Chapter 9

Introduction

Ageing is associated with physiological changes including shifts in body composition \([1, 2]\) towards lower muscle mass and accompanied lower muscle strength \([3-5]\). If muscle mass and muscle strength are below a clinically relevant threshold, it is called sarcopenia \([6]\). Sarcopenia is associated with negative health outcomes \([7-15]\) and contributes to high healthcare costs \([16, 17]\). A consensus definition of sarcopenia including diagnostic criteria is needed. Furthermore, raising awareness among healthcare professionals is of utmost importance. The aim of this thesis was to compare prevalence rates of sarcopenia using different sets of diagnostic criteria and to assess associations between candidate diagnostic measures of sarcopenia and muscle-related clinical parameters. Three diverse relevant populations of older adults were used encompassing geriatric outpatients, healthy young and old participants and a general population of young-to-middle aged and old adults. Furthermore, the aim of this thesis was to provide insight into the current awareness among healthcare professionals.

Main findings

Definition of sarcopenia

Chapter two showed that prevalence rates of sarcopenia vary within the same population of older adults and are highly dependent upon the applied set of diagnostic criteria. Moreover, agreement between the diagnostic criteria was minimal. These results indicate the importance of defining sarcopenia in a uniform way and the need to reach consensus on the diagnostic criteria for sarcopenia. Chapter three showed low concordance between diagnostic criteria for sarcopenia and diagnostic criteria for frailty indicating that these are two separate conditions and should not be intermingled with each other. Sarcopenia and frailty are based on different constructs and require a different treatment approach.

Diagnostic measures of sarcopenia

Chapter four showed that the assessment of maximal handgrip strength is dependent on the number of attempts, independent of age and health status. It was also showed that three attempts are needed if handgrip strength is considered as a continuous variable. If handgrip strength is considered as a discrete variable to assess low handgrip strength (dynapenia) using a cut-off value, it was showed that two attempts are sufficient in younger populations.
whereas in middle-aged and older populations the percentage of misclassification should be taken into account when using two attempts.

When comparing the association between muscle-related clinical parameters and diagnostic measures of sarcopenia, chapter five showed that parameters of malnutrition were most strongly associated with both relative and absolute muscle mass in geriatric outpatients and less strong associations were found with muscle strength and physical performance. Chapter six showed that serum albumin was most strongly associated with relative muscle mass in healthy young participants whereas serum albumin was not associated with any of the diagnostic measures in healthy old participants. Chapter seven showed that the association of instrumented physical activity measures and diagnostic measures of sarcopenia was highly dependent on age in a general population. Instrumented physical activity measures were most strongly associated with handgrip strength in young-to-middle aged adults and most strongly associated with gait speed in older adults. Results of these chapters add evidence essential for the development of the most clinically valid definition of sarcopenia.

**Awareness among healthcare professionals**

Chapter eight showed that healthcare professionals with a specific interest in sarcopenia are familiar with the concept of sarcopenia. Although an increase in the use of diagnostic measures was found five months after attending a lecture cycle on sarcopenia, application in clinical practice was hampered mostly by lack of knowledge, availability of equipment and time constraints to perform diagnostic tests. For the management of sarcopenia, the percentage of consulting the physiotherapist/exercise therapist and the dietitian, who are both required for the treatment, did not change after five months. These results indicate that educational lectures could be a first step to raise awareness among healthcare professionals, however, the implementation of diagnosis and management of sarcopenia requires further attention.

**Reflection**

**Definition of sarcopenia**

A consensus definition for sarcopenia is currently lacking and the use of different sets of diagnostic criteria results in non-comparable prevalence rates. Agreement between the currently used diagnostic criteria is minimal (Chapter two). Therefore, different groups of
sarcopenic older adults would be identified with potential different phenotypic characterization. This could have a subsequent impact on the effectiveness of interventions because someone can be classified based on low muscle mass only or on a combination of low muscle mass, muscle strength and physical performance. There are only a few studies assessing the agreement between diagnostic criteria and assessing the intra-individual prevalence rates of sarcopenia. In line with our results, these studies also showed minimal agreement between diagnostic criteria in middle-aged adults [18] and community-dwelling older adults [19]. Combining diagnostic criteria has an impact on prevalence rates. Prevalence rates using a single diagnostic criterion only including muscle mass or only muscle strength were found to be higher than using the combination of diagnostic criteria of muscle mass and muscle strength [19]. This indicates that low muscle mass and low muscle strength do not necessary coincide within a single individual. The use of a combination of diagnostic criteria in the definition of sarcopenia compared to the use of a single diagnostic criterion should be based on the one that has the strongest predictive value on health outcomes such as falls, physical disability, activities of daily living dependency and mortality and subsequently on the effectiveness of sarcopenia interventions.

