

Aus dem Zentrum für Innere Medizin der Universität zu Köln
Klinik und Poliklinik für Innere Medizin II der Universität zu Köln
Direktor: Universitätsprofessor Dr. med. Th. Benzing

Prevalence and diagnostics of sarcopenia and its prognostic feature in older, hospitalized patients

Inaugural-Dissertation zur Erlangung der Doktorwürde
der Medizinischen Fakultät
der Universität zu Köln

vorgelegt von
Anne Ferring
aus Luxemburg, Luxemburg

promoviert am 28. Juli 2026

Dekan: Universitätsprofessor Dr. med. G. R. Fink

1. Gutachterin: Universitätsprofessorin Dr. med. Dr. M. C. Polidori Nelles

2. Gutachter: Prof. Dr. Stefan Sauerland

Erklärung

Ich erkläre hiermit, dass ich die vorliegende Dissertationsschrift ohne unzulässige Hilfe Dritter und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe; die aus fremden Quellen direkt oder indirekt übernommenen Gedanken sind als solche kenntlich gemacht.

Bei der Auswahl und Auswertung des Materials sowie bei der Herstellung des Manuskriptes habe ich Unterstützungsleistungen von folgenden Personen erhalten:

Frau Universitätsprofessorin Dr. med. Dr. M. C. Polidori Nelles

Frau Dr. med. Anna Maria Affeldt (geb. Meyer)

Weitere Personen waren an der geistigen Herstellung der vorliegenden Arbeit nicht beteiligt. Insbesondere habe ich nicht die Hilfe einer Promotionsberaterin/eines Promotionsberaters in Anspruch genommen. Dritte haben von mir weder unmittelbar noch mittelbar geldwerte Leistungen für Arbeiten erhalten, die im Zusammenhang mit dem Inhalt der vorgelegten Dissertationsschrift stehen.

Die Dissertationsschrift wurde von mir bisher weder im Inland noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde vorgelegt.

Die dieser Arbeit zugrunde liegende prospektive klinische Studie wurden von mir in Zusammenarbeit mit Frau Universitätsprofessorin Dr. med. Dr. M. C. Polidori Nelles, Leiterin des Schwerpunkts für Klinische Altersforschung der Klinik II für Innere Medizin der Uniklinik Köln, Köln, Deutschland, Frau Dr. Anna Maria Affeldt, Fachärztin der Klinik II für Innere Medizin der Uniklinik Köln, Köln, Deutschland, Luisa Mück, Jill Stegemann, Laura Wiebe, Doktorandinnen des Schwerpunkts Klinische Altersforschung an der Klinik II für Innere Medizin an der Uniklinik Köln, und unter statistischer Beratung durch Frau Ingrid Becker vom Institut für Medizinische Statistik und Bioinformatik der Uniklinik Köln, Köln, Deutschland, entwickelt.

Die auf der Station 17 der Klinik II für Innere Medizin durchgeführten Untersuchungen im Rahmen der Vun nix kütt nix-Studie habe ich, gemeinsam mit den Doktorandinnen Luisa Mück, Jill Stegemann und Laura Wiebe unter Aufsicht der Universitätsprofessorin Dr. med. Dr. M. Cristina Polidori Nelles und der Stationsärztin Dr. med. Anna Maria Affeldt vorgenommen. Die telefonischen Nachbeobachtungen wurden durch Luisa Mück, Jill Stegemann, Laura Wiebe und mich vorgenommen.

Die Anleitung zur von mir selbst durchgeführten statistische Auswertung der Daten erfolgte durch Frau Ingrid Becker. Die dieser Dissertationsschrift zugrunde liegende Publikation *"Prognostic Features of Sarcopenia in Older Hospitalized Patients: A 6-Month Follow-Up Study"* in der Zeitschrift Journal of Clinical Medicine wurde eigenständig von mir verfasst.

Das Lektorat *Mentorium* hat die Endfassung dieser Arbeit grammatikalisch und sprachlich überarbeitet, hat jedoch weder einen Anteil an der geistigen noch an der inhaltlichen Gestaltung dieser Arbeit.

Falls ich mich im Rahmen dieser Arbeit auf Ergebnisse anderer Arbeiten beziehe, habe ich dies kenntlich gemacht.

Erklärung zur guten wissenschaftlichen Praxis:

Ich erkläre hiermit, dass ich die Ordnung zur Sicherung guter wissenschaftlicher Praxis und zu Umgang mit wissenschaftlichem Fehlverhalten (Amtliche Mitteilung der Universität zu Köln AM 132/2020) der Universität zu Köln gelesen habe und verpflichte mich hiermit, die dort genannten Vorgaben bei allen wissenschaftlichen Tätigkeiten zu beachten und umzusetzen.

Luxemburg, den 30.03.2026

Unterschrift:

Danksagung

Mein aufrichtiger Dank gilt allen Patientinnen und Patienten, die an unserer klinischen Studie teilgenommen haben. Ihr Vertrauen und Ihre Geduld haben diese Arbeit erst ermöglicht. Viele der Gespräche und Begegnungen werden mir in besonderer Erinnerung bleiben.

Ein besonderer Dank geht an meine Doktormutter, Frau Polidori. Ich bewundere Ihre Leidenschaft, Ihr unermüdliches Engagement und wie Sie die Altersmedizin mit Weitsicht und Herzblut voranbringen. Auch wenn ich nicht den Weg in die Geriatrie gewählt habe, prägen mich Ihre Ideen und Ihr Blick auf ältere Patienten täglich.

Danke auch an Anna. Ohne deine Begeisterung und deinen ansteckenden Enthusiasmus für die Studie, hätte ich diesen Weg wohl nicht eingeschlagen. Trotz deiner zahlreichen Aufgaben hattest du stets ein offenes Ohr und standst mir jederzeit zur Seite. Deine Unterstützung und Zuversicht haben mich durch viele Phasen dieser Arbeit getragen.

Mein Dank gilt ebenfalls allen Coautoren des Papers, insbesondere Frau Becker für ihre wertvolle Unterstützung bei der statistischen Beratung, sowie Laura, Luisa und Jill für die gemeinsame Rekrutierung auf Station. Doch Luisa und Jill - ihr wart nicht nur meine treuen Weggefährtinnen während der Dissertation, sondern habt die letzten Jahre unvergesslich gemacht. Eure Unterstützung und Freundschaft bedeuten mir unendlich viel und gehen weit über die Promotion hinaus. Dies gilt natürlich auch für alle anderen Freundschaften die ich über die vielen Jahre in Köln knüpfen konnte, die ich namentlich nicht alle erwähnen kann.

Mama und Papa - Danke für eure Unterstützung, eure Liebe, euer Vertrauen und eure stetigen Ermutigungen, meinen eigenen Weg zu gehen. Ihr unterstützt mich in jeder Entscheidung, auch wenn es manchmal etwas länger dauert, bis ich diese tatsächlich treffe. Auch dem Rest meiner Familie gilt ein großer Dank, insbesondere Lisi, die nicht müde wurde, bei jedem Familienfest nach dem neuesten Stand der Dissertation zu fragen und mir damit immer wieder den nötigen Anstoß und Motivation gegeben hat.

Zu guter Letzt möchte ich noch Charel danken; für deine bedingungslose Liebe und Unterstützung, dass du immer hinter mir stehst, mich ermutigst, meine Ziele zu verfolgen, und nie müde wirst, meine spontanen Entscheidungen mitzugehen.

für Boma & Bopa,
wenn ich auch nur ein bisschen werde wie ihr, dann freue ich mich aufs Älterwerden.

Contents

ABBREVIATIONS	8
1. ZUSAMMENFASSUNG (DEUTSCH)	9
2. INTRODUCTION	11
2.1 How to age in good health?	13
2.2 Geriatric Medicine - a milestone	14
2.2.1 Frailty and its consequences	15
2.2.2 The Comprehensive Geriatric Assessment	17
2.2.3 The Multidimensional Prognostic Index	18
2.3 Sarcopenia	19
2.3.1 Origin and Definition	19
2.3.2 Prevalence of sarcopenia	22
2.3.3 Pathogenesis and pathophysiology of sarcopenia	24
2.3.4 Primary and secondary sarcopenia, acute and chronic sarcopenia	25
2.3.5 Diagnostics of sarcopenia	26
2.4 EWGSOP Algorithm to classify Sarcopenia	26
2.4.1 Step A - Case finding using SARC-F	27
2.4.2 Step B - Assessment of sarcopenia by muscle strength	29
2.4.3 Step C - Confirmation of sarcopenia by muscle mass	30
2.4.4 Step D - Determination of severity by physical performance	32
2.5 The role of sarcopenia in the German health care system	33
2.6 Research question and aim of the work	34
3. PUBLICATION	36

4.	DISCUSSION	49
4.1	Findings of the "Vun nix kütt nix"-study	49
4.2	Key findings on sarcopenia, prognosis and outcomes in older patients	49
4.3	Prevalence of sarcopenia in the study population	54
4.4	The value of a consistent and globally used definition of sarcopenia	56
4.5	Limitations and problems along the conduction of the study	57
4.6	Conclusion and research outlook	59
5.	REFERENCES	61
6.	SUPPLEMENTS	70

Abbreviations

ADL	=	Activities of Daily Living
ANOVA	=	Analysis of Variance
ASMM	=	Appendicular Skeletal Muscle Mass
BIA	=	Bioelectrical Impedance Analysis
BMI	=	Body Mass Index
CGA	=	Comprehensive Geriatric Assessment
CIRS	=	Cumulative Illness Rating Scale
ESS	=	Exton Smith Scale
EWGSOP	=	European Working Group on Sarcopenia in Older People
EQ-5D-5L	=	European Quality of Life 5 Dimensions 5 Level
GDS	=	Geriatric Depression Scale
GS	=	Geriatric Syndromes
GR	=	Geriatric Resources
HGS	=	Hand Grip Strength
IADL	=	Instrumental Activities of Daily Living
MNA-SF	=	Mini Nutritional Assessment - Short Form
MPI	=	Multidimensional Prognostic Index
PROMs	=	Patient Reported Outcome Measures
RCT	=	Randomized Controlled Trial
RSES	=	Rosenberg Self-Esteem Scale
SPI	=	Selbst Pflege Index
SPMSQ	=	Short Portable Mental Status Questionnaire
TIDP	=	Tailored Intersectoral Discharge Program
TUG	=	Timed Up and Go - test
VAS	=	Visual Analogue Scale
WHO	=	World Health Organization
NS	=	No Sarcopenia
PS	=	Probable Sarcopenia
CS	=	Confirmed Sarcopenia
SS	=	Severe Sarcopenia

1. Zusammenfassung (deutsch)

Aufgrund des demografischen Wandels und bemerkenswerter Fortschritte in der Medizin, wächst die Bevölkerungsgruppe der über 60-Jährigen rasant und die durchschnittliche Lebenserwartung älterer Menschen wird voraussichtlich weiter steigen. Das öffentliche Gesundheitssystem sieht sich demnach mit einem dringenden Handlungsbedarf konfrontiert, um dieser älteren Bevölkerung mit erheblichem Risiko des Funktionsverlustes gerecht zu werden und den Alterungsprozess positiv beeinflussen zu können. Die größte Herausforderung besteht demnach darin, dass die zusätzlichen Lebensjahre nicht durch einen schlechten Gesundheitszustand und funktionelle Einschränkungen geprägt sind, sondern die Funktionalität, und auch die Lebensqualität in genau diesen Jahren aufrecht erhalten werden. Das vorrangige Ziel besteht demnach darin, die Anzahl an behinderungsfreien Jahren zu maximieren und den Zeitraum der Morbidität und Gebrechlichkeit in der alternden Bevölkerung zu verkürzen. Um genau diese Aspekte des Alterns besser greifen zu können und die multidimensionalen Aspekte der Gebrechlichkeit darstellen zu können, wurden umfassende geriatrischen Assessments (Comprehensive Geriatric Assessment CGA) zum Goldstandard für den diagnostischen Prozess in der Geriatrie. Der daraus abgeleitete Multidimensionale Prognostischer Index (MPI) bietet eine weitere Grundlage, um den älteren Menschen in seiner vielfältigen, komplexen und multidimensionalen Art wahrzunehmen und sowohl physische, psychische, funktionelle und soziale Aspekte zu erheben, sowie die multidimensionale Frailty und Prognose zu quantifizieren. Als wichtiger, die Prognose beeinflussender Baustein, bleibt der zunehmende Funktionsverlust zu nennen. Aufgrund des demografischen Wandels nimmt demnach auch die Prävalenz von Krankheiten wie der Sarkopenie, definiert als ein allgemeiner und fortschreitender, altersbedingter Rückgang von Muskelmasse, Kraft und Funktion stetig zu. Wie genau sich die Sarkopenie jedoch auf die Prognose älterer Patienten, mit dem hochgradig prädiktiven Wert des MPI gemessen, auswirkt, ist noch nicht ausreichend erforscht und soll in dieser Dissertation weiter beleuchtet werden.

Basis dieser vorliegenden Dissertation ist die Studie mit dem Titel "*Vun nix kütt nix* - Patient, Geriater und Hausarzt als multiprofessionelles Team für ein intersektorales Entlassungsmanagement". Diese Interventionsstudie befasste sich mit dem Thema des Entlassungsmanagements für ältere, multimorbide Patienten in der Akutversorgung. Primäres Ziel der Studie war es, die Effektivität eines Tailored Intersectoral Discharge Program (TIDP) bei der Optimierung des Übergangs von der stationären in die ambulante Versorgung und bei der Verbesserung der Behandlung multimorbider Personen durch gemeinsame klinische Entscheidungsfindung zu untersuchen. In einer Subanalyse, die die Hauptgrundlage dieser Dissertation bildet, wurde sich auf die Sarkopenie konzentriert, die Probleme, die mit ihrer

Diagnose einhergehen, und ihren Einfluss auf den Gesundheitszustand, die Frailty und die Prognose von älteren Patienten.

Die *"Vun nix kütt nix"* - Studie konnte zeigen, dass die intersektorale Triade aus Hausarzt, Patient und Geriater in der Lage ist, die Gebrechlichkeit bei akut hospitalisierten Patienten zu reduzieren und die Stimmung, wie auch das Selbstwertgefühl zu verbessern. Obwohl kein signifikanter Effekt der Intervention auf die Rehospitalisierungsraten nachgewiesen werden konnte, lieferte die Studie neue Erkenntnisse bezüglich Verringerung der Gebrechlichkeit und Verbesserung der Patientenbezogenen Ergebnissen (Patient Reported Outcome Measures, PROMs) in Form von höherem Selbstwertgefühl und weniger depressiven Symptomen. Darüber hinaus konnte in der Sekundäranalyse gezeigt werden, welcher multifaktoriellen Einfluss die Sarkopenie auf die Prognose, die Gebrechlichkeit und die kurzfristigen Ergebnisse älterer, multimorbider Patienten haben kann. Signifikante Unterschiede zwischen Patienten mit Sarkopenie und denen ohne Anzeichen für Sarkopenie konnten nicht nur in Bezug auf körperliche Parameter und Komorbiditäten, sondern auch hinsichtlich der selbst wahrgenommenen Lebensqualität, des Wohlbefindens und des Selbstwertgefühles aufgezeigt werden.

Die vorliegenden Analysen an stark phänotypisierten Patienten konnten demnach die klinische Relevanz von Sarkopenie durch ihre Quantifizierung mittels PROMs und einer gut etablierten CGA-basierten Messung von Prognose und multidimensionaler Frailty aufdecken. Perspektivisch sollten die Ergebnisse dafür genutzt werden, weitere Forschung unter Verwendung der etablierten diagnostischen Kriterien für Sarkopenie zu betreiben, und zu untersuchen, ob zusätzliche krankenhausinterne Bewegungs- oder/und Ernährungsinterventionen oder Rehabilitationsprogramme, die speziell auf den individuellen, mit Sarkopenie verbundenen Status ausgerichtet sind, eine präventive Wirkung auf den weiteren klinischen und ambulanten Verlauf haben könnten.

2. Introduction

"Aging is not lost youth but a new stage of opportunity and strength."

Betty Friedan (1921-2006)¹

The human species is constantly faced with unprecedented challenges, be it through global warming and its associated effects, antimicrobial and drug resistance or pandemics like the recently experienced SARS-CoV-2 (Severe Acute Respiratory Syndrome CoronaVirus type 2) outbreak, which profoundly impacted not only the healthcare sector but also interpersonal dynamics and community spirit. One of these challenges which is no longer elusive and difficult to assess is constant acceleration of aging, a phenomenon that can be observed worldwide. The longevity revolution is evident in the drastic rise in life expectancy, as can also be seen in the example of Germany. While men born in Germany in 1950 had a mean life expectancy of 64.6 years, newborn male babies born in 2020 can expect to reach 78.9 years and those born in 2060 even 84.4 years. The expected numbers are even higher for women; according to statistical forecasts, average life expectancy in 2060 could rise to 88.8 years for women born in Germany². This shows the extreme extent to which life expectancy has increased in recent decades, and at the same time makes it clear that our healthcare system is facing a challenge that has never been more present and obvious. On the one hand, this increase in life expectancy is a testament to remarkable advancements and progress in the medical field, effectively reducing infant mortality and combating once-deadly infectious diseases like tuberculosis or AIDS. Significant investments have also been made in preventing chronic conditions such as cardiovascular diseases, diabetes and cancer. Furthermore, people have been encouraged to embrace healthier lifestyles with reduced tobacco use, increased physical activity, and a greater focus on healthy nutritious diets and living, culminating in an overall understanding of health, all of which are beginning to bear fruit. On the other hand, in light of these tremendous developments, our healthcare system is confronted with an unprecedented challenge, given the substantial number of older patients requiring individualized and time-intensive help. The population segment of persons older than 60 years is the most rapidly growing one and mean life expectancy in older individuals is predicted to continue increasing which therefore goes hand in hand with an increase of people at risk of functional decline. Countries' health systems and their workforces all over the world are facing an enormous challenge³.

