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Phenotyping older patients needing intensive treatment

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9
ENGLISH SUMMARY
NEDERLANDSE SAMENVATTING
LIST OF ABBREVIATIONS
LIST OF CONTRIBUTING AUTHORS
LIST OF PUBLICATIONS
CURRICULUM VITAE
DANKWOORD

ENGLISH SUMMARY

Introduction

The world's population is ageing: almost every country in the world is experiencing growth in the number older persons in their population (Eurostat Statistics 2017). With increasing age, the prevalence of disease increases, resulting in a high proportion of older adults suffering from multiple (chronic) diseases (also called multimorbidity) [1]. Higher age is accompanied with multimorbidity, ageing-associated diseases and is also associated with the presence of geriatric conditions. Examples of geriatric conditions are: a decreased ability to perform activities of daily living (or functional impairment), cognitive impairment, delirium and falls [2, 3]. A way of phenotyping older patients is the use of a geriatric assessment. A geriatric assessment is used to explore the different domains of somatic status, mental functioning, physical functioning and social functioning.

Because of the multimorbidity and the complex interaction between the different domains, clinical decision making in older patients can be challenging for clinicians, patients and caregivers. It is known that a higher age and multimorbidity are associated with many adverse health outcomes such as disability, institutionalization, poorer quality of life and higher rates of side effects after treatment [4, 5]. However, only few studies have assessed the association of a geriatric assessment with outcomes in vulnerable older patients with severe diseases, such as head and neck cancer, esophageal cancer or end-stage renal disease [5]. Especially in these vulnerable older patients with severe treatments can have major impact on outcomes such as disability and quality of life.

Aim of the thesis

This thesis has three aims. The first aim is to quantify the lack of evidence in the literature regarding the report of elements of a geriatric assessment in older adults participating in clinical trials. The second aim is to study the association between the outcome of a geriatric assessment and adverse health outcomes in older patients with various severe diseases. The third aim is to assess the determinants of a patient reported outcome measurement in an older patient population.

Summary of the key findings

In **chapter 2**, we aimed to evaluate whether it is insightful what kind of older patients participated in randomized controlled trials (RCTs). We analysed the published RCTs in 2012 and evaluated what proportion of trials, specifically designed for older patients, reported on elements of the domains of the geriatric assessment in the patient characteristics (i.e. in the population descriptives or the in- and exclusion criteria). We found

that only 34% of all trials (participants had a mean age ≥ 60 years) report elements of the domains in the patient characteristics. The percentage of reported geriatric domains increased when the age limit was higher, however, that only presented a small percentage of all included trials.

In **chapter 3 and 4** we studied the association of functional or cognitive impairment, social environment and frailty with adverse health outcomes in patients with head and neck cancer and in patients with esophageal cancer with a review of the literature. In both patient groups we showed that impairment in functional performance, depression and social environment were highly prevalent. In patients with head and neck cancer the majority of the studies reported a statistically significant association of impairment in functional and cognitive performance, mood or social environment with a higher risk of adverse outcome. In patients with esophageal cancer, functional or cognitive impairment or frailty were associated with adverse health outcomes, but the studies were relatively small.

In **chapter 5** we studied the association of geriatric assessment and one-year mortality in older patients with cancer in the head and neck region. We analysed the data of a cohort study in which all patients aged 70 years and older, diagnosed with head and neck cancer, received a geriatric assessment prior to their treatment. We showed that geriatric impairments were highly prevalent. Furthermore, we found that the mortality rate was high, even in the patient treated with a curative intention. Malnutrition and mobility were independently associated determinants with one-year mortality.

In **chapter 6** we aimed to describe in detail the patterns of cognitive functioning and identifies nephrologic, geriatric and neuroradiologic determinants associated with an impaired cognitive function in older patients reaching end-stage renal disease (ESRD) and who have not started with renal replacement therapy (yet). We analysed the data from the Cognitive decline in Older Patients with End stage renal disease (COPE) study. All patients with end-stage renal disease received a full nephro-geriatric work-up. We showed that older patients reaching ESRD have a high prevalence of impaired memory, executive function and psychomotor speed. High age, low education, low functional status, frailty, higher burden of white matter hyperintensities on MRI and a history of vascular disease were determinants. The patterns of cognitive impairment and brain changes on MRI are suggestive of vascular cognitive impairment.

In **chapter 7**, we aimed to identify the determinants associated with self-rated health in an older population visiting the Emergency Department (ED). We used the data of the Acutely Presenting Older Patients (APOP) study in which a patient reported outcome

measurement was described in older patients visiting the emergency department (ED) of the LUMC or the Alrijne Hospital. As patient reported outcome measurement we used self-rated health. We found that a decline in SRH after an ED visit in older patients is at least partly dependent on factors of functional capacity and functional decline.

DISCUSSION

As mentioned previously, only a small proportion of the randomized controlled trials (RCTs) specifically included older adults, and the geriatric characteristics in these RCTs were underreported. This finding supported our hypothesis that for clinicians it is unclear to which older patients the results can be applied. Because of the ageing population and the increasing prevalence of multiple (chronic) diseases at higher age [1], there will be a need of improving the scientific evidence in older adults. To achieve this, several steps should be taken. Researchers should start to systematically report the geriatric characteristics of older patients in all RCTs and make RCTs more accessible for older adults to participate. Furthermore, alternative research methods, like observational studies, should be considered. However, the importance and the specific aspects of conducting research in older adults should firstly be recognized by researchers, clinicians, research grant providers and sponsors.

In this thesis we describe that aspects of the geriatric assessment are associated with adverse health outcomes. This finding endorses the importance of taking geriatric characteristics into account in patients who possibly need intensive treatment (e.g. surgery, chemotherapy or radiation therapy or a combination). Importantly, it is not necessary to administer a complete geriatric assessment to all patients. A two-stepped model, in which all patients undergo a short simple screening, and only those with abnormal test scores undergo a complete geriatric assessment, is suggested[6].

An example where all the above described aspects are combined is the 'Triage of Elderly Needing Treatment' (TENT)-study. In this study all patients who possibly need intensive treatment (e.g. surgery, chemotherapy or radiation therapy or a combination), the geriatric characteristics are taken into account and all patients are followed for complications of treatment, mortality, functional status and quality of life up to 12 months after treatment.

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