Weight loss of 5% or more predicts loss of fat free mass during palliative chemotherapy in patients with advanced cancer – a pilot study

Susanne Buskermolen
Jacqueline A.E. Langius
Hinke M. Kruizenga
Gerdien C. Ligthart-Melis
Martijn W. Heymans
Henk M.W. Verheul

Nutrition and Cancer 2012;64(6):826-832
Abstract

Purpose: The cut-off value of critical weight loss is still subject of discussion. In this pilot study, we investigated whether \( \geq 5\% \) weight loss in the past year predicts changes in nutritional status in patients with advanced cancer during treatment with palliative chemotherapy.

Methods: In 20 patients with advanced cancer undergoing palliative (combination) chemotherapy, body weight, fat free mass (FFM) and cachexia were measured prior to the start and at nine weeks of treatment. History of weight loss was used to test differences in development of nutritional parameters during chemotherapy with use of independent sample t-tests.

Results: At baseline, ten of twenty patients had lost \( \geq 5\% \) body weight during the past year and five patients were cachectic. The change in FFM in the first 9 weeks of chemotherapy was significantly worse in patients with \( \geq 5\% \) weight loss compared to patients with \( <5\% \) weight loss (mean difference: 3.5 kg (\( p=0.001 \))). Data also suggest that \( \geq 5\% \) weight loss predicts shorter survival (\( p=0.03 \)).

Conclusion: We found that patients with \( \geq 5\% \) weight loss prior to chemotherapy have a deterioration in nutritional status during chemotherapy and may have a shorter survival. These results have to be confirmed in a larger study including a robust survival analysis.
Introduction

Disease-related undernutrition is a well-known problem in patients with cancer. Incidence rates vary depending on tumour site and tumour stage from 9% (in urological cancer) up to 85% (in pancreatic cancer) at diagnosis (1). Most patients who are about to receive palliative chemotherapy are at nutritional risk or already malnourished before start of the treatment (2). Weight loss and several nutrition-associated problems are associated with diminished quality of life (3), lower response to chemotherapy (3-5) and poor survival (3-9). In addition, patients with advanced cancer with weight loss prior to chemotherapy develop more frequent and more severe toxicity compared to patients without weight loss (5;6;10) and may receive ineffective chemotherapy due to significantly more treatment delay and dose reductions (6).

Weight loss is the result of an imbalance between energy intake and energy expenditure. Dietary intake can be impaired by side-effects of the anti-tumour therapy, for example nausea, vomiting and altered taste in case of chemotherapy (1). An increased energy expenditure can be caused by metabolic alterations induced by the tumour, known as the cachexia syndrome. “Cachexia is a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass” (11). In patients with cancer, cachexia is thought to be caused by the primary reaction of the host tissue of the patient to cancer and by substances produced by tumour cells (12;13). The literature on incidence and prevalence rates of cachexia is scarce because of the lack of a classification system until 2008 (11).

Screening for undernutrition is mandatory in Dutch hospitals. Currently, all patients with cancer are screened with the Short Nutritional Assessment Questionnaire (SNAQ) (14). Recently, a set of criteria to define cachexia has been described (11). The cut-off value of weight loss used in this set of criteria to define cachexia, 5% weight loss in the past year, is stricter than the currently used cut-off values in the SNAQ, ≥5% in the past month or ≥10% in the past six months (11;14). Based on this refinement of the criteria, it should be evaluated whether this stricter cut-off value is a predictor for a deterioration in nutritional status in patients with cancer receiving palliative chemotherapy.

The aim of this pilot study was to investigate whether this stricter cut-off value, weight loss of 5% or more in the past year, is associated with changes in body weight, fat-free mass, hand grip strength and mid-upper arm muscle circumference during palliative chemotherapy in patients with advanced cancer.
Chapter 3

Materials and methods

Patients
Patients aged 18 years or older with advanced cancer (proved recurrence or metastases) who were scheduled for first- or second line palliative chemotherapy treatment at the department of Medical Oncology of the VU University Medical Center Amsterdam were invited to enter the study. Patients with pleural fluid effusion, severe pitting oedema or ascites were excluded because nutritional status measurements are inadequate in these conditions. The research protocol was approved by the Medical Ethics Committee of the VU University Medical Center Amsterdam and the study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Informed consent was obtained from all participants.

