Research Article

Assessment of muscle mass with computerised tomography in patients with incurable gastrointestinal cancer. A prospective single centre study

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ABSTRACT

Objective
Body composition is often affected in patients with incurable cancer, but the prevalence of sarcopenia is unknown. Our aim was to evaluate sarcopenia as predictor of overall survival in a cohort of patients with incurable gastrointestinal cancer and furthermore to evaluate if this cohort had different characteristics than patients, from an identical cohort who accepted participation in a RCT.

Design and methods
In this single centre study, we prospectively included a cohort of patients with incurable gastrointestinal cancer nutritionally at risk (NRS 2002≥2). Patients were screened but refused participation in an RCT testing supplemental HPN. To assess sarcopenia, data on skeletal muscle mass (SMM) from the cross-sectional area of L3 were assessed using computerized tomography scan (CT scan). SMM evaluation was included if a CT scan was available within 60 days from the inclusion date. Differences in survival were tested according to sarcopenia and modified Glasgow Prognostic Score (mGPS). Survival was compared between the patients who refused to participate in the RCT and patients who actually did participate.

Results
Eligible for inclusion were 187 patients, and 165 had a CT scan available for analysis. Most prevalent diagnosis was pancreatic cancer (52%), median age was 70.5 (41.2–89.4), median BMI 22.3 (14.4–36.8) and 99% were receiving chemotherapy. Sarcopenia was present in 78% of the overall cohort, more women (88%) than men (70%) were sarcopenic at inclusion. There was a positive correlation between BMI and SMM, but SMM accounted for only 8% of the variance in BMI.

Conclusions
Prevalence of sarcopenia was high in this cohort of patient with incurable gastrointestinal cancer; SMM did positively correlate to BMI, but only accounted for minor variations. mGPS was in the multivariate cox regression model predictive of survival and sarcopenia did not add to this elevated risk.
Introduction

Patients with incurable cancer often develop alterations in body composition, which has a negative impact on prognosis [1, 2]. The change in body composition in cancer patients often includes loss of muscle mass associated with functional disability and mortality [3-5]. Multifarious adverse effects of chemotherapy often increase these challenges [6-8]. As reported in a recent study by Choi et al. body composition has proved a prognostic factor in patients with incurable cancer [9]. Loss of skeletal muscle mass (SMM) is a result of impaired food intake, inflammation, and absence of physical activity. It is still uncertain if loss of muscle mass in patients with incurable cancer can be reversed and perhaps this will improve the outcome. However, it is likely that this is only possible in patients without severe inflammation and with a life expectancy above three months [10]. In a recent study by Feliciano et al [11] on patients with colorectal cancer the risk of death was nearly doubled in patients with sarcopenia and inflammation at time of diagnoses. In previous studies mGPS, based on ‘crp’ and ‘albumin’, has been valuable as a prognostic tool in patients with incurable cancer [12, 13].

Recruitment of patients with incurable cancer to clinical trials is often challenging and in a recent review on methodology, characterising clinical trials in palliative care, it was reported that only one third (36.8%) of the presented studies succeeded in including the number of patient estimated necessary in the sample size calculations [14].

It is questionable if patients participating in clinical trials have better outcomes, but recently an individual benefit of study participation was proven in young adults with cancer [15, 16]. Furthermore, another concern could be that patients participating in clinical trials basically have different demographic characteristics e.g. sex, age, and grade of disease, which may result in poor generalizability of study results.

It is generally accepted that mGPS is predictive for survival in patients with cancer, and some studies have suggested a worse prognosis if combined with sarcopenia. Aim of the present study was to evaluate the prevalence of sarcopenia in a cohort of patients with incurable gastrointestinal cancer and to evaluate the predictive value of sarcopenia for overall survival.

