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Original article

The association of weight loss with one-year mortality in hospital patients, stratified by BMI and FFMI subgroups

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SUMMARY

Background: The European Society for Clinical Nutrition and Metabolism (ESPEN) has recently published consensus-based criteria for the diagnosis of malnutrition; in subjects identified at nutritional risk the diagnosis is confirmed by either BMI <18.5 kg/m^2 or weight loss in combination with low BMI or low FFMI. Concerns have been raised whether this definition correctly classifies malnutrition in patients with normal weight or overweight and concomitant weight loss. Therefore, the aim of this research is to assess the association between weight loss and one-year mortality in hospitalized patients, stratified by BMI and FFMI subgroups.
Methods: This prospective study included 769 patients admitted to the VU University Medical Center. Critical weight loss (CWL) was defined as >5% weight loss in the previous month or >10% weight loss in the previous six months. The association between CWL and one-year mortality was analyzed with a priori stratification by BMI cut-off values (</≥20.0 kg/m^2 for patients <70 years and </≥22.0 kg/m^2 for patients ≥70 years) and FFMI cut-off values (derived from BIA measurements, </≥15 kg/m^2 for females and </≥17 kg/m^2 for males). Mortality risks were calculated (HR, 95% CI).
Results: CWL occurred in 35% of patients and was associated with an increased one-year mortality rate vs. no-CWL (25% vs. 15%, $p = 0.001$), HR for mortality risk 1.76 (1.26–2.45)). CWL + low FFMI was associated with higher mortality risk (HR 1.95 (1.20–3.17), whereas CWL + normal FFMI was not (HR 1.37 (0.85–2.21)). Among patients with normal/high BMI, those with CWL had a significantly higher mortality risk compared to those without critical weight loss, however additionally adding FFMI to that model showed that a low FFMI was crucial in the observed association with mortality (CWL + normal BMI + low FFMI, HR 2.69 (1.29–5.65); CWL + normal BMI + normal FFMI, HR 1.38 (0.84–2.27)).
Conclusion: – Patients with critical weight loss have a higher one-year mortality compared to patients with no critical weight loss. FFMI seems to play a crucial role in this association, as normal weight patients with normal FFMI had lower mortality rates than their counterparts with low FFMI.

1. Introduction

In 2015, the European Society for Clinical Nutrition and Metabolism, published a consensus-based minimum set of malnutrition criteria, with the aim “to unify international terminology, to effectively provide nutritional interventions, and to document clinically relevant malnutrition”, see Fact box 1 [1].

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Fact box 1
ESPEN diagnostic criteria for malnutrition [1].

The ESPEN diagnostic criteria for malnutrition [1]. In subjects that have been identified as being at risk for malnutrition (by a validated screening tool) malnutrition is confirmed/defined as:

- **BMI** of <18.5 kg/m^2

or

- Combination of **unintentional weight loss** (>5% weight loss over the last three months or >10% weight loss indefinite of time) with either:

BMI of <20 kg/m^2 (<22 kg/m^2 in patients 70 years and older)
or
FFMI of <15 kg/m^2 for females and <17 kg/m^2 for males

As this set of malnutrition criteria is based on consensus, validation studies are required to substantiate the chosen methods and cut-off points. Experts in the field have questioned whether this consensus definition correctly identifies nutritional risk in overweight patients who have experienced considerable weight-loss [2]. The ESPEN consensus group suggests that a patient is only considered to be malnourished if the weight loss had led to a considerable depletion of energy or protein reserves, represented by BMI or FFMI below the suggested cut-off points. A patient with unintentional weight loss but with (still) normal energy and protein reserves is considered to be a patient at risk, but not yet malnourished.

Although multiple previous studies have shown that unintentional weight loss in patients leads to a higher mortality risk [3–10], only few studies have studied whether the impact of weight loss is different for patients in the higher or lower BMI and FFMI subcategories [3]. Therefore, this study was designed to investigate the impact of critical weight loss (CWL) on one-year mortality, stratified by BMI and FFMI subgroups according to the ESPEN diagnostic criteria for malnutrition.

2. Methods

2.1. Study design and population

The study population consisted of two samples from the VU University Medical Center (VUmc, Amsterdam, The Netherlands). The first study (Study 1) was performed to determine the cost-effectiveness of early screening and treatment of malnutrition [11]. This study cohort consisted of consecutive adult inpatients admitted to the wards of general internal medicine or general surgery. Patients were included between April 2002 and October 2002, and between February 2003 and June 2003 [11]. Data collection took place at the first day of admission to hospital.