But what exactly does it mean to age and what are the inevitable steps in the process of aging? Generally, when contemplating aging and the population of older adults, various age-related conditions such as a decrease in hearing and vision, decelerated and precarious mobility, back

pain or declining social memory come to mind. From a scientific and biological point of view, the process of aging involves multitudinous complex factors that lead to molecular and cellular damage, which then in turn manifest themselves in a decrease in physical, mental, or functional efficiency⁴. However, these changes are by no means linear or uniform for every aging person, neither are they concordant with a person's chronological age. They rather are as individual and diverse as the human beings themselves. Since the release of the book "Evolutionary Biology of Aging" by Michael R. Rose in 1991, the proposed definition of aging as "a persistent decline in the age-specific fitness components of an organism due to internal physiological deterioration"⁵ has often been used and adapted by other evolutionary biologists. As the body ages, it experiences declines at the cellular, molecular, epigenomic, organic and various other levels, rendering it more vulnerable and increasing the likelihood of becoming frail or developing a chronic disease⁶. Over time, these changes and physical alterations can no longer be compensated for and eventually lead to death. However, aging does not have to be an accumulation of deterioration that inevitably leads to death, but it can also bring an array of positive effects. The crucial goal is that the years that are added to people's lives are not compromised by poor health status and functional limitations. Therefore, the primary objective is to maximize the disability-free years and to compress the period of morbidity and mortality in the aging population⁷. To achieve this objective, medical care needs to be tailored to the individual needs of the patients rather than being solely disease-orientated. Otherwise, health care systems are confronted with immense costs and a significant burden of illnesses and functional limitations⁸. Considering the increasing complexity of patient's problems due to demographic changes, follow-up care for older patients after their stay in the hospital as well as the interface between acute inpatient and outpatient care are gaining importance to minimize the risk of inefficient, over-, or undertreatment. A narrow collaboration among providers both intra- and intersectoral would therefore be required, but unfortunately is often rather neglected due to lack of time or appropriate remuneration.

To facilitate personalized care for older patients and gain an optimal overview of their relevant dimensions such as their functional status, mental health, and socio-medical parameters, the usage of the Comprehensive Geriatric Assessment (CGA)⁹⁻¹¹ and the derived Multidimensional Prognostic Index (MPI)¹²⁻¹⁵ have proven effective. Consequently, MPI can assist physicians and other healthcare professionals in making improved clinical decisions regarding diagnostics and treatment of older patients, enabling targeted discharge management and better patient outcomes overall¹⁶.

The cornerstone of this dissertation is the study titled *"Vun nix kütt nix" - Patient, geriatrician and general practitioner as a multi-professional team for intersectoral discharge management*". This intervention study addresses the previously broached issue of discharge management for

older, multimorbid patients in acute care. The primary aim of the study was to investigate the effectiveness of a Tailored Intersectoral Discharge Program (TIDP) in optimizing the patient's inpatient-outpatient transition and improving the treatment of multimorbid individuals through shared clinical decision-making. A secondary analysis, which forms the main basis of this dissertation, focuses on sarcopenia, the problems that come along with its diagnosis, and its influence on older patients' health status, frailty, and prognosis.

The following chapters provide an overview of the challenges posed by an aging population and the current state of geriatric medicine, including assessment tools such as the CGA and MPI. The concepts of frailty and sarcopenia, along with their diagnostic approaches, will also be introduced, with particular attention to the difficulties in precisely defining and diagnosing sarcopenia. The dissertation briefly presents the results of the primary study, with the findings from the secondary analyses discussed in detail and critically evaluated in the context of current research.

Throughout the dissertation, only the male form will be used when referring to individuals or groups. This is done solely to enhance readability but naturally includes both female and male individuals in context.

2.1 How to age in good health?

"The trick is growing up without growing old." - Casey Stengel (1890-1975)

Over the last few decades, it has become increasingly clear that the ultimate goal of aging is not simply to grow old indefinitely at any cost, but to age while maintaining good health and well-being. This shift in perspective emphasizes the importance of prevention and early intervention, enabling individuals to reach old age without compromising their health and quality of life. It is therefore not just the longevity that matters; equally important is the condition in which one can experience those later years. While some individuals may enjoy excellent health both physically and mentally in their 70s and beyond, remaining "fit as a fiddle", others may experience frailty and weakness even earlier in life. The question therefore arises as to what factors impact upon this desired healthy aging and which precise conditions dictate how the further future will look? How can the number of people experiencing positive aging trajectories be maximized to the fullest?

In their retrospective cohort study of centenarians¹⁷, Evert et al. suggest a classification of centenarians into three clinically distinguishable morbidity patterns: patients remaining free of the diagnosis of a chronic disease until the age of 100, formed the group of the "escapers", as they were able to outrun a condition causing many deaths annually and worldwide. The

"*delayers*" were diagnosed with a chronic disease after reaching the age of 80, while the "*survivors*", who comprised the largest proportion of the study population, described individuals who received their first diagnosis of a chronic disease before reaching 80 years of age but survived beyond it¹⁷. With their publication, the authors aimed to develop a method capable of forecasting "health-related survivorship outcomes" of the older, since each person undergoes an individual and unique development and responds differently to various conditions. However, the key question remains: How does one become an "*escaper*" and to what extent can one directly influence this outcome, or is it largely determined by genetics? It remains an important topic to pinpoint at which junctures an intervention is possible and necessary in order to achieve the goal of healthy living.

2.2 Geriatric Medicine - a milestone

Interest in the process of aging and maintaining health can be traced back to the times of Hippocrates, but it was not until a century ago that geriatrics began to find true integration within the medical field, especially in the United States and in the United Kingdom¹⁸. The need for a specialized and specific professional group became inevitable in order to face the challenges arising from increasing life expectancy. In the early twentieth century, Ignatz Leo Nasher published a paper proposing the term "geriatrics" to refer to the field focusing on diseases in older age. The term originated from the Greek words "*geron*" (meaning "old person") and "*iatrikos*" (meaning "medical science") and being the counterpart to what pediatrics is for the youngest segment of the population¹⁹. The first impetus for the implementation of geriatrics in a medical student's curriculum, as well as the establishment of a separate word for older chronically ill patients was published by British doctor Marjory W. Warren in 1943 in her article "*Care of chronic sick - A case for treating chronic sick in blocks in a general hospital*"²⁰. She was also the first to establish an organized geriatric medicine unit in a British hospital and promoted innovative methods by highlighting the importance of a multidisciplinary approach to meet the needs of older patients and abandoning the assumption that a disease can no longer be cured merely because of a certain age. In another paper she stressed the need for geriatrics to be recognized as a distinct branch of medicine, deserving of greater attention and support: "until the subject is recognized as a special branch of medicine in this country it will not receive the sympathy and attention it deserves"^{20,21}. This important step, the recognition by the British National Health Service (NHS) of geriatrics as a medical specialty finally occurred in the 1950s, paving the way for its development and expansion in other countries as well²².

In modern Geriatric Medicine, the focus remains on multidisciplinary teams, early active involvement and rehabilitation, tailored interventions, all with a patient-centered rather than disease-focused approach. A patient-centered approach presupposes "providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions"^{23,24}. To achieve this, highly trained professionals are essential and patients need to be perceived in the context of their individual pasts, with their current desires and decision-making regarded as a cooperative process rather than a confrontation of the patient with a unilateral, already settled plan²⁵. While challenging, this approach yields rewards in the form of higher satisfaction and well-being on the part of the patients, which in turn can positively impact the prognosis, shorten the duration of treatment and thus reduce healthcare costs²⁶.

2.2.1. Frailty and its consequences

Due to its high prevalence in older people, frailty is a significant multidimensional geriatric syndrome that has garnered increasing attention in Geriatric Medicine²⁷. It is characterized as a multidimensional, age-associated decline in function as well as in the reserve of multiple physiological systems and capacities²⁸, leading to a certain state of vulnerability, representing the visual expression of aging²⁹. Being a multidimensional and highly prevalent state in the process of aging, it is associated with an increased risk of falls, hospitalization, disability and mortality³⁰. It is a condition brought about by the deterioration of multiple physiological systems which occur naturally with aging, resulting in a state in which changes in health and increased vulnerability occur when triggered by sudden, even minimal stressors³¹. In other words, a small and seemingly trifling event that one would not expect to trigger a noticeable reaction can lead to a significant and disproportionate change in a person's health state. These can be small events like the introduction of a new medication, a minor infection, or surgery that can subsequently result in states of dependency, immobility, instability or delirium, while a fit and robust older person would react with a temporary small decline in function, followed by a return to previous homeostasis³¹. Despite significant effort in research in the last two decades, a consensus on the definition of frailty has not yet been reached. In 2001, Fried et al. defined a "physical phenotype of frailty" based on the presence of at least three out of five components³⁰, the first being unintentional weight loss of at least 10 pounds in the last year. As other characteristics, they defined weakness (determined by low grip strength), self-reported exhaustion indicating poor endurance and energy, slow gait speed and a low level of physical activity³⁰. Patients showing one or two of these characteristics were considered as „prefrail" or in other words in an intermediate state while those without any of those 5 characteristics were considered "robust"³⁰. However, as these characteristics focus on the state of extreme

physical vulnerability, this model neglects, in relative terms, the multidimensionality associated with frailty. More recent models consider various dimensions, such as cognition, genetics, psychological or socio-economic domains^{32,33}. With the frailty index published by Rockwood and Mitnitski, a measurable way to quantify the vulnerability was proposed by considering frailty as an "accumulation of deficits"³⁴. In their stochastic approach, various potential deficits, geriatric syndromes, functional restrictions and social deficiencies are assessed and combined in one score, thereby taking into account a wider range of factors than the phenotypical approach of Fried. It is also worth mentioning that frailty should not be regarded as a static state, but as a constantly changing and dynamic process with regular shifts between the different states of frailty³⁵. The overall picture of frailty can be seen as the terminal point of a dynamic progression starting with functional integrity and well-being and then developing in a slow and sometimes imperceptible process still with the potential to be reversed, but more commonly worsening over time³⁵. When it comes to assessment and diagnostics, various methods are available, differing in their extent and clinical context, but with a common characteristic of determining the elevated likelihood of adverse outcome²⁷. Multiple studies across different subpopulations and settings could consistently show a correlation between frailty and mortality³⁶⁻³⁸. Moreover, associations with frailty were demonstrated when considering falls, dependency, disabilities, depression, poor social interaction or hospitalisations³⁹⁻⁴⁴.

In summary, even though an international consensus for a definition and assessment of frailty is still under development at present, some key points have emerged: Firstly, frailty is a complex and multidimensional condition, influenced not only by physical components but also by social, cognitive, psychological and many other factors²⁷. Secondly, it is a predominantly age-related condition, but not exclusive to aging, as not all individuals experience frailty as they grow old. It therefore should be viewed as a separate condition that may occur alongside the physiological aging process³³. And third, frailty is an evolving, dynamic condition with fluctuations between different frailty states over a period of time³⁵.

Adverse outcomes that have been proven to come along with sarcopenia, an age-related loss of muscle mass and function, that will be covered in detail in the following chapters of this thesis, are comparable to many of those being associated with frailty⁴⁵. At the present time, the relationship between sarcopenia and frailty is yet to be fully understood and it remains unclear whether sarcopenia acts as a "mediator" to many of the adverse outcomes that arise with frailty or if it is a clinical manifestation of frailty^{46,47}. It even seems as if the question is similar to the one asking whether the chicken or the egg came first, and until now there is no answer to this question either. However, it is evident that both sarcopenia and frailty present

important overlaps in their influence on prognosis, and both represent an issue bringing certain challenges in the future, when considering the fact that people are getting older and age-related loss of muscle function together with frailty will be common co-occurrences of aging. Another commonality both frailty and sarcopenia share is the challenge of correctly identifying and treating patients. By virtue of vague and inconsistent definitions, medical personnel have to meet the challenge of identifying patients at risk appropriately and proactively before they even become frail or sarcopenic. For this to succeed, a comprehensive approach is urgently needed.

2.2.2. The Comprehensive Geriatric Assessment

The UK health-care system was a pioneer in recognizing the importance of a multidisciplinary approach that does not exclusively focus on disease management but on enhancing the quality of life and overall outcomes of older individuals. This groundbreaking concept gave rise to the CGA, which has become a cornerstone of modern Geriatric Medicine. It has become one of the most important tools for creating an overarching concept for facilitating treatment and long-term tracking of older patients, as well as clinical decision making.

Developed by Marjory Warren in the late 1930's⁹ in order to meet the challenges posed by increasing age, the standard of CGA has evolved significantly in 1987 due to the pooling of various experts in that field by the National Institutes of Health NIH^{48,49}. In 1991, Rubenstein et al. defined the CGA as *"a technique for multidimensional diagnosis of frail, older people with the purpose of planning and/or delivering medical, psychosocial, and rehabilitative care"*⁵⁰. Ellis et al. in 2017 further emphasized its complexity and overarching purpose, describing it as *"a multi-dimensional diagnostic and therapeutic process that is focused on determining a frail older person's medical, functional, mental, and social capabilities and limitations with the goal of ensuring that problems are identified, quantified, and managed appropriately"*⁵¹.

It is perspicuous that for a process as complex as aging is in its entirety, a tool combining and incorporating all those elements was needed to be able to provide best possible care for the older population. The power and strength of the CGA lies in its ability to synergize mental, physical and functional status, while simultaneously evaluating social capabilities, quality of life and environmental factors, thus offering an objective insight into the overall health status of older patients⁴⁸. All the information gathered by means of the CGA is intended to provide an individualized treatment approach with the aim of stimulating independence and quality of life of the patients⁵². However, despite decades of interest and research, no general agreement on the best CGA tool has been reached. There are many elements that can be included in the CGA and a huge variety of comprehensive assessment tools have been elaborated. The CGA therefore is not a defined, rigid bundle of questionnaires, but rather a multidisciplinary concept

integrating different valid and reliable tools of geriatric domains thought to be the foundation for the diagnostic and treatment process of older patients.

Typically, the CGA includes gathering information about self-care abilities and activities of daily living, accomplishing functional tasks, mobility, activity status, fall history, pain, depressive symptoms and social environment. Additionally cognition, mood, medication intake, nutrition status, urinary continence, living situation and financial as well as social support are items that contribute to the CGA^{9,53}. Numerous meta-analyses have demonstrated that comprehensive geriatric assessment enhances detection of geriatric challenges and issues and can lead to improvements in functional status⁵³⁻⁵⁵. In their newest generalized information, Ward et al. summarize that CGA *"is based on the premise that a systematic evaluation of frail older persons by a team of health professionals may identify a variety of treatable health problems and lead to better health outcomes"*⁵³.

2.2.3. The Multidimensional Prognostic Index

Initially developed and validated to predict mortality, the MPI has also become an important prognostic tool for evaluating frailty^{32,56}. It is derived from eight domains of the CGA: the Katz's Activities of Daily Living (ADL)⁵⁷ for daily dependence, Lawton's Instrumental Activities of Daily Living (IADL)⁵⁸, the Cumulative Illness Rating Scale (CIRS)⁵⁹ for comorbidity assessment, Exton Smith Scale (ESS)⁶⁰ for ulcer risk assessment, Mini Nutritional Assessment Short Form (MNA-SF)⁶¹ for nutritional status evaluation, Short Portable Mental Status Questionnaire (SPMSQ)⁶² for cognitive assessment, as well as data regarding medication intake and cohabitation status.

Each item within these domains is scored according to the presence of problems, classified as none (= 0 points), minor (=0.5 points), or major (= 1 point). Based on these 8 subcategories, a mathematical algorithm is used to calculate the final MPI score, classifying the patients into three risk groups for "all-cause mortality"⁶³. Low risk corresponds to MPI < 0.34, moderate risk to MPI between 0.34 and 0.66, and high risk for overall mortality to MPI > 0.66⁵⁶.

In their multidimensional domain analysis comparing different frailty instruments, Pilotto et al. demonstrated that the MPI exhibits the highest prognostic accuracy when it comes to mortality prediction in older, hospitalized patients⁶³. At this point, numerous studies have established the importance of the MPI, making it a globally-used instrument to predict both short- and long-term mortality and frailty⁶³.

It should also be emphasised that the MPI's accuracy extends beyond the geriatric internal medicine setting. It has been proven effective in various inpatient domains including but not limited to Oncology^{13,64}, Nephrology⁶⁵, Gastroenterology⁶⁶, Cardiology¹⁴ or Cardiac surgery for patients undergoing transcatheter aortic valve implantation TAVI¹⁵. In conclusion, the MPI stands as a crucial tool for predicting mortality and frailty, and its versatility and effectiveness have been confirmed in diverse medical settings.

Although evidence suggests that sarcopenia significantly influences poor outcomes related to frailty, an association between sarcopenia and MPI is, to our current knowledge, yet to be established^{67,46,68}.

2.3 Sarcopenia

2.3.1. Origin and Definition

For a long time, the phenomenon of aging was far away from occupying the center of interest in medical research. It was not until the Twentieth Century when a shift occurred and medical research began focusing more specifically on human aging and all that it entails. What became apparent very quickly and impressively, was the age-related changes of physiological functions, be it in the area of hearing, vision, basal metabolic rate, renal or lung function or cognitive capabilities⁶⁹. Among these changes, what could not be overlooked by either the affected individuals or the researchers were the age-related changes in motility and movement, as well as the diminishing of muscle mass over the period of life⁷⁰. In 1988, Irwin H. Rosenberg drew attention to the significant decline of lean body mass with progressive aging and laid the first stone for a widespread definition of a health condition that had already been observed at that time but not at all defined or further described:

*"No decline with age is more dramatic or potentially more functionally significant than the decline in lean body mass... Why have we not given it more attention?"*⁷⁰

Rosenberg at that point introduced the term "sarcopenia" for the first time. The roots of this term's origin are based on the Greek words „sarx" for flesh and „penia" for loss⁷⁰, collectively referring to the scarcity of "meat". It defined an important and in Rosenberg's words "dramatic" change in body composition (most of all a progressive paucity of skeletal muscle mass) and related functions. Rosenberg's publication paved the way for further exploration and research on this geriatric topic. Over time, the definition has been further elaborated and broadened to develop a concept that goes beyond the mere loss of muscle mass. In 2010 an important milestone in the process of definition development was established with the incorporation of muscle function into the concept of sarcopenia, being of more predictive value on outcomes⁷¹⁻

⁷³. From this point on muscle mass has no longer been considered the only factor influencing or contributing to sarcopenia and the importance of muscle function and therefore strength, endurance and performance has become more and more clear⁷⁴. This shift in perspective attracted increased scientific interest that is also reflected very clearly in the number of publications on sarcopenia in the medical database of PubMed. While a total of 880 publications could be found in the period from the late 1980s to 2009, the number of publications increased to more than 10,400 hits in the following decade.