Patients and methods

Study design

Data were analysed from a prospective cohort of patients with incurable gastrointestinal cancer who were consecutively screened and offered participation in a RCT [17]. Patients were recruited in relation to the clinical randomized study of parenteral nutrition, in which they declined to participate. Extraction from the medical records and data entry in the database was completed by a physician and two specially trained nurses. Results from the RCT were not the scope of this work, and therefore these data are reported elsewhere [17].

Ethics

Ethical approval was obtained from the local Ethics Committee (S-20120094). Permission to use the data from the patients who declined to participate in the RCT was obtained from the Danish Patient Safety Authority (3-3013-1763/1). Patients who participated in the RCT all gave written informed consent. Permission for data handling and storage was obtained from the Danish Data Protection Act (16/24969).

Patients

Patients attending the Oncology Outpatient Clinic for clinical evaluation or scheduled treatment with chemotherapy were screened using NRS 2002 which is the mandatory screening tool used in the Danish Hospital setting. Patients were approached by the primary investigator or the project nurse during chemotherapy. Inclusion criteria were: incurable gastrointestinal cancer (locally advanced or metastatic), age >18 years, WHO performance status (PS) 0-2 and nutritionally at risk according to NRS 2002 score ≥2) AND who declined to participate in the previously published RCT [17-19]. Exclusion criteria were: non-compliance, expected survival<3months, Short Bowel Syndrome or actual treatment with home parenteral nutrition. Chemotherapy was not an exclusion criterion. Patients were evaluated from May 2014 until November 2016 at a Danish University hospital.

Definitions

Baseline characteristics were recorded at the time of screening. Data on demographics, modified Glasgow Prognostic Score (mGPS), unplanned admissions and survival were obtained from patient’s medical record. Computerised Tomography (CT) images completed for routine care; staging and follow up of the cancer were used for evaluation of SMM. Additionally, patients were asked the main reason for not wanting to participate in the RCT. Body surface Area (BSA) was calculated using the formula by Du Bois [20].

Sarcopenia

The term sarcopenia was in the study based exclusively on muscle mass since no data on muscle function was available. Analyses of muscle mass were included if a CT scan was available within 60 days from the inclusion date. Muscle mass was manually marked by hand by the same person, a trained radiographer for all scans, and evaluated using Osirix software (Osirix version 7.0. Pixmeo, Switzerland, 2015). The radiographer was blinded to the outcome including the overall survival.
CT images were analysed at the level of L3, using the cross-sectional area as a predictor of whole-body muscle mass. The cross-sectional area of SMM at the level of L3 is closely related to whole body muscle area [21]. To quantify the muscle, mass the Hounsfield unit threshold used was within the range -29 to + 150 HU [22, 23]. All tissue values were normalized for height (cm²/m²) and expressed as skeletal muscle index (SMI).

CT evaluated muscle mass and the criteria for sarcopenia was based on cut-offs from the study by Martin et al, with stratified definitions for sarcopenia accounting for BMI [4]. Threshold values with BMI < 25 L3 skeletal muscle index ≤43 cm²/m² for men and L3 skeletal muscle index ≤41 cm²/m² for women at BMI ≥25 threshold values were 53 cm²/m² and 41 for men and women, respectively. To estimate the whole body muscle mass, the following equation was used in our study: total body fat-free mass (FFM) (kg) = 0.3* [skeletal muscle at L3 (cm²)] + 6.06 (r=0.94) [3].

Cachexia

At baseline all included patients had either anorexia or had had a marked weight loss >5%. Therefore, patients may all be characterized with some degree of cachexia [10]. Since no biomarkers of cachexia exist at the time being, we evaluated the patients using SMI and mGPS.

Survival analyses

Overall survival was estimated from date of refusal until the last day of observation. Overall survival was analysed according to sarcopenia and mGPS.

Unplanned admissions

Included were unplanned admissions due to incidents of acute illness from the time of screening/ inclusion to end of observation.