The second study (Study 2) represents an ongoing patient cohort, in which parameters of nutritional status are collected as part of an in-depth nutritional assessment by a dietitian, either on referral by the treating physician, or as part as protocolled care for patients at increased nutrition risk (i.e. preoperative work-up for patients with carcinoma's of the upper gastrointestinal tract). This sample consists of adult inpatients and outpatients from different wards of the VUmc. Patients were included from February 2008 until February 2015.

For the present study, adult patients 18 years or older were included (Fig. 1). Patients with missing values on FFMI (derived from bioelectrical impedance (BIA)) were excluded as well as patients with reported edema or amputations [12]. Patients from Study 1 were additionally excluded if their expected hospital stay was less than 24 h, if they were not able to give informed consent or if they could not be weighed. Study 1 was approved by the medical ethical review committee of the VUmc and was carried out in accordance with the Declaration of Helsinki [11]. Measurements from Study 2 were obtained during regular dietetic consultations and were collected with the purpose to optimize nutritional care. Informed consent was waved as data were collected as part of routine care.

2.2. Data collection & variables

2.2.1. Survival

The primary outcome for this study was one-year mortality, measured from the day of nutritional assessment. Both the digital hospital information system and the Municipal Personal Records Database were checked to determine survival status. There were no missing data on survival.

2.2.2. Weight loss

The main determinant of this study was weight loss. Weight loss during the past month and during the past six months before measurement was obtained by recall. For this study, critical weight loss (CWL) was defined as >5% weight loss in the previous month and/or >10% weight loss in the previous six months [13]. Weight loss of ≤5% in the previous month and/or ≤10% in the previous six months was defined as no critical weight loss (non-CWL group).

2.2.3. Anthropometric data

Actual weight was measured on a calibrated scale (SECA) with an accuracy of 0.1 kg. Height was either recalled or measured. Height was measured with a calibrated telescopic measuring rod (SECA) and was expressed in meters (m) with an accuracy of 1 cm. Weight was measured in 510 patients (66%) and recalled in 200 patients (26%). In 59 patients (8%) it was unknown whether weight was measured or recalled. Height was measured in 61 patients (8%) and recalled in 648 patients (84%). In 60 patients (8%) it was unknown whether height was measured or recalled.

BMI (weight/height^2) was calculated from weight and height and expressed in kg/m^2. The (age specific) cut-off values for BMI according to the ESPEN diagnostic criteria for malnutrition were used as a priori stratification in the analysis between weight loss and one-year survival; </≥20.0 kg/m^2 for patients <70 years and </≥22.0 kg/m^2 for patients ≥70 years [1].

2.2.4. Body composition

Measurements of body composition were performed by BIA according to a standardized protocol [14]. In Study 1, body composition was measured using a Xitron 4000B analyzer (Xitron technologies, San Diego, CA, USA). In Study 2 body composition measurements were performed with either a Bodystat 1500 MDD (Bodystat Ltd, Douglas, Isle of Man, British Isles), a Quadscan 4000 (Bodystat Ltd, Douglas, Isle of Man, British Isles) or a BodyScout (Fresenius Kabi, Bad Homburg, Germany). All devices were calibrated before use. Inpatients were measured at bedside; outpatients were requested to lie down on a bed for five minutes before measurement.

Based on resistance and reactance at 50 kHz, fat free mass (FFM, kg) was calculated according to the Geneva equation [15]. Subsequently FFMI was calculated as FFM/height^2.

The sex specific cut-off values for FFMI according to the to the ESPEN diagnostic criteria for malnutrition were used as a priori

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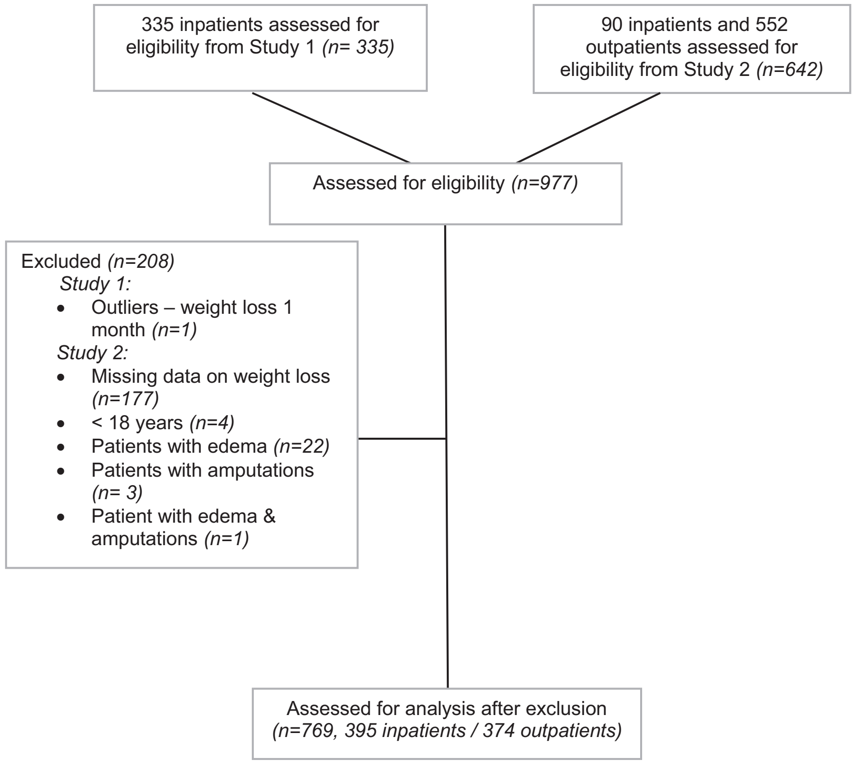