Study design
In this observational prospective study markers of nutritional status: body weight (BW), fat free mass (FFM), handgrip strength, mid-arm muscle circumference (MUAMC), appetite and cachexia were determined prior to the first chemotherapy cycle (week 1) and after nine and eighteen weeks, according to the methods described below. A year after the last patient was included, survival data were obtained from the electronic medical record of each patient.

Markers of nutritional status
Body weight was measured (with patients wearing light indoor clothes without shoes) within 0.1 kg on a calibrated scale (Seca type 888). History of body weight was inquired or obtained from the medical record. A weight loss history of at least 5% in one year was used as cut-off value to compare groups in outcome.

Intra- and extracellular fluids (ICF and ECF respectively), total body water (TBW) and fat free mass (FFM) were determined using a bio-electrical impedance spectroscopy. The measurements were performed prior to chemotherapy, before infusion with fluids, with the patient in supine position, using a bio-impedance spectrum analyzer (Xitron 4200, Xitron Technologies, inc. San Diego, CA, USA). The measurements were conducted at least two weeks after the previous chemotherapy infusion. Two current electrodes (tetra-polar electrodes (3 M red Dot AG/AgCl)) were placed at the non-dominant side at the clean dorsal surfaces of hand and foot on the distal portion of the second metacarpal and metatarsal, respectively. Two detector
electrodes were placed at the posterior wrist between the styloid processes of the radius and ulna and at the anterior ankle between the tibial and fibular malleoli. TBW and FFM were calculated from resistance and reactance by using the Hanai equation (15).

Handgrip strength was measured using a hydraulic hand dynamometer (Baseline, Fabrication Enterprises, USA). The test was performed sitting, with the shoulder adducted and neutrally rotated, elbow flexed at 90 degrees, forearm and wrist in neutral position. Patients were instructed to perform two maximal isometric contractions. Both maximal values were recorded to the nearest 0.5 kg, and the mean of the two measurements was used to compare with age- and sex dependent reference values (<lowest tertile) for hand grip strength from Bohannon et al (16). Mid-upper arm circumference (MUAC) was measured in duplo at the midpoint of the non-dominant upper arm between the acromion process and the tip of the olecranon process, using a tape measure. To calculate the mid-arm muscle circumference, the triceps skin fold (TSF) was measured in duplo by a trained dietician at the same point using a John Bull skin fold calliper. The mean value of these measurements was recorded. Mid-arm muscle circumference was calculated by: \[ \text{MUAMC} = (\text{MUAC} - (\pi \times \text{TSF})) \]
and compared to the reference values of Frisancho et al (17).

Questionnaires
Appetite was assessed using the self-report version of the Simplified Nutritional Appetite Questionnaire (18). With this 4-item questionnaire, a score between 4 and 20 points can be obtained with a lower score indicating deterioration in appetite. A score \( <14 \) indicates significant risk of at least 5% weight loss within six months (18). Patients filled out the Multidimensional Fatigue Inventory (MFI-20) for the assessment of fatigue (19). The questionnaire consists of 20 questions in five domains: General Fatigue, Physical Fatigue, Reduced Activity, Reduced Motivation and Mental Fatigue. Each question is answered on a 5-point Likert scale, with a result of a score between 4 and 20 points per domain; a higher score indicates more fatigue (19). For the purpose of this study, the Physical Fatigue domain is used for the definition of cachexia.

Biochemical parameters
The laboratory values C-Reactive Protein (CRP), serum albumin and haemoglobin were measured in a non-fasted state before infusion with chemotherapy. Plasma
concentrations of CRP were measured with an automated latex-enhanced immunoturbidimetric assay on a Modular P analyzer (Roche Diagnostics, Almere, The Netherlands) (20). Serum albumin concentrations were chemically determined on a Modular P analyzer (Roche Diagnostics, Almere, The Netherlands) (21). Whole blood haemoglobin was determined with spectrophotometry on a Cell-Dyn Sapphire analyzer (Abbott Diagnostics, Hoofddorp) (22). All analyses were performed at department of Clinical Chemistry of the VU University Medical Center.