Statistical Analysis

Descriptive statistics are presented as median and range if not stated otherwise. For comparison of continuous outcome variables unrelated t-test or Mann-Whitney U test, (Wilcoxon two-sample test) was used when appropriate. Ordinal scale data was analysed using Fisher’s exact test.

A multivariable logistic regression was used to analyse the association between unplanned admissions and SMI. Univariate and multivariate logistic regression was used to analyse variables associated with sarcopenia. Correlation between SMM and BSA as well as SMM and BMI were evaluated using Pearson’s correlation coefficient.

Kaplan-Meier curves according to sarcopenia and to mGPS were presented for all patients participating in this study. Cox proportional hazards regression analyses were used to test for predictors of mortality in a subgroup of patients who had a valid CT scan within 60 days from inclusion. Results from the univariate analyses are presented, along with results from a multivariate Cox regression model including variables if p<0.10 in the univariate model. To test for strength of the model Harrell’s C, concordance was performed after the regression analyses. Using Kaplan-Meier and Log-rank we compared the differences in overall survival according to RCT participation or not. All analyses were performed using Stata (Version15. Statistical software, College station, Texas: StataCorp LLC).

Results

Demographics

Five hundred and sixty-four patients with incurable gastrointestinal cancer were screened for participation in the RCT. Of these 323 patients did not fulfill the inclusion criteria; 245 (43%) were screened to have risk score <2, 30 (5%) were evaluated to be non-compliant, 14 (2%) had a life-expectancy<3 months, 12 (2%) had performance status 3, six (1%) were already receiving HPN, five (1%) had Short Bowel Syndrome, and 11(2%) were not included for a unknown reason. A total of 187 patients who declined to participate in the RCT were included in the present study.

Twenty-three patients (12%) were scanned more than 60 days within the days of the interview and thus were not included in the Kaplan-Meier or the cox regression analyses on muscle mass and survival. Half of the patients had pancreatic cancer, were median 71 years, and had a median BMI 22.3 and 99% were receiving chemotherapy at the time of observation.

Sarcopenia

Majority of the patients in our cohort had sarcopenia. We found a vast difference for the number of patients estimated to be malnourished using BMI (11%) and the patients estimated to be sarcopenic using computerized tomography scan at L3 level (78%). Sarcopenia was found in patients with BMI ranging from 14.7kg/m² – 36.8 kg/m². Median BMI in patients was 22.8 kg/m² in patients with sarcopenia and 22.1 kg/m² in patients without sarcopenia (Table 2). We found a strong positive correlation (Pearson’s coefficient = 0.72, p<0.01) between
SMM and Body Surface Area (BSA). SMM explaining 52% of the variation in BSA. As well there was a small but significant positive correlation (Pearson's coefficient= 0.28, p<0.01) between SMM and BMI, SMM explaining only 8% of the variation in BMI.

Table 1: Demographics and characteristics of a population of 187 patients with incurable gastrointestinal cancer.

<table>
<thead>
<tr>
<th>N (%)</th>
<th>cohort</th>
<th>Percentage %</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>187</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>89</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>98</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>70.5</td>
<td>41.2-89.4</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18.5 (underweight)</td>
<td>21</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>18.5-24.9 (normal weight)</td>
<td>117</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>25.0-29.9 (overweight)</td>
<td>40</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>≥30 (Obese)</td>
<td>9</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Tumour site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oesophagus</td>
<td>4</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>34</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Duodenum</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>96</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Bile duct</td>
<td>14</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>34</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>NET</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Performance Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>26</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>115</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>46</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>mGPS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>100</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>52</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>34</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Palliative chemotherapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No chemo</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Single agent chemotherapy</td>
<td>42</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Combination chemotherapy</td>
<td>144</td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>Re-admissions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No admissions</td>
<td>29</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>One admission</td>
<td>46</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Two or more admissions</td>
<td>112</td>
<td>60</td>
<td></td>
</tr>
</tbody>
</table>

*mGPS=Modified Glasgow Prognostic Score
(0=albumin>35,crp<10,1=CRP>10, albumin>35, 2=CRP>10, albumin<35

In a simple logistic model, sex was the only risk factor for sarcopenia, but the significance disappeared when analysed in the multivariate model. In the multivariate model the risk of sarcopenia was significantly higher in women (OR 3.67, p<0.01).
We found no significant in survival according to sarcopenia (Figure 1). Survival was in median 289 days (104-1109) and 212 days (6-980). In the cox regression model sarcopenia was not predictive of survival.