In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) published their first consensus on definition and diagnosis to facilitate a clinical approach in age-related sarcopenia⁷⁵. Representatives from the European Geriatric Medicine Society, the European Society for Clinical Nutrition and Metabolism, the International Association of Gerontology and Geriatrics European Region and the International Association of Nutrition and Aging were significantly involved in the findings of the published consensus. They clarified the need to consider both muscle mass and function to diagnose sarcopenia, acknowledging that muscle strength is not exclusively and solely dependent on muscle mass and that their interaction is not linear, explaining the limited clinical value if considering only mass⁷⁴. Subsequently, in 2011, the International Working Group on Sarcopenia published an operational definition, defining sarcopenia as *"the age-associated loss of skeletal muscle mass and function. Sarcopenia is a complex syndrome that is associated with muscle mass loss alone or in conjunction with increased fat mass"*⁷⁶. The purpose of the consensus was to create an easy approach to assess potentially affected patients and to deliver an objective definition. Also in 2011, the Society for Sarcopenia, Cachexia and Wasting Disorders (SSCWG) proposed the term *"sarcopenia with limited mobility"* as a definition for a patient with decreased muscle mass and in need of therapeutic treatment due to poor physical performance⁷⁷.

An important milestone was achieved in 2016 by veering away from the concept of sarcopenia as an event occurring incidentally in the aging process but to classify it as a recognized official disease in the International Classification of Diseases and Related Health Problems (ICD-10) in the United States and later in the German ICD-system (ICD-10-GM) in 2018⁷⁸. This recognition marked a shift from perceiving sarcopenia as a geriatric syndrome to a distinct medical condition⁷⁹. The ICD-code M62-5- also incorporates the loss of muscle mass together with reduced functionality and is therefore considerably more precise than the definition only focusing on muscle mass.

However, unawareness and overburdening with diagnostic steps, as well as lack of the required specific tools have shaped the day-to-day clinical practice. Moreover, the growth in

interest is not yet manifesting in better patient care and outcomes such as fewer falls, fractures, hospitalizations, and mortality. This is also the reason why the EWGSOP published an update of their previous original definition in January 2019 *"to increase consistency of research design, clinical diagnoses and ultimately, care for people with sarcopenia"*⁸⁰. Clinical progress and research-based updates over the last decade have been used by the experts of EWGSOP in order to deliver a clear and comprehensive definition of sarcopenia, that is also largely supported by the Asian Working Group on Sarcopenia⁷³. Although it is certainly not the only definition that exists, it is the one most commonly used, also by other international scientific expert groups such as the European Geriatric Medicine Group or the International Association of Gerontology and Geriatrics European Region. In general, the definition incorporates low muscle strength *"as a key characteristic of sarcopenia"*, low muscle mass as an important indicator to confirm the diagnosis and poor physical performance to rank severity. The exact parameters incorporated into the updated version of the EWGSOP2 definition of sarcopenia and a more detailed overview of diagnostic approaches will be highlighted later in this dissertation, but at this point it can already be stated that case-finding, diagnosis and evaluation are to be significantly facilitated.

Having discussed the progress made in defining sarcopenia and the ongoing efforts to achieve a unified definition, it is essential to shed light on the current state of research and interest in this area. As already mentioned before, a total of 880 publications can be found in the period between the late 1980s and 2009 but more than 10,400 publications in the following decade, and in 2022 alone a staggering 3,334 results can be found when searching using the term "sarcopenia" in the PubMed database. This again proves the tremendous interest the topic has garnered, particularly in recent years.

Unfortunately, despite all efforts to create a unified definition, there are still significant discrepancies in the various studies and scientific papers addressing the topic of sarcopenia. Furthermore, it is not only the exact definition of the term which poses an obstacle to worldwide comparability, but above all the wide range of diagnostic options that are used to evaluate different aspects of sarcopenia, which unfortunately still differ even after the publication of a comprehensive definition. Despite publication of definitions that clarify deteriorated muscle function as a condition for diagnosis, sarcopenia continues to be conflated with pure loss of muscle mass in many studies. This lack of a global consensus between widely used definitions is of course still hindering both the field of research and the implementation of sarcopenia into clinical practice.

This is why the Global Leadership Initiative in Sarcopenia (GLIS)⁸¹ was recently formed with the goal of finally establishing a universal and global definition of sarcopenia which from that

point on will be used in every upcoming paper. As a first step, the international GLIS aims to fuse and form a definition of sarcopenia that is all-encompassing and can be universally acknowledged and circulated. It is formed by the Australian and New Zealand Society for Sarcopenia and Frailty Research (ANZSSFR), Asian Working Group for Sarcopenia (AWGS), European Working Group on Sarcopenia in Older People (EWGSOP) and Sarcopenia Definitions and Outcomes Consortium (SDOC), therefore uniting expert groups from all over the world⁸¹. Once a global conceptual definition of sarcopenia is available, effort will be devoted to operationalizing the elements involved, and to publish assessments, cutoffs, algorithms, and outcome measures⁸². Whether a final and worldwide enforceable consensus will be found in the near future remains to be seen, as it would represent another revolution in the field of sarcopenia research. Until then, the definition by Cruz-Jentoft, as one of the best-known experts in the field of sarcopenia, provides an overarching and comprehensible basis:

" Sarcopenia has been defined as a progressive and generalized skeletal muscle disorder that involves the accelerated loss of muscle mass and function. Sarcopenia is associated with increased adverse outcomes including falls, functional decline, frailty, and mortality." ⁸³

2.3.2. Prevalence of sarcopenia

The decline of neuromuscular performance and function, as well as the debilitation experienced by individuals as they age, are widely recognized as inevitable steps in the aging process of every human being. Even without any specific underlying diseases, observing the body's decreased functionality compared to the peak years of youth is a common experience for seniors and they observe that the body is not as functional anymore as it used to be in their twenties. Over the past decades, several cross-sectional studies have compared muscle function and strength in healthy, young probands and older women and men^{84,85}.

Overall, the worldwide estimated prevalence of sarcopenia varies significantly, ranging from 5 to 13% for individuals in their sixth or seventh decade, highly depending on the measurement tool used for screening^{86,87}. For those aged 80 years or above, the estimated prevalence is even higher, ranging from 11 to 50% being affected by sarcopenia^{87,88}. These marked variations in the prevalence of sarcopenia according to setting and population might be attributable to widely unclearly defined diagnostic criteria and the fact that despite increased awareness for sarcopenia in the last decade, comprehensive translation into clinical practice and standardized assessment are yet to be achieved at the time of writing^{80,89}.

Nonetheless, regardless of the differences and varying numbers, there is a consensus that the prevalence of sarcopenia generally increases with advancing age⁸⁸⁻⁹¹. For instance, in the

German KORA-Age study conducted in 2017, the EWGSOP1 definition published in 2010 was used to diagnose sarcopenia, and accordingly the prevalence in patients ≥ 65 years from the region of Augsburg was investigated⁸⁸. They found an average prevalence of sarcopenia of 5.7% (7.5% in women, 4.0% in men) with linear increase in prevalence with age both for men and women. Specifically, the prevalence rose from 2.2% in the group of 65-69 year old to 12.4% in those aged 80 years and above⁸⁸.

A systematic review by Cruz-Jentoft et al., which included 18 studies, also using the EWGSOP consensus definition, reported a prevalence of 1 to 29% in community-dwelling individuals, 14 to 33% (up to 68% in men) in populations living in long-term care facilities, and 10% in the hospitalized population⁸⁹. It should be noted, however, that the results concerning prevalence in hospitalized patients are primarily based on those of only one study by Gariballa et al.⁹². In a more recent review published by Papadopoulou et al., prevalence of 23% in hospitalized men and 24% in hospitalized women were found, with an overall pooled prevalence of 13% across all populations⁹³. A systematic review studying sarcopenia in populations living in residential facilities again shows how large the range in prevalence can be, reporting numbers between 17.7% and 87%⁹⁴. If considering recent studies that evaluate prevalence by reverting diagnosis criteria based on the updated version by EWGSOP2, lower prevalence has been identified compared to when using EWGSOP1 criteria^{91,95}.

Accordingly, this chapter more than clearly highlights the substantial variation in sarcopenia prevalence in the literature, which is probably influenced by the specific population that is studied (e.g. individuals living in the community, in nursing homes, or hospitalized patients), the diagnostic criteria employed and the different tools used for assessments. Nevertheless, the undeniable fact remains that sarcopenia is a prevalent condition among the older population and it represents a fundamental point of action in every geriatric setting. It is highly probable that the number of unreported or undetected cases is extremely high and that an enormous number of patients therefore misses the opportunity of being treated in an early and potentially treatable stage of their condition.

In conclusion, understanding the prevalence of sarcopenia is crucial in addressing the healthcare needs of an aging population. While variations in prevalence estimates exist due to diverse study populations and diagnostic criteria, it is evident that sarcopenia is a common condition affecting older individuals. Early detection and intervention are paramount for improving the quality of life and functional independence of those affected by this condition. Continued research and standardized assessment approaches are therefore essential to better address and manage sarcopenia in geriatric settings.

2.3.3. Pathogenesis and pathophysiology of sarcopenia

Similar to all other organs, skeletal muscles are likewise not spared from physiological, age-related changes. Structural and functional changes affect the human skeletal muscles, characterized primarily by increasing atrophy. In fact, the exact pathomechanism of sarcopenia remains incompletely established to date and is believed to have a multifactorial and relatively complex genesis involving biochemical, molecular, and physiological changes⁹⁶.

One known aspect is that the biosynthesis of muscle protein already begins to decrease in early adulthood, usually starting around the age of 30 and then continuously declining at a rate of about 3-8% per decade⁹⁷. Subsequently, from the sixth decade onwards, muscle strength is presumably shrinking by approximately 1-2% per year⁹⁸. Previous studies have highlighted the reduction in both the number and size of muscle fibers as a significant contributor for aging atrophy and different mechanisms have been proposed to be associated with age-related muscle loss. Specifically, Lexell et al. observed that muscle fibers in younger individuals (aged 30 to 50 years) were firmly packed in well-preserved fascicles, whereas older individuals (aged 70 to 80 years) showed less compact packing with visible differences in fiber size and shape⁹⁹. Also, in older muscles, fewer and smaller fibers could be observed and it was stated that the reduction of type-2 fibers primarily led to the reduction in size. In concordance with previous studies, a reduction of the cross-sectional area in thigh muscle could be reported⁹⁹⁻¹⁰¹. Buford et al. stated that decline in organelles, cytoplasmic substances as well as muscle protein can result in an increased level of atrophy or apoptosis¹⁰². In 2013, Nilwik et al. agreed with the assumption that the reduced size of type-2 fibers is the main reason leading to a decline in muscle mass¹⁰³. Oxidative stress¹⁰⁴, ascent levels of apoptotic pathways in skeletal myocytes¹⁰⁵ and denervation of muscle fibers¹⁰⁶ also seem to have an important impact on the incremental decline of skeletal muscle mass and performance.

Another important phenomenon is that with advancing age, the body is no longer able to utilize the consumed proteins in the same way it would have done earlier in life. In fact, the aging muscles seem to respond to a reduced extent to anabolic stimuli which in turn leads to impaired protein synthesis that is indispensable for the preservation of the muscular system¹⁰⁷. This phenomenon has been referred to as "anabolic resistance" ¹⁰⁸.

Concomitantly with a decrease in sensitivity to anabolic stimuli, conditions with chronically elevated levels of inflammatory markers, displayed by interleukin (IL)-6 and C-reactive protein (CRP) were found to be associated with an increase in muscle protein catabolism, therefore leading to an increasing state of disability¹⁰⁹. A recent systematic review published in 2020 by

Tuttle et al. found chronically elevated inflammatory markers to be significantly associated with lower muscle strength and mass¹¹⁰.

Due to these changes (i.e. the impaired reaction to anabolic stimuli and the accelerated catabolism), in combination with a decline in quantity and quality of satellite cells (i.e. the muscle's stem cells with, in contrast to myofibers, ability for differentiation, proliferation and regeneration¹¹¹), the potential for regeneration diminishes, making age-related muscle atrophy and injuries more challenging to counteract effectively^{112,113}.

In the last decade, the pathophysiology of age-related muscle loss has definitely attracted increased interest in research. Nevertheless, understanding the entire complexity of these processes will require further investigation and certainly take some more time. As life expectancy increases, with people reaching a lifespan of over 80 years becoming the norm rather than the exception, the accompanying extensive loss of muscle mass and strength will continue to feature prominently in the daily work of clinicians. A comprehensive and improved understanding of the aging process and its impact "on human neuromuscular function" is therefore crucial for developing effective interventions and treatments for sarcopenia⁹⁸.

2.3.4. Primary and secondary sarcopenia, acute and chronic sarcopenia

For a better overview, the terms primary, secondary, acute and chronic sarcopenia which have already been touched upon in the foregoing are given an proper introduction in this chapter. The categorization into primary and secondary sarcopenia is based on the cause of its development: if no specific factor other than the physiological aging process is apparent for the development of sarcopenia, it can be referred to as "primary"⁸⁰ or "sarcopenia of aging"¹¹⁴. As described in the previous chapter on pathogenesis, mitochondrial and satellite cell dysfunction, changes in muscular architecture or reduced protein turnover are causes of age-related loss of muscle mass and function¹¹⁵.

Sarcopenia is considered "secondary" if it develops due to factors other than the aging process. These factors can include underlying systemic diseases, often accompanied by inflammatory processes such as cancer, COPD, chronic kidney or cardiovascular disease and many more¹¹⁶. However, poor nutritional behavior, physical inactivity and unhealthy lifestyle can likewise contribute towards the development of a secondary sarcopenia⁸⁰.

Additionally, further classification can be done through the duration of the symptoms. Over the last decades of research, it became increasingly apparent that there is a difference between

the loss of muscle function which becomes noticeable in acute care setting and a slowly progressing loss which takes several years and may not be obvious at first. Specifically, sarcopenia lasting less than 6 months can be categorized as acute, typically associated with sudden illnesses or injuries and the immobility that comes along with them, whereas sarcopenia persisting for more than 6 months is classified as chronic. Chronic sarcopenia is commonly linked to progressive and long-term health conditions, amplifying the risk of mortality⁸⁰. Distinguishing between acute and chronic sarcopenia aims to emphasize the importance of regularly assessing individuals who may be prone to sarcopenia, with the goal of monitoring the pace of its development or deterioration. By doing so, healthcare professionals can identify early signs of sarcopenia progression and unfavorable outcomes, enabling timely intervention with treatments designed to prevent or postpone its advancement. These observations are expected to provide valuable insights and facilitate proactive measures to mitigate the impact of sarcopenia⁸⁰ although the concept still needs to be further developed and strengthened by additional research¹¹⁷.

Whether the distinction between acute and chronic sarcopenia will prevail and evolve remains to be seen. Currently, the ICD-10 code for sarcopenia (ICD-10-CM code M62.84) does not include a specific classification⁷⁹. Similarly, the clinical guideline by the International Conference on Sarcopenia and Frailty research (ICFSR) does not provide distinct recommendations specifically tailored to acute and chronic sarcopenia¹¹⁸.

2.3.5. Diagnostics of sarcopenia

One important aspect that makes uniformity in the definition of sarcopenia so challenging is the wide range of diagnostic tools and the lack of consensus on diagnostic criteria. Over the last two decades, several expert groups put significant effort into developing a definition of sarcopenia based on specific diagnostic criteria. In our study, we chose to employ the EWGSOP2⁸⁰ algorithm due to its comprehensive and structured diagnostic criteria, providing a clinically relevant framework for identifying and categorizing sarcopenia in our patient population. In the following, available and widely used diagnostic equipment will be distinguished and briefly presented.

2.4 EWGSOP Algorithm to classify Sarcopenia

In 2010, the EWGSOP published a first definition for sarcopenia with the objective of improving detection and handling for patients with sarcopenia⁷². The EWGSOP proposed the division of sarcopenia into three successive stages, based on the severity of the disease: Isolated decline

in muscle mass without functional detriment was named *Presarcopenia*. The combination of both reduced muscle mass and function (either physical performance or objectified muscle strength) was categorized as *sarcopenia*. If all three (muscle mass, physical performance and muscle strength) were impaired, this state was defined as *severe sarcopenia*⁷⁵.

At the beginning of 2018 this definition was contemporized using the research and clinical evidence that had been recorded in the previous 10 years, leading to an updated version both of the definition for sarcopenia and the algorithm used for case-finding⁸⁰. In the updated EGWSOP2 guidelines, sarcopenia is now characterized not only by the consecutive loss of muscle tissue, but also by low muscle strength, quantity, quality and poor physical capacity. Also, the previously introduced term "Presarcopenia" was dropped again and conditions previously summarized as "Presarcopenia" should henceforth be considered as "low muscle mass" or "Probable Sarcopenia". With their recommendations, the working group is following the goal to aggrandize the awareness of the muscle disease and its risks at the same time. They present an updated version of an algorithm visualizing the step-by-step procedure for case-finding, diagnosis and determining of severity of sarcopenia, clearly presented to facilitate use in clinical practice as well as in studies and research⁸⁰. In the secondary analysis that forms the cornerstone of this thesis, we also used this step-by-step procedure to subdivide our study population. The experts of the EWGSOP2 group recommend a pathway of Find-Assess-Confirm-Severity (abbreviated as F-A-C-S). For a better overview we have additionally named these single steps in alphabetical order, i.e. Step A, Step B, Step C and Step D. In the subsection, the step-by-step approach is discussed and the individual steps are examined in further detail.

