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ORIGINAL ARTICLE

Study investigating the role of skeletal muscle mass estimation in metastatic spinal cord compression

H. Gakhar[1] · A. Dhillon[1] · J. Blackwell[4] · K. Hussain[1] · R. Bommireddy[1] · Z. Klezl[1,3] · J. Williams[1,2,4,5]

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Abstract
Background Age-related loss of functional muscle mass is associated with reduced functional ability and life expectancy. In disseminated cancer, age-related muscle loss may be exacerbated by cachexia and poor nutritional intake, increasing functional decline, morbidity and accelerate death. Patients with spinal metastases frequently present for decompressive surgery with decision to operate based upon functional assessment. A subjective assessment of physical performance has, however, been shown to be a poor indicator of life expectancy in these patients. We aimed to develop an objective measure based upon lean muscle mass to aid decision making, in these individuals, by investigating the association between muscle mass and 1-year survival.
Methods Muscle mass was calculated as total psoas area (TPA)/ vertebral body area (VBA), by two independent blinded doctors from CT images, acquired within 7 days of spinal metastases surgery, at the mid L3 vertebral level. Outcome at 1 year following surgery was recorded from a prospectively updated metastatic spinal cord compression database.
Results 86 patients were followed for 1 year, with an overall mortality of 39.5 %. Mortality rates at 1 year were significantly high among patients in the lowest quartile of muscle mass, compared with those in the highest quartile (57.1 vs 23.8 %, $p = 0.02$).
Conclusion Death within 1 year in individuals with spinal metastases is related to lean muscle mass at presentation. Assessment of lean muscle mass may inform decision to operate in patients with spinal metastases.

Keywords Metastatic spinal cord compression · Sarcopenia · Lean muscle mass

✉ H. Gakhar
gul34@yahoo.com

J. Williams
john.williams7@nhs.net

[1] Spinal Unit, Division of Surgery, Royal Derby Hospital, Derby DE223NE, UK

[2] MRC/Arthritis Research UK Centre for Musculoskeletal Ageing Research, Royal Derby Hospital Centre, University of Nottingham, Nottingham DE22 3DT, UK

[3] 3rd Medical School, Charles' University Prague, Prague, Czech Republic

[4] Anaesthetic Department, Division Surgery, Royal Derby Hospital, Derby DE223NE, UK

[5] School of Graduate Entry Medicine and Health, Derby City General Hospital, University of Nottingham, Derby DE22 3DT, UK

Introduction

For achieving rapid pain relief, preservation of neurological function and maintenance of activities of daily living, surgical decompression remains the preferred treatment for metastases within the spine [1]. However, although the decision to operate is commonly based upon a meticulous and complex overall assessment of the clinical and radiological information available, surgery is not offered in all instances. When assessing outlook and informing the decision-making process, various prognostic scores have been developed to aid this difficult decision-making process [2–5]. Previous studies have highlighted the inadequacy of such preoperative scoring systems, suggesting that the decision to treat is often based upon subjective

functional and radiological patient appraisal, which may lack objective prognostic value [6].

Conversely, despite skeletal muscle wasting often being obscured by tissue oedema and body weight changes, computed tomography (CT)-based measurements of body composition have shown depletion of skeletal muscle mass (sarcopenia), to be good a predictor of survival in patients complaining of gastrointestinal and lung cancer and also following liver transplantation [7–11]. There has, therefore, been a recent recognition that sarcopenia is a clinically important phenomenon with predictive value in cancer patients [12].

Denoting a skeletal muscle mass greater than two standard deviations below that of a typical healthy adult [13], sarcopenia has been associated with functional impairment and disability [13, 14], risk of fractures and falls [13], increased length of hospital stay [15], nosocomial infections [16] and decreased survival [17] in non-malignant diseases. Moreover, severe muscle depletion is associated with reduced physical ability, unfavourable treatment outcomes and increased mortality in cancer and non-cancer patients [18–23]. Studies in patients with malignant diseases [23, 24] and non-malignant conditions [25, 26] have shown that sarcopenia and associated increased fat mass result in particularly poor physical functional ability and clinical outcome [27].

Data addressing the importance of the preservation of skeletal muscle mass are, however, limited in patients with metastatic spinal cord compression. The aim of the present study was therefore to investigate the influence of skeletal muscle mass on survival following surgical treatment in patients with metastatic spinal cord compression.

