Epidemiology of disease-related undernutrition and the impact on postoperative adverse outcome in cardiac surgery
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CHAPTER 1

GENERAL INTRODUCTION AND OUTLINE OF THIS THESIS
Introduction

In the Netherlands, open-heart surgery is performed in sixteen hospitals nationwide. In 2008, 16,877 open-heart operations were carried out including coronary artery bypass graft (CABG) both with and without cardiopulmonary bypass, valvular surgery and other types of surgery. Cardiac surgery patients are at a relatively high risk of disability, morbidity and of adverse effects on quality of life and life expectancy. Risk reduction wherever feasible and possible is the standard approach to minimizing adverse outcome and should start preoperatively. Nowadays physical exercise and nutritional intervention therapies to optimize the preoperative condition of patients are prescribed to high-risk patients undergoing cardiac surgery. An often overlooked preoperative condition for adverse outcome after cardiac surgery is disease-related undernutrition (DUR). A common tool used to identify undernourished patients is body mass index (BMI; body weight in kg/m²). In cardiac surgery it has been extensively shown that patients with a low preoperative BMI are at higher risk for postoperative complications, infections and mortality than even obese and severely obese patients. Therefore, to further reduce the risk of complications after cardiac surgery, identification of DRU should be integrated into the selection process of preoperative management strategies. Although BMI helps to identify the undernourished, it does not give exact information on body composition. Body mass consists of metabolically-active, fat-free mass (FFM) and fat mass. It has been demonstrated in chronic obstructive pulmonary disease (COPD) patients that a low FFM is a stronger predictor for mortality than a low BMI. Patients with a normal BMI may still suffer from DRU because of a low FFM. For example, if only BMI is used to identify the undernourished, some cardiac surgery patients with a low FFM might be misclassified as well-nourished. It is evident that these misclassifications may lead to inappropriate nutritional treatment and possible postoperative complications. The general aim of this thesis is to improve the identification of DRU and thereby treatment of the undernourished cardiac surgery patients. The more specific objectives of each individual study are delineated in the respective chapters.

Disease related undernutrition

Terminology

The terms undernutrition and malnutrition are often used interchangeably. It can be argued that the term malnutrition represents both undernutrition and overnutrition. Both terms may refer to nutritional problems on a macronutrient and/or micronutrient level. Macronutrients comprise carbohydrates, fat and proteins. Micronutrients are vitamins, minerals, and spore elements. This thesis focuses on a
negative macronutrient balance with or without micronutrient deficiencies. In other words, this thesis focuses on the protein-energy undernutrition part of malnutrition in patients undergoing cardiac surgery and will be referred to as ‘disease-related undernutrition (DREU)’ or simply ‘undernutrition’.

**Definition**

In 1993, DREU was described as ‘a state resulting from lack of uptake or intake of nutrition, leading to altered body composition, reflected by a decreased body cell mass (BCM), and diminished function’ \(^9\). In 2003, a similar definition for DREU was given by the British Association of Parenteral and Enteral Nutrition (BAPEN) \(^8\) in which it was specified that in addition to function loss DREU should also include deterioration of clinical outcome. DREU was described as ‘a state of nutrition in which primarily a deficiency of energy and/or protein causes measurable adverse effects on body composition, function, and clinical outcome’ \(^8\). In 2006 the European Society for Clinical Nutrition and Metabolism (ESPEN) \(^10\) published a corresponding definition. However, it should be noted that currently there is still no universally agreed definition of DREU \(^11-15\).

**Mechanism**

It has been extensively shown that DREU is associated with a higher risk for developing infectious and non-infectious complications, increased morbidity and mortality, poorer quality of life, prolonged hospital stay, and increased costs \(^4;7;8;16-18\). It is hypothesized that DREU reflects decreased FFM, or more specifically decreased BCM resulting in a higher risk for adverse outcome \(^11-15;19\). The lower the level of metabolically-active FFM, or the more FFM is lost, the less well the body can respond to a stressful event such as trauma, disease or surgery. The other way around, inflammatory activity that is associated with trauma, disease and surgery contributes to the pathogenesis of DREU, or more specifically to the pathogenesis of muscle wasting. As outlined by Soeters and Schols \(^13\), there is an increased proliferation of the immune system (liver, spleen, immune cells elsewhere in the body, and wounds) in the defense against a stressful event. The synthesis of acute phase proteins by the immune system is increased. Muscle mass functions as an important source of amino acids for this protein synthesis \(^19-22\). Thereby, the response to a stressful event consists of loss of muscle mass - and to a lesser extent skin, possibly bone protein and other solids (calcium and phosphate) - and gain in organ or tissue mass responsible for our defense against the stressful event - the immune system \(^13\). The summed effect of this redistribution of protein is that protein is lost at whole body level. This loss of protein, i.e. muscle mass, leads to a vicious circle in which a healthy response to renewed exogenous stressful events is inhibited even more. In health, FFM is the rough equivalent of BCM and muscle mass (*Figure 1.1*).
Reference standard for DRU in this thesis