Fig. 1. Flowchart of patients included in this study.

stratification in the analysis between weight loss and one-year mortality; $</\geq 15$ kg/m^2 (females) and $</\geq 17$ kg/m^2 (males) [1].

2.3. Statistical analysis

Before analyses, continuous variables were checked for normality. The variables age, weight, height, weight loss, BMI and FFMI were checked and outliers were excluded before analysis. Age and FFMI were presented as means with standard deviations. BMI was positively skewed and presented as median and interquartile range (IQR). The variables; gender, inpatient/outpatient status, weight loss (CWL versus non-CWL), BMI cut-off values and FFMI cut-off values were presented with numbers and percentages.

Independent t-tests were used to test the differences in age and FFMI between the critical weight loss group and the non-critical weight loss group, Mann–Whitney U test was used for BMI. Chi-squared tests (X^2) were used to test the difference in gender, inpatient/outpatient status, age $</\geq 70$ years, BMI cut-off values and FFMI cut-off values between the critical weight loss group and the non-CWL group.

Survival analyses were performed with Kaplan–Meier curves (*p*-value) and Cox's proportional hazard models (Hazard Ratio, 95% confidence interval, *p*-value). First, log rank tests were used to test the difference in one-year mortality between patients with/without CWL, with/without BMI respectively FFMI below the ESPEN cut-off points, and with/without CWL split by BMI $</\geq 18.5$. Kaplan–Meier curves were inspected to determine whether the proportional hazard assumption was met. Subsequently, the association between weight loss (CWL compared to non-CWL), BMI (under and over the cut-off points of 18.5 and 20/22 kg/m^2) and the interaction weight loss and BMI was analyzed.

Finally, to understand the results, subsets were made to show the association between weight loss (CWL compared to non-CWL) and one-year mortality with a priori stratification by BMI cut-off values (BMI $</\geq 18.5$ kg/m^2 and BMI $</\geq 20.0$ kg/m^2 (without BMI <18.5 kg/m^2) for patients <70 years or $</\geq 22.0$ kg/m^2 (without BMI <18.5 kg/m^2) for patients ≥ 70 years) and FFMI cut-off values ($</\geq 15$ kg/m^2 for females and $</\geq 17$ kg/m^2 for males), and possible combinations. Hazard ratios represent mortality risk.

Interaction or confounding by age, gender and inpatient/outpatient status was investigated but none of these variables were effect modifiers (based on significance) or confounders (based on $\geq 10\%$ change in the beta of the independent variable). Statistical analyses were performed using IBM SPSS Statistics 23. *p*-values of <0.05 were considered statistically significant.

3. Results

Before exclusion, the study population consisted of 977 patients, 335 patients from Study 1 and 642 patients from Study 2. Two hundred eight patients were excluded, mostly because of missing data on weight loss (flow chart, Fig. 1), resulting in 769 included patients.

3.1. Patient characteristics

Patient characteristics are shown in Table 1. The mean age of the study population was 60 ± 6 years and fifty-five percent of the patients (*n = 419*) were male. The proportion of inpatients and outpatients was almost equally distributed. The specialisms represented were: surgery/surgical oncology (*n = 451, 59%*), internal medicine (*n = 187, 24%*), medical oncology (*n = 73, 10%*), gastroenterology (*n = 26, 3.5%*), pulmonology (*n = 22, 3%*), and other (*n = 10, 0.5%*). Thirty-five percent (*n = 270*) of the patients presented with CWL, more outpatients than inpatients (56% versus 44%).

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Table 1
Baseline characteristics of the total study population ($n = 769$).