Materials methods

Patients and study design

As part of an ongoing evaluation of the Royal Derby Hospital spinal service performance, anonymized data from all patients who underwent surgical treatment for metastatic spinal cord compression from 2009 to 2013 were analysed. Data were taken from our prospectively maintained database within the department of spinal surgery. For this study, we considered all patients with metastatic spinal cord compression who had surgery and who had a CT staging scan in the week prior to surgical treatment. Final analysis included all patients who had a minimum follow-up of 1 year or until death within 1 year of CT scan.

Image analysis

Two independent observers visually analysed CT scans. Axial sections were taken at the mid vertebral level of the third lumbar vertebra (L3). Freely available Image J software, from the National Institute of Health (NIH, Maryland, USA), was used to quantify vertebral and psoas muscle cross-sectional area. Cross-sectional surface area was calculated for the psoas muscles at the third lumbar vertebra (L3) and divided by the cross-sectional surface area of the L3 vertebra, for all patients within the study (TPA/VBA) Fig. 1. Total psoas muscle surface area divided by L3 vertebral body area obtained using this method, was further compared to TPA /height^2 in metres for a subset of patients for whom height was extractable from the database. Muscle bulk at the L3 level is therefore presented either as mm^2/m^2 or as a unit less value depending upon the method of normalization.

Two medically qualified independent blinded evaluators calculated psoas muscle mass and L3 vertebral body surface area for all patients. Demographic and clinico-pathological data were extracted from the spinal unit database.

Statistical analysis

Parametric data are expressed as mean +/− standard deviation or median and interquartile range for non-parametric data. All p values are two sided, and levels of significance are p values of <0.05. Kaplan–Meier plots were used to determine the effect of muscle mass on 1-year mortality. Statistical analysis was completed using SPSS (SPSS for Windows, version 16.0; SPSS).

Results

Patient demographics

In total, 86 individuals were included in the study and followed for 1 year following decompression of spinal

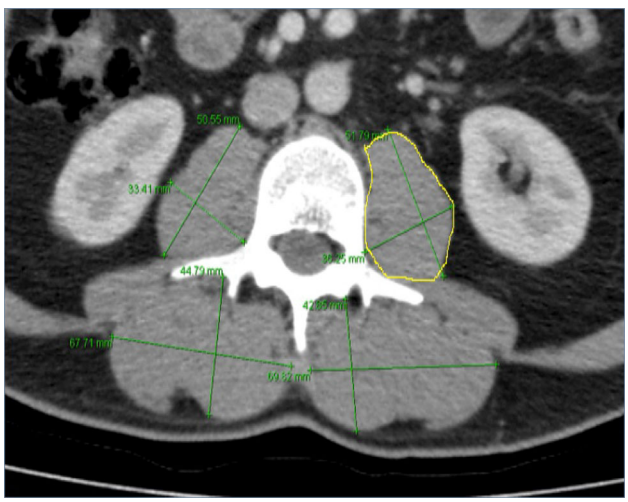

Fig. 1 Cross-section at the level of L3 depicting use of Image J software to calculate circumference of the psoas muscle (*yellow line*)

metastases (male 44:female 42). In our series, lumbar spine was the most common site of metastasis, followed by thoraco–lumbar junction and then thoracic spine. For descriptive purposes, the results have been presented in two groups. Group A formed by patients who were alive at 1 year and group B by patients who were dead at 1 year. Patient characteristics are described in Table 1.

There was no difference in gender between groups (Group A: M:F 26:26 vs Group B: M:F 18:16; $p = 0.83$), with individuals in group B significantly of older age [Group A:62 years (53–71.75) vs Group B:68 years (61.75–76.25)]; $p = 0.04$). Patients presented with a variety of primary cancers, with lymphoma (18), breast (14), renal (14), lung (13) and prostate (12), the most common presenting primaries. Individuals were more likely to be dead within the year if primary tumour site was lung when compared to breast or lymphoma ($p < 0.01$). There was no other significant difference in survival chance between other primary tumours.

Estimation of muscle mass

Individuals who died within the year had significantly lower lean muscle mass on initial CT compared to those alive at the end of 1 year (Group A:2.26 (1.70–2.67) vs Group B:1.95 (1.54–2.29); $p = 0.05$). There was good inter observer reliability in calculating the psoas muscle and L3 vertebral body surface area. ($r^2 = 0.97$; $p < 0.001$) Fig. 2.

