The measurement of body composition and outcome in critically ill patients

Impact of the research

Impact of critical illness

Every year more than 76.000 patients are admitted to Dutch ICU's. With a minimum cost of €2500 per admission, the total costs of Intensive Care Medicine exceeds 200 million euros. The in-hospital mortality of this entire population is 13% and from this it can be calculated that every day more than 25 patients die in Dutch hospitals after an ICU admission. An ICU admission is often associated with discomfort, pain and anxiety for the patient and emotional distress for the patient's relatives. For many relatives it is extra difficult to cope with this distress when the ICU admission has an adverse outcome and "all the suffering has been in vain". The aim of this thesis was to study the association between (changes in) body composition and outcome in critical illness and to provide the scientific field with new data and new tools that may advance the use of body composition analysis in the outcome prediction of patients with critical illness.

Associations and causal relations

In chapter 2 we confirmed previous observations that sarcopenia on ICU admission is associated with an increased hospital mortality. However, our research shows that this association is primarily determined by co-morbidities that are known to be associated with both muscle loss and high mortality, such as chronic renal insufficiency and cancer. Therefore, we concluded that, in our cohort, sarcopenia is not an independent risk factor for hospital mortality in critical illness. These findings underline the importance of carefully addressing confounding factors when studying the association between muscle mass and disease outcome. To improve pathophysiological and prognostic knowledge it is important to study associations between risk factors and outcome. In many cases specific risk factors are studied because a causal relation is presumed. Appealing hypotheses of causal relationships are often rapidly and broadly embraced and disseminated as without further challenging the actual causality of an association. Our findings remind researchers to keep challenging and deepen existing hypotheses, even if these are based on a plausible (patho)physiological background.

Reliability of sequential body composition analysis

Analysis of CT images at the level of vertebra L3 is an established method to determine muscle mass, muscle quality and fat mass. The interobserver agreement of the analysis of a single image is excellent. However, the coefficient of variation of a tissue area measured by CT is actually unknown. Sequential CT-scans are increasingly used to quantify changes in body composition over a period of time. In chapter 3 we observed a considerable spread in the measured changes in muscle area between individual patients over a relative short period

of time. Although this spread can be explained (partly) by pathophysiological variation, the question arises whether other physiological source of variation such as intestinal air content or even non-physiological sources of variation such as the position of a patient in the scanner affect the reliability of sequential CT scans for body composition analysis. Before sequential CT scans are widely implemented in body composition research, the coefficient of variation of sequential CT scans should be clarified. It can be conceived that changes in body composition can only be reliably measured when the coefficient of variation is much lower than the relative changes in tissue areas. It is also conceivable that edema affects point measurements of tissue areas in critically ill patients. To what extent this affects the interpretation of body composition remains to be seen.

Standardization of research methods

There is increasing awareness of the importance of standardization in clinical research. Standardization facilitates comparability and reproducibility of the results of different studies. Also, in the view of the growing importance of meta-analyses and in view of the advent of machine learning and other artificial intelligence tools standardization of methods and outcome parameters is important. In clinical research standardized core outcome sets are increasingly advocated and used. In order to optimally integrate the knowledge on the role of body composition in health and disease, yielded by different studies, it is important to develop generally accepted definitions and reference values. In chapter 3, we showed that the use of external reference values for sarcopenia leads to more accurate grouping and more robust conclusions than the use of reference values that are relative to a cohort under study. This probably holds true for many other epidemiological studies where the grouping factor has a skewed distribution within the studied cohort. In chapter 4 we propose a method to determine external reference values for visceral obesity measured using CT scans, these findings need to be validated but encourage the scientific field to take a further step towards standardization of definitions of advert body types. In chapter 5 we have used these reference values to study the association between visceral obesity and outcome in critical illness. We found no statistically significant association between visceral obesity and outcome following ICU admission. However, the results neither rule out the existence of the obesity paradox which states that (mild) obesity is protective in critical illness. These findings still warrant further investigation and validation in larger and more defined populations. In addition, pathophysiological explanations pointing at a possible causal relation between obesity and better outcome after critical illness should be investigated.