Measurement of cancer cachexia
Cancer cachexia\(^a\) was defined as (11): At least 5% unintentional weight loss in 12 months or less in the presence of underlying illness PLUS three of the following five criteria: decreased muscle strength (lowest tertile), fatigue, anorexia (<14 points on Simplified Nutritional Appetite Questionnaire (18)), low fat free mass index (<10\(^{th}\) percentile) and abnormal biochemistry (haemoglobin < 7.5 mmol/l, albumin < 32 g/L or C-reactive protein > 5 mg/L). Respectively, hand grip strength, MFI-20, Short Nutritional Appetite Questionnaire, MUAMC and laboratory value measurements were used for this definition. For decreased muscle strength, the reference values of Bohannon et al (16) were used (lowest tertile). Fatigue was defined as the score of the domain physical fatigue of the MFI-20 fatigue questionnaire (19) above 15 points. This is based on a mean value plus one standard deviation from a general population (23).

New cachexia criteria only include weight loss, inflammation and anorexia (24;25). Based on these opinion papers, we defined cachexia\(^a\) as ‘At least 5% unintentional weight loss with the presence of inflammation and anorexia.’ The cut-off values chosen for inflammation and anorexia are respectively C-reactive protein > 5 mg/L and <14 points on Simplified Nutritional Appetite Questionnaire (18).

Statistical analysis
Descriptive statistics (means ± SD, or median and interquartile ranges, as appropriate) was used to describe the study sample with regard to baseline characteristics. To explore selective dropout, differences in baseline variables for drop-outs versus patients who completed the third measurement were tested using chi-square tests, independent t-tests or Mann-Whitney U-tests as appropriate. Statistical analysis of the nutritional status during chemotherapy is only performed on the first two measurements, because of a high dropout rate during the study. Independent t-tests and chi-square tests were used to test differences in markers of nutritional status.
between patients with at least 5% weight loss in the past year versus patients with < 5% weight loss. Survival analysis was performed using the Log-rank test (for the difference between the group with and without ≥5% weight loss at baseline). Statistical analysis was performed using SPSS for Windows version 17.0. P-values < 0.05 were regarded statistically significant.

Results

Flow chart and baseline characteristics
A total of 33 patients with advanced cancer and scheduled to have chemotherapy were assessed for eligibility to enter the study during the three months of inclusion. Eleven patients were excluded according to the exclusion criteria (n=9 due to fluid problems, n=2 due to language problems). Twenty-two patients were found eligible to enter the study, of which two patients eventually did not want to participate because of other priorities (Figure 1).

Twenty patients completed the baseline measurement; 12 men and 8 women. Mean age was 64.6 (± 8.1) years. In these 20 patients, 12 different tumour types were present, of which colorectal cancer was the most prevalent (n=6, 30%) (Table 1). At baseline, ten of the twenty patients had lost weight of 5% or more during the past year. Nine of ten patients with weight loss of 5% or more in the past year had lost their bodyweight in the past six months. Five of ten patients with weight loss of 5% or more met the criteria of cachexia according to the criteria of Evans (11)(cachexia\textsuperscript{a}) and also five of ten patients with weight loss of 5% were classified cachectic when inflammation and anorexia was present (cachexia\textsuperscript{b}). Four of five cachectic patients were identified as cachectic by both cachexia definitions. Sixty percent of the patients had low hand grip strength (below the lowest tertile) There was no association between a low hand grip strength and inquired weight loss history; the prevalence of a low hand grip strength was equal in both groups (Table 1).
Assessed for eligibility (n=33)

Excluded (n=13) according to the exclusion criteria:
- Fluid problems: n=9
- Language problems: n=2
Declined to participate (n=2)

Recruited, completed baseline measurement (n=20)

Lost to follow-up (chemotherapy stopped) (n=4)
- Missed second measurement) (n=1)

Completed second measurement (9 weeks) (n=15)

Lost to follow-up (died) (n=6)

Completed third measurement (18 weeks) (n=10)

Figure 1. Recruitment and dropout of patients
Pre-treatment weight loss predicts loss of FFM