Table 2: CT evaluated muscle mass and the proportion of patients being sarcopenic and sarcopenic obese.

<table>
<thead>
<tr>
<th></th>
<th>Non-participants</th>
<th>RCT participants</th>
<th>P</th>
<th>Missing (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>163</td>
<td>47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMI* (cm²/m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>37.6 (23.4-52.9)</td>
<td>37.4 (18.4-54.5)</td>
<td>0.60</td>
<td>(24/0)</td>
</tr>
<tr>
<td>Men</td>
<td>34.5 (23.4-47.6)</td>
<td>32.7 (18.4-47.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFM*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>39.8 (25.4-62.5)</td>
<td>38.4 (22.0-55.6)</td>
<td>0.24</td>
<td>(24/0)</td>
</tr>
<tr>
<td>Men</td>
<td>34.2 (25.4-44.5)</td>
<td>31.7 (22.0-42.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT sarcopenicc</td>
<td></td>
<td></td>
<td>0.73</td>
<td>(24/0)</td>
</tr>
<tr>
<td>ALL</td>
<td>128 (78)</td>
<td>38 (81)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>67 (88)</td>
<td>15 (88)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>61 (70)</td>
<td>23 (77)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarcopenic obesed</td>
<td></td>
<td></td>
<td>0.34</td>
<td>(24/0)</td>
</tr>
<tr>
<td>Not sarcopenic, not obese</td>
<td>34 (21)</td>
<td>8 (17)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarcopenic Obese</td>
<td>7 (4)</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>1 (1)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarcopenic</td>
<td>121 (74)</td>
<td>38 (81)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data were presented as Median (Range) N (%)

* SMI= Skeletal Muscle Index, CT measured muscle mass at L3 divided by height².

*FFM = Fat free mass= 0.3*CT musclemass(kg) + 6.06 (1)

*Sarcopenic = SMI <43 for men and SMI <41 for women at BMI 20-24.9; SMI<53 for men, SMI<41 for women at BMI≥25kg/m²

*Sarcopenic and obese, obesity = BMI ≥30kg/m²

Figure 1: Overall survival according to sarcopenia. No significant difference was found.

Figure 2: Overall survival according to mGPS. Significant difference was found when tested using cox regression.
Overall survival and mGPS

At six months 72%, 54% and 41% were still alive with mGPS 0, mGPS 1 and mGPS 2, respectively. At twelve months 35%, 21% and 9% were still alive with mGPS 0, mGPS 1 and mGPS 2, respectively (Figure 2). Median survival was for mGPS 0 268 days, mGPS 1 193 days, and for mGPS 2 136 days.

Table 3: Univariate and multivariate Cox regression analyses including patients with incurable cancer and an available CT scan for evaluation of skeletal muscle mass (SMM) within 60 days and an available mGPS