2.4.1. Step A - Case finding using SARC-F

The algorithm starts with the recommendation for screening. In order to obtain a general overview of the possible presence of sarcopenia, the *SARC-F* („Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls“) score can provide characteristic information. It was developed in 2013 by John Morley and Theodore Malmstrom and first published in English¹¹⁹. Being a five-item questionnaire based on self-reported capabilities, it is a quick and informative tool that can be used in community-dwelling patients just as well as in hospitalized persons, and even the general practitioner treating persons living alone can get an overview of possible risks after only a few minutes. Patients are being asked to evaluate and rank their limitations in strength, walking, stair climbing, rising from a chair and their history of falls¹¹⁹. Meanwhile, the *SARC-F* score has become an important screening tool, also validated in varying large populations as in the study of African and American Health (AAH), in the National Health and Nutrition Examination study (NHANES) analyzing non-institutionalized individuals in the United States and the Baltimore Longitudinal Study of Aging (BLSA)¹²⁰. In all these

populations, the SARC-F score was able to deliver consistent and significant prediction concerning the patient's outcome. Also in an older, Chinese population, SARC-F score was solid in predicting physical limitation and mortality rates¹²¹. It is therefore an important tool that can be easily and rapidly used for identifying persons at risk of adverse outcome, regardless of their origin or environment. When it comes to evaluating muscle strength and performance, SARC-F shows low to moderate sensitivity but very high specificity, meaning that the tool provides high potential to rule out sarcopenia but rather low contingency in identifying every case¹²². Severe cases of sarcopenia will, however, be detected in the majority of cases¹²³. The relatively low sensitivity can also be put into perspective when considering that the SARC-F score is based on subjective perception of the patient's own limitations and therefore is not an objective measurement of muscle mass, representing the prerequisite for sarcopenia diagnosis. This is also the reason why the EWGSOP2 in their new consensus suggests the score for identification and *"as a way to introduce assessment and treatment of sarcopenia into clinical practice"*⁸⁰. The recommendation is to use the SARC-F score in order to screen for people at risk for sarcopenia and its adverse outcomes and to identify patients in need of further investigations and treatment at an early stage, all in accordance with other statements like Bahat et al.: *"SARC-F questionnaire stands as one of the best tools to evaluate sarcopenia in every day practice"*¹²⁴.

For the category *Falling*, the patient can indicate the number of falls during the last year with 0 falls = 0 points, 1-3 falls = 1 point and ≥ 4 falls = 2 points. *Strength* is assessed by asking about the difficulties the patient perceives by lifting 5kg. One can answer if one encounters no problems at all (0 points), some problems (1 point) or is unable to do so (2 points). *Walking* is measured by contextualizing the patient's problems if he has to walk in a room or if he requires any help to do so (0= no problems; 1= some problems; 2= unable to do/using aids). *Rise from a chair* and *Stair climbing* are assessed by asking how much difficulty arises while transferring from a bed or a chair respectively, how challenging it is to climb 10 steps (0= no problems; 1= some problems; 2= unable to do). After adding up the points of every item, the total score reaches from 0 to 10 points with a score of 0-3 points defined as healthy or at low risk for sarcopenia while every patient presenting ≥ 4 points in total is expected to be at higher risk for poor muscle function and sarcopenia^{119,120}. Patients with SARC-F < 4 points were classified into the *"No Sarcopenia"* (NS) group. Unfortunately, at the time of the assessments starting in October 2019, a validated translation of the original SARC-F score published by Malmstrom¹¹⁹ was not yet available. However, since the patients on the ward were German speakers, we translated the questionnaire in advance to the best of our knowledge. In June 2020, the translation, adaptation, and validation of the German version of the SARC-F was performed for the first time and it could be shown that *"the German version of the SARC-F is a suitable*

tool for case finding of probable sarcopenia"¹²⁵. After subsequent review and comparison with the translation we selected for the assessments, we determined that there were no major deviations from the translation proposed by Drey et al, so that our collected values could be considered valid. **Figure 1** shows the German version of the SARC-F that was used in the study.

Figure 1: SARC-F questionnaire used in the study, based on Malmstrom TK, Miller DK, Simonsick EM, Ferruci L, Morley JE. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. J Cachexia Sarcopenia Muscle, 2016 Mar;7(1):28-36. doi:10.1002/jcsm.12048

ITEM UND FRAGE	ANTWORT	PUNKTEWERT
KRAFT Wie viele Probleme haben Sie ein ca. 5 kg schweres Gewicht zu heben und zu tragen?	Keine Probleme	0
	Etwas Probleme	1
	Starke Probleme/ Unmöglich	2
GEHEN Wie viele Probleme bereitet es Ihnen durch einen Raum zu gehen?	Keine Probleme	0
	Etwas Probleme	1
	Sehr schwierig/ Benötigte Hilfsmittel / Unmöglich	2
AUFSTEHEN Wie viele Schwierigkeiten haben Sie vom Bett oder Stuhl aufzustehen?	Keine Probleme	0
	Etwas Probleme	1
	Sehr schwierig/ unmöglich ohne Hilfe	2
TREPPENSTEIGEN Wie viele Schwierigkeiten haben Sie beim Treppengehen von 10 Stufen (ein Stockwerk)	Keine Probleme	0
	Etwas Probleme	1
	Sehr schwierig/ unmöglich ohne Hilfe	2
STÜRZE Wie oft sind Sie im letzten Jahr gestürzt?	Gar nicht	0
	1 – 3 Stürze	1
	4 oder mehr Stürze	2
	GESAMT	

2.4.2. Step B - Assessment of sarcopenia by muscle strength

As mentioned previously, with the SARC-F score being a self-assessing and therefore subjective tool, it of course needs clinical and objectifiable measurements to estimate the actual decline of the different sarcopenia parameters. A popular method for exactly this

scenario is the measurement of *Hand Grip Strength* (HGS) due to its simplicity, low cost and widespread availability. It is very easy to perform, the purchase of an appropriate dynamometer is affordable and the results of grip strength testing can provide a solid impression of overall strength¹²⁶. In addition, HGS has already been associated with a variety of unfavorable outcomes in past studies: low grip strength has been shown to correlate with functional disability¹²⁷, neural morbidity¹²⁸ and mortality¹²⁹, to name but a few of the various associated health-conditions. The only requirement to assess hand grip strength is the use of a handheld, calibrated dynamometer although standardized and consistent measurement still has to be further examined to better compare results of different studies and move the application into everyday clinical practice¹³⁰. According to EWGSOP2, *"because of its ease of use, grip strength is advised for routine use in hospital practice, in specialty clinical settings, and in community healthcare"*⁸⁰.

With the help of a dynamometer, the grip strength can quickly be classified as normal or low and thereby providing information regarding possible sarcopenia. Patients who provided clinically insignificant values in these first two steps were not considered to be at acute risk for sarcopenia and could be re-evaluated at a later time⁸⁰. For those showing clinically significant values in the first and in the second step, evaluation of the muscle quantity or quality should be performed subsequently for confirmation (Step C).

Another method to evaluate muscle strength would be the chair rise or chair stand test. As can already be deduced from the name of the test, patients are asked to stand up five times from a sitting position, each time without using their arms. The results can provide information about the strength and endurance of the quadriceps muscle group and therefore evaluate functional performance¹³¹. As in the secondary analysis forming the basis for this thesis, only the HGS and not chair rise test or any other test evaluating strength in lower extremities was performed, this aspect will not be discussed further in this context.

2.4.3. Step C - Confirmation of sarcopenia by muscle mass

If muscle strength was found to be low, tests for muscle quantity followed. Numerous validated methods in widespread use are available to assess muscle quantity and muscle mass. The use of *Bioelectrical Impedance Analysis (BIA)* is very popular due to its widespread availability, cost-effectiveness and portability and was also used in our study. During BIA, body water, body fat, muscle mass, body cell mass and other metrics of body composition are estimated by utilizing the specific conductivities of the different tissue types in the human body¹³². Since both the intra- and extracellular fluids are excellent conductors of electrical current, alternating

current induces a phase shift between the ohmic resistance component also called resistance (R) and the capacitive component, also known as reactance (X_c)¹³². Both parameters provide an impression of extra- and intracellular fluid status, as well as cell membrane mass. After running a BIA, Appendicular Skeletal Muscle Mass (ASMM) can be estimated and used for classification of sarcopenia. Nevertheless, especially in older probands, this estimation of body composition from the raw bioimpedance parameters can be challenging, as they are extremely susceptible to interference and highly depending on the hydration state. Measurement can come with a high error rate in patients with altered body composition. As constant hydration status and absence of fluid imbalance is rather rare, considering the number of geriatric patients with cardiac insufficiency and therefore edema and with multimorbidity also having a potential impact on body composition, BIA data cannot always be considered error-free and accurate¹³³. Obtaining usable values and increased precision requires some standardized conditions to be fulfilled during measurement. The first thing to pay attention to is the proband's body position; measurements should be taken in a recumbent position, with arms and legs outstretched, ensuring that no parts of the body are crossed or touching any part of the bed. Also the intake of food or fluids can show some effects on the results during the first hour and should therefore be, if possible, avoided just before the test¹³⁴. A factor that may also influence the BIA results is exercising shortly before the test and correspondingly altered body temperature¹³⁵. In our analysis, however, this is a point that does not need to be given weight, since the measurement in the probands was made shortly after admission to the geriatric ward and it can therefore be assumed that exercise was not performed recently beforehand. If one takes this information into account, it quickly becomes clear that the BIA measurement used by itself can often only provide a moderate overview, however, as a non-invasive, inexpensive and portable tool that does not require much time to use it is ideally suited for everyday clinical use.

Another possibility for evaluating and quantifying muscle mass is the use of radiological density measurement (Dual-Energy X-Ray Absorptiometry, DXA), Computed Tomography (CT) or Magnetic Resonance Imaging (MRI). For clinical trials, EWGSOP2 favors the usage of ASMM by DXA, while MRI and CT imaging are more likely to be used in the evaluation of muscle mass in cancer patients since they are already routinely used for diagnosis, staging, and treatment response⁸⁰. On the other hand this method has not yet been validated for all patient groups and represents a considerable additional effort in terms of time and cost when used in geriatric patients who would not necessarily have required extensive diagnostic imaging.

2.4.4. Step D - Determination of severity by physical performance

In order to quantify the physical performance of older people, there are again numerous methods from which to choose, for example by measuring gait speed, chair stand test, 400-m walk test, timed-up-and-go test (TUG) or Short Physical Performance Battery (SPPB), to name but a few¹³⁶. In our study population, the TUG test was performed. Performance was assessed by timing how long it took a patient to stand from a chair, walk 3 meters, return, and sit down. A time of ≥ 20 seconds was considered indicative of low physical performance for both women and men^{80,137,138}. It is important to mention that not only severe sarcopenia, if confirmed, is to be understood as a definitive diagnosis, but even a probable sarcopenia is reason enough to *"trigger assessment of causes and start intervention"*⁸⁰. **Figure 2** illustrates the new diagnostic algorithm of the EWGSOP 2 guideline and **Figure 3** shows the cut-off points used for the different steps.

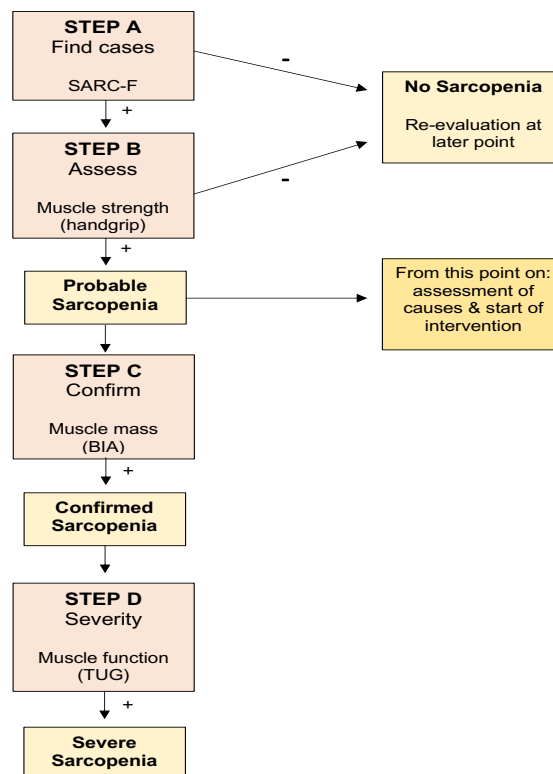


Figure 2: Diagnostic algorithm following EWGSOP2-guideline by Cruz-Jentoft et al.⁸⁰

Cut-off points used (EWGSOP2):			
	women	men	references
SARC-F (total):	≥4		Malmstrom et al. ¹¹⁹
for low strength (handgrip in kg):	<16 kg	<27 kg	Dodds et al. ¹³⁹
for low muscle quantity (BIA ASM/height ²):	<5.5 kg/m ²	<7.0 kg/m ²	Gould et al. ¹⁴⁰
for low performance (TUG in s):	≥ 20s		Bischoff et al. ¹⁴¹

Figure 3: Cut-off points for sarcopenia on the basis of EWGSOP2 consensus by Cruz-Jentoft et al.⁸⁰

2.5 The role of sarcopenia in the German health care system

On the occasion of the "International Day of the Elderly" on October 1st 2017, the German Society of Internal Medicine (DGIM) pointed out that age-related muscle loss as well as its serious adverse outcomes is still underestimated and not provided the necessary attention¹⁴². The disease sarcopenia has serious, multifaceted consequences not only for each affected individual, but also for society and the whole healthcare system. At this point, few studies assessing the direct and indirect costs of sarcopenia have been published, making it difficult to get an idea of the exact "economic burden-of-illness"¹⁴³. In 2019, Bruyère et al. published a systematic review with the aim of shedding more light on the consequences of sarcopenia from a public health perspective, concluding that in the majority of the studies included, healthcare costs were significantly higher in people with sarcopenia than in those without¹⁴³. And even if these results are based on very heterogeneously conducted studies, which do not necessarily allow a definitive conclusion regarding the economic burden of sarcopenia to be drawn, the higher costs can definitely be explained by the numerous impacts accompanying the disease. As already mentioned in previous chapters, sarcopenia brings increased functional restrictions¹⁴⁴, number of falls^{68,145,146}, mortality¹⁴⁴, loss of physical independence¹⁴⁷ as well as more frequent and longer hospital stays^{136,144,148}. All of these adverse outcomes not only have a negative impact on the quality of life of the individuals affected but also lead to higher utilization of resources, therefore making a measurable impact on the increased cost that the healthcare system has to shoulder^{143,144,148-150}. For example, with sarcopenia being associated with a higher risk of falls¹⁴⁵ and therefore subsequent hospitalizations, the cost of these hospitalizations for fall-related injuries is substantial and can place a significant burden on healthcare systems. Put simply, sarcopenia leads to increasing physical disability and dependence, which in return comes with an increased need for assistance, for example in daily living, whether through need for extensive rehabilitation periods, home care services, admission to nursing facilities or, in a worst case scenario admission to hospital^{144,148}. An Italian

study, for example, found that sarcopenic older people have a longer length of stay in rehabilitation facilities and are more likely to require readmission within 30 days after discharge¹⁴⁶. Furthermore, sarcopenia is often associated with other comorbidities and geriatric syndromes and is in turn associated with higher costs and increased healthcare expenditure¹⁵⁰. Sarcopenia clearly poses substantial public health challenges. Individually, it increases the risk of disability, loss of independence, adverse comorbidity outcomes, institutionalization, and mortality. At the societal level, it represents a major health burden, driving considerable healthcare costs and fostering dependency among older adults. As the population aged 60 years and older is steadily growing³ and the incidence of sarcopenia simultaneously increasing with age, the significant economic burden that sarcopenia brings along will not decrease in the years ahead unless early detection, diagnostic, and appropriate therapies are improved and one is able to act at a time before significant and irreversible damage has occurred requiring more costly assistance.

2.6 Research question and aim of the work

With increasing life expectancy, the previously largely overlooked disease of sarcopenia is gaining importance. Systematic and continuous evaluation of sarcopenia should be a crucial component in every geriatric setting, if not in all general internal medicine wards and for all general practitioners. Fortunately, the interest and acknowledgment of progressive decline in muscle mass and function has been growing over the past several decades, leading to focused research and studies aimed at creating structured guidelines. In addition, sarcopenia is no longer just a hummingbird issue in the geriatric field with research also taking place in other specialties like oncology¹⁵¹, nephrology¹⁵² or gastroenterology¹⁵³, to name but a few. The interest therefore has visibly risen, but no general agreement has been reached in terms of definition and even more importantly exact and comprehensive diagnosis of sarcopenia. The definitions used, diagnostic tools and cut-off values are not consistent and results therefore are not globally transferable. The gap between awareness of the condition and consecutive screening and diagnosis has not yet been narrowed¹⁵⁴ and even after decades of research and thousands of studies on sarcopenia, the situation that "most cases of sarcopenia go undiagnosed"⁸³ persists. Nevertheless, the challenge lies not only in the lack of a consistent definition and diagnostic process, but also that structured, transmissible guidelines are still missing, making an adaptation into clinical practice rather difficult. Despite these difficulties, early diagnosis and treatment of sarcopenia are crucial and it is of great importance that healthcare providers are aware of these precise challenges so that they can use a comprehensive approach to diagnose sarcopenia, including assessing muscle mass, strength,

and function, as well as considering comorbidities and other factors that may affect muscle health⁸⁰.