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total group (n=20)</th>
<th>&lt; 5% WL (n=10)</th>
<th>≥ 5% WL (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Age (years) a</td>
<td>64.6 (8.1)</td>
<td>64.0 (7.7)</td>
<td>65.1 (8.8)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>12 (60)</td>
<td>6 (60)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Cancer type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oesophageal/stomach</td>
<td>2 (10)</td>
<td>0 (0)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>4 (20)</td>
<td>1 (10)</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>6 (30)</td>
<td>5 (50)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>1 (5)</td>
<td>0 (0)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Breast and gynaecology</td>
<td>2 (10)</td>
<td>1 (1)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Other sites</td>
<td>5 (25)</td>
<td>2 (20)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Planned chemotherapy protocol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line</td>
<td>18 (90)</td>
<td>9 (90)</td>
<td>9 (90)</td>
</tr>
<tr>
<td>Second line</td>
<td>2 (10)</td>
<td>1 (10)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 18.5</td>
<td>2 (10)</td>
<td>1 (1)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>18.5-25.0</td>
<td>10 (50)</td>
<td>4 (40)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>&gt; 25.0</td>
<td>8 (40)</td>
<td>5 (50)</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Cachexia a.b</td>
<td>5 (25)</td>
<td>NA</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Cachexia b.c</td>
<td>5 (25)</td>
<td>NA</td>
<td>5 (50)</td>
</tr>
<tr>
<td>FFMI &lt; 10th percentile</td>
<td>2 (11)</td>
<td>0 (0)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>MUAMC &lt; 10th percentile</td>
<td>2 (10)</td>
<td>1 (1)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Hand grip strength lowest tertile</td>
<td>12 (60)</td>
<td>6 (60)</td>
<td>6 (60)</td>
</tr>
</tbody>
</table>


a Mean (sd)
b Cachexia a. defined according to the definition of Evans et al (11) Not applicable in group with weight loss <5% because weight loss of 5% or more is a component of the cachexia definition.
c Cachexia b. based on the presence of inflammation and anorexia. Not applicable in group with weight loss <5% because weight loss of 5% or more is a component of the cachexia definition.

Primary endpoint

Patients with 5% weight loss or more at baseline had a significant decline in fat free mass during chemotherapy (mean difference compared to patients with <5% weight loss: 3.5 kg (p=0.001)). History of weight loss was not associated with changes in hand grip strength and mid-upper arm muscle circumference (Table 2).
Table 2. Change in weight, fat free mass, phase angle, hand grip strength and mid-upper arm muscle circumference (week 9 compared to week 1) for subgroups with <5% weight loss versus ≥ 5% weight loss at baseline

<table>
<thead>
<tr>
<th></th>
<th>&lt; 5% WL (n=7) Mean ± SD</th>
<th>≥ 5% WL (n=8) Mean ± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ Weight (kg)</td>
<td>-1.00 ± 2.70</td>
<td>-2.18 ± 3.64</td>
<td>0.482</td>
</tr>
<tr>
<td>Δ FFM (kg)</td>
<td>2.00 ± 1.38</td>
<td>-1.48 ± 1.58</td>
<td>0.001*</td>
</tr>
<tr>
<td>Δ ICF (l)</td>
<td>1.73 ± 1.26</td>
<td>0.03± 1.66</td>
<td>0.049*</td>
</tr>
<tr>
<td>Δ PA (degrees)</td>
<td>-0.38 ± 0.98</td>
<td>-0.77 ± 0.78</td>
<td>0.442</td>
</tr>
<tr>
<td>Δ Hand grip strength (kg)</td>
<td>-0.94 ± 9.12</td>
<td>-1.29 ± 4.16</td>
<td>0.928</td>
</tr>
<tr>
<td>Δ MUAMC (mm)</td>
<td>-4.88 ± 16.62</td>
<td>-2.57 ± 10.95</td>
<td>0.760</td>
</tr>
</tbody>
</table>

Δ : Change. FFM: Fat free mass, ICF: Intracellular fluids; PA: Phase Angle, MUAMC: Mid-upper arm muscle circumference
* Statistical significant for the difference between two groups

Cachexia criteria

There were no statistical significant differences in hand grip strength, mid-upper arm muscle circumference and laboratory values (haemoglobin, albumin and c-reactive protein) between patients with weight loss of 5% or more at baseline versus patients with <5% weight loss at baseline (cachexia criteria, Table 3).