<table>
<thead>
<tr>
<th>Number</th>
<th>Survival</th>
<th>Crude model</th>
<th>Adjusted Model^a</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Median survival (Range)</td>
<td>HR 95% CI P</td>
</tr>
<tr>
<td>Non-sarcopenic</td>
<td>164</td>
<td>35 219 (18-980)</td>
<td></td>
</tr>
<tr>
<td>Performance</td>
<td>0 (ref)</td>
<td>24 316 (59-1109)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>98 262 (6-891) 1.60 0.96-2.67 0.07 1.71 1.01-2.90 0.04*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>42 122 (15-788) 3.93 2.23-6.92 &lt;0.01** 4.28 2.36-7.74 &lt;0.01**</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>165</td>
<td>219 (6-1109) 1.01 0.99-1.02 0.38 1.00 0.98-1.02 0.92</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Men</td>
<td>86 209 (12-980)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>78</td>
<td>250 (6-1109) 0.78 0.56-1.08 0.14 0.77 0.54-1.10 0.15</td>
<td></td>
</tr>
<tr>
<td>mGPS^c</td>
<td>0 (ref)</td>
<td>15 268 (12-891)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>117 193 (23-1109) 1.48 1.01-2.17 0.05 1.59 1.01-2.90 0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>32 136 (6-482) 2.69 1.75-4.13 &lt;0.01** 4.28 2.37-7.74 &lt;0.01**</td>
<td></td>
</tr>
</tbody>
</table>

^aAdjusted model including sarcopenia, mGPS, performance, age and sex.
^bSarcopenic = L3 skeletal muscle index ≤52.4 cm²/m² for men and for women L3 skeletal muscle index ≤38.5 cm²/m²
^c'm2/m²' cmGPS=Modified Glasgow Prognostic Score; (0=albumin>35,crp<10,1=CRP>10, albumin>35, 2=CRP>10, albumin<35

Unplanned admissions

Unplanned admissions were frequent and only 15% were not admitted at all. Number of admissions ranged from 1 to 9 per patient. A limited number of patients had more than four admissions (9%). We did not identify any predictors of risk of admission.

Discussion

In this study mGPS was a strong predictor of survival, and there was no predictive value of sarcopenia. Sarcopenia was found in patients with a wide range of BMI’s. We found a strong positive correlation between SMM and BSA. Length of survival was not dependent on RCT participation. Finally, we did not find that patient with sarcopenia had a higher risk of admissions.

At baseline majority of the patients had sarcopenia, and sarcopenia had a predictive value for overall survival but only in the univariate cox regression model. Compared to the patients who declined to participate in the previously reported RCT by Obling et al. the patients in this cohort were similar regarding tumour site, performance and sex [15]. SMM did not differ between the two cohorts, and neither did the percentage of
patients with sarcopenia. Participants in the RCT testing sHPN were younger, had lower BMI, but did not have a better outcome than the ones who refused participation.

The prevalence of sarcopenia in this study was higher than in previously published studies. This is not surprising, since the included patients were all screened to be nutritionally at risk at inclusion, with either eating disabilities or preceding loss of weight. The discrepancy between number of patients being underweight and the number being sarcopenic highlights the need for the use of other parameters than BMI to assess the nutritional encounters. Using Body Mass Index (BMI) or weightloss as criteria for study inclusion may not be accurate in patients with cancer, since fluid imbalance will affect these parameters [24]. As well, it may be considered if the screening tool NRS 2002, originally developed for the use in hospitalized patients, is sufficiently accurate to identify the patients before the severe decrease in muscle mass or the decline in mGPS.

Drug distribution is affected by body composition, which may be the reason for patients with sarcopenia being more susceptible to toxicity during chemotherapy than patients without sarcopenia [6, 7, 25]. In a cohort of colon cancer patients receiving combination chemotherapy, lean body mass was evaluated to be a significant predictor of neuropathy and toxicity [26]. Furthermore, a previous study on patients with non-metastatic colon cancer receiving chemotherapy found an association between toxicity and low SMI [27]. Prescription of chemotherapy as single agent or combination therapy is dependent on performance status but not on mGPS or sarcopenia. Dosage of chemotherapy is at the time being, calculated from BSA, which may not be accurate since SMM only explained half of the variation in BSA [20]. BSA did not correspond perfectly to the muscle mass findings, which make us consider if other parameters should be included when calculating chemotherapy dosage to minimize the risk of toxicity. Nutritional status and impaired mobility were predictive of overall survival in a recent study [28]. A study on aging patients with cancer suggested a multivariate model including functional capacity to prevent toxicity [29]. Also, the review by Hopkins et al. suggests using muscle mass to individualize the chemotherapy and to a greater extent avoid side effects [30].

