Epidemiology of disease-related undernutrition and the impact on postoperative adverse outcome in cardiac surgery
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Nowadays physical exercise and nutritional intervention therapies to optimize patients’ preoperative condition are prescribed to high-risk patients undergoing cardiac surgery. An often overlooked preoperative condition predisposing to adverse outcome after cardiac surgery is disease-related undernutrition (DRU). A common tool used to identify undernourished patients is low body mass index (BMI, kg/m²). In cardiac surgery it has been extensively shown that patients with a preoperatively low BMI are at a 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. 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. These misclassifications may lead to inappropriate nutritional treatment and possible postoperative complications. Information about the impact of other items identifying DRU such as unintentional weight loss (WL), or metabolically-active body mass components such as FFM or muscle mass in patients undergoing cardiac surgery is lacking.

In this thesis the possibilities to improve identification of DRU and thereby treatment of undernourished cardiac surgery patients were investigated.

In Chapter 2 preoperative protein and energy intake and postoperative adverse outcome were assessed in preoperatively well-nourished, non-hospitalized cardiac surgery patients of 65 years of ages or older. Hundred patients were assessed scheduled for cardiac surgery in the Academic Medical Center in Amsterdam, the Netherlands. Comparison of low protein intake ($\leq 0.98 \, \text{g/kg/d}$) with high protein intake ($>0.98 \, \text{g/kg/d}$) demonstrated that a low protein intake did not result in more complications or prolonged length of stay. In low-risk operative patients in particular, a high energy intake ($>22 \, \text{kcal/kg/d}$) resulted in more postoperative complications than a low energy intake ($\leq 22 \, \text{kcal/kg/d}$) (33.3% and 13.2%, respectively; (Odds ratio (OR) 5.0; 95% Confidence Interval (CI) [1.5-16.9]). A preoperative protein intake $\leq 0.80 \, \text{g/kg/d}$ was seen in 22.6%, and an energy intake $\leq 25 \, \text{kcal/kg/d}$ in 72.2% of the patients. The outcome of this study suggests that detecting and correcting a preoperative low protein or energy intake is of no clinical relevance in the well-nourished, non-hospitalized elderly patients awaiting cardiac surgery. In contrast, caloric overfeeding may be associated with an increased complication rate. Consequently, we recommend in the area of nutritional interventions, to screen before you intervene. After screening for DRU patients who may benefit from nutrition assessment and intervention are identified.
Chapter 3 describes a systematic review selecting quick-and-easy undernutrition screening tools with high diagnostic accuracy for the general hospital inpatient and outpatient population. A valid, quick-and-easy undernutrition screening tool is an essential requisite to treat undernutrition. Without standardized screening protocols at best half of undernourished patients are identified by medical and nursing staff. Studies were included if they met following criteria: The study determined the diagnostic accuracy of a quick-and-easy screening tool in an adult population. The screening tool was compared to an acceptable reference standard for DRU. The reference standard for DRU resulted in a dichotomous classification: DRU present or absent. The study included data to abstract sensitivity and specificity. The methodological quality was formally assessed using the QUADAS (checklist for quality assessment in analytical accuracy studies) in those studies in which the nutritional screening tools had a relevant sensitivity and specificity (>65%). After this quality assessment it was concluded that no studies for the general hospital outpatient population were of adequate quality. For the general hospital inpatient population only the Short Nutritional Assessment Questionnaire (SNAQ) and the Malnutrition Screening Tool (MST) were studied with a high rating to the criteria specified. The diagnostic accuracy of the MST seemed slightly better than the SNAQ. However, the MST study had a lower QUADAS ‘score’ for blinding and the cut-off point of the MST for positive screening was defined post hoc. From our systematic review it was concluded that the high applicability combined with clinical relevant sensitivity and specificity make both the MST and the SNAQ the most accurate tools ready to implement at the general hospital inpatient population. No studies were carried out in a cardiac surgery population.