	Total	Patients with critical weight loss	Patients with no critical weight loss	p-value
n (%)	769 (100)	270 (35.1)	499 (64.9)	
Age (years)[A]	60.0 (15.5)	61.2 (14.8)	59.3 (15.8)	0.111
<70 years (%)	545 (70.9)	189 (70.0)	356 (71.3)	0.696
≥70 years (%)	224 (29.1)	81 (30.0)	143 (28.7)	
Male (%)	419 (54.5)	154 (57.0)	265 (53.1)	0.296
Inpatient (%)	395 (51.4)	118 (43.7)	277 (55.5)	0.002
BMI (kg/m^2)[B]	23.8 (5.9)	22.4 (6.2)	24.6 (6.0)	<0.001
BMI cut-off values (%)				
<18.5 kg/m^2 [C]	72 (9.4)	39 (14.4)	33 (6.6)	<0.001
≥18.5 kg/m^2 [C]	697 (90.6)	231 (85.6)	466 (93.4)	
<20.0 kg/m^2|<22.0 kg/m^2 [D]	182 (23.7)	94 (34.8)	88 (17.6)	<0.001
≥20.0 kg/m^2|≥22.0 kg/m^2 [D]	587 (76.3)	176 (65.2)	411 (82.4)	
FFMI (kg/m^2)[A]				
Females	15.5 (2.2)	14.8 (2.2)	15.8 (2.1)	<0.001
Males	18.1 (2.1)	17.4 (2.1)	18.4 (2.1)	<0.001
FFMI cut-off values (%)				
<15.0 kg/m^2|<17.0 kg/m^2 [E]	283 (36.8)	129 (47.8)	154 (30.9)	<0.001
≥15.0 kg/m^2|≥17.0 kg/m^2 [E]	486 (63.2)	141 (52.2)	345 (69.1)	

[A] = Mean (SD) [B] = Median (IQR) [C] = Cut-off values includes all subjects [D] = Cut-off value 20 kg/m^2 applies for subjects <70 years and cut-off value 22 kg/m^2 applies for subjects ≥70 years [E] = Cut-off value 15 kg/m^2 applies for females and cut-off value 17 kg/m^2 applies for males.

BMI was significantly lower in patients with CWL, compared to the non-CWL group. Also, a larger proportion of patients with CWL presented with BMI or FFMI below the ESPEN cut-off points.

3.2. Survival

For each of the determinants of the ESPEN definition, one-year survival was calculated. One-year survival for patients with/without CWL was 75.2% and 85.2% respectively (log rank, $p = 0.001$). Figure 2A shows the accompanying Kaplan–Meier curve. One-year survival for patients with BMI <18.5 kg/m^2 vs. BMI ≥18.5 kg/m^2 was 77.8% and 82.1% (log rank: $p = 0.333$). For patients with BMI <20/22 kg/m^2 vs. patients with BMI ≥20/22 kg/m^2 one-year survival was 76.4% and 83.3% (log rank, $p = 0.026$) and for patients with FFMI <15/17 kg/m^2 vs. patients with FFMI ≥15/17 kg/m^2 one-year survival was 76.0% and 85.0% respectively (log rank, $p = 0.001$). The one-year survival for patients with/without CWL and BMI <18.5 kg/m^2 was 71.8% and 84.8% respectively. For patients with/without CWL and BMI ≥18.5 kg/m^2 this 75.8% and 85.2% respectively (log rank, $p = 0.007$) (Fig. 2B).

3.3. Impact of critical weight loss on mortality

Table 2 shows one-year mortality data for patients with critical weight loss versus patients without critical weight loss, for subsets according to the ESPEN criteria. Data show that CWL is of less relevance in patients with a BMI between 18.5 and 20/22 kg/m^2, in patients with a normal FFMI, and in patients with a normal BMI combined with a normal FFMI.

Patients with CWL and patients with combinations of CWL with BMI ≥18.5 kg/m^2, BMI ≥20/22 kg/m^2, FFMI <15/17 kg/m^2, and combined high BMI/low FFMI had a higher mortality rates. In contrast, CWL combined with BMI <18.5 kg/m^2, BMI between 18.5 and 20/22 kg/m^2, FFMI ≥15/17 kg/m^2, combined low BMI/low FFMI, combined low BMI/high FFMI, and combined high BMI/high FFMI was not associated with higher mortality.