mGPS and not sarcopenia was in this study predictive of survival in opposition to previously reported findings. The large number of patients with sarcopenia and the inclusion of patients at different stages of advanced cancer disease may have influenced the results. It is possible that some patients stopped losing weight and some had an ongoing weight loss depending on tumour burden and inflammatory status. In a recent prospective observational study on 67 patients with metastatic colorectal cancer, muscle area (CT measured) decreased significantly during palliative chemotherapy and the loss of muscle mass was independently associated with survival [1]. As reported in a recent study by Choi et al body composition has proved as a prognostic factor in patients with incurable cancer and sarcopenia receiving chemotherapy [9]. In that study there was a predictive value of loss of muscle mass during chemotherapy, whereas BMI did not show any significant value.

Prognostication in patients with incurable cancer is important since there is a correlation between life expectancy and symptom burden. Patients with fewer and less severe symptoms often have longer life expectancy [31]. In a previous study on patients with incurable cancer it was shown that a high symptom burden was associated with prolonged hospitalization and higher number of readmissions [32]. Malnutrition, which was found in 41% of the total population screened for inclusion in this study, leads to a wide range of symptoms. It seems logical to treat the symptoms accompanying malnutrition in an attempt to prevent the burdensome hospitalizations.

A general understanding is that patients with cancer participating in clinic trials have an improved outcome because of the increased attention from the project workers [33, 34]. This was not confirmed by the results from our study. Overall survival was not significantly different in the patients who participated in this study compared to patients participating in the RCT. We could not confirm the previous reported findings of a superior outcome for the patients participating in RCT in terms of survival [35].

Although patients and their relatives do expect the professionals to take care of weight loss during cancer treatment [36] many patients did not want to participate in the clinical trial offering dietary counselling and supplemental home parenteral nutrition under circumstances of randomization. Reasons for not wanting to participate in the RCT varied, and we found no pattern in the reasoning. Almost one third of the patients stated being too stressed or overwhelmed as the main reason for not participating. Patients with incurable cancer in general experience high rates of stress due to the insecurity of the course of disease. From previous studies it is documented that patients in palliative care abstain from participation in clinical trials if the intervention is thought to be complex with risk of side–effects and if the support from the relatives is non-existent [37, 38].

The population studied was heterogenous in terms of diagnoses and therefore also in type of chemotherapy. Patients were analysed at different stages of disease and were only included if nutritionally at risk. Previous studies have stated sarcopenic obesity as a negative predictor of mortality in patients with incurable cancer [39, 40]. In our study population only, a minority were obese since the patients were preselected, and therefore subgroup analysis including sarcopenic obesity was impossible.
In future studies addressing outcome and therapeutic intervention in patients with incurable cancer including nutritional status, muscle mass and muscle function could improve characterization of patient groups and may perhaps improve individual dosing of chemotherapy resulting in less toxicity.

Conclusion

We found a high prevalence of sarcopenia in this cohort of patients with incurable cancer. The high prevalence of sarcopenia found was surprising and make us wonder if a diminished nutritional state in patients with incurable cancer is not recognized and not treated. mGPS was a strong predictor of survival and sarcopenia did not add to this elevated predictive value of mGPS.

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Data availability

Data are available from the correspondent author upon request

Statement of authorship

Authors contributed equally to the design of the study. SRO collected the data and analysed and interpreted the data in close collaboration with BW, PP and JK. SRO, BW, PP and JK drafted and critically revised the manuscript. Final draft of the manuscript was approved by all contributing authors.

Conflicts of interest

Primary investigator received funding from the Danish national Cancer society and Baxter International Corporation to run the RCT.

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