Within our study group, we were able to normalize the lean muscle mass in relation to vertebral body in all 86 patients. For a subset of 38 of these individuals, height was also extracted from the available database, with correlation plots of TPA/VBA vs TPA/ Height^2 showing a close relationship between these two measures of muscle bulk. ($r = 0.77$, $p < 0.0001$) Fig. 3.

Survival analysis

Calculated normalized lean muscle mass was analysed as quartiles, with 23.8 % mortality in the highest quartile within a year compared to 57.1 % mortality in the lowest quartile ($p = 0.02$) Fig. 4.

Primary cancer

Individuals with a lung, gastrointestinal or "other" primary malignancies were more likely to be dead at 1 year, with all three groups having 1-year survival rates less than 50 %. These groups are also the groups with the lowest muscle mass on CT at presentation Fig. 5. Of the malignancies recorded, lung primary patients had a significantly lower muscle mass on CT than breast and lymphoma patients ($p < 0.01$). There was no significant difference in muscle mass at presentation between all other malignancy groupings.

Discussion

We demonstrate that the simple and easy to perform normalized measure of psoas cross-sectional area utilizing vertebral body area correlates well with normalization

Table 1 Comparison of demographics between patients who were alive at 1 year with those who were dead at 1 year

	Alive at 1 year	Dead at 1 year	*p* value	Statistical test
Age	62 years (IQR 53–71.75)	68 years (IQR 61.75–76.25)	0.04	Mann Whitney test
Gender (M/F)	26/26	18/16	0.83	Fisher's Exact test
Muscle mass (arbitrary units)	2.26 median (IQR 1.70–2.67)	1.95 median (IQR1.54–2.29)	0.05	Mann Whitney test
Muscle mass				
Highest quartile	16	5	0.02	Log-rank test(highest to lowest quartiles)
Mid high quartile	14	8		
Mid low quartile	13	9		
Lowest quartile	9	12		
Primary cancer				
Breast	12	2	<0.01	Kruskall Wallis with Dunn's multiple comparisons (Lung more likely deceased at 1 year that Breast or Lymphoma)
Lymphoma	16	2		
Gastrointestinal	3	4		
Prostate	6	6		
Renal	9	5		
Lung	3	10		
Other	3	5		

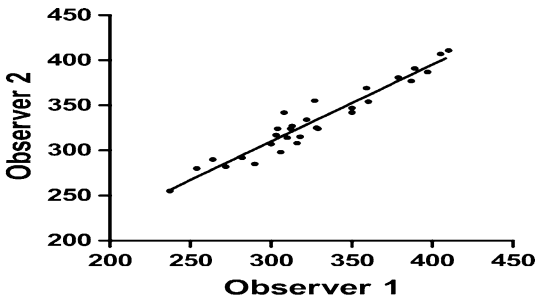

Fig. 2 Figure showing correlation between independent observers in assessing muscle mass from staging CT scans

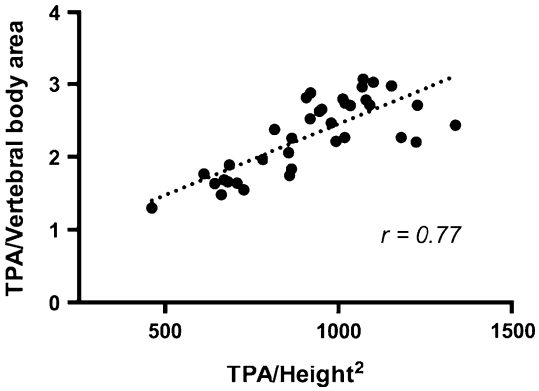

Fig. 3 Graph showing correlation between normalized muscle mass using height (TPA/Height^2) and vertebral body surface area (TPA/VBA)

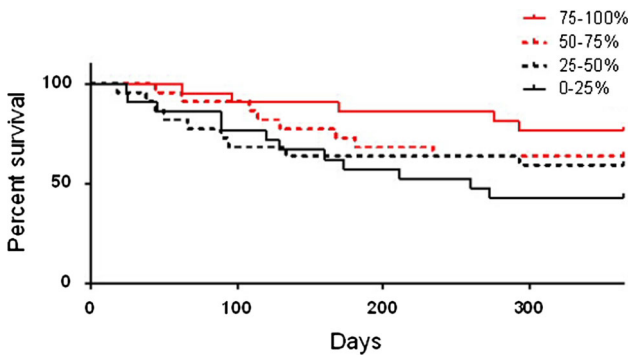

Fig. 4 Kaplan Meier plot showing survival by quartile of muscle mass

using patient height. Moreover, we show that this measure is a useful predictor of 1-year mortality following decompression of the spinal cord for metastases.