Cox proportional hazards analyses predicting one-year mortality were performed for patients with CWL compared to patients with no CWL, with subanalyses stratified by BMI and FFMI subcategories and subsequent combinations (Fig. 3). This figure shows that CWL on itself, or CWL in combination with BMI ≥18.5, BMI ≥20/22, FFMI<15/17, BMI ≥20/22 in combination with FFMI<15/17 was predictive of higher mortality. In contrast CWL combined with low BMIs (both BMI <18.5 and BMI between 18.5 and 20/22), and CWL combined with higher FFMI (≥15/17) was not predictive for increased mortality.

4. Discussion

To our knowledge, this is the first study that investigates the association between CWL and one-year mortality in hospitalized patients, stratified by BMI and FFMI subgroups according to the ESPEN diagnostic criteria for malnutrition.

The main question to be answered was whether the ESPEN definition would correctly classify patients with normal weight or overweight and weight loss as malnourished, as these patients meet the cut-off points for depletion (low BMI or low FFMI) only after considerable weight loss. To study this question, which is extremely relevant in the present era of overweight, we studied CWL in relation to one-year mortality, stratified by BMI and FFMI subgroups.

This study showed that patients with CWL and a normal FFMI were nót at increased one-year mortality risk, whereas those who presented with CWL and a low FFMI had an increased mortality risk. A higher mortality risk was also observed in patients with CWL and a combined higher BMI/low FFMI but not in patients with CWL and a combined higher BMI/high FFMI. These findings underline the importance of FFMI measurements in the assessment of malnutrition.

An increased mortality risk was also observed for patients with CWL and a higher BMI. At first sight this would suggest that patients with a higher BMI and concomitant weight loss would incorrectly not be classified malnourished by the ESPEN definition. However, further subgroup analyses showed differences between CWL + high BMI + low FFMI versus CWL + higher BMI + high FFMI. Only patients with a low FFMI had increased mortality risks. These results suggest that the ESPEN assumption that CWL only becomes of relevance when protein stores get depleted may be correct. Note that subsamples were small and that replication in larger samples is warranted.

Not surprisingly and in line with previous publications, patients with either CWL, or a low BMI, or a low FFMI had higher mortality rates than patients with normal values. The fact that this was not statistically significant for BMI <18.5 or BMI between 18.5 and 22 kg/m^2 may be explained by the fact that the assumption of proportional hazards was not met during the first 3 months;

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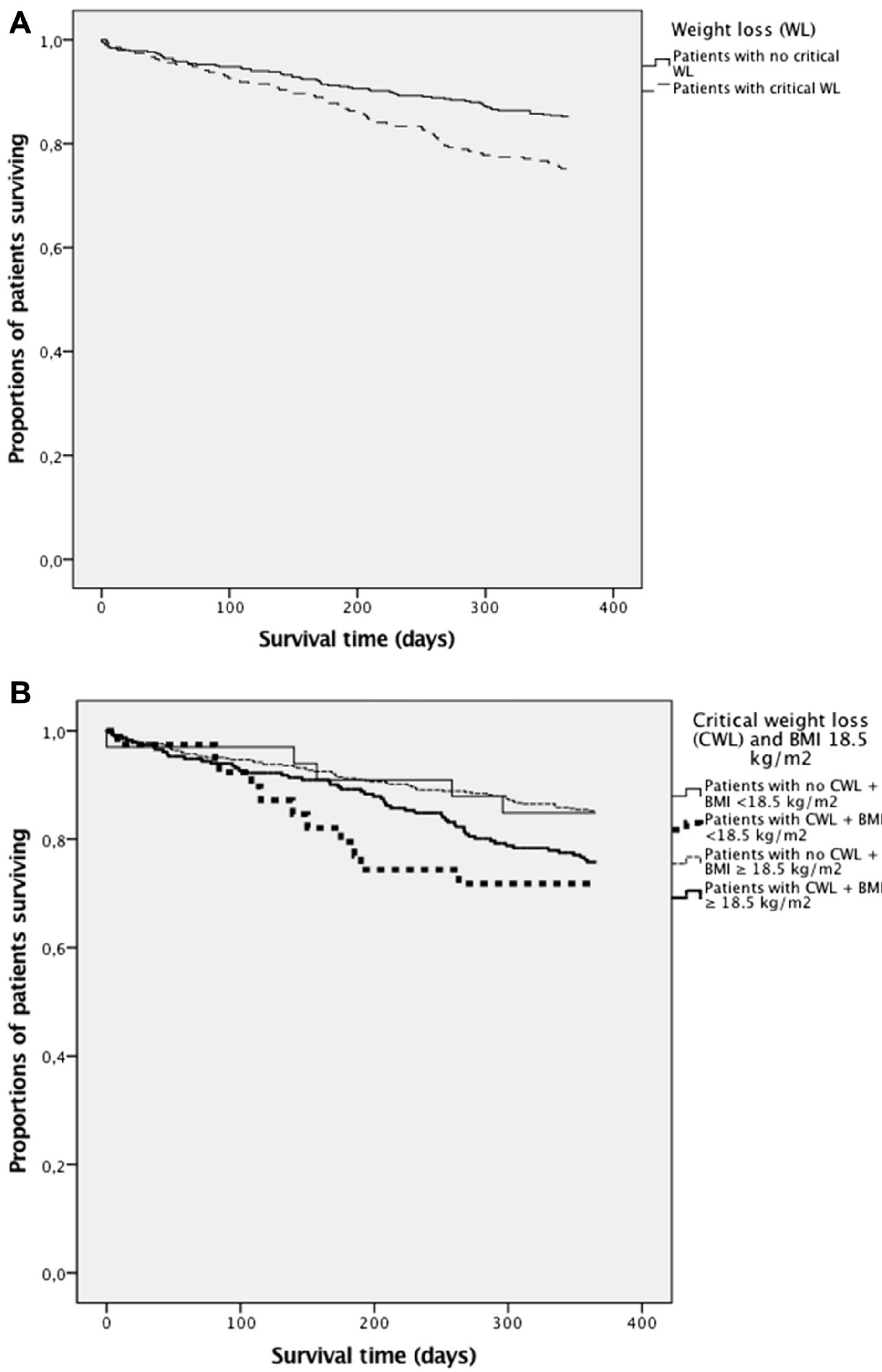

