New insights in pulmonary cachexia

Valorisation

This chapter describes the valorisation of the research illustrated in this thesis, which is essentially the creation of value from knowledge [1,2]. This chapter therefore summarizes and reflects on how the findings of this thesis can be utilized outside the scientific field. First we will describe the main public relevance. Next, the main findings and their impact for health care and the future plans will be discussed.

According to the World Health Organization, chronic obstructive pulmonary disease (COPD) and lung cancer are both in the top 10 world's biggest killers. Globally, it is estimated that in 2015 3.17 and 1.69 million deaths were caused by COPD and lung cancer, respectively [3,4]. With ageing and rising smoking prevalence in developing nations, the prevalence of COPD and lung cancer is expected to further increase in the coming years [5,6]. Although COPD and lung cancer are primarily lung diseases, both often coexist with cachexia [7,8], which encompasses depletion of skeletal muscle and/or adipose tissue. Cachexia is associated with a range of adverse clinical outcomes including reduced exercise capacity [9], decreased health status [10] and diminished quality of life [11], it interferes with treatment efficacy [12] and impacts mortality rates [13].

Prevention and timely treatment of cachexia in patients with COPD and lung cancer requires adequate and early identification of patients at risk and detailed understanding of the pathophysiology involved. Overall, the research described in this doctoral thesis focussed on new insights in order to disentangle disrupted energy metabolism in cachexia. Cachexia is a complex process being a consequence of changes in the control of metabolism. This thesis focussed on putative triggers of increased energy metabolism in COPD and in lung cancer, amongst others with use of standard-of-care medical images.

In COPD, the prevailing believe is that increased energy metabolism is caused by high workload of breathing. An intervention to enhance breathing mechanics by reducing hyperinflation is an unique model to test this hypothesis. While this intervention to enhance breathing mechanics has resulted in improved pulmonary function and improved physical activity level, no systemic effects on the energy balance were observed.

Cachexia has long been regarded as a muscle wasting disorder, but more recently adipose tissue has started to gain attention as possible target for cachexia. In the overall disease trajectory in COPD there were no leads for a role of increased adipose tissue metabolism in cachexia. However, its role in a phase when cachexia develops progressively and patients exhibited metabolic derangements is unknown. In order to measure increased adipose tissue metabolism, extensive cold exposure followed by scanning is currently the only reliable protocol in a clinical setting. Nevertheless, this study protocol turned out to be too strenuous for the fragile cachectic population. Consequently, development of more appropriate study methodologies

to investigate the role of brown adipose tissue for this vulnerable population is subject for future research.

In the context of cachexia in lung cancer, extensive analysis of baseline standard-of-care medical images found no potential to predict future cachexia development. However longitudinally, this thesis showed a clear added value for the use of clinically acquires computed tomography scans for evaluation of body composition. Muscle wasting is clinically relevant and body composition data have the potential to improve risk stratification and personalize lifestyle interventions. It is therefore important to link longitudinal body composition analysis to evaluation of regular care images in order to gain more insight in cachexia development at an early stage. Currently, quantification of body composition occurs manually, which is a time consuming process. Automated methods will facilitate integration into regular clinical care. Thereby, imaging based tumour response evaluation during anti-tumour therapy can be combined with body composition analysis and can be captured in radiology reports. This should be combined with recording of body weight during each hospital visit of the patient in order to closely monitor and to assess risk stratification.

Optimal therapeutic intervention in cachexia depends on both proper insight into the precise mechanisms and timely identification of patients at risk. This research provided new scientific insights in the aetiology and showed a clear added value for the use of clinically acquires computed tomography scans for evaluation of body composition. Hopefully this will prove valuable for future research and contribute to optimization of current treatments and contribute to new treatment options for cachexia.

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