.8)		0.582
SOSGOQ2.0 pain					
Baseline	38	55 (30.1–79.8)	45.6 (41.9–49.3)	51.2 (43.6–58.8)	0.197
12 weeks	25	53.3 (34.3–72.3)	54.7 (50.0–59.5)		0.826
SOSGOQ2.0 physical function					
Baseline	39	93.3 (64.6–111.0)	45.9 (36.8–55.1)	47.5 (–12.0 to 107.0)	0.017
12 weeks	26	90.0 (68.5–122.0)	56.6 (46.2–66.9)		0.022
SOSGOQ2.0 mental health					
Baseline	39	83.3 (47.5–119.0)	55.8 (48.0–63.7)	40.6 (–9.0 to 90.0)	0.054
12 weeks	25	79.2 (31.7–126.0)	81.5 (71.3–91.8)	81.5 (71.3–91.8)	0.909
SOSGOQ2.0 social function					
Baseline	39	41.6 (20.9–62.3)	53.3 (48.7–58.3)	61.1 (13.3–109.0)	0.203
12 weeks	25	47.2 (4.1–90.1)	60.9 (53.4–68.8)		0.205
EQ-5D summary index					
Baseline	37	0.77 (0.60–0.94)	0.44 (0.32–0.55)	0.48 (0.10–0.87)	0.190
12 weeks	24	0.87 (0.58–1.15)	0.57 (0.42–0.73)		0.166

HRQOL, health related quality of life.

nutritional intake problems reported the presence of two or more physical symptoms, such as vomiting or mouth sores, impairing nutritional intake.

The median body mass index (BMI) for patients with a PG-SGA global score A was 24.4 (range, 22.9–32.6), compared to a median BMI of 25.2 (range, 19.2–35.9) for patients with a PG-SGA global score B and a median BMI of 22.8 (range, 22.3–29.7) for patients with a PG-SGA global score C.

HRQOL

At baseline, the mean SOSGOQ2.0 overall score was 68.3, 51.4, and 51.3 for patients with a PG-SGA global score A, B, and C ($P=0.015$), respectively. In addition, malnourished patients had worse baseline SOSGOQ2.0 physical function, social function and mental health scores compared to well-nourished patients. Comparison across all PG-SGA global scores at 12 weeks post-surgery, showed a mean

SOSGOQ2.0 overall score of 67.4 ($N=3$) for PG-SGA A patients, and a score of 63.2 ($N=22$) for the PG-SGA B and C patients combined ($P=0.582$) (Table 2).

Based on the numeric nutritional risk score, the mean SOSGOQ2.0 score was 57.7, 50.0, and 52.4 for patients with a PG-SGA score between 0–3, 4–8, and 9 or above ($P=0.133$), respectively. Comparison across all PG-SGA scores 12 weeks post-surgery, showed a mean overall SOSGOQ2.0 score of 63.9 ($N=7$) for patients with a PG-SGA score between 0–4, a score of 63.4 ($N=12$) for patients with a PG-SGA score between 5–8 and 64.2 ($N=5$) for patients with a PG-SGA score of 9 or above ($P=0.990$).

At baseline, the mean EQ-5D-3L summary index was 0.77, 0.44, and 0.48 for PG-SGA A, B, and C ($P=0.190$), respectively. In addition, the impairment in the ability to perform daily activities was greater in malnourished compared to well-nourished patients ($P=0.080$). Comparison across the PG-SGA global scores 12 weeks post-surgery, showed a mean EQ-5D-3L summary index of

0.87 (N=3) for PG-SGA A patients and a mean index of 0.57 (N=21) for PG-SGA B and C patients combined (P=0.166) (Table 2).

At baseline, the mean EQ-5D-3L summary index was 0.56, 0.49, and 0.32 for patients with a PG-SGA score between 0–3, 4–8, and 9 or above (P=0.226), respectively. Comparison across all PG-SGA scores at 12 weeks post-surgery, showed a mean EQ-5D-3L score of 0.68 (N=7) for patients with PG-SGA score between 0–3, a mean index of 0.65 (N=12) for patients with a PG-SGA score between 4–8 and 0.46 (N=5) for patients with a PG-SGA score of 9 or above (P=0.495).