Fig. 2. Kaplan–Meier curves expressing one-year survival in A: patients with critical weight loss and patients with no critical weight loss ($p = 0.001$) and B: patients with critical weight loss and patients with no critical weight loss, stratified by BMI <18.5/≥18.5 kg/m^2 ($p = 0.007$).

thereafter the hazard ratio indicates a proportional effect and survival curves diverged. In addition, few patients and even fewer deaths were included in the very low BMI category, possibly indicating a lack of power.

Patients with a combination of CWL and a BMI between 18.5 and 20/22 kg/m^2 or the combination of CWL + low BMI + low FFMI were not at increased mortality risk compared to those without CWL. Although this may seem surprisingly unexpected at first sight, results can be explained by the fact that patients with a low BMI of a combination of low BMI/low FFMI are already depleted in energy and protein reserves. Whether this is combined or not combined with CWL seems to be of less relevance. Also, the number of events was rather small and HRs tended towards increased risk, so the negative results may as well indicate a lack of power.

Several earlier studies have described an association between weight loss and survival [3–10,16–20]. Newman et al. showed that weight loss (defined as weight loss of 5% or more over in a 3-year period) was associated with an increased risk of mortality in older adults (HR 1.66; 95% CI 1.18–2.33) [3]. Wijnhoven et al. showed that unintentional weight loss was associated with an

Table 2
One-year mortality data for patients with critical weight loss versus patients without critical weight loss, for all patients and according to the different ESPEN malnutrition criteria.

Patients (*n*)	Critical weight loss, *n*	Dead, *n* (%)	No critical weight loss, *n*	Dead, *n* (%)	*p*-value
All patients (769)	270	67 (25%)	499	74 (15%)	**0.001**
BMI <18.5 (72)	39	11 (28%)	33	5 (15%)	0.173
BMI ≥18.5 (697)	231	56 (24%)	466	69 (15%)	**0.003**
BMI between 18.5 and 20/22 (110)[A]	55	15 (27%)	55	12 (22%)	0.543
BMI ≥20/22 (587)[A]	176	41 (23%)	411	57 (14%)	**0.006**
FFMI <15/17 (283)[B]	129	41 (32%)	154	27 (17%)	**0.006**
FFMI ≥15/17 (486)[B]	141	26 (18%)	345	47 (14%)	0.196
BMI between 18.5 and 20/22 and FFMI <15/17 (88)[A B]	45	13 (29%)	43	10 (23%)	0.595
BMI between 18.5 and 20/22 and FFMI ≥15/17 (22)[A B]	10	2 (20%)	12	2 (17%)	0.804
BMI ≥20/22 and FFMI <15/17 (124)[A B]	46	17 (37%)	78	12 (15%)	**0.006**
BMI ≥20/22 and FFMI ≥15/17 (463)[A B]	130	24 (18%)	333	45 (13%)	0.200

p-values <0.05 are shown in bold.
[A] = Cut-off value 20 kg/m^2 applies for subjects <70 years and cut-off value 22 kg/m^2 applies for subjects ≥70 years.
[B] = Cut-off value 15 kg/m^2 applies for females and cut-off value 17 kg/m^2 applies for males.

