

## **Sarcopenia – an overlooked prognostic indicator in lung cancer**

Muscle wasting (sarcopenia) is seen in approximately 42% of lung cancer patients and associated with poor prognosis. During the last two decades the understanding of skeletal muscles as an organ of more than just movement has arisen. More evidence confirms muscles as modulator of the immune system by release of peptides and myokines. Skeletal muscles production of cytokines, such as IL-7 and IL-15, is shown to be essential for maintenance of immune function and development of lymphocytes suggesting that muscle wasting may influence the immune capacity. The amount of these molecules has been shown to be proportionally associated with skeletal muscle mass, supporting a link between sarcopenia and immune function. In addition, sarcopenia has also been related to tumor cell sensitivity to immunotherapy as a secondary effect of deficient immune function. This is further supported by the fact that patients with sarcopenia and advanced NSCLC treated with immunotherapy have been shown to be less effective. In addition, patients with sarcopenia often develop insulin resistance, which has been shown to be important for tumor progression. Against this background, it is therefore imperative to elucidate the relationship between sarcopenia and NSCLC.

CT-verified sarcopenia, often expressed as the muscle cross-sectional area at the level of the third lumbar vertebra, has been suggested in a single systematic review as a possible strong prognostic factor for complications and mortality in patients with NSCLC. However, the study references small studies with different cancer stages, different ways of defining sarcopenia and assessing muscle mass. The hypothesis of this study is that pre- and postoperative sarcopenia, measured as CTverified sarcopenia, is an unfavorable prognostic factor in surgically treated NSCLC patients with increased risk of post-operative complications, risk of relapse and poor overall survival. The overall objective of the present study is to investigate the prognostic significance and clinical consequences of pre- and post-operative sarcopenia in NSCLC patients.

The project will be conducted as a nationwide, epidemiological study where all Danish patients diagnosed and surgically treated for NSCLC between 2003-2020 will be included (approximately 14.000 patients). The Danish Lung Cancer Registry will be used to identify patients. The database contains information on patient characteristics, type of treatment, complications and survival. Statistics Denmark (DST) provides data on socioeconomic position. All data are linked with CTderived muscle mass data from patients to describe the relation between sarcopenia and NSCLC.

This study is a national cohort study using register data and data collected from CT-scans to investigate a potential novel association between sarcopenia and prognosis for patients treated for lung cancer and at this stage we need more knowledge before implementing patient views.

This study may contribute significantly to understand the progression and prevalence of sarcopenia in lung cancer patients. Moreover, it will elucidate whether sarcopenia is more pronounced in certain stages of lung cancer. This study can create the basis for implementation of sarcopenia as a prognostic predictor and it may contribute to improved assessment of patients' general health status and prognosis as well as planning the individual patient's course of treatment in terms of pre- and postoperative rehabilitation. As sarcopenia may not only be an unfavorable prognostic indicator in lung cancer, but also other types of cancer, such as pancreatic cancer, oesophageal cancer, colon cancer, ovarian cancer, cervical cancer, stomach cancer, breast cancer, knowledge from this study may extend beyond large parts of the cancer area and influence the treatment of cancer in general in the future.