Phenotyping older patients needing intensive treatment

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8 GENERAL DISCUSSION

KEY FINDINGS

This thesis has three key findings. First, only a small proportion of the randomized controlled trials (RCTs) specifically included older adults, and the geriatric characteristics in these RCTs are underreported. Second, we show that geriatric impairments, such as cognitive impairment and functional dependency, are prevalent, and associate with adverse health outcomes in older patients with head and neck cancer and in patients with esophageal cancer. Third, self-rated health is partly dependent on factors of functional capacity and functional decline. This chapter reviews these key findings, discusses the implications for research and for clinical practice, and provides perspectives for future research.

IMPLICATIONS FOR RESEARCH

Increasing the number of representative older adults in research

In **chapter 2** we report that only a small proportion of the published RCTs targeted older adults. RCTs and meta-analyses are generally considered to provide the highest 'level of evidence', and the results of these RCTs or meta-analyses are used to compose clinical guidelines. Since older adults are underrepresented in these trials and the included participants are often not representative for the older adults seen in clinical practice, it is questionable whether these clinical guidelines are applicable for older adults. 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. In **chapter 2** we show that geriatric characteristics are underreported, even in the RCTs specifically designed for older adults. Consequently, this results in a low external validity; i.e. it is unclear to which older adults the results can be applied. Since older patients are very heterogeneous with respect to for example, cognitive functioning and/or physical capacity, extrapolating research outcomes based on chronological age or disease stage alone may lead to undertreatment as well as overtreatment [2, 3]. So, when older adults are participating in research, in my opinion, geriatric characteristics should always be reported. Ideally a guideline is available which includes a standard set of geriatric characteristics, and that imposes for example, that at least one aspect of each geriatric domain should be reported. There is already a guideline available addressing 'physical frailty' [4]. This could be helpful in characterising older adults in research and therewith make the participants comparable between the diverse studies.

To increase the representative number of older adults participating in RCTs, the RCTs should be conducted differently. For instance, by applying less stringent exclusion criteria or by making RCTs more accessible for older adults to participate. One suggestion could be to plan home visits, so older (vulnerable) adults are more willing to participate. There is already a guideline available on how to perform an RCT in older adults. This guideline suggests to combine research activities with routine hospital visits, to plan research visits at home or to provide telephone follow up [5]. However, these adaptions make RCTs more complex and more expensive, while resources are limited.

Other research methods, like observational studies, may be valuable alternatives to consider. Observational studies can generate a large amount of reliable data, are easily accessible and often cheaper than an RCT since randomization is unnecessary [6]. Besides, observational studies often have less exclusion criteria, and the included participants may therefore more broadly represent patients seen in daily practice [7, 8]. Furthermore, (international) databases, originally established for improving the quality of care, can also be used for research purposes. An example from the Netherlands is the Dutch Institute of Clinical Auditing (DICA), which is a registry with information on patients and disease characteristics as well as outcomes relevant for patients, such as functional performance in the period after a hip fracture. Data from these (international) databases may even be combined with local study data. For example, when studying geriatric characteristics in patients with esophageal cancer, the study data can be combined with disease and treatment specific information registered in the Netherlands Cancer Registry (NCR) database. When studying diseases in older adults, collaboration with other institutions in order to increase inclusion rates can be necessary. Major challenges in these collaborations are the standardization of clinical care and to facilitate the systematic registration and collection of data for research purposes. In the future perspectives we describe such an initiative.

The importance and the specific aspects of conducting research in older adults should firstly be recognized by researchers, clinicians, research grant providers and sponsors. This can be achieved by providing more education. One of our initiatives is the development an e-learning for medical professionals, but also accessible for non-medical professionals, about evidence-based medicine in the older patient. All the aspects described above (i.e. the importance of conducting research in older adults, the current gaps and the needs) are discussed in this e-learning, see also www.iemo.nl/elearning.