In this dissertation both the difficulties and opportunities of diagnostics will be highlighted and discussed. Basis and cornerstone of this thesis is the prospective study "*Vun nix kütt nix*" and the secondary analysis of sarcopenia "Prognostic Features of Sarcopenia in Older Hospitalized Patients: A 6-Month Follow-Up Study"¹⁵⁵ derived from it. In addition to the evaluation of the prevalence of sarcopenia using the step-by-step procedure by EWGSOP2 on our group of hospitalized geriatric patients, the aim of this dissertation was also the further investigation of the role of sarcopenia in relation to the patient's prognosis as measured by the MPI and Patient reported outcome measures (PROMs). A secondary analysis was performed to identify differences in demographic characteristics between subgroups of sarcopenia, to analyze how it is associated with MPI, and to evaluate the overall prognosis and frailty for the individual. Furthermore, the necessity of detailed and consecutive screening and diagnosis will be highlighted regarding possible benefits for the individual as such, but also regarding the healthcare system. The objective is to present the interrelationships more thoroughly and to understand the importance of consecutive screening for sarcopenia for people over 60 at the latest, assuming that too few people are properly diagnosed and treated with this disease in clinical and outpatient facilities.

3. Publication

Article

Prognostic Features of Sarcopenia in Older Hospitalized Patients: A 6-Month Follow-Up Study

Anne Ferring ¹, Luisa Mück ¹, Jill Stegemann ¹, Laura Wiebe ¹, Ingrid Becker ², Thomas Benzing ^{1,3}, Anna Maria Meyer ^{1,*} and Maria Cristina Polidori ^{1,3,†}

¹ Department II of Internal Medicine and Center for Molecular Medicine Cologne, Faculty of Medicine and University Hospital Cologne, University of Cologne, 50937 Cologne, Germany; anneferring@hotmail.de (A.F.)

² Institute of Medical Statistics and Computational Biology, University Hospital of Cologne, 50937 Cologne, Germany

³ CECAD, Faculty of Medicine and University Hospital Cologne, University of Cologne, 50937 Cologne, Germany

* Correspondence: anna.meyer@uk-koeln.de; Tel.: +49-221-478-39256

† These authors contributed equally to this work.



Citation: Ferring, A.; Mück, L.; Stegemann, J.; Wiebe, L.; Becker, I.; Benzing, T.; Meyer, A.M.; Polidori, M.C. Prognostic Features of Sarcopenia in Older Hospitalized Patients: A 6-Month Follow-Up Study. *J. Clin. Med.* **2024**, *13*, 3116. <https://doi.org/10.3390/jcm13113116>

Academic Editors: Francisco Guillen-Grima and Urban Emmenegger

Received: 20 March 2024

Revised: 19 May 2024

Accepted: 22 May 2024

Published: 26 May 2024



Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Abstract: Background: Sarcopenia is associated with adverse health outcomes. Understanding the association between sarcopenia, multidimensional frailty, and prognosis is essential for improving patient care. The aim of this study was to assess the prevalence and prognostic signature of sarcopenia in an acute hospital setting co-led by internists and geriatricians. **Methods:** Sarcopenia was assessed by applying the European Working Group on Sarcopenia in Older People (EWGSOP2) algorithm, including the SARC-F score, handgrip strength, bioelectrical impedance analysis (BIA), and Timed Up and Go (TUG) test, to 97 older multimorbid inpatients (76.5 ± 6.8 years, 55% women). The patients underwent a Comprehensive Geriatric Assessment (CGA) including an evaluation of Geriatric Syndromes (GSs) and Resources (GR) and prognosis calculation using the CGA-based Multidimensional Prognostic Index (MPI), European Quality of life—5 Dimensions (EQ-5D-5L) scale, Rosenberg Self-Esteem Scale (RSES), and Geriatric Depression Scale (GDS). Information on survival and rehospitalizations was collected 1, 3, and 6 months after discharge. **Results:** Sarcopenia was present in 63% (95% CI: 54–72%) of patients and categorized as probable (31%), confirmed (13%), and severe sarcopenia (18%). Sarcopenic patients showed significantly higher median MPI-values ($p < 0.001$), more GSs ($p = 0.033$), fewer GR ($p = 0.003$), lower EQ-5D-5L scores ($p < 0.001$), and lower RSES scores ($p = 0.025$) than non-sarcopenic patients. Six months after discharge, being sarcopenic at baseline was predictive of falls ($p = 0.027$) and quality of life ($p = 0.043$), independent of age, gender, and MPI. **Conclusions:** Sarcopenia is highly prevalent in older hospitalized multimorbid patients and is associated with poorer prognosis, mood, and quality of life up to 6 months after discharge, independent of age, sex, and MPI as surrogate markers of biological age.

Keywords: sarcopenia; EWGSOP2; MPI; prognosis; frailty; comprehensive geriatric assessment; older people

1. Introduction

Ongoing demographic change is disclosing an unprecedented clinical landscape, which includes rapidly increasing mortality rates due to multimorbidity [1] and a greater prevalence of geriatric syndromes. Among these changes, the prevalence of sarcopenia, defined as a generalized and progressive, age-related decline in muscle mass, strength, and function [2], is constantly rising. While prevalence estimates might be largely underdiagnosed due to a lack of universally accepted diagnostic algorithms for long periods, solid evidence links sarcopenia to adverse outcomes such as frailty, rehospitalization, mortality, falls, loss of independence, and depression [3–5]. Since 2018, the definition and stepwise diagnostic approach of the European Working Group on Sarcopenia in Older People 2

(EWGSOP2) [6] has provided a standardized research approach to the question of the adverse outcomes and prognosis of sarcopenia. The prognosis of older patients, crucial for avoiding frailty and iatrogenic conditions during clinical decision making, is difficult to accurately evaluate due to the increasingly biopsychosocial and heterogeneous nature of poor outcomes with advancing age. Several Comprehensive Geriatric Assessment (CGA)-based risk scores have proven more useful than illness-centered tools for predicting disease trajectories in older adults [7–9]. Among these, the Multidimensional Prognostic Index (MPI) [10] is a well-established, highly validated tool used to quantify patients' multidimensional frailty and prognosis [7,11]. The aim of the present investigation was to evaluate the prevalence and prognostic blueprint of sarcopenia as defined by the EWGSOP2 criteria in older multimorbid patients undergoing geriatric treatment in a recently established acute hospital setting co-led by internists and geriatricians.

2. Methods

Study Design and Patients: To achieve the above-described aim, data obtained from older multimorbid inpatients included in an RCT investigating the effects of a tailored individualized discharge program (TIDP) compared with usual rehabilitative care [12] in an acute clinical ward co-led by geriatricians and internists were used. As a recently established innovative ward of the large metropolitan University Hospital of Cologne designed to cover the needs of the older population of multimorbid patients requiring potentially disabling disease-centered high-performance medicine [12], patients undergo early complex geriatric rehabilitation (ECGR), and the ward is co-led by internists and geriatricians equally responsible for clinical decision making [12]. Patients 60 years old or older were included if they were admitted due to acute disease or relapse of a chronic condition, multimorbid (with synchronous presence of two or more chronic conditions that require long-term treatment [13]), and suffering from at least two geriatric syndromes requiring typical rehabilitative care.

For the purpose of the present analysis, patients with incomplete SARC-F-scores ($n = 1$), without values for handgrip strength ($n = 4$), and who had not undergone Bioelectrical Impedance Analysis (BIA, $n = 8$) were excluded from the secondary analysis. The final sample size comprised 97 patients (Figure 1).

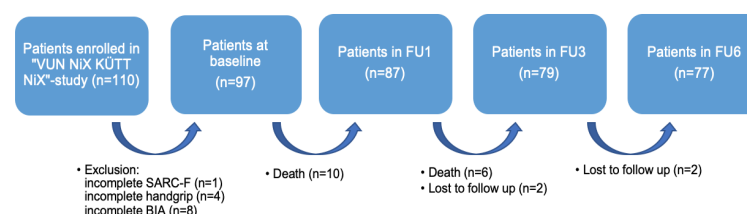


Figure 1. Flow chart for the secondary analysis. Notes: FU = Follow-Up; SARC-F = strength, assistance with walking, rise from a chair, climb stairs, and falls; BIA = Bioelectrical Impedance Analysis.

Study Procedures: As previously described, patients underwent, together with acute disease standard-of-care treatment and ECGR, a CGA that included an assessment of the MPI [10], calculated based on its eight subdomains: the Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) for the functional status, the Cumulative Illness Rating Scale (CIRS) for comorbidities, Exton Smith Scale (ESS) for pressure score risk, Mini Nutritional Assessment Short Form (MNA-SF) for nutritional status, the Short Portable Mental Status Questionnaire (SPMSQ) for cognitive status, and medication intake and living condition. By summing the values of each respective severity domain and dividing the sum by 8, the MPI value was obtained, and patients were allocated into three risk groups. These groups indicate the risk of mortality and other adverse outcomes, including hospitalization, admission to long-term care facilities, or homecare need. MPI-1

patients have a score between 0 and 0.33, indicating a low risk; MPI-2 patients have a score of 0.34–0.66, indicating moderate risk; and MPI-3 patients have a score of 0.67–1, indicating they are at high risk [10,11,14]. Additionally, Geriatric Syndromes (GS) and Resources (GR) [15] and Patient-Related-Outcome-Measures (PROMs) including Geriatric Depression Scale (GDS) [16], European Quality of life-5 Dimensions (EQ-5D-5L) for health-related quality of life (HRQoL) [17], and Rosenberg Self-Esteem Scale (RSES) [18] scores were collected for all patients. For the assessment of quality of life, the German version of the EQ-5D-5L, which generates an index score on a scale from −0.66 (representing a state worse than death) to 1 (indicating full health), was used [17]. The RSES is a self-assessment that is evaluated through a set of ten statements, resulting in a score between 0 and 30, while scores below 15 indicate low self-esteem [18]. Information about hospitalizations and falls during the year preceding admission, nursing needs (grade of care according to the German nursing care insurance, spanning from grade 0 to 5 [19]), and number of ECGR days was collected. Information on laboratory values including albumin and total protein levels on admission and discharge was also available. Patients were assigned randomly to either receive ECGR alone or in combination with a tailored intersectional discharge program (TIDP). The TIDP group received an interprofessional discharge treatment plan, which included personalized counselling tailored to various aspects and a reference guidebook. One, three, and six months after discharge, all patients underwent follow-up via telephone to collect information about mortality, rehospitalizations, falls, and nursing needs, as well as EQ-5D-5L and GDS.

Diagnosis of Sarcopenia: The assessment of sarcopenia was performed using the EWGSOP2 algorithm [6] (Figure 2). In Step A, the patients' scores on the SARC-F scale, consisting of five items, namely, strength, falls, walking assistance, rise from a chair, and stair climbing, were evaluated. With a total score ranging from 0 to 10 points, patients with ≥ 4 points are expected to be at higher risk for sarcopenia [20] and were included in Step B. In Step B, measurement of muscle strength was assessed via handgrip strength in kg [21] for both sides using a standardized Jamar dynamometer. Patients performed maximal isometric contractions three times with both hands, with 15 s breaks in between. The highest value was used as the handgrip strength value in the present analysis. If handgrip strength was low (<16 kg for women and <27 kg for men), the corresponding patient's status was classified as Probable Sarcopenia (PS) and they were included in Step C. In Step C, BIA-determined body composition and muscle mass were analyzed, using the BIACORPUS RX 4004M developed by MEDI CAL HealthCare GmbH at the time of admission. For a valid estimation of Appendicular Skeletal Muscle Mass (ASMM), the equation created by Sergie et al. was used: $ASMM\ (kg) = -3.964 + (0.227 \times (height^2/Resistance)) + (0.095 \times weight) + (1.384 \times sex\ (with\ m = 1; f = 0)) + (0.064 \times Reactance)$ [22]. ASMM was normalized in relation to each subject's height to obtain the ASMM index in kg/m^2 . After the EWGSOP2 cut-off points for low muscle quantities ($<5.5\ kg/m^2$ for women and $<7\ kg/m^2$ for men [6]) were applied, patients were diagnosed with Confirmed Sarcopenia (CS) and were included in Step D. In Step D, TUG test was used for quantifying severity of sarcopenia [23]: the time taken by a participant to rise from a sitting position, walk 3 m, return, and sit down again was measured with a stopwatch in seconds. As cut-off points for both women and men, ≥ 20 s indicated Severe Sarcopenia (SS).

Statistical Analysis: All statistical analyses were performed using IBM SPSS (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA, version 28.0, Property of IBM Corp.) software. Descriptive statistics are expressed in absolute numbers and relative frequencies for categorical variables. Mean (standard deviation (SD)) and median (interquartile range (IQR)) are used for numerical variables. The Kolmogorov–Smirnov test was performed to test for normal distribution. Univariate tests such as Chi-square and Fisher's exact test were used to test for associations of frequencies, using univariate ANOVA for means and Mann–Whitney-U for medians.



Figure 2. Flowchart of study population after EWGSOP2 stepwise procedure for the diagnosis of sarcopenia. Notes: SARC-F = strength, assistance with walking, rise from a chair, climb stairs, and falls; BIA = Bioelectrical Impedance Analysis; ASM = Appendicular Skeletal Mass; TUG = Timed Up-and-Go test.

Linear and logistic regression analyses were used to test the influence of sarcopenia groups at admission on outcomes and were adjusted for age, sex, and MPI on admission, unless otherwise specified. FU outcomes were further adjusted for intervention (TIDP) and the respective scales on admission whenever assessed. Bonferroni-corrected post hoc analysis, a univariate test, was used for 4-group comparison between the different groups for sarcopenia. Significance level was set at 0.05 (two-sided) to account for multiple pairwise comparisons.

Registration, Participant Consent, and Ethics: The study that this secondary analysis is based upon is registered at the German Clinical Trials Register (DRKS00015996), and the authors declare that this study respects the ethical standards for human experimentation that are stated in the Declaration of Helsinki of 1975, as revised in 2000, as well as the national law. The original RCT was approved by the Ethical Committee (EK 18-394) of the University Hospital of Cologne, Germany, and each patient or proxy respondent signed informed consent forms.

3. Results

3.1. Characteristics of the Study Population

The demographic and clinical characteristics of the 97 patients are presented in Table 1. Mean age of the study population was 76.5 (SD 6.8) years, 55% were female. In Step A and B, 37% (95% CI: 28–48%) of the patients (n = 36) were diagnosed as having no sarcopenia. In Step B, 31% (95% CI: 23–40%) (n = 30) had SARC-F scores ≥4 and low handgrip and were diagnosed as Probable Sarcopenia (PS). As 13% (95% CI: 7–21%) (n = 13) additionally showed low ASMM in the BIA, they were diagnosed as Confirmed Sarcopenia (CS) in Step C. In Step D, according to TUG test, 19% (95% CI: 11–26%) of the patients (n = 18) were diagnosed with Severe Sarcopenia (SS). Prevalence of sarcopenia in the study sample therefore was 63% (95% CI: 54–72%), including PS, CS and SS (Figure 2).

Table 1. Comparison of sarcopenic and non-sarcopenic patients according to EWGSOP2 criteria for sarcopenia.

	Total (n = 97)	No Sarcopenia (n = 36; 37%)	Sarcopenia (n = 61; 63%)	Probable Sarcopenia (PS) (n = 30; 31%)	Confirmed Sarcopenia (CS) (n = 13; 13%)	Severe Sarcopenia (SS) (n = 18; 19%)	p-Value ^{a,b}
Age (years), mean (SD)	76.5 (6.8)	76.3 (6.9)	76.7 (6.8)	77.3 (7.2)	75.7 (8.0)	76.6 (5.2)	0.752
Female, n (%)	53 (55)	25 (70)	28 (46)	10 (36)	7 (47)	11 (61)	0.024
Length of hospital stay (days), mean (SD)	20.4 (12.5)	17 (7.2)	22.3 (14.5)	24.2 (18.8)	19.3 (8.1)	22 (10.8)	0.043
Number of GCT (days), median (IQR)	16 (11–22)	14.5 (8–17)	17.0 (15–23)	21.5 (14.8–23)	17.0 (13.5–19)	15.0 (14.5–22.3)	0.006 *
Grade of care, n (%)	65 (75)	19 (56)	46 (89)	20 (83)	12 (86)	14 (93)	<0.001 *
BMI, median (IQR)	24.2 (21.2–27.2)	24.1 (19.9–27.05)	24.4 (21.4–27.26)	26.4 (22.55–30.32)	23.6 (21–27)	21.5 (18.93–26.4)	0.563
Hospitalized in the last year, n (%)	78 (82)	25 (71)	53 (88)	25 (86)	12 (92)	16 (89)	0.038
Falls in the last year, n (%)	52 (54)	13 (36)	39 (64)	17 (57)	11 (85)	11 (61)	0.008
Scores upon admission							
MPI Value, median (IQR)	0.56 (0.44–0.69)	0.43 (0.31–0.56)	0.56 (0.44–0.69)	0.53 (0.44–0.63)	0.56 (0.44–0.66)	0.69 (0.63–0.94)	<0.001 **
MPI-Group, n (%)	MPI-1	15 (15)	11 (31)	4 (7)	3 (11)	1 (6)	<0.001 **
	MPI-2	56 (58)	21 (58)	35 (57)	18 (64)	10 (67)	
	MPI-3	26 (27)	4 (11)	22 (36)	7 (25)	4 (27)	
ADL, mean (SD)	3.9 (1.8)	5.1 (1.0)	3.2 (1.7)	3.5 (1.8)	3.6 (1.4)	2.6 (1.7)	<0.001 *
IADL, mean (SD)	4.1 (2.6)	5.9 (2.2)	3.1 (2.3)	3.6 (2.3)	2.9 (2.4)	2.4 (2.0)	<0.001 *
CIRS, mean (SD)	6.3 (1.8)	5.7 (1.8)	6.7 (1.8)	6.3 (1.5)	6.2 (1.7)	7.5 (2.0)	0.011 *
MNA-SF, mean (SD)	7.3 (3.0)	8.2 (3.0)	6.8 (2.8)	7.8 (2.7)	6.7 (2.8)	5.2 (2.4)	0.024 *
SPMSQ, mean (SD)	1.64 (2.18)	0.92 (1.13)	2.1 (2.5)	1.47 (1.59)	2.23 (2.68)	3.00 (3.45)	0.011 *
ESS, mean (SD)	15.3 (2.7)	16.8 (2.3)	14.4 (2.7)	15.2 (1.9)	13.5 (2.8)	13.6 (2.6)	0.003 *
Number of medications, mean (SD)	10.7 (4.5)	9.6 (3.6)	11.4 (4.5)	11.9 (5.3)	9.9 (4.0)	11.5 (4.7)	0.224 *
EQ-5D-5L, median (IQR)	0.62 (0.37–0.85)	0.79 (0.57–0.92)	0.53 (0.29–0.76)	0.55 (0.28–0.79)	0.57 (0.33–0.70)	0.52 (0.30–0.64)	<0.001 *
GDS, median (IQR), n = 96	3.5 (2–6)	3 (2–5)	4.5 (2–7)	3 (2–7)	6 (3.5–11.5)	4 (2–5.5)	0.696 *
RSES, mean (SD)	25.2 (3.8)	26.3 (3.0)	24.5 (4.0)	25.3 (3.3)	23.2 (5.2)	24.2 (4.1)	0.025 *

Table 1. Cont.