Table 3. Sub criteria of cachexia (baseline measurement)

<table>
<thead>
<tr>
<th></th>
<th>&lt; 5% WL (n=10) n (%)</th>
<th>≥ 5% WL (n=10) n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cachexia</td>
<td>0 (0)</td>
<td>5 (50)</td>
<td>NA*</td>
</tr>
<tr>
<td>Handgrip strength &lt; lowest tertile</td>
<td>6 (60)</td>
<td>6 (60)</td>
<td>1.00</td>
</tr>
<tr>
<td>Fatigue ≥15 points</td>
<td>2 (20)</td>
<td>4 (40)</td>
<td>0.63</td>
</tr>
<tr>
<td>MUAMC &lt;10th percentile</td>
<td>1 (10)</td>
<td>1 (10)</td>
<td>1.00</td>
</tr>
<tr>
<td>Appetite &lt;14 points</td>
<td>4 (40)</td>
<td>7 (70)</td>
<td>0.37</td>
</tr>
<tr>
<td>Laboratory values (min. 1 of 3 abnormal)</td>
<td>5 (50)</td>
<td>9 (90)</td>
<td>0.14</td>
</tr>
<tr>
<td>Haemoglobin &lt; 7.5 mmol/l</td>
<td>2 (22)</td>
<td>5 (50)</td>
<td>0.35</td>
</tr>
<tr>
<td>Albumin &lt; 32g/l</td>
<td>0 (0)</td>
<td>1 (10)</td>
<td>1.00</td>
</tr>
<tr>
<td>CRP ≥ 5 mg/l (n=17)</td>
<td>5 (63)</td>
<td>7 (78)</td>
<td>0.62</td>
</tr>
<tr>
<td>Appetite &lt;14 points in combination with CRP ≥ 5 mg/l</td>
<td>2 (20)</td>
<td>5 (56)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

MUAMC: Mid-upper arm muscle circumference CRP: C-Reactive Protein
* P-value for cachexia is not applicable because weight loss is used to define cachexia.
Assessment of dropouts
Of the 20 included patients, 15 (75%) completed the measurement after 9 weeks and 10 patients (50%) completed the third measurement (after 18 weeks). Main reason for dropping out was termination of chemotherapy administration (n=4) and death of patients (n=6) (Figure 1). The patients who dropped out before the third measurement had a worse appetite at baseline compared to the patients who completed the third measurement (medians: 12.5 and 15.5, respectively) (p=0.05).

Figure 2. Individual weight change: weight loss in the first nine weeks of chemotherapy was a predictor for dropping out before the third measurement (p<0.01).
Furthermore, 4 out of 10 dropouts met the criteria of cachexia at baseline, while only 1 patient out of 10 in the group who completed the third measurement had cachexia. Weight loss during the first 9 weeks of chemotherapy was a predictor for dropping out before the third measurement ($p<0.01$, Figure 2).

**Survival**

In the group of patients with weight loss of 5% or more at baseline, a shorter survival compared to patients with 0-5% weight loss at baseline was found ($p=0.03$, Figure 3).

![Cumulative survival plot](image)

*Figure 3. Kaplan-Meier plot: cumulative survival for ≥5% weight loss versus <5% weight loss at baseline. Log-rank test, P-value for the difference: 0.029*

Furthermore, a shorter survival in patients who lost fat free mass during the first nine weeks of chemotherapy compared to the patients with stable fat free mass was also found ($p=0.04$) (Data not shown).
Discussion

As far as we know this is the first study which uses the new cachexia cut-off value of weight loss to investigate its association with nutritional status parameters in patients with advanced cancer receiving palliative chemotherapy. The objective was to evaluate whether this new cut-off value is associated with other parameters of the nutritional status during palliative chemotherapy. We also evaluated whether this new cut-off value of weight loss may be related to some extent to survival in this heterogeneous group of patients. We found that weight loss of more than 5% prior to chemotherapy resulted in a decrease of fat free mass in the first nine weeks of chemotherapy and an association with a shorter survival in this heterogeneous patient group was suggested.

Our results are in line with the results of Halpen-Silveria et al (27). They found that severe malnutrition at admission (PG-SGA score C) was an independent predictor of loss of fat free mass during the course of chemotherapy when compared to wellnourished patients (PG-SGA score A). However, the cut-off value they used (PG-SGA-score C: ≥5% weight loss in 1 month or more than 10% in 6 months) is much stricter than the cut-off value in our study (≥5% weight loss in the past year), and even with the small number of patients in our study an impressive difference in fat free mass change was found.