We focused on the body composition part of the definitions of DRU as described above. At the start of this thesis we considered a reference standard for DRU acceptable if it included at least 1) ‘unintended weight loss (WL) or another anthropometric measurement such as FFM or arm muscle circumference unintended decreasing over time’, and 2) ‘an estimate or measurement of current body composition such as BMI’. This description of an acceptable reference standard was based on discussions with experts in the field and most probably represents the decreased and/or low status of metabolically-active BCM. It was also based on most relevant items - unintended WL and BMI - referred to in the literature as able to identify those patients who will benefit from nutritional intervention resulting in improved clinical outcome\(^8,23\).

Undernutrition in cardiac surgery

In the Netherlands, undernutrition is present in about 25-40% of hospital inpatients and in 10-20% of the preoperative outpatient population\(^24,25\). Also patients undergoing cardiac surgery are prone to DRU, probably due to their relatively advanced age and the presence of heart failure. Elderly patients are at risk for sarcopenia - loss of muscle mass and function due to ageing\(^15,26,27\). Chronic heart failure patients are at risk for cardiac cachexia - loss of mainly muscle mass, anorexia and weakness due to a hypermetabolic condition due to systemic inflammatory processes, or other (as yet unraveled) disease-related pathological changes\(^15,28,29\). Both sarcopenia and cardiac cachexia lead to DRU\(^15\). In particular as advanced age and co-morbidities are no longer contra-indi-
cations to cardiac surgery, these patients have a higher likelihood of being undernourished and are more vulnerable to developing postoperative complications. Previous studies have shown that approximately one-quarter of cardiac surgery patients are likely to be preoperatively undernourished in terms of a low BMI. They are at higher risk for postoperative infectious and non-infectious complications and mortality, higher even than obese and severely obese patients.

Although BMI helps to identify the undernourished, it does not give exact information on body composition or changes. Information about the impact of unintended WL, or metabolically-active body components such as FFM, BCM or muscle mass in patients undergoing cardiac surgery is lacking. For example, patients with a normal BMI may still be suffering from undernutrition because they have a low FFM. Thus, if only BMI is used to identify the undernourished, some cardiac surgery patients with a low FFM might be misclassified as well-nourished. It is evident that misclassifications lead to inappropriate nutritional treatment and possibly preventable complications. Research assessing the prevalence of DRU based on body mass components such as FFM, and their association with adverse outcome in patients undergoing cardiac surgery is required.

Methods of assessing body composition

There are several ways to measure FFM or BCM. There are reference methods and field methods. Reference methods for BCM are total body potassium counting (TBK), neutron activation analysis (TBN - total body nitrogen) and multiple dilution techniques. Reference methods to assess FFM are air displacement plethysmography (BodPod), dual-energy X-ray absorptiometry (DXA), and deuterium dilution. These reference methods are time consuming, expensive and not practical. Against these reference methods more practical field methods can be validated. A promising field method of assessing FFM and BCM is bioelectrical impedance spectroscopy (BIS). BIS measurements are done in a few minutes while the patient lies in supine position with legs apart and arms abducted. Two electrodes are placed on the dorsum of the hand and two on the dorsum of the foot. A weak electrical current is introduced into the body and tissue conductivity measured. At low frequency, the electrical signal travels predominantly through the extracellular space, whereas high-frequency signals travel through extra- and intracellular space. There are three different bio-impedance techniques namely single-frequency bio-impedance analysis (SF-BIA), multi-frequency bio-impedance analysis (MF-BIA), and BIS. The BIS has more potential in illness and fluid shifts than the single and the fixed multi-frequency BIA. BIS measures impedance at a range of non-fixed, multi-frequencies and uses physical models instead of population dependent regression equations to determine extracellular water (ECW), intracellular water (ICW) and total body water (TBW). From TBW (ECW + ICW), FFM is calculated.
Screening methods to identify risk for DRU