	Total (n = 97)	No Sarcopenia (n = 36; 37%)	Sarcopenia (n = 61; 63%)	Probable Sarcopenia (PS) (n = 30; 31%)	Confirmed Sarcopenia (CS) (n = 13; 13%)	Severe Sarcopenia (SS) (n = 18; 19%)	p-Value ^{a,b}	
GS, mean (SD)	7.1 (2.2)	6.3 (2.1)	7.6 (2.2)	7.4 (2.1)	7.8 (2.0)	7.7 (2.4)	0.033 *	
GR, mean (SD)	7.3 (2.2)	8.2 (1.7)	6.8 (2.3)	7.4 (2.1)	6.1 (2.3)	6.4 (2.6)	0.003 *	
More GR than GS, n (%)	78 (80)	34 (94)	44 (72)	22 (79)	10 (67)	12 (67)	0.007 *	
Low Handgrip, n (%)	71 (73)	10 (14)	61 (100)	30 (42)	13 (18)	18 (25)	<0.001 *	
TUG test ≥ 20 s, n (%)	63 (81)	27 (87)	36 (77)	17 (90)	1 (10)	18 (100)	<0.001 *	
Blood levels								
Albumin upon Admission, g/L, mean (SD)	32.2 (6.1)	35.2 (5.5)	30.5 (5.8)	31.0 (5.4)	29.9 (7.4)	29.9 (5.4)	<0.001	
Albumin Discharge, g/L, mean (SD)	31.5 (8.7)	33.9 (8.5)	30.5 (8.7)	29.2 (10.9)	32.0 (5.8)	31.3 (6.9)	0.109	
Total Protein upon Admission, g/L, mean (SD)	65.0 (9.4)	66.9 (9.1)	65.0 (9.4)	63.9 (8.6)	61.5 (10.4)	65.7 (10.2)	0.134	
Total Protein Discharge, g/L, mean (SD)	63.4 (10.8)	63.9 (15.6)	63.1 (7.6)	61.9 (7.3)	64.9 (5.0)	63.7 (9.5)	0.752	
Follow-Up								
Falls, n (%)	during hospital stay, n = 97	8 (8)	1 (3)	7 (12)	4 (13)	2 (15)	1 (6)	0.132 *
	FU1, n = 89	19 (21)	2 (6)	17 (32)	10 (37)	2 (17)	5 (33)	0.004 *
	FU3, n = 83	25 (30)	4 (12)	21 (43)	11 (42)	2 (22)	8 (57)	0.002 *
	FU6, n = 84	28 (33)	4 (12)	24 (48)	12 (44)	2 (22)	10 (71)	0.027 *
	FU1, n = 68	0.65 (0.34–0.87)	0.83 (0.60–0.95)	0.51 (0.31–0.80)	0.58 (0.31–0.85)	0.62 (0.11–0.82)	0.34 (0.24–0.67)	0.013 *
EQ-5D-5L, median (IQR)	FU3, n = 54	0.74 (0.38–0.85)	0.86 (0.66–0.93)	0.59 (0.30–0.79)	0.51 (0.29–0.79)	0.65 (0.1–0.77)	0.63 (0.22–0.84)	0.002 *
	FU6, n = 63	0.65 (0.37–0.85)	0.78 (0.45–0.91)	0.56 (0.37–0.82)	0.71 (0.42–0.86)	0.19 (0.01–0.66)	0.58 (0.43–0.68)	0.043 *
	FU1, n = 85	26 (31)	8 (24)	18 (35)	12 (43)	2 (22)	4 (27)	0.070 *
Rehospitalization, n (%)	FU3, n = 85	35 (41)	12 (36)	23 (44)	14 (50)	4 (44)	5 (33)	0.473 *
	FU6, n = 74	43 (50)	15 (46)	28 (54)	17 (61)	4 (44)	7 (47)	0.451 *

Table 1. Cont.

		Total (n = 97)	No Sarcopenia (n = 36; 37%)	Sarcopenia (n = 61; 63%)	Probable Sarcopenia (PS) (n = 30; 31%)	Confirmed Sarcopenia (CS) (n = 13; 13%)	Severe Sarcopenia (SS) (n = 18; 19%)	p-Value ^{a,b}
Mortality, n (%)	alive after 1 month	87 (90)	34 (94)	53 (87)	26 (87)	12 (92)	15 (83)	0.240 *
	alive after 3 months	79 (83)	32 (91)	47 (78)	24 (80)	10 (83)	13 (72)	0.268 *
	alive after 6 months	79 (83)	32 (91)	47 (78)	24 (80)	10 (83)	13 (72)	0.268 *
GDS, mean (SD)	FU1, n = 61	4.2 (3.1)	3.2 (2.6)	4.9 (3.4)	4.5 (3.2)	5.6 (4.4)	5.3 (2.7)	0.035 *
	FU3, n = 53	3.9 (3.1)	3.2 (2.6)	4.6 (3.2)	4.5 (3.2)	5.6 (4.4)	5.3 (2.7)	0.080 *
	FU6, n = 53	4.7 (3.1)	4.0 (2.9)	5.3 (3.2)	4.1 (2.5)	6.8 (5.0)	3.6 (2.2)	0.121 *
RSES, median (IQR)	FU1, n = 60	27 (24–28.5)	27 (25–29)	26 (24–28)	26 (24–28)	25.5 (18–27.75)	28 (26.5–29)	0.744 *
	FU3, n = 61	28 (25–29)	29 (27.5–30)	27 (24–28)	27 (24–28)	27 (15.75–27.25)	27 (24–29)	0.002 *
	FU6, n = 53	28 (25–29)	28 (25–29)	27.5 (25–29)	28 (27–30)	24.5 (14.25–28.5)	25 (22–28.75)	0.444 *

Notes: Patients were subdivided into sarcopenia groups using the EWGSOP2 algorithm. SD = standard deviation; IQR = Interquartile Range; CCT = Geriatric Complex Treatment; BMI = Body Mass Index; MPI = Multidimensional Prognostic Index; ADL = Katz's Activities of Daily Living; IADL = Lawton's Instrumental Activities of Daily Living; CIRS = Cumulative Illness Rating Scale; MNA-SF = Mini Nutritional Assessment Short Form; SPMSQ = Short Portable Mental Status Questionnaire; ESS = Exton Smith Scale; EQ-SD-5L = EuroQol Quality of Life—5 Dimensions (5-Level Version); GDS = Geriatric Depression Scale; RSES = Rosenberg Self-Esteem Scale; GSs = Geriatric Syndromes; GR = Geriatric Resources; FU = Follow-Up. ^a After testing for normal distribution (Kolmogorov–Smirnov) and interpreting the histogram, the Mann–Whitney–U test was performed for medians, *t*-test was conducted for means, and Chi-squared test was conducted for frequencies. ^b Indicated *p*-values are those for the comparison between No Sarcopenia and Sarcopenia groups, significant at 5%, significant *p*-values highlighted in bold. * After linear/logistic regression analysis was conducted, results were adjusted for age, sex, and MPI. ** After linear/logistic regression analysis was conducted, results were adjusted for age and sex.

3.2. Association between Sarcopenia, Prognosis, and Outcomes

The median MPI value upon admission was 0.56, indicating moderate frailty and risk of poor outcomes at follow up, with sarcopenic patients showing significantly higher MPI values, independently of age and sex, compared to non-sarcopenic patients ($p < 0.001$, Table 1, Figure 3). Linear regression analysis revealed a significant difference between MPI values upon admission for the non-sarcopenic group and SS patients ($p < 0.001$) as well as between PS and SS patients ($p = 0.009$). With respect to the MPI subdomains upon admission and adjusted for age and sex, sarcopenic patients presented significantly higher CIRS values (6.7 vs. 5.7, $p = 0.011$), lower ADL (3.2 vs. 5.1, $p < 0.001$) and IADL (3.1 vs. 5.9, $p < 0.001$) values, lower ESS (14.4 vs. 16.8, $p = 0.003$) values, lower MNA-SF (6.8 vs. 8.2, $p = 0.024$) values, and higher SPMSQ (2.1 vs. 0.9, $p = 0.011$) values compared to non-sarcopenic patients. Bonferroni-corrected post hoc tests revealed a significant difference between the ADL values of non-sarcopenic and PS ($p < 0.001$, $M_{Diff} = 1.72$, 95%-CI[0.73–2.71]), CS ($p = 0.018$, $M_{Diff} = 1.47$, 95%-CI[0.17–2.76]), and SS patients ($p < 0.001$, $M_{Diff} = 2.42$, 95%-CI[1.32–3.63]), as well as significant differences in the remaining MPI subdomains (Table 2). All the p -values of significant differences of the pairwise comparison between the groups are shown in Table 2. RSES ($p = 0.025$) and EQ-5D-5L ($p < 0.001$) values upon admission were significantly lower in patients with sarcopenia compared to those for non-sarcopenic patients. Patients with sarcopenia presented significantly more GSs ($p = 0.033$) and fewer GR ($p = 0.003$) and a higher prevalence of grade of care at admission ($p = 0.012$) and needed more ECGR days (18.5 vs. 13.7 days, $p = 0.006$) when compared to non-sarcopenic patients (Table 1). Patients with sarcopenia had significantly lower serum albumin levels at the time of admission ($p < 0.001$, Table 1) than non-sarcopenic patients. Patients with sarcopenia suffered significantly more falls in the preceding year ($p = 0.008$) and during FUs ($p = 0.004$) independently of age, gender, MPI upon admission and discharge, and TIDP. Also, patients with sarcopenia had lower EQ-5D-5L scores ($p < 0.001$) in all follow-ups; after one month, higher GDS scores ($p = 0.035$); and, after three months, lower RSES scores ($p = 0.002$) when compared to non-sarcopenic patients (Table 1) and after adjustment for age, gender, MPI, and TIDP.

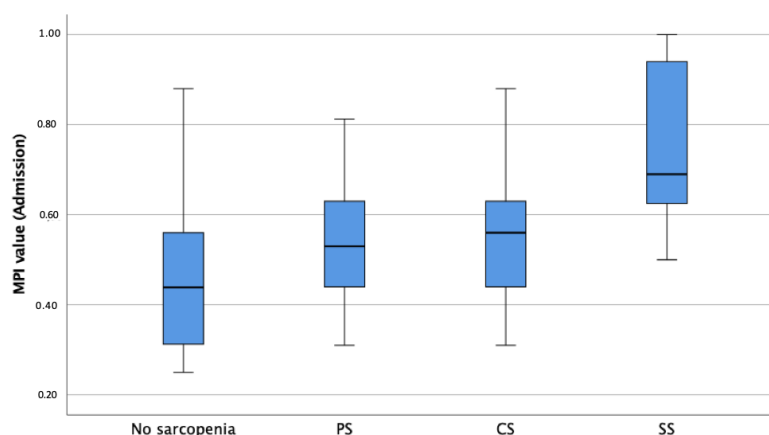


Figure 3. Boxplots showing sarcopenia groups according to EWGSOP2 in association with MPI-prognosis at admission. Notes: MPI = Multidimensional Prognostic Index; PS = Probable Sarcopenia; CS = Confirmed Sarcopenia; SS = Severe Sarcopenia.

Table 2. Post hoc tests for pairwise comparison for MPI subdomains.

		M _{Diff}	95%-CI	p-Value
ADL				
No Sarcopenia	PS	1.72	0.73–2.71	<0.001 *
	CS	1.47	0.17–2.76	0.018 *
	SS	2.47	1.32–3.63	<0.001 *
PS	CS	−0.25	−1.58–1.08	1.0
	SS	0.76	−0.44–1.95	0.547
CS	SS	1.0	−0.45–2.46	0.398
IADL				
No Sarcopenia	PS	2.35	0.86–3.84	<0.001 *
	CS	3.07	1.12–5.02	<0.001 *
	SS	3.53	1.79–5.27	<0.001 *
PS	CS	0.721	−1.28–2.72	1.0
	SS	1.18	−0.62–2.98	0.667
CS	SS	0.457	−1.17–2.65	0.815
CIRS				
No Sarcopenia	PS	−0.64	−1.79–0.51	0.826
	CS	−0.54	−2.04–0.97	0.559
	SS	−1.81	−3.15–0.46	0.003 *
PS	CS	0.10	−1.44–1.65	1.0
	SS	−1.17	−2.55–0.22	0.154
CS	SS	−1.27	−2.96–0.42	0.277
MNA-SF				
No Sarcopenia	PS	0.361	−1.48–2.20	1.0
	CS	1.502	−0.91–3.91	0.576
	SS	3.03	0.88–5.18	0.002 *
PS	CS	1.14	−1.33–3.61	1.00
	SS	2.67	0.45–4.89	0.010 *
CS	SS	1.53	−1.18–4.24	0.794
SPMSQ				
No Sarcopenia	PS	−0.55	−1.93–0.83	1.00
	CS	−1.31	−3.12–0.49	0.317
	SS	−2.08	−3.73–0.44	0.006 *
PS	CS	−0.76	−2.62–1.09	1.00
	SS	−1.53	−3.23–0.16	0.100
CS	SS	−0.769	−2.83–1.29	1.00
ESS				
No Sarcopenia	PS	1.54	0.00–3.09	0.051
	CS	3.24	1.21–5.26	<0.001 *
	SS	3.17	1.36–4.97	<0.001 *
PS	CS	1.70	−0.38–3.77	0.182
	SS	1.62	−0.24–3.49	0.127
CS	SS	−0.73	−2.35–2.21	0.182

Notes: Bonferroni-corrected post hoc test for parametric values. * *p*-values of pairwise comparison between the groups, significant at level 0.05. MPI = Multidimensional Prognostic Index; M_{Diff} = Mean Difference; CI = Confidence Interval; PS = Probable Sarcopenia; CS = Confirmed Sarcopenia; SS = Severe Sarcopenia; ADL = Katz's Activities of Daily Living; IADL = Lawton's Instrumental Activities of Daily Living; CIRS = Cumulative Illness Rating Scale; MNA-SF = Mini Nutritional Assessment Short Form; SPMSQ = Short Portable Mental Status Questionnaire; ESS = Exton Smith Scale.

4. Discussion

The present study shows a high prevalence of sarcopenia within an over-60 population segment admitted to an acute geriatric ward. Furthermore, this analysis highlights the clinical relevance of sarcopenia in terms of PROMs, quantified prognosis, and multidimensional frailty. A longitudinal association between sarcopenia's severity and life-determining outcomes, such as further falls, but also quality of life and self-esteem, was shown.

To the best of our knowledge, this is the first report of a significant association between sarcopenia, diagnosed according to the EWGSOP2-algorithm; multidimensional prognosis and frailty measured using the MPI; and health outcomes at three different timepoints. The MPI was shown to be highly accurate in forecasting poor outcomes with advancing age in different patient populations [7,11,24,25]. For the present group of patients, the MPI was shown to be able to accurately monitor the success of ECGR vs. usual care administered to similarly frail patient populations [12]. Importantly, this study showed that the longitudinal changes quantified by the MPI are clinically relevant in terms of rehospitalization and mortality rates up to 6 months after discharge [12]. The ability of MPIs to capture clinically relevant outcomes in the longitudinal health trajectory of older patients with sarcopenia is also clear in this analysis. In fact, one further major observation of the present investigation is the dose–response association between MPI scores and sarcopenia severity and related outcomes at follow-ups. This result is not surprising from a pathophysiological point of view, as a highly sensitive multidimensional tool can seize at best the multifactorial, individual, dynamic nature of the aging process [11], especially under stress conditions such as those in hospitalization. However, there are few clinical studies using a quantifiable, scaled CGA that can be used as a readout to address the clinical impact of sarcopenia in terms of multidimensional frailty and prognosis severity.

Most of the MPI subcategories were shown to be closely interwoven with sarcopenia. Among these, the role of nutrition is particularly noteworthy. There is substantial evidence demonstrating a strong correlation between nutrition and muscle mass, strength, and overall function in older adults, underscoring the critical significance of nutrition both in preventing and managing sarcopenia [26].

As mentioned above and in line with the literature [5,27], one more crucial finding yielded by the present analysis is the longitudinal association of sarcopenia severity not only with previous falls but, importantly, with life-determining outcomes such as further falls in FUs when compared to non-sarcopenic patients. This information is particularly relevant from the perspective of its independence from chronological age, sex, and the MPI. Not only does the MPI—like every CGA—act as a surrogate marker of biological age [7], but it contains several sarcopenia-related factors that are usually difficult to disentangle in real life, such as cognitive performance and nutritional status [7]. The independent nature of sarcopenia as a risk condition for falls underlines the importance of its precise diagnosis at every possible medical visit.