Treatment outcomes

A total of six adverse events were documented in six patients. Adverse events included neurological deterioration in two patients, a pulmonary embolism, transient urinary retention, a pathological femur fracture and symptomatic humeral metastases. Overall median length of hospital stay was 6 days (range, 1–100 days). No association between nutritional status and the occurrence of adverse events or length of hospital stay could be determined. The median follow-up for survival was 18 months; at last follow-up only 23 patients (59%) were still alive. Patients presenting with a PG-SGA score between 0 and 8 had a mean survival of 33.4 months compared to 21.5 months for those presenting with a PG-SGA score of 9 or above (P=0.386). The mean survival time was 32.8 months for PG-SGA B patients and 26.6 months for PG-SGA C patients (P=0.451). Both PG-SGA A patients were alive at final follow-up with a mean follow-up of 20.3 months.

Discussion

As spinal metastases normally indicate advanced disease, treatment goals for patients with spinal metastases shift from cure to comfort, with the primary goals of relieving pain and maintaining or improving HRQOL. Symptom management is herein essential, as symptom control has been associated with improved HRQOL but also with improved survival (20,21). Pain, treatment related side effects and other physical symptoms may all impair nutritional intake, leading to malnutrition. Malnutrition is common among cancer patients and has been associated with increased morbidity and mortality, and significantly contributes to the disease burden (11-14). Nutritional status is potentially modifiable by adequate nutritional support and could thereby improve

HRQOL and treatment outcomes. The purpose of this study was to obtain preliminary data regarding the nutritional status of patients with spinal metastases who underwent surgical treatment. In addition, we aimed to explore the potential relationship between nutritional status and length of stay, adverse events, HRQOL and survival. We demonstrated that according to the PG-SGA, 92% (N=36) of our patients were moderately or severely malnourished. Based on the numeric nutritional risk score, 72% of the patients required a nutritional intervention. Malnourishment was associated with lower HRQOL scores at baseline. However, no statistically significant association between malnutrition and the occurrence of adverse events, length of stay, survival or post-treatment HRQOL could be determined in the present study.

Several studies have reported worse HRQOL scores in patients with malnutrition as compared to well-nourished patients. In a retrospective study Gupta *et al.* evaluated the association between nutritional status, including the SGA, and HRQOL with the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (QLQ-C30) in 58 patients with stage III–IV colorectal cancer (22). The authors demonstrated that well-nourished patients had significantly better HRQOL scores on the global, physical, pain and role scales of the QLQ-C30 as compared to malnourished patients (22). These results are in agreement with the results from our study, which showed lower baseline SOSGOQ2.0 total and SOSGOQ2.0 physical function scores in malnourished patients as compared to well-nourished patients. Although statistically non-significant, differences between well-nourished and malnourished patients in EQ-5D total scores, EQ-5D usual activity levels, SOSGOQ2.0 mental health and social function were clinically relevant. No difference in pain could be determined between malnourished and well-nourished patients in our study.

Our results found no association between malnutrition as defined by the PG-SGA global score or the PG-SGA nutritional risk score and survival. This is in contrast with other previously published studies on the association between malnutrition and survival in other oncology populations. Tan *et al.* conducted a prospective cohort study in 114 patients with advanced cancer and demonstrated a significant association between malnutrition and mortality (7). Severely malnourished patients (PG-SGA C) had a median survival of 5.6 months, as compared to a median survival of 11.1 months for moderately malnourished patients (PG-SGA B) and a median survival of 18.8 months for

well-nourished patients (PG-SGA A) (7). In comparison, the mean survival time of severely malnourished patients in our study was 26.6 months as compared to 32.8 months for moderately malnourished patients, which showed no statistically significant difference. This difference in statistical significance may be explained by our limited sample size resulting in a potential type 2 statistical error, and the skewed distribution of the patients among the different PG-SGA categories, with the majority of the patients being classified as moderately malnourished.