In 2000, the Dutch Dietetic Association initiated a national campaign to increase awareness of DRU with the title: “Eat well to get well” (Wie beter eet wordt Sneller Beter). The goal of this campaign was to draw the attention of society and health care professionals to DRU. This campaign was followed by the first Dutch DRU screening\textsuperscript{35}. This screening demonstrated that despite the high prevalence and overall understanding that DRU increases complications, costs and length of hospital stay\textsuperscript{36-38}, half of all undernourished hospitalized patients remained unrecognized by medical and nursing staff, and therefore went untreated\textsuperscript{35}. In 2005, the expert group “Eat well to get well” received financial funding from the Ministry of Health, Welfare and Sports (VWS) to nationally implement an effective screening procedure for DRU on hospital admission and thereby optimal nutritional treatment. To make this plan a success, it was considered necessary by the Dutch Dietetic Association and the expert group “Eat well to get well” to reach national consensus about the nutritional screening tools to be used. Therefore, on 29 November 2005 a national consensus meeting was organized at the Academic Medical Center, Amsterdam. To reach national consensus about the nutritional screening tools to be used, the results of our review (Chapter 3 of this thesis) were presented and discussed at this consensus meeting. A major subject of debate was the clinical relevance of registering the parameter low BMI in addition to unintended WL only to identify the undernourished. Or, translated into nutritional screening tools, the question remaining was; ‘Is the SNAQ (Short Nutritional Assessment Questionnaire) method\textsuperscript{39} (Figure 1.2) as accurate as the MUST\textsuperscript{40} (Malnutrition Universal Screening Tool) method (Figure 1.3) to identify DRU?’ The MUST includes BMI and the SNAQ does not.

At the end of the discussion the SNAQ and the MUST were the tools recommended

<table>
<thead>
<tr>
<th>Did you lose weight unintentionally?</th>
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<tbody>
<tr>
<td>• More than 6 kg in the last 6 months</td>
</tr>
<tr>
<td>• More than 3 kg in the last month</td>
</tr>
</tbody>
</table>

| Did you experience a decreased appetite over the last month? | 1 |
|-------------------------------------------------------------|

| Did you use supplemental drinks or tube feeding over the last month? | 1 |
|---------------------------------------------------------------------|

**Figure 1.2** Short Nutritional Assessment Questionnaire (SNAQ)\textsuperscript{39}. Score: 0 or 1 point; well nourished, 2 points; moderately undernourished, 3 points or more; severely undernourished.
<table>
<thead>
<tr>
<th>BMI kg/m²</th>
<th>Score</th>
</tr>
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<tbody>
<tr>
<td>&gt;20</td>
<td>0</td>
</tr>
<tr>
<td>18.5-20</td>
<td>1</td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>2</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Unplanned weight loss in past 3-6 months</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5%</td>
<td>0</td>
</tr>
<tr>
<td>5-10%</td>
<td>1</td>
</tr>
<tr>
<td>&gt;10%</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acute disease effect score</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>If patient is acutely ill and there has been or is likely to be no nutritional intake &gt;5 days</td>
<td>2</td>
</tr>
</tbody>
</table>

Figure 1.3 Malnutrition Universal Screening Tool (MUST)⁴⁰. Score: 0; low risk, 1; medium risk, ≥ 2; high risk of DRU.

to screen for DRU on hospital admission to internal medicine as well as surgical patients⁴¹. Following the recommendations of the Dutch Dietetic Association and the expert group “Eat well to get well” the question remained whether the SNAQ or the MUST was most accurate in identifying undernourished patients undergoing cardiac surgery.

Outline of this thesis

This study aimed to investigate the possibilities to improve identification of DRU and thereby treatment of the undernourished patients undergoing cardiac surgery.

The overall aims of the work presented in this thesis are:

- To determine the prevalence of DRU based on parameters other than low BMI in patients undergoing cardiac surgery.
- To assess DRU based on parameters other than low BMI in relation to the risk of adverse outcomes after cardiac surgery such as infection, prolonged length of intensive care unit (ICU) and hospital stay, and quality of life.
- To suggest a screening procedure to optimize the identification and with that treatment of undernourished cardiac surgery patients.
In Chapter 2 the association between preoperative energy and protein intake and postoperative adverse outcome in well-nourished cardiac surgery patients is investigated. Chapter 3 presents a systematic review looking at diagnostic accuracy of quick-and-easy nutritional screening tools in hospital in- and outpatients. Chapter 4 reports on the prevalence of unintended WL and low BMI in patients undergoing cardiac surgery and their association with postoperative adverse outcome. Chapter 5 describes the additional benefit of actually measuring FFM. Chapter 6 describes agreement between the BIS and DXA methods in assessing FFM in patients undergoing cardiac surgery. Chapter 7 reports on the impact of cardiac-surgery-induced undernutrition two months after operation. Chapter 8 describes the clinical relevance of using the quick-and-easy undernutrition screening tools SNAQ, MUST and cardiac-surgery-specific MUST (CSSM), in identifying undernourished cardiac surgery patients. Chapter 9 presents a general discussion of the main findings. It also highlights the implications for practice and future research.

References
General introduction


General introduction