There are further important observations from this analysis that should be discussed. First of all, an association between sarcopenia and the presence of more GSs [28] was confirmed. With sarcopenia being ICD-10-listed since 2018 in Germany and recognized as an independent disease, its influence on other GSs may become the center of interest of studies in the future. Moreover, it was shown for the first time that significantly more patients with sarcopenia had a grade of care at the time of admission to the hospital. The concept of the care grade was added to the German social security system in order to ensure appropriate long-term care [19]. With significantly more patients with sarcopenia having a grade of care compared to those without sarcopenia, an influence on disability and an impressive decline in independence was once again confirmed. Also for the first time, a significant association between fewer GR and sarcopenia was observed, while its structured assessment is not yet part of the clinical routine in Germany [15].

A significant association between sarcopenia and depression, lower quality of life, and lower self-esteem during hospitalization and at follow-ups was observed. While a high prevalence of depression symptoms and lower quality of life have already been as-

sociated with sarcopenia [29–31], the present data confirm these observations and shed light on another under-investigated but highly important factor of resilience and stress resistance in advanced age-self-esteem [12]. Given the established associations between lower self-esteem, reduced physical activity, and frailty [32] and the potential of improved self-esteem to mitigate readmissions and prevent functional decline [33,34], it is imperative to acknowledge the interplay between sarcopenia and low self-esteem in sarcopenia management.

In this secondary analysis, the prevalence of sarcopenia based on the EWGSOP2 algorithm applied to older multimorbid hospitalized patients showed a high rate of 63% compared to previously reported prevalence ranging between 9% and 51% [35]. However, as we assessed hospitalized patients, this high prevalence is likely due to the geriatric nature and frailty of the studied population. Overall, it remains difficult to compare the exact prevalence of sarcopenia due to the heterogeneity of the study populations as well as the various assessments, definitions, and cut-offs used. Huemer et al. recently suggested using a higher cut-off for low handgrip strength than the one used in EWGSOP2, a measure that could potentially identify more individuals at risk for sarcopenia [36] by preventing early exclusion through grip strength in the first steps of the algorithm. This adjustment would increase the prevalence of sarcopenia even further than that currently observed, presenting even greater public health relevance and promoting even more concern for this largely unmet medical need [2,37–39]. Contrariwise, no significant difference could be found regarding rehospitalization or mortality. This, however, is not consistent with the results of previous studies that showed significant correlations between the degree of muscle wastage and increased number of hospitalizations as well as higher mortality [40]. In examining the disparities between our study's results and those reported in previous research, it is crucial to consider several factors that may account for these variations. Prior studies demonstrating an association between sarcopenia and mortality and analyzing patient groups similar to the group in this study in terms of setting (inpatients), age (older than 65), and sarcopenia definition (EWGSOP2) stand out for their length of follow-up of at least 3 years and larger sample size [41,42]. As mentioned above, a significant association between sarcopenia and number of falls was shown in this analysis. As low strength and low muscle mass contribute to the impairment of balance [43,44] and are therefore associated with falls, and, at the same time, with falls being one of the main mechanisms relating sarcopenia to mortality, it is possible that the length of the follow-up period was decisive for the inconsistent result in terms of mortality in this analysis. It is therefore possible that studies with larger sample sizes and longer follow-up periods are needed to rule out this inconsistency.

Limitations of this analysis: One limitation was the relatively small sample size of this study population, with 97 patients included. However, the patient population was highly phenotyped [12], and several of the observations confirm what is already reported in the literature. Another limitation is the relatively short follow-up period, i.e., 6 months, which was predetermined as per the original RCT protocol. This duration may not have captured the full spectrum of changes and outcomes associated with sarcopenia, most notably when it comes to long-term implications and mortality. Also, the use of a complete case analysis from an RCT limits the generalizability of the results. The limited availability of longer-term, comprehensive longitudinal studies in the field of sarcopenia underscores the need for further research in order to better understand the trajectory and impact of this condition over extended periods.

5. Conclusions

In conclusion, sarcopenia was shown to be significantly associated with MPI prognosis, PROMs (depression, quality of life, self-esteem, and GR), and adverse outcomes (falls, grade of care), independent of age, gender, and TIDP. This suggests that sarcopenia has prognostic significance for older hospitalized patients, and its consideration might be useful for shared decision making in a clinical setting. With the prevalence of sarcopenia among older adults

being high and increasing and with this condition, in fact, being underdiagnosed [27,45], the newly established definition for the diagnostic steps of sarcopenia appears particularly important for systematic early detection and management of this highly unfavorable disorder.

Author Contributions: Conceptualization and design of the clinical trial, A.M.M. and M.C.P.; performed the experiments, A.F., L.M., J.S., L.W., A.M.M. and M.C.P.; analyzation of the data, A.F., A.M.M. and I.B.; writing—original draft preparation, A.F.; writing—review and editing, A.M.M. and M.C.P.; visualization, A.F.; critical revisions, A.F., A.M.M., I.B., T.B., M.C.P., L.M. and J.S. All authors have read and agreed to the published version of the manuscript.

Funding: The RCT leading to these results received funding from Wilhelm Woorst-Stiftung für Alternsforschung im Stifterverband with the Wilhelm Woorst-Preis für Alternsforschung 2019 for which the authors are very grateful (Grant T0011-33.646). The authors have no competing interests to declare that are relevant to the content of this article.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the University Hospital of Cologne, Germany (EK 18-394), approved on 25 February 2019.

Informed Consent Statement: Informed consent was obtained from all subjects or proxy involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy.

Conflicts of Interest: The authors declare no conflicts of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

1. WHO. *World Report on Ageing and Health*; WHO: Geneva, Switzerland, 2015.
2. Cruz-Jentoft, A.J.; Sayer, A.A. Sarcopenia. *Lancet* **2019**, *393*, 2636–2646. [\[CrossRef\]](#)
3. Chang, K.-V.; Hsu, T.-H.; Wu, W.-T.; Huang, K.-C.; Han, D.-S. Is sarcopenia associated with depression? A systematic review and meta-analysis of observational studies. *Age Ageing* **2017**, *46*, 738–746. [\[CrossRef\]](#)
4. Bianchi, L.; Ferrucci, L.; Cherubini, A.; Maggio, M.; Bandinelli, S.; Savino, E.; Brombo, G.; Zuliani, G.; Guralnik, J.M.; Landi, F.; et al. The Predictive Value of the EWGSOP Definition of Sarcopenia: Results from the InCHIANTI Study. *J. Gerontol. Ser. A* **2015**, *71*, 259–264. [\[CrossRef\]](#)
5. Yeung, S.S.Y.; Reijnierse, E.M.; Pham, V.K.; Trappenburg, M.C.; Lim, W.K.; Meskers, C.G.M.; Maier, A.B. Sarcopenia and its association with falls and fractures in older adults: A systematic review and meta-analysis. *J. Cachexia Sarcopenia Muscle* **2019**, *10*, 485–500. [\[CrossRef\]](#)
6. Cruz-Jentoft, A.J.; Bahat, G.; Bauer, J.; Boirie, Y.; Bruyère, O.; Cederholm, T.; Cooper, C.; Landi, F.; Rolland, Y.; Sayer, A.A.; et al. Sarcopenia: Revised European consensus on definition and diagnosis. *Age Ageing* **2019**, *48*, 16–31. [\[CrossRef\]](#)
7. Zampino, M.; Polidori, M.C.; Ferrucci, L.; O’neill, D.; Pilotto, A.; Gogol, M.; Rubenstein, L. Biomarkers of aging in real life: Three questions on aging and the comprehensive geriatric assessment. *GeroScience* **2022**, *44*, 2611–2622. [\[CrossRef\]](#)
8. Rodriguez-Pascual, C.; Paredes-Galan, E.; Vilches-Moraga, A.; Ferrero-Martinez, A.I.; Torrente-Carballido, M.; Rodriguez-Artalejo, F. Comprehensive geriatric assessment and 2-year mortality in elderly patients hospitalized for heart failure. *Circ. Cardiovasc. Qual. Outcomes* **2014**, *7*, 251–258. [\[CrossRef\]](#)
9. Dodson, J.A.; Hajduk, A.M.; Geda, M.; Krumholz, H.M.; Murphy, T.E.; Tsang, S.; Tinetti, M.E.; Nanna, M.G.; McNamara, R.; Gill, T.M.; et al. Predicting 6-month mortality for older adults hospitalized with acute myocardial infarction: A cohort study. *Ann. Intern. Med.* **2020**, *172*, 12–21. [\[CrossRef\]](#)
10. Pilotto, A.; Ferrucci, L.; Franceschi, M.; D’Ambrosio, L.P.; Scarcelli, C.; Cascavilla, L.; Paris, F.; Placentino, G.; Seripa, D.; Dallapiccola, B.; et al. Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. *Rejuvenation Res.* **2008**, *11*, 151–161. [\[CrossRef\]](#) [\[PubMed\]](#)
11. Pilotto, A.; Custodero, C.; Maggi, S.; Polidori, M.C.; Veronese, N.; Ferrucci, L. A multidimensional approach to frailty in older people. *Ageing Res. Rev.* **2020**, *60*, 101047. [\[CrossRef\]](#) [\[PubMed\]](#)
12. Meyer, A.M.; Bartram, M.P.; Antczak, P.; Becker, I.; Benzing, T.; Polidori, M.C. A Tailored Discharge Program Improves Frailty and Mood in Patients Undergoing Usual Rehabilitative Care: A Randomized Controlled Trial. *J. Am. Med. Dir. Assoc.* **2022**, *23*, 1962.e1–1962.e13. [\[CrossRef\]](#)
13. Mercer, S.; Furler, J.; Moffat, K.; Fischbacher-Smith, D.; Sanci, L. *Multimorbidity: Technical Series on Safer Primary Care*; World Health Organization: Geneva, Switzerland, 2016.

14. Volpato, S.; Bazzano, S.; Fontana, A.; Ferrucci, L.; Pilotto, A. Multidimensional prognostic index predicts mortality and length of stay during hospitalization in the older patients: A multicenter prospective study. *J. Gerontol. Ser. A Biomed. Sci. Med. Sci.* **2015**, *70*, 325–331. [\[CrossRef\]](#)
15. Meyer, A.M.; Becker, I.; Siri, G.; Brinkkoetter, P.T.; Benzing, T.; Pilotto, A.; Polidori, M.C. The prognostic significance of geriatric syndromes and resources. *Aging Clin. Exp. Res.* **2020**, *32*, 115–124. [\[CrossRef\]](#)
16. Leshner, E.L.; Berryhill, J.S. Validation of the geriatric depression scale-short form among inpatients. *J. Clin. Psychol.* **1994**, *50*, 256–260. [\[CrossRef\]](#)
17. Devlin, N.J.; Brooks, R. EQ-5D and the EuroQol group: Past, present and future. *Appl. Health Econ. Health Policy* **2017**, *15*, 127–137. [\[CrossRef\]](#)
18. Roth, M.; Decker, O.; Herzberg, P.Y.; Brähler, E. Dimensionality and Norms of the Rosenberg Self-esteem Scale in a German General Population Sample. *Eur. J. Psychol. Assess.* **2008**, *24*, 190. [\[CrossRef\]](#)
19. Baake, C.P. *Begutachtungsverfahren NBA—Pflegergrad bei Erwachsenen*; Walhalla Digital: Regensburg, Germany, 2017.
20. Malmstrom, T.K.; Morley, J.E. SARC-F: A simple questionnaire to rapidly diagnose sarcopenia. *J. Am. Med. Dir. Assoc.* **2013**, *14*, 531–532. [\[CrossRef\]](#)
21. McGrath, R.P.; Kraemer, W.J.; Snih, S.A.; Peterson, M.D. Handgrip strength and health in aging adults. *Sports Med.* **2018**, *48*, 1993–2000. [\[CrossRef\]](#)
22. Sergi, G.; De Rui, M.; Veronese, N.; Bolzetta, F.; Berton, L.; Carraro, S.; Bano, G.; Coin, A.; Manzato, E.; Perissinotto, E. Assessing appendicular skeletal muscle mass with bioelectrical impedance analysis in free-living Caucasian older adults. *Clin. Nutr.* **2015**, *34*, 667–673. [\[CrossRef\]](#) [\[PubMed\]](#)
23. Herman, T.; Giladi, N.; Hausdorff, J.M. Properties of the ‘timed up and go’ test: More than meets the eye. *Gerontology* **2011**, *57*, 203–210. [\[CrossRef\]](#) [\[PubMed\]](#)
24. Meyer, A.M.; Becker, I.; Siri, G.; Brinkkötter, P.T.; Benzing, T.; Pilotto, A.; Polidori, M.C. New associations of the Multidimensional Prognostic Index. *Z. Für Gerontol. Und Geriatr.* **2019**, *52*, 460–467. [\[CrossRef\]](#)
25. Dent, E.; Martin, F.C.; Bergman, H.; Woo, J.; Romero-Ortuno, R.; Walston, J.D. Management of frailty: Opportunities, challenges, and future directions. *Lancet* **2019**, *394*, 1376–1386. [\[CrossRef\]](#)
26. Robinson, S.M.; Reginster, J.-Y.; Rizzoli, R.; Shaw, S.C.; Kanis, J.A.; Bautmans, I.; Bischoff-Ferrari, H.; Bruyère, O.; Cesari, M.; Dawson-Hughes, B.; et al. Does nutrition play a role in the prevention and management of sarcopenia? *Clin. Nutr.* **2018**, *37*, 1121–1132. [\[CrossRef\]](#)
27. Beaudart, C.; Zaaria, M.; Pasleau, F.; Reginster, J.-Y.; Bruyère, O. Health outcomes of sarcopenia: A systematic review and meta-analysis. *PLoS ONE* **2017**, *12*, e0169548. [\[CrossRef\]](#)
28. Suzan, V.; Kanat, B.B.; Yavuzer, H. Association of sarcopenia with geriatric syndromes and neutrophil/lymphocyte ratio. *Medicine* **2022**, *11*, 645–650. [\[CrossRef\]](#)
29. Li, Z.; Tong, X.; Ma, Y.; Bao, T.; Yue, J. Prevalence of depression in patients with sarcopenia and correlation between the two diseases: Systematic review and meta-analysis. *J. Cachexia Sarcopenia Muscle* **2022**, *13*, 128–144. [\[CrossRef\]](#)
30. Tsekoura, M.; Kastrinis, A.; Katsoulaki, M.; Billis, E.; Gliatis, J. Sarcopenia and its impact on quality of life. In *GeNeDis 2016: Genetics and Neurodegeneration*; Springer: Berlin/Heidelberg, Germany, 2017; pp. 213–218.
31. Beaudart, C.; Demonceau, C.; Reginster, J.Y.; Locquet, M.; Cesari, M.; Jentoft, A.J.C.; Bruyère, O. Sarcopenia and health-related quality of life: A systematic review and meta-analysis. *J. Cachexia Sarcopenia Muscle* **2023**, *14*, 1228–1243. [\[CrossRef\]](#)
32. Guerrero-Escobedo, P.; Tamez-Rivera, O.; Amieva, H.; Avila-Funes, J.A. Frailty is associated with low self-esteem in elderly adults. *J. Am. Geriatr. Soc.* **2014**, *62*, 396–398. [\[CrossRef\]](#)
33. Heppner, H. Soft skills: Somewhat different doping. *Z. Für Gerontol. Und Geriatr.* **2018**, *51*, 160–164. [\[CrossRef\]](#) [\[PubMed\]](#)
34. Beswick, A.D.; Rees, K.; Dieppe, P.; Ayis, S.; Goberman-Hill, R.; Horwood, J.; Ebrahim, S. Complex interventions to improve physical function and maintain independent living in elderly people: A systematic review and meta-analysis. *Lancet* **2008**, *371*, 725–735. [\[CrossRef\]](#) [\[PubMed\]](#)
35. Papadopoulou, S.; Tsintavis, P.; Potsaki, G.; Papandreou, D. Differences in the prevalence of sarcopenia in community-dwelling, nursing home and hospitalized individuals. A systematic review and meta-analysis. *J. Nutr. Health Aging* **2020**, *24*, 83–90. [\[CrossRef\]](#) [\[PubMed\]](#)
36. Huemer, M.-T.; Kluttig, A.; Fischer, B.; Ahrens, W.; Castell, S.; Ebert, N.; Gastell, S.; Joeckel, K.-H.; Kaaks, R.; Karch, A.; et al. Grip strength values and cut-off points based on over 200,000 adults of the German National Cohort—A comparison to the EWGSOP2 cut-off points. *Age Ageing* **2023**, *52*, afac324. [\[CrossRef\]](#)
37. Bauer, J.; Morley, J.E.; Schols, A.M.W.J.; Ferrucci, L.; Cruz-Jentoft, A.J.; Dent, E.; Baracos, V.E.; Crawford, J.A.; Doehner, W.; Heymsfield, S.B.; et al. Sarcopenia: A Time for Action. An SCWD Position Paper. *J. Cachexia Sarcopenia Muscle* **2019**, *10*, 956–961. [\[CrossRef\]](#) [\[PubMed\]](#)
38. Stuck, A.K.; Basile, G.; Freystaetter, G.; de Godoi Rezende Costa Molino, C.; Lang, W.; Bischoff-Ferrari, H.A. Predictive validity of current sarcopenia definitions (EWGSOP2, SDOC, and AWGS2) for clinical outcomes: A scoping review. *J. Cachexia Sarcopenia Muscle* **2023**, *14*, 71–83. [\[CrossRef\]](#)
39. Bernabei, R.; Landi, F.; Calvani, R.; Cesari, M.; Del Signore, S.; Anker, S.D.; Bejuit, R.; Bordes, P.; Cherubini, A.; Cruz-Jentoft, A.J.; et al. Multicomponent intervention to prevent mobility disability in frail older adults: Randomised controlled trial (SPRINTT project). *BMJ* **2022**, *377*, e068788. [\[CrossRef\]](#) [\[PubMed\]](#)