increased 3-year mortality risk in community-dwelling older adults (HR for unintentional weight loss due to medical reasons <72 y: 2.43; 95% CI 1.52–3.88/HR for unintentional weight loss due to medical reasons ≥72 y: 1.62; 95% CI 1.23–2.14/HR for unintentional weight loss due to unknown reasons: 1.98; 95% CI 1.49–2.62) [9]. In two community based cohorts, Allison et al. showed that weight loss was associated with increased mortality rate; each standard deviation of weight loss (4.6 kg in first cohort/6.7 kg in second cohort) increased the hazard rate, by 29% in the first cohort (95% CI: 14–47%) and by 39% in the second cohort (95% CI: 25–54%) [10].

We have not identified any previous studies combining CWL and FFMI to predict mortality risk, however a few studies have investigated the association between FFMI as a stand-alone measurement and mortality in specific patients groups. Schols et al. reported that FFMI was an independent predictor of mortality in patients with chronic obstructive pulmonary disease (COPD) [21].

Bigaard et al. showed that a low FFMI was an independent predictor of all-cause mortality in a large Danish community dwelling cohort of over 50.000 participants [22]. Hollander et al. showed that a FFMI ≤16.7 kg/m^2 in men or a FFMI ≤14.6 kg/m^2 in women, which are comparable with the cut-off values used in the ESPEN diagnostic criteria for malnutrition, impaired survival in patients with cystic fibrosis before and after lung transplantation [23].