Including relevant endpoints for older adults in research

With increasing age, treatment goals are changing. Compared to younger patients, older patients give more importance to quality of life and maintaining functional dependency than to length of life [9-11]. Endpoints relevant for patients can be measured using patient reported outcome measurements (PROMs). In **chapter 7** we show that self-rated health, one example of a PROM, is partly dependent on factors as functional capacity and functional decline. Until now, PROMs are not structurally taken into account as relevant outcome in research. One reason is the lack of a "golden instrument" for measuring PROMS in older adults. It is not desirable that older adults, often suffer from multiple diseases, have to fill several overlapping disease-specific questionnaires. A solution could be one standard set of health outcome measures specific for older persons, regardless of the disease. The International Consortium for Health Outcomes Measurement (ICHOM), an international consortium with goal to increase value-based healthcare, recently developed such a standard set [12]. It is debatable if this set is usable in the Netherlands, but it can be a good starting point for further investigation of outcome measures that would be relevant for clinicians, health care policies and researchers.

IMPLICATIONS FOR CLINICAL PRACTICE

In **chapter 3, 4 and 5** we report that geriatric impairments are prevalent in patients with head and neck cancer and esophageal cancer. The finding that geriatric impairments are so prevalent stresses the importance to a more holistic approach of the patient, rather than only taking their disease into consideration. Furthermore, geriatric impairments might influence the shared decision process. For example, cognitive impairment can directly influence the patients' shared decision making capacity by limiting the amount and speed of information processing [13]. The association of geriatric impairments with adverse health outcomes is described in diverse patient groups in **chapter 3, 4 and 5.** This finding is in line with literature in other diseases where it has been described that geriatric impairments predict several health outcomes including mortality, disability and cognitive functions[14].

The discussion above endorses that geriatric characteristics are important to consider when making personalized clinical treatment decisions. However, it is remains unclear which instrument or tests to explore the geriatric characteristics are the most helpful in treatment decision making or in predicting successful outcomes relevant for older adults. It is doubtful that there will ever be one perfect instrument usable and suitable for all different diseases and settings. From this thesis it is recommended to start exploring the geriatric characteristics as part of routine clinical care instead of waiting for the 'best' assessment

without taking geriatric characteristics into account at all. Importantly, it is not necessary to administer a complete comprehensive geriatric assessment (CGA) to all patients. Several two-stepped models have been described in literature, in which all patients undergo a short simple screening, and only those with abnormal test scores undergo a complete CGA [15]. For example, the geriatric-8 (G8) has a good sensitivity for detecting geriatric impairments and for identifying the patients who will benefit most from a complete CGA [16]. Taken together, I recommend that all older patients needing an intensive treatment should undergo some geriatric screening for example by using a two-stepped model.

FUTURE PERSPECTIVES

We have described several steps that can be taken to improve evidence-based medicine and personalized treatment decision making in older adults. The 'Triage of Elderly Needing Treatment' (TENT)-study is a good example combining all the described steps. In four hospitals in the Netherlands a routine clinical care pathway is implemented for older patients (aged 70 years or older), who possibly need intensive treatment (e.g. surgery, chemotherapy or radiation therapy or a combination). These patients receive a geriatric screening and on indication a comprehensive geriatric assessment prior to the start of treatment. We designed the TENT-study based on this routine clinical care pathway. All patients are followed for complications of treatment, mortality, functional status and quality of life up to 12 months after treatment. The TENT-study has several aims. First, to describe the prevalence of geriatric impairments in diverse patient populations needing invasive treatment and to explore the association with outcomes after treatment. Second, to develop a tool which can help in making informed treatment decisions and to, ultimately, increase the rate of favourable outcomes after treatment and increase the quality of care for older patients. The TENT-study started in January 2016 in the LUMC and since July of 2018 has been extended into a multicentre study. The first results of the TENT-study are expected mid-2019.

The TENT-study exemplifies how geriatric screening can be integrated into the daily practice and how to use clinical data in a large multicentre observational study focussing on the older adult needing intensive treatment. This also demonstrates the opportunities when collaborating with other institutions, standardizing routine clinical care and combine it with research. We hope that in the future the format of the TENT-study may serve as a template for implementing standardized routine clinical care pathways for older adults needing intensive treatment. Ultimately, we hope that the evidence gathered by the TENT-study can be used to improve research and evidence-based care for older adults needing intensive treatment.

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