Clinical Nutrition xxx (2017) 1–8

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

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

Marian A.E. de van der Schueren [a, b, c, *, 1], Malon de Smoker [a, d, 1], E. Leistra [a, e], H.M. Kruizenga [a, c, f]

[a] Department of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands
[b] Department of Nutrition and Health, Faculty of Health and Social Studies, HAN University of Applied Sciences, Nijmegen, The Netherlands
[c] Dutch Malnutrition Steering Group, Amsterdam, The Netherlands
[d] Department of Dietetics, Albert Schweitzer Ziekenhuis, Dordrecht, The Netherlands
[e] Department of Health Sciences, Faculty of Earth and Life Sciences, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands
[f] Dutch Dietetic Association, Houten, The Netherlands

ARTICLE INFO

Article history:
Received 10 April 2017
Accepted 22 August 2017

Keywords:
Malnutrition
Mortality
Weight loss
ESPEN diagnostic criteria for malnutrition
Body mass index
Fat free mass index

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.

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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].

* Corresponding author. VU University Medical Centre, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands.
E-mail address: m.devanderschueren@vumc.nl (M.A.E. de van der Schueren).
[1] Authors share first authorship.

http://dx.doi.org/10.1016/j.clnu.2017.08.024
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Please cite this article in press as: de van der Schueren MAE, et al., The association of weight loss with one-year mortality in hospital patients, stratified by BMI and FFMI subgroups, Clinical Nutrition (2017), http://dx.doi.org/10.1016/j.clnu.2017.08.024

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 $\leq$5% in the previous month and/or $\leq$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; </$\geq$20.0 kg/m^2 for patients <70 years and </$\geq$22.0 kg/m^2 for patients $\geq$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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