Numerous studies reported increased adverse outcomes after cardiac surgery in patients with low BMI. Little is known yet, however, about the impact of preoperative unintended WL in cardiac surgery patients. In Chapter 4 the prevalence and association of unintended WL in view of low BMI adjusted for a validated set of preoperative risks, inflammatory activity and duration of extracorporeal circulation with postoperative adverse outcome was explored. Nutritional data from 331 cardiac surgery patients were collected within 24 hours of hospital admission and linked to the standard postoperative complication registration database. Preoperative DRU ≥ 10% unintended WL in the preceding six months and/or BMI ≤ 21.0 kg/m² - was present in 9.1% of the study population (4.3% and 4.8%, respectively). It was observed that preoperative unintended WL of ≥ 10% in the preceding six months was associated with a prolonged length of stay in hospital independent from low BMI (adj. OR 7.1; 95% CI [1.8-28.1]). Preoperative BMI ≤ 21.0 kg/m² was associated with an increased occurrence of postoperative infections and prolonged stay in ICU independent from ≥ 10% unintended WL in the preceding six months (adj. OR 4.6; 95%CI [1.2-17.8] and adj. OR 5.3; 95%CI [1.3-21.8], respectively). Based on this study, we recommend special attention
for cardiac surgery patients with preoperative ≥ 10% unintended WL in the preceding six months or a BMI ≤ 21.0 kg/m² because both parameters are independently associated with adverse outcome. When for preoperative screening of cardiac surgery patients a tool without scoring on a low BMI is used, approximately half of the undernourished cardiac surgery patients are missed. This is because, as shown by our study, half of the preoperatively undernourished cardiac surgery patients suffer from unintended WL and the other half from a low BMI with minor overlap.

Chapter 5 describes the additional benefit to actually measure body composition to detect DRU in patients awaiting cardiac surgery. BMI or unintended WL do not give information on exact body composition. Body mass consists of metabolically-active FFM and fat mass. Additionally, several studies showed that a low FFM index (FFMI, kg/m²) is a stronger predictor for mortality than a low BMI. A prospective observational study was conducted. Preoperative FFM was determined by bioelectrical impedance spectroscopy (BIS) in 325 adult patients admitted for elective cardiac surgery. The results showed that a low FFMI, present in 8.3% of patients, was independently associated with the occurrence of infections after cardiac surgery (18.5% vs. 4.7%, adj. OR 6.9; 95%CI [1.8-27.7]). A low FFMI also tended to be associated with a higher risk for a longer postoperative stay at the ICU (adj. Hazard ratio (HR):0.7; 95%CI [0.4-1.1]). When classifying patients as undernourished by traditional methods - BMI ≤ 21.0 kg/m² and/or ≥ 10% WL in the preceding six months - half of patients with a low FFMI were misclassified and scored as well-nourished. Based on this study we advocate that FFMI should be the leading parameter in classifying and treating undernourished cardiac surgery patients.