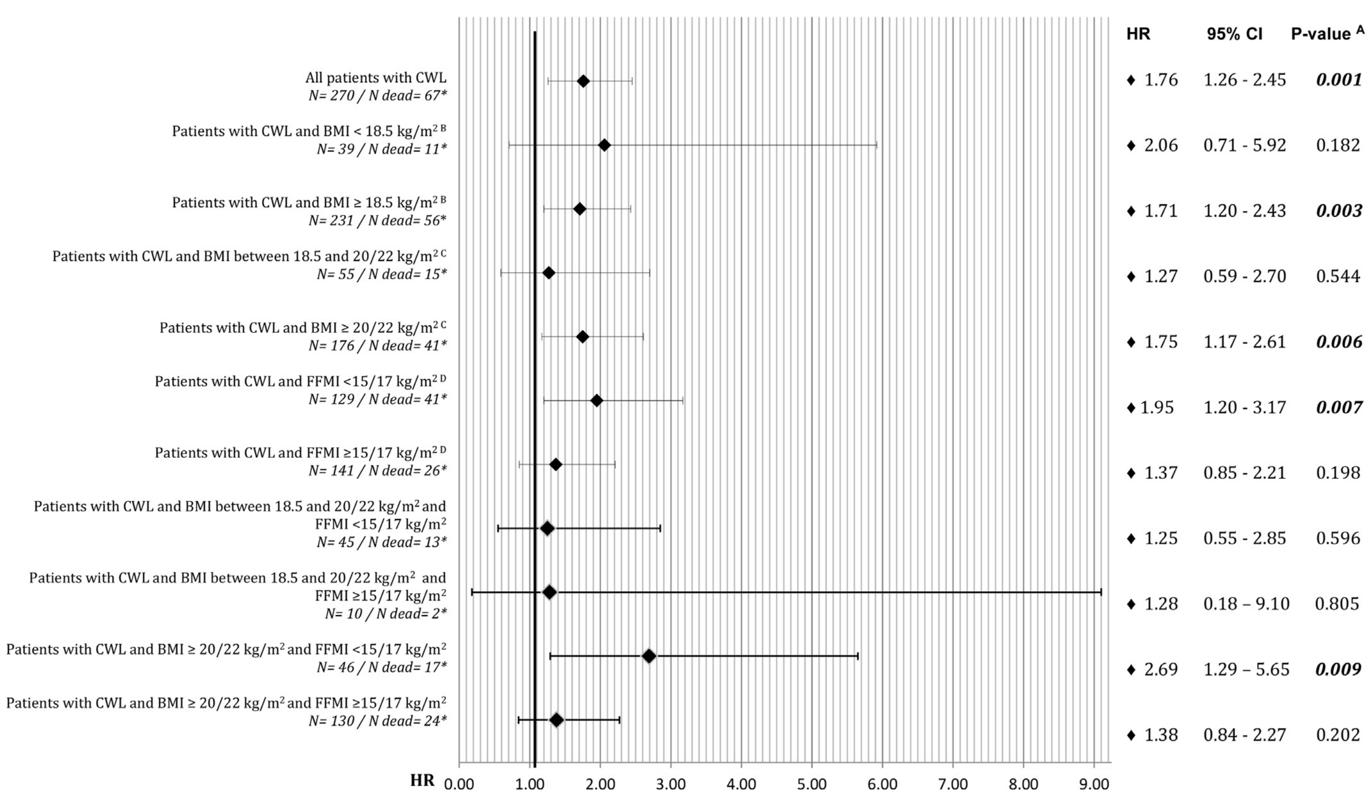

Fig. 3. Cox regression analysis on the association between patients with critical weight loss compared to patients with no critical weight loss and one-year mortality in total cohort and stratified by BMI and FFMI subgroups. [A] = *p*-values <0.05 are shown in bold. [B] = Cut-off values includes all subjects. [C] = Cut-off value 20 kg/m^2 applies for subjects <70 years and cut-off value 22 kg/m^2 applies for subjects ≥70 years. [D] = Cut-off value 15 kg/m^2 applies for females and cut-off value 17 kg/m^2 applies for males. * = The distribution of N/N dead represents patients with critical weight loss. Abbreviations: CWL = Critical Weight loss, HR = Hazard Ratio, CI = Confidence Interval.

4.1. Strengths and limitations

A strength of this study is the generalizability of the results. For Study 1, all consecutively admitted inpatients were included, therefore selection bias did not occur. Patients from Study 2 were only selected if they were referred for an in-depth nutritional assessment. This may have induced selection bias as they were likely to be malnourished. This is supported by the relatively normal BMI of included patients; whereas approximately half of the Dutch adult population is overweight, the percentage of overweight patients in Study 2 was 27.6%. Herewith, this study does not apply to an obese population. Measuring body composition is a standard procedure in diagnosing nutritional status of patients with a positive malnutrition screening score and in certain high-risk patients groups (i.e. upper gastrointestinal surgery) but is not always done in the patients with mild malnutrition. Therefore the study population of Study 2 may not be a representative reflection of a general hospital population.

Also, the study cohort was relatively young, so no conclusions can be drawn about the geriatric population, although they have the highest burden of malnutrition.

For this study, CWL was defined based on more than 5% weight loss in the past month or more than 10% weight loss in the past 6 months. This is slightly different from the ESPEN consensus definition, but we do not think that this may have affected the results.

A shortcoming of this study is that weight was only measured in 66% of all patients. However this reflects daily clinical practice; recalled weight may be less accurate then measured weight. This applies to height in even larger extent, as height was measured in only 8% of the patients. Haverkort et al. showed that patients tend to overestimate their height and underestimate their body weight [24]. This can lead to misclassification and therefore information bias because height and weight are needed to calculate weight loss, BMI and FFMI, and to subsequently subdivide patients into the CWL group or no CWL group and to stratify patients into the BMI and FFMI subgroups. As the mean weight of patients with measured weight was not significantly different from the mean weight of patients with recalled weight (73 ± 18 kg versus 75 ± 16 kg, $p = 0.103$), we assume that this has not influenced our results.

We did not record whether weight loss had occurred involuntary of voluntary. The impact of intentional weight loss on survival is different than the impact of unintentional weight loss on survival [3–10,16–20,25]. However, given our clinical practice, we assume that the majority of our patients with weight loss had lost weight unintentionally.

Another limitation of this study is that different BIA devices were used to calculate FFMI. It is well known that different devices measure differently [26], and this may have influenced the assessment of FFMI. The electrodes, used to perform the BIA measurements, were the same for all measurements though.

Finally, despite checking for possible confounders, it was not possible to adjust for well-known confounders like disease severity or care complexity because these data were not available for the total sample.

5. Conclusion

This study provides insight in the association between CWL and mortality, stratified by BMI and FFMI subgroups. The results show that one-year mortality is higher in patients with CWL compared to patients with no CWL. Further analyses suggest that depletion of protein reserves plays a crucial role, because patients with low FFMI showed a significant association between CWL and one-year mortality whereas patients with a normal FFMI did not show this association. This influence of low FFMI was also observed in subgroups of patients with normal BMI, stressing the importance of FFMI measurements in the assessment of malnutrition. Due to small subgroups, re-evaluation in larger datasets is warranted.

The results of this study suggest that the ESPEN definition, which only defines a patient malnourished if weight loss occurs in parallel with depletion of protein or energy reserves, may be correct in doing so.

Conflict of interests

None declared.

Authorship

HK and MdvdS designed the study protocol.
MdS, HK and MdvdS analyzed and interpreted the data.
MdS and MdvdS drafted the manuscript.
All authors approved the final version of the manuscript.

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