**Diagnostic measures of sarcopenia**

The diagnostic measure(s) i.e. muscle mass, muscle strength, physical performance, which are most strongly associated with muscle-related clinical parameters should be included in the definition of sarcopenia. Table 1 gives an overview of the studies relating standardized diagnostic measures of sarcopenia with muscle-related clinical parameters in different populations. The three studies included in this thesis (Chapters five, six, seven) and four previous studies [9, 20-22] were summarized since all these studies used standardized diagnostic measures of sarcopenia, which allows for direct comparison of effect sizes. Results are summarized based on p-values; note that p-values are highly dependent on the sample size and do not reflect the magnitude of the effect sizes. Overall, the association between diagnostic measures and muscle-related clinical parameters was found to be highly dependent on the muscle-related clinical parameter and population. Results are still inconclusive on which diagnostic measure(s) i.e. relative and absolute muscle mass, muscle strength, physical performance, could be most accurate to include in the definition of sarcopenia. In addition, confounders such as fat mass also play a role since additional adjustments attenuated some associations in the fully adjusted models. Furthermore, the
different roles of muscle as internal organ such as in the glucose regulation or the role as a motor such as in physical activity could explain the inconclusive results.

Standardization of the diagnostic measurement methods is important to allow for comparison. For the measurement of muscle mass, a device should be used which can make an accurate distinction between muscle mass and fat mass such as a direct-segmental multi-frequency bio-electrical impedance analyser [23]. Handgrip strength is a frequently used measure for muscle strength, a proxy for total muscle strength, and is included in several sets of diagnostic criteria for sarcopenia [24-26]. A standardized protocol measuring maximal handgrip strength is lacking [27, 28] which should include the number of attempts (Chapter four), position of the arm and instructions. Knee extension strength is a measure for muscle strength of the lower limbs and often used for research purposes but the use in clinical practice is limited due to the equipment and training on how to perform the test. Furthermore, the additional value of knee extension strength compared to handgrip strength should first be established i.e. the agreement between both measures and comparing associations with health outcomes. Standardization of the measurement of gait speed encompasses instructions regarding the pace, but also the distance of the walking test as it has been shown that gait speed is dependent on the used walk test [29].

**Awareness among healthcare professionals**

Education to raise awareness among healthcare professionals is necessary for the implementation of the diagnosis and management of sarcopenia. In addition, an important step is that sarcopenia is recently recognized as an independent condition by the International Classification of Disease, Tenth Revision, Clinical Modification (ICD-10-CM, code M62.84) [30, 31]. This is necessary for both research and clinical practice and especially for the improvement of diagnosis and management including the required interventions for sarcopenia. Furthermore, it is important to also raise awareness among lay people on sarcopenia, the prevention and its treatment.
Table 1. Overview of studies relating standardized diagnostic measures of sarcopenia with muscle-related clinical parameters in different populations

<table>
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<tr>
<th></th>
<th>Healthy participants</th>
<th>General population</th>
<th>Geriatric outpatients</th>
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<tbody>
<tr>
<td></td>
<td>Physical performance</td>
<td>Bone mineral density</td>
<td>Serum albumin</td>
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<td></td>
<td>Young</td>
<td>Old</td>
<td>Young</td>
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<tr>
<td>Minimal adjusted model</td>
<td>-</td>
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<td>Relative muscle mass</td>
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<tr>
<td>Absolute muscle mass</td>
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<tr>
<td>Muscle strength</td>
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<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Physical performance</td>
<td>NA</td>
<td>NA</td>
<td>+/-</td>
</tr>
<tr>
<td>Fully adjusted model</td>
<td>+/-</td>
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<td>Relative muscle mass</td>
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<tr>
<td>Physical performance</td>
<td>NA</td>
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NA not applicable. ++; p-value <0.001, +; p-values ≥0.001 and <0.05, +/-; p-values ≥0.05 and <0.10 (suggesting a trend), -=; p-values ≥0.10.
Clinical implications and future research

Several steps are required to reach consensus on the definition and these steps may run in parallel to each other. First, further studies are needed in diverse populations of older adults to determine the appropriate diagnostic measures and to derive cut-off values related to clinically relevant outcomes. Sarcopenia should be related to clinically relevant outcomes such as falls, physical disability, activities of daily living dependency and mortality, and should be seen as a separate condition and not be intermingled with frailty and malnutrition. The use of different diagnostic criteria in future research is recommended to explore if diagnostic criteria act differently in the association with clinically relevant outcomes. Second, future studies should also focus on the standardization of the measurement methods of the diagnostic measures. Standardization also requires consensus about the measurement methods and arrangements need to be made on these methods. Third, raising awareness among healthcare professionals is of great importance and educating them on the diagnosis and management of sarcopenia. Fourth, implementation of the diagnosis and management of sarcopenia require many other factors next to raising awareness such as the acquisition of diagnostic measurement devices, re-organization of care, collaboration between healthcare professionals, the perceived needs and benefits of the innovation, and organizational factors. The ICD-10 code will help with the implementation of the diagnosis and management of sarcopenia and to raise more awareness among healthcare professionals. Furthermore, lay people should also be educated about the clinical relevance of the ageing muscle and sarcopenia. Future research should also focus on the appropriate interventions for sarcopenia and explore this in diverse populations.
Chapter 9

References