This present study lends weight to the growing body of evidence within the literature supporting the view that muscle wasting is associated with reduction in functional capacity and life expectancy in a variety of cancer states and following oncological surgery. Skeletal muscle and adipose tissue in this region (L3) correspond well to whole-body tissue mass in non-malignant populations [28–31],

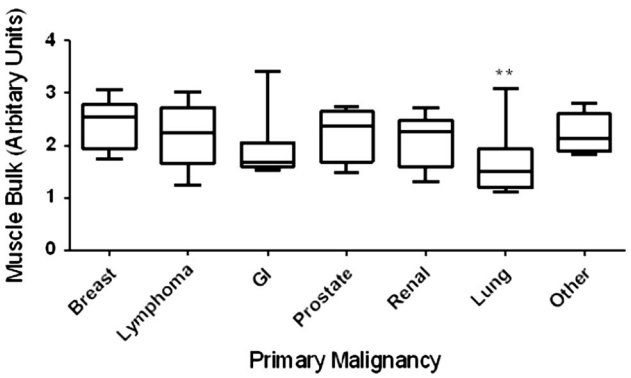

Fig. 5 *Box*-and-*whisker plot* of the total cross-sectional area of skeletal muscle mass in various primary cancers. *Boxes* represent median values and interquartile ranges, *whiskers* represent the 5th and 95th percentile

and have been repeatedly validated [32] and used [32–36] for assessment of body composition in patients with cancer. Using simple readily available software (Image J), estimation of muscle mass can be shown to be strongly correlated with prognosis in this patient population. Given the demonstrated shortcomings of subjective functional and radiological preoperative assessment in this population, this approach may be helpful in the clinical decision-making process. Similar results have been obtained in other studies both in the context of prognosis and treatment efficacy [8–10, 12, 22].

Not only do our results demonstrate, on direct comparison of muscle mass at presentation, a significantly lower muscle mass in patients subsequently dead within 1 year, but also additionally show a reduced chance of survival for those individuals within the lowest quartile of muscle bulk at presentation compared to those within the highest at 1 year using Kaplan–Meier plots. This raises the possibility of the incorporation of CT-assessed muscle mass into routine pre-surgical assessment to aid determination of decision to treat. These results mirror the finding that individuals with lung, gastrointestinal or other cancers and who are more likely than not to be dead at 1 year (all have 1-year survival less than 50 %), are also the groups with the lowest muscle mass on CT estimation.

We acknowledge that there are limitations to our study. Firstly, this study is a retrospective evaluation of a prospectively maintained database, potentially affecting data quality. There may also be an element of selection bias as we have only included patients who have had surgical treatment for metastatic spinal cord compression. Secondly, individuals who died within 1 year of surgery were significantly older than those who survived. The reduction in muscle mass and function with age is well documented [37], notwithstanding this we believe that the clear relationship between lowest quartile of muscle mass and outcome that we demonstrate is likely a result of a muscle loss

associated limitation in functional capacity and not a result of chronological age alone. Thirdly, due to difficulty in obtaining height from our spinal database, and in contrast to the previous literature published in the field, we have employed vertebral body area to normalize muscle bulk at the L3 vertebra. We believe that this is a justified approach for calculating muscle mass given the frequent omission of height and weight measures from patient documentation. In addition, measurement of vertebral body area is simply acquired from CT in conjunction with psoas muscle area. Furthermore, subset analysis in this study of individuals in whom height, psoas area and vertebral body area were available, shows a high correlation between TPA/VBA and TPA/Height^2. Finally, we accept that this is a relatively small study and that larger observational studies need to be undertaken to confirm our findings and allow for the incorporation of muscle mass into current measures of outcome.

In conclusion, current methods for assessing outcome in patients presenting for decompression of metastatic spinal cord lesions are suboptimal. Preoperative assessment of muscle bulk on CT scan predicts the likelihood of survival at 1 year in this patient population and may further empower the surgeon in the surgical decision-making process.

Conflict of interest None.

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