According to the PG-SGA global score, 82% of the patients in our study were moderately malnourished and 10% were severely malnourished. Although it is known that malnutrition is common among cancer patients, malnutrition rates among patients with spinal metastases were previously unknown. In comparison, in the study of Gupta *et al.* that included stage III–IV colorectal cancer patients, 59% of the patients were well-nourished, 38% were moderately malnourished and 3% were severely malnourished. The nutritional status of the patients in the present study was evaluated with the short form of the PG-SGA. Historically, many different questionnaires, laboratory values and anthropometric measurements have been used to evaluate the nutritional status (23,24). The PG-SGA was specifically designed for and validated within the oncology population and has been accepted by the Oncology Nutrition Dietetic Practice Group of the American Dietetic Association as the gold standard measure for nutritional risk assessment in cancer patients (15). The full PG-SGA consists of two parts, one part that is completed by the patient and the second part that is completed by a physician or trained dietician. The part that is completed by the patient is also referred to as the PG-SGA short form. The PG-SGA short form has also been shown to be a valid measure for the evaluation of nutritional status and has been associated with length of stay, HRQOL, and survival (25). An advantage of using the (short-form) PG-SGA rather than anthropometric measurements or laboratory values is that the PG-SGA is able to identify symptoms that impair adequate nutritional intake thereby enabling direct dietary or other medical interventions. In addition, the PG-SGA is likely more sensitive to changes over a short period of time as compared to laboratory values.

A major limitation of this study was the limited sample size. However, enrolment and follow-up of patients with spinal metastases in cohort studies is challenging given their limited life expectancy. An explorative statistical approach

was used rather than an ante hoc sample size calculation as a result the sample size limited the ability to perform extensive analyses and is likely to be underpowered to detect smaller, but still clinically relevant, statistically significant differences in HRQOL, survival and the occurrence of adverse events between the different categories of malnutrition. In addition, this study was conducted in a single tertiary care center limiting the generalizability of the results. Finally, the effects of a nutritional intervention to improve nutritional status or symptoms were not evaluated in our study. The PG-SGA was used solely for observational research purposes; patients might have received nutritional interventions based on the discretion of their treating physician (e.g., medical oncologist), which might have influenced the results.

Inadequate nutritional intake prohibits maintenance of muscle mass, thereby significantly contributing to the development of sarcopenia and frailty. Sarcopenia is defined as the loss of muscle mass, combined with a decline in strength and/or muscle function (26). Frailty is a complex syndrome, reflecting a state of increased vulnerability to effects of stressors and increased risk of adverse health outcomes (27). Frailty may be appreciated as the accumulation of functional deficits, which may be expressed by an index. The Metastatic Spinal Tumour Frailty Index (MSTFI) was developed in response to the lack of data regarding frailty and clinical outcomes in patients with spinal metastases (28). This index was developed using a large nationwide database and includes nine independent parameters that were significantly associated with adverse events and survival (28). One of the parameters included in the MSTFI is malnutrition. The odds for the occurrence of an adverse event among malnourished patients was 2.11 times the odds of the occurrence of an adverse event of well-nourished patients, emphasizing the importance of assessing malnutrition in this patient population (28).

Conclusions

This study is the first to demonstrate that malnutrition as determined by the PG-SGA short is highly prevalent among patients with spinal metastases. In addition, malnutrition was associated with lower baseline SOSGOQ2.0 overall scores, SOSGOQ2.0 physical functioning scores, mental health, and social functioning scores, as well as lower baseline overall EQ-5D scores and EQ-5D usual activity scores. No significant association between malnutrition and the occurrence of adverse events, length of stay, post-

treatment HRQOL or survival could be determined. The results of this study support the need for future larger studies to evaluate the prognostic significance of malnutrition and the influence of nutritional interventions in patients with spinal metastases.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The local institutional review board approved the research protocol (No. 15-475) and all patients provided written informed consent.

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