Preoperative risk assessment of adverse outcomes in onco-geriatric surgical patients

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Introduction and outline of the thesis
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Worldwide, the burden of cancer increases. In 2015 there were 17.5 million incident cancer cases, compared with 14.9 million in 2013 and 8.5 million in 1990\textsuperscript{1, 2}. A total of 16% to 35.6% of the increase in incident cancer cases can be attributed to population aging. Moreover, most solid tumours occur in the elderly population\textsuperscript{1, 3}. As surgery plays an important role in the multimodality treatment of solid tumours, surgeons are being confronted with more and more onco-geriatric patients.

The heterogeneity of the onco-geriatric population poses a big challenge for clinicians when dealing with this growing number of patients, as it makes the decision-making process more complex. On the one hand, this challenge comes to expression by onco-geriatric patients receiving substandard treatment\textsuperscript{4, 5}, likely due to the assumption that increasing age itself is associated with reduced fitness for treatment and the complexity of predicting a geriatric patient’s response to treatment\textsuperscript{6-9}. On the other hand, the risk of overtreatment exists, with increased risks of adverse outcomes and impaired quality of life. In order to allocate appropriate treatments to patients, it is necessary to identify which of the onco-geriatric patients are fit and which are vulnerable or frail. Fit onco-geriatric patients are thought to be able to withstand major stressors like cancer surgery, possibly comparable to their younger counterparts. Frailty is, although not unambiguously defined in literature, ‘a loss of resources in several domains of functioning’ and results in increased vulnerability to stressors. Therefore, frail patients are at increased risk of adverse postoperative outcomes\textsuperscript{10}.

The Geriatric Assessment (GA) was originally developed by geriatricians to handle complex health care issues in frail elderly in a multidimensional and interdisciplinary manner\textsuperscript{11, 12}. It comprises the evaluation of multiple domains, most commonly physical, functional, psychological and socio-environmental\textsuperscript{11, 12}. Geriatric oncology adopted the GA, with the aim of identifying multidomain impairments that 1) were previously unrecognized and might influence the treatment plan, 2) are associated with an increased risk of adverse posttreatment outcomes and 3) might be amenable to a targeted intervention\textsuperscript{13, 14}.

Performing a full GA in every onco-geriatric patient is not feasible in a busy surgeon’s practice, nor necessary, as the majority of patients is fit for surgery\textsuperscript{11, 15}. Consensus as to what constitutes a complete GA and what are items or screening tools that can reliably assess the domains included is lacking, which hampers implementation in clinical practice\textsuperscript{16, 17}. This is partly due
of outcomes between studies and the great variety regarding the population under study, the domains included, and the methods used to assess those domains$^{16, 17}$. To provide a complete overview of the evidence available to date on the predictive value of separate GA domains and the different tools to assess them, regarding adverse postoperative outcomes in onco-geriatric patients, a systematic review of systematic reviews was performed (chapter 2). The goal of this systematic review was to provide for scientifically substantiated recommendations to facilitate the implementation of a preoperative GA in daily clinical practice.

To easily identify which patients are at risk for adverse outcomes and who thus might benefit from further assessment, time-saving screening tools need to be investigated$^{18}$. For this reason, the Preoperative Risk Estimation for Onco-geriatric Patients (PREOP)-study was designed by members of the surgical taskforce of the International Society of Geriatric Oncology (SIOG). Patients of 70 years of age or older, undergoing elective surgery for a solid tumour, were included in this prospective multicentre cohort study. The PREOP-study investigated the predictive ability of a set of screening tools regarding 30-day postoperative outcomes. The first analysis focused on the predictive value of the Timed Up and Go (TUG) regarding the risk of adverse outcomes up to 30-days postoperatively and compared it to the predictive ability of the well-known American Society of Anaesthesiologists (ASA)-classification, that is readily available for all surgical patients (chapter 3). The TUG is an easy to administer tool that was developed with the purpose of identifying frail elderly by quantifying functional mobility$^{19}$. Repeatedly, the TUG was found to be able to identify the level of physical disability in community dwelling elderly and to predict adverse outcomes in patients undergoing surgery and receiving chemotherapy$^{20-29}$. Data on the predictive value of the TUG in the onco-geriatric surgical population were lacking until now.

The second analysis of the PREOP-study compared the geriatric screening tools, that touch on all domains that generally compose a GA, regarding their ability to predict the risk of major 30-day complications (chapter 4). This analysis enhances comparability between different screening tools and GA domains and with other studies that might focus on only a few of the domains. Subsequently a preoperative risk score was developed, to stratify patients according to their risk of major 30-day complications.

Next, we looked into further detail at preoperative nutritional status in the same population (chapter 5). Though infrequently included in a GA$^{16, 30}$, this domain is often affected in
onco-geriatric patients (32% to 64.2% at nutritional risk or malnourished)\textsuperscript{31-33}. It is likely that nutritional impairment is a multifactorial problem in onco-geriatric patients, caused by cancer and its treatment, as well as factors associated with increasing age. For example, nutritional impairment is more prevalent in patients with advanced disease and intra-abdominal tumours\textsuperscript{34-37}. Furthermore, the infamous side-effects of chemotherapy and radiotherapy, such as nausea, vomiting and mucositis, can increase the risk of nutritional impairment even further\textsuperscript{35, 37}. Finally, other geriatric domains, including mood, functional status, polypharmacy and socio-environmental factors, are presumably associated with an impaired nutritional status as well\textsuperscript{35, 38}. In chapter 5 we analysed the associations between preoperative nutritional impairment, impairments in other geriatric domains and the risk of adverse postoperative outcomes in onco-geriatric surgical patients, as this might lead to targeted interventions to optimise patients for surgery and tailored treatment that hopefully will improve postoperative outcomes\textsuperscript{39}.

Finally, we completed the PREOP-study by addressing long-term outcomes in onco-geriatric surgical patients (chapter 6). Data on long-term outcome measures in onco-geriatric surgical patients are scarce and seem under-exposed, whilst the life expectancy of elderly might be higher than one often thinks: life expectancy at 70 years of age is approximately 14 to 17 years, and octogenarians have a life expectancy of 8 to 10 years\textsuperscript{40, 41}. Moreover, elderly rate maintaining their preoperative level of functioning as one of the most important outcomes, emphasizing the importance of knowing the long-term risk of institutionalisation\textsuperscript{42}. This final chapter provides data on survival up to five years postoperatively and the impact on postoperative living situation up to two years postoperatively. Furthermore, the predictive ability of the PREOP risk score regarding these outcomes is analysed.

With this thesis, we aim to raise awareness to the fact that the onco-geriatric patient population is not simply an older version of its younger counterpart. The heterogeneity of this population complicates the decision-making process and emphasizes the need for tailored treatment. The PREOP-study eventually aimed to support these processes. The general discussion and my stand upon future perspectives, can be read in chapter 7.
References


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