There are several options to measure FFM. In Chapter 6 agreement in FFM between the portable, bedside BIS and relatively expensive, non-portable dual-energy X-ray absorptiometry (DXA) in patients undergoing cardiac surgery was assessed. In 26 patients scheduled for cardiac surgery attending the preoperative outpatient clinic, body composition measurements by BIS and DXA were performed two weeks prior to and two months after cardiac surgery. BIS overestimated preoperative and postoperative FFM by 2 kg compared to DXA (2.3 kg (95%CI: -3.5-8.1 kg) and 2.1 kg (95%CI: -4.5-8.7 kg), respectively). BIS underestimated FFM change by - 0.5% (95%CI: -8.4-7.5%). The large inter-individual variation between BIS and DXA assessed FFM hinders the interchange-ability of BIS and DXA in routine clinical practice. For example, BIS assessed FFMI may be approximately 1.5 kg/m² below or 3 kg/m² above FFMI assessed by DXA. This variation may lead to misclassifications and thereby inappropriate nutritional treatment and possible postoperative complications. DXA is limited by its lack of differentiation in hydration state of FFM. In clinical practice this differentiation is essential as extracellular water (ECW) reflects hydration and intracellular water (ICW) reflects nutritional status. The evaluation of nutritional therapy should include dynamic assessment of body composition. We
suggest the use of the more sophisticated DXA method to assess FFM in parallel to BIS but with a lower frequency of assessment. In addition, fluid balance and inflammatory status has to be integrated into the nutritional assessment of cardiac surgery patients to correctly interpret BIS and DXA measurements and therapy efficacy. In Chapter 7 postoperative losses of skeletal muscle mass (SMM) in relation to complications, quality of life, re-admission and one-year mortality after cardiac surgery was assessed. SMM is the component of FFM most sensitive to losses in disease and ageing. In 29 patients scheduled for cardiac surgery visiting the preoperative outpatient clinic SMM using DXA was assessed two weeks prior and two months after cardiac surgery. Postoperatively, one out of four patients lost ≥5% SMM. When analyzed separately, a ≥5% decline in leg SMM was associated with a decline in experienced vitality (88% vs. 35%, OR 13.0; 95%CI [1.3-128.1]). In contrast, a ≥5% loss of arm SMM was associated with fewer in-hospital complications (33.3% vs. 69.2%, OR 0.2; 95%CI [0.04-0.98]). These patients were characterized by a higher preoperative FFMI. In line with Chapter 5, the results of this study suggest that a preoperatively higher FFMI indicates better ability to cope with operative stress, resulting in fewer complications. Further, this study illustrates that two months after cardiac surgery ≥5% of postoperative loss of muscle mass is still present in a quarter of patients, and associated with decreased vitality. Both preoperative and postoperative nutritional intervention combined with physical exercise programs to increase lean body mass and thereby improve postoperative recovery after cardiac surgery seem to have potential.

We recommend that FFMI measurements should be integrated into the standard preoperative assessment to identify, assess and treat the undernourished starting several weeks prior to cardiac surgery. To reduce extra workload and costs of measuring body composition during screening quick-and-easy undernutrition screening tools such as the Malnutrition Universal Screening Tool (MUST) or the SNAQ both tools recommended in the Netherlands can be helpful to clinical practice. In Chapter 8 the accuracy of the MUST and SNAQ to detect undernutrition measured by a low FFMI were compared. SNAQ and MUST-related questions and preoperative FFMI using BIS were determined in 325 adult patients admitted for elective cardiac surgery. Sensitivity for detecting low FFMI was 59% and 19% for the MUST and SNAQ, respectively. This means that approximately 80% of cardiac surgery patients with a low FFMI will be misclassified as well-nourished if screened using the SNAQ. These misclassified undernourished patients may not receive their beneficial nutritional intervention. In addition, although less, still 40% of cardiac surgery patients will be misclassified as well-nourished if screened using the MUST. Further, it was observed that the accuracy of the MUST improved when age and gender were added to the nutritional screening process. Moreover, a relatively high sensitivity of 74% for the CSSM was observed. Further research to evaluate our cardiac-surgery-spe-
cific MUST (CSSM) is needed prior to implementing.
In conclusion, DRU is relatively common in patients undergoing cardiac surgery and associated with postoperative adverse outcome. To correctly identify and treat undernourished patients awaiting cardiac surgery FFMI should be measured in addition to BMI and unintended WL only two to six weeks prior to surgery. If positively screened for DRU, further diagnostic assessment incorporating body composition using BIS and with a lower frequency DXA has to take place. Based on this assessment, patient-tailored dietary treatment can be prescribed and its effect evaluated. Future research should further unravel the mechanism behind specific nutritional interventions and possible benefits. A large multicentre clinical trial has to point out if preoperative and postoperative nutritional intervention combined with physical exercise started during the waiting period before elective surgery and re-started during the early and long-term postoperative phases benefit undernourished patients awaiting elective cardiac surgery. As a result of these interventions, recovery after cardiac surgery may be improved.