We found no associations between weight loss category at baseline and hand grip strength change during chemotherapy. Although loss of muscle strength is thought to be correlated to loss of muscle mass with ageing in physiological studies, correlations in older adults appear to be inconsistent and not very robust (28), which is in line with our negative results.

Multiple studies show that weight loss is a predictor for survival, with variable cut-off values used for weight loss. For example, PG-SGA B/C versus PG-SGA A (8;29), the highest tertile of weight loss versus the lowest tertile (7) and any weight loss versus stable weight (4-6). The univariate survival analysis in this small patient group showed that even small amounts of weight loss (5% or more in one year) may worsen prognosis.

For the estimation of fat free mass, bio-impedance analysis is an easy, non-invasive method that can be performed bed-side. Its validity in patients with cancer is sometimes questioned because of an increased hydration state in these patients, better known as tumour-induced hyperhydration (30). Fat free mass can be overestimated by the use of total body water measurement. Therefore, hydration
abnormalities such as pleural fluid effusion, severe pitting oedema or ascites were exclusion criteria for participation in this study.

In our study, five of ten patients with weight loss were in a cachectic state according to the definition of Evans (referred to as cachexia\textsuperscript{a}) (11) and also according to our definition based on the opinion papers of Muscaritoli \textit{et al.} and Fearon \textit{et al.} (referred to as cachexia\textsuperscript{b}) (24;25), four of five were similar patients. This is a prevalence of 20-25% in the total study population. Before classification, the prevalence of cachexia was estimated higher based on weight loss alone (31). In patients with pancreatic cancer, the prevalence of cachexia fell from 80% to 20% when cachexia was classified in a multidimensional form (31).

An interesting finding in our study is the contribution of individual items to the two definitions of cachexia. There were no statistical significant differences in hand grip strength, mid-upper arm muscle circumference and laboratory values (albumin, haemoglobin and c-reactive protein) (cachexia\textsuperscript{a}) between patients with weight loss of 5% or more at baseline versus patients with <5% weight loss at baseline. Also, presence of inflammation in combination with anorexia (cachexia\textsuperscript{b}) was not statistical significant different between the two weight loss groups. This is in contrast to the findings of O’Gorman \textit{et al.} (32). They found that patient with more than 5% weight loss had diminished appetite, increased inflammation and diminished anthropometric measurements compared to weight-stable patients with advanced gastrointestinal cancer.

Next to patients with gastrointestinal cancer, we also included patients with other tumour types, this may be an explanation for conflicting results. The importance of individual items of the cachexia diagnostic tool such as hand grip strength, mid-upper arm muscle circumference and albumin, needs to be reconsidered and should be further evaluated in larger prospective trials, differentiating for tumour location.

The best way to treat cancer cachexia is to cure cancer, and in that way normalizing the metabolic abnormalities induced by the tumour and/or tumour/host interactions. For some years, attempts have been made to reverse loss of fat free mass with different interventions in patients with cancer. Two often used examples are progestational agents and N-3 polyunsaturated fatty acids. Progestational agents like megastrol acetate improves appetite and is associated with weight gain. Nevertheless, an increase of fat mass rather than fat free mass is achieved and there is no benefit in quality of life (33). To attack metabolic changes, N-3 polyunsaturated fatty acids are of consideration because of their possible anticachectic properties (34;35). Supplementation of N-3 fatty acids might preserve fat free mass (36;37).
A limitation of this study is its small sample size. As a consequence, all statistical tests described are univariate and results have to be interpreted with caution, especially considering the survival analyses. Nevertheless, these results contribute to science in a hypothesis-generating manner.

This pilot study demonstrated that patients with weight loss of 5% or more prior to chemotherapy have a deterioration in nutritional status during chemotherapy. In addition, a potential relation of weight loss of 5% or more with survival became apparent. These results have to be confirmed in a larger study including a robust survival analysis, in order to clarify which cut-off value of weight loss can be used best as a criterion for undernutrition in patients with cancer.
References

Pre-treatment weight loss predicts loss of FFM