40. Xu, J.; Wan, C.S.; Ktoris, K.; Reijnierse, E.M.; Maier, A.B. Sarcopenia is associated with mortality in adults: A systematic review and meta-analysis. *Gerontology* **2022**, *68*, 361–376. [[CrossRef](#)] [[PubMed](#)]
41. Bianchi, L.; Maietti, E.; Abete, P.; Bellelli, G.; Bo, M.; Cherubini, A.; Corica, F.; Di Bari, M.; Maggio, M.; Martone, A.M.; et al. Comparing EWGSOP2 and FNIH Sarcopenia Definitions: Agreement and 3-Year Survival Prognostic Value in Older Hospitalized Adults: The GLISTEN Study. *J. Gerontol. Ser. A* **2019**, *75*, 1331–1337. [[CrossRef](#)] [[PubMed](#)]
42. Malafarina, V.; Malafarina, C.; Biain Ugarte, A.; Martinez, J.A.; Goñi, I.A.; Zulet, M.A. Factors Associated with Sarcopenia and 7-Year Mortality in Very Old Patients with Hip Fracture Admitted to Rehabilitation Units: A Pragmatic Study. *Nutrients* **2019**, *11*, 2243. [[CrossRef](#)] [[PubMed](#)]
43. Bijlsma, A.Y.; Pasma, J.H.; Lambers, D.; Stijntjes, M.; Blauw, G.J.; Meskers, C.G.; Maier, A.B. Muscle strength rather than muscle mass is associated with standing balance in elderly outpatients. *J. Am. Med. Dir. Assoc.* **2013**, *14*, 493–498. [[CrossRef](#)]
44. Muir, S.W.; Berg, K.; Chesworth, B.; Klar, N.; Speechley, M. Quantifying the magnitude of risk for balance impairment on falls in community-dwelling older adults: A systematic review and meta-analysis. *J. Clin. Epidemiol.* **2010**, *63*, 389–406. [[CrossRef](#)]
45. Coletta, G.; Phillips, S.M. An elusive consensus definition of sarcopenia impedes research and clinical treatment: A narrative review. *Ageing Res. Rev.* **2023**, *86*, 101883. [[CrossRef](#)] [[PubMed](#)]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

4. Discussion

4.1 Findings of the "Vun nix kütt nix"-study

The study *"Vun nix kütt nix' - Patient, geriatrician and general practitioner as a multiprofessional team for intersectoral discharge management"* is among the first to provide evidence that an intersectoral, multiprofessional collaboration involving patients, geriatricians, and general practitioners may contribute to reductions in frailty among acutely hospitalized patients, while simultaneously improving patient-reported outcomes such as mood and self-esteem. It offered new evidence with putting focus on hospitalized patients and potential risk factors for rehospitalization: unawareness on the patient's part, but also uninformed GP and frailty during acute medical treatment. The study and its findings can operate as a model for improved transition between hospital stay and post-discharge treatment with beginning of intervention already during hospitalization instead of a delayed start. Although no significant effect of the intervention on rehospitalization rates could be shown, it was demonstrated that the TIPD approach yielded significant benefits in reducing frailty and improving PROMS in terms of higher self-esteem and fewer depressive symptoms.

Detailed key findings along with conclusions and implications of the randomized controlled trial "Vun nix kütt nix" can be consulted in the original publication "A tailored discharge program improves frailty and mood in patients undergoing usual rehabilitative care" published by Meyer et al. in 2022 in the Journal of the American Medical Directors Association (JAMDA)¹⁵⁶.

4.2 Key findings on sarcopenia, prognosis and outcomes in older patients

The primary finding of this secondary analysis is the detection of the multifactorial influence of sarcopenia on the prognosis, frailty and short-term outcomes of older, multimorbid patients. Significant differences between patients showing signs of sarcopenia and those with no indications for sarcopenia could be highlighted not only regarding physical parameters and comorbidities, but also when it comes to self-perceived quality of life, well-being and self-esteem¹⁵⁵.

While previous research has established that sarcopenia is linked to adverse clinical trajectories in older adults¹⁵⁷, to date, this study uniquely investigates a significant relationship between sarcopenia - diagnosed using the structured EWGSOP2-algorithm - multidimensional prognosis assessed by the MPI, and health outcomes evaluated at three distinct timepoints. Previous studies have demonstrated that the MPI provides a reliable means of predicting adverse outcomes in aging populations across diverse clinical settings^{12,28,32,158}. In the cohort

analyzed here, the MPI proved effective in tracking the impact of the TIDP intervention relative to standard care delivered to similarly frail patients¹⁵⁶. Notably, the changes in MPI observed over time were associated with meaningful clinical endpoints, including rehospitalization and mortality up to six months post-discharge, highlighting the index's utility for monitoring longitudinal patient trajectories¹⁵⁶.

Our findings demonstrate a significant association between sarcopenia on admission and the MPI on admission, independent of sex and chronological age. Upon more detailed group comparison, post-hoc test revealed that MPI values of the non-sarcopenic patients are significantly different when compared to those with severe sarcopenia, the same as when comparing values of PS and SS patients. Also for the subcategories of the MPI, significant differences could be found if groups were being compared to those patients with severe sarcopenia. As the classification into the group of SS requires low physical performance (tested with the help of TUG), this step of the algorithm seems to be filtering out the individuals that are particularly affected or in higher risk for adverse outcome. These findings are consistent to previous studies, linking impaired motoric capabilities tested with TUG to higher risk for falls¹⁵⁹⁻¹⁶¹, even if an exact predictive ability is limited.

This analysis further highlights the capacity of the MPI to reflect clinically meaningful outcomes over the longitudinal course of older patients with sarcopenia. One of the key findings is the observed dose-response relationship between MPI scores, the severity of sarcopenia and as well corresponding follow-up outcomes¹⁵⁵. From a pathophysiological perspective, this is consistent with expectations, as a multidimensional, highly sensitive instrument is particularly suited to capture the complex, dynamic, and individualized nature of the aging process³², especially under stressors such as an acute hospitalization. Despite this, relatively few clinical investigations have employed a quantifiable, scaled CGA as a tool to systematically evaluate the impact of sarcopenia on multidimensional frailty and prognostic trajectories.

Notably, many of the MPI subdomains appear to be closely interwoven with sarcopenia, with nutritional status playing a particularly important role. In this context, significant associations between the presence of sarcopenia and the MNA-SF-score could be demonstrated. Although several studies already have explored this relationship, definitive conclusions remain lacking. Both malnutrition and sarcopenia are highly prevalent conditions among older adults and can occur either independently or in combination. Malnutrition, in particular, has also been recognized as a key contributor to the development and progression of sarcopenia, influencing muscle protein synthesis, functional reserve and overall physical performance and therefore being part of the complex pathogenesis of sarcopenia¹⁶². A growing body of evidence indicates a strong relationship between nutritional status and multiple dimensions of musculoskeletal

health, including muscle mass, strength, and functional capacity. Inadequate intake of protein, micronutrients, and energy can accelerate the loss of muscle tissue, exacerbate frailty, and increase vulnerability to adverse outcomes such as falls, hospitalization, and loss of independence. These findings highlight the critical importance of early nutritional assessment and intervention as part of a comprehensive strategy to prevent or mitigate sarcopenia, supporting both functional preservation and overall quality of life in the aging population^{162,163}.

In accordance to previous studies, associations between sarcopenia and reduced functionality, by reverting to Katz ADL and Lawton IADL were shown in our analysis as well^{164,165}. This link may be mediated by the loss of muscle strength and physical function that are crucial for the diagnosis of sarcopenia and those significantly associated with ADL and IADL performance in older adults^{166,167}. By the same token, well-developed muscle strength was shown to be protective against functional declining below the threshold where dependence according to ADL and IADL occurs¹⁶⁸, which then also explains the association between sarcopenia and higher disability. Our findings regarding the association of sarcopenia with adverse outcomes, impaired function and increased disability are also confirmatory of previous longitudinal studies^{88,92,145,146,169,170}. But the MPI gives us the opportunity to determine the prognosis not only unidimensional about mortality or rehospitalization, but as a multidimensional tool it gives us information about frailty and the multi-layered prognosis of an older person. Additionally, with sarcopenia exerting a significant influence on the MPI-values, independently of the confounding effects of chronological age and sex, this supports the assertion that sarcopenia itself plays a pivotal role in contributing to the observed outcomes.

As already mentioned, our findings regarding the association of sarcopenia with adverse outcome and increased disability are in accordance with previous longitudinal studies. For example, Phillips et al. showed in the KORA-Age study that the presence of sarcopenia has an important impact on disability in older patients and leads to higher disability scores, giving a reliable idea of the capacity to accomplish activities of daily living⁸⁸. Gariballa et al. concluded that older people with sarcopenia present a worse clinical outcome over 6 months when compared to a similar population group without sarcopenia⁹². They showed prolonged length of hospital stay, more depressive symptoms and lower serum albumin concentration in people with diagnosed sarcopenia. Landi et al. showed in their iSIRENTE study, that falls in participants with sarcopenia are more than three times more likely and that depression is more prevalent¹⁴⁶. The systematic review and meta-analysis of Yeung et al. also found positive correlation between the presence of sarcopenia and falls and fractures, regardless of the study design, sex, population or sarcopenia definition¹⁴⁵.

The present analysis further demonstrates that increasing sarcopenia severity is associated with clinically meaningful outcomes over time. Beyond a higher burden of prior falls, sarcopenic patients showed an elevated risk of subsequent falls during both the year before admission and the follow-up period when compared with non-sarcopenic individuals. Importantly, these associations persisted irrespective of chronological age, gender, or baseline MPI, underscoring the independent prognostic relevance of sarcopenia severity when it comes to life-determining outcomes. Taken together, these findings emphasize that the MPI - like every CGA-based instrument- extends beyond a mere reflection of chronological aging by capturing elements of biological vulnerability. Importantly, it integrates multiple domains that are closely interwoven and related to sarcopenia and are often difficult to disentangle in routine clinical practice, such as cognitive function and nutritional status. The observation that sarcopenia remains independently associated with fall risk further highlights the need for accurate and systematic identification of sarcopenia at every appropriate and possible point of medical contact.

In our present cohort, sarcopenia was not directly associated with higher rates of rehospitalization, an increase in the grade of care or mortality during the follow-up period. This observation stands in opposition to earlier studies reporting a clear relationship between the extent of muscle loss and both increased hospitalization rates and mortality¹⁷¹. From a pathophysiological perspective, this discrepancy may be explained by the complex and time-dependent mechanisms through which sarcopenia exerts its clinical impact. Sarcopenia represents a chronic, progressive condition characterized by reduced muscle mass, impaired neuromuscular function and decreased physiological reserve, which may not translate into hard endpoints such as mortality within a relatively short observation period.

While no direct association with mortality was observed in the current analysis, a robust association between sarcopenia and increased incidence of falls could be demonstrated. Given that reduced muscle strength and diminished muscle mass are key contributors to impaired physical function and instability or lack of balance^{172,173}, being associated with falls, and with falls in turn representing one of the principal pathways through which sarcopenia may translate into increased mortality risk¹⁷¹, the relatively short follow-up period of this study may have limited the ability to detect such downstream outcomes. In this context, falls may represent an intermediate clinical endpoint linking sarcopenia to mortality, rather than mortality being an immediate consequence of muscle loss itself. Mortality related to sarcopenia may therefore emerge only after a longer time lag, following recurrent falls, complications or functional decline. Previous studies reporting significant associations between sarcopenia and mortality were typically characterized by substantially larger sample sizes and considerably longer observation periods - often extending beyond three years^{174,175}. Such timeframes may

be necessary for the cumulative effects of recurrent falls, immobility, inflammatory burden and secondary complications to manifest as increased mortality or sustained care dependency. Therefore, the absence of a detectable mortality signal in the present analysis does not contradict the biological relevance of sarcopenia, but rather underscores the importance of long-term observation to really capture its downstream consequences. Consequently, future studies with extended follow-up durations, larger cohorts and sufficient statistical power appear necessary to fully capture the long-term prognostic implications of sarcopenia and to further elucidate its relationship with mortality and care dependency.

Several additional findings emerging from this analysis merit closer consideration. Most notably, the close relationship between sarcopenia and the accumulation of geriatric syndromes was corroborated¹⁷⁶. While earlier studies also conceptualizing sarcopenia itself as a geriatric syndrome and demonstrating its association with adverse conditions such as falls, cognitive decline, polypharmacy and malnutrition^{177,178}, the present data further emphasized its central role within the broader geriatric syndrome network. Not surprisingly, geriatric syndromes of immobility and instability were more prevalent among sarcopenic patients, highlighting once again its functional consequences. Since the formal introduction of sarcopenia as an independent diagnosis in the ICD-10-system in Germany since 2018, increasing attention has been directed toward its potential impact on other geriatric syndromes. These findings support the notion that sarcopenia may not merely coexist with, but actively contribute to the development and progression of additional geriatric conditions, thereby amplifying overall vulnerability in older patients. Understanding these interdependencies may therefore represent an important focus of future geriatric research and clinical practice.

Beyond this, the present study provides novel evidence that sarcopenia is already linked to an increased prevalence of an established grade of care already at the time of hospital admission. In the German social security system, the grade of care is a standardized instrument designed to quantify long-term care dependency by assessing impairments in mobility, self-care, cognitive and communicative abilities, as well as the capacity to organize everyday life independently¹⁷⁹. The markedly and significantly higher proportion of sarcopenic patients with an assigned grade of care at admission when compared to non-sarcopenic patients (89% vs. 59%) indicates that functional limitations related to sarcopenia are not merely acute or hospitalization-related phenomena, but reflect sustained loss of autonomy preceding inpatient treatment^{88,170}. This findings once again highlight the substantial impact of sarcopenia on disability and everyday functioning, particularly with regard to activities of daily living and independent mobility. From a clinical perspective, this association emphasizes the importance of timely identification and targeted management of sarcopenia, not only to prevent acute adverse outcomes but also to mitigate progression toward chronic dependency and institutional care.

Also, a novel and clinically relevant finding is the association between sarcopenia and reduced availability of geriatric resources. While the structures assessment of GR is not yet routinely integrated into clinical practice in Germany¹⁸⁰, the observed imbalance between fewer resources and increased vulnerability among sarcopenic patients highlights an often overlooked dimension of the condition.

Taken together, the present findings extend the understanding of sarcopenia beyond somatic manifestations by highlighting its close relationship with PROMs. Throughout hospitalization and follow-up, sarcopenia was consistently associated with higher levels of depressive symptoms (GDS), reduced quality of life (EQ-5D-5L) and lower self-esteem (RSES). Previous studies have already linked sarcopenia to diminished psychological resilience, supporting the notion that physical decline and internal coping resources are closely interconnected in older age¹⁸¹. The present results align with these observations and further emphasize the bidirectional relationship between physical functioning and psychosocial well-being. While an increased burden of depressive symptoms and impaired quality of life in sarcopenic individuals has been documented previously^{182,183}, the current analysis adds an important and comparatively underexplored dimension by demonstrating a robust association between sarcopenia and lower self-esteem¹⁵⁶. Self-esteem represents a key component of resilience and stress resistance in advanced age and may influence health behaviors, physical activity, and engagement in rehabilitation. Given existing evidence linking low self-esteem to reduced physical activity and frailty¹⁸⁴, as well as data suggesting that strengthening self-esteem may help prevent functional decline and hospital readmissions^{185,186}, these findings underscore the need to integrate psychosocial dimensions into the clinical management of sarcopenia. Addressing sarcopenia as a multidimensional condition may therefore be essential to improving both functional and patient-centered outcomes in older adults.

4.3 Prevalence of sarcopenia in the study population

In this secondary analysis, sarcopenia defined according to the EWGSOP2 criteria was highly prevalent among hospitalized patients, affecting nearly two thirds of the study population (63%, 95% CI: 54-72%). This proportion exceeds prevalence estimates reported in earlier investigations, which range widely between 9% (95% CI: 7-11%) and 51% (95% CI: 37-66%)^{93,87,88}, depending on population characteristics and study design. The markedly higher prevalence observed in our present cohort is most plausibly explained by the specific clinical context and setting in which the patients were recruited. Unlike many previous studies that assessed sarcopenia primarily in community-dwelling or relatively healthy older adults, the current analysis focusses on patients admitted to an acute geriatric internal medicine ward.

This setting inherently comprises individuals with complex health profiles, characterized by the coexistence of multiple diseases, acute medical events and functional impairment. Moreover, inclusion criteria of the study required the presence of multimorbidity (defined as multiple health conditions or synchronous presence of two or more chronic conditions that require long-term treatment¹⁸⁷) as well as at least two geriatric syndromes necessitating rehabilitative intervention. Against this background, the relatively high prevalence of sarcopenia identified in this cohort appears to reflect the advanced frailty and vulnerability of the population rather than an overestimation related to diagnostic criteria.

Indeed, recent data from a neurological rehabilitation setting employing comparable inclusion and diagnostic criteria reported similarly high prevalence rates of sarcopenia, reaching up to 79%¹⁸⁸. These findings support the notion that sarcopenia is particularly common in clinical populations characterized by complex chronic disease. Chronic medical conditions such as diabetes mellitus, cardiovascular disease, COPD or metabolic syndrome have consistently been associated with an increased risk for sarcopenia^{116,189,190}, which may partly explain the elevated prevalence observed in our study population, composed exclusively of patients with longstanding and chronic medical conditions. In addition, with mean age of 76.5 ($\pm$ 6.8) years, the study cohort represents an advanced-aged population, in whom age-related declines in muscle mass and strength are more pronounced, thereby further increasing the likelihood of sarcopenia. Beyond age and comorbidity, lifestyle-related factors, such as physical inactivity and sedentary behavior, poor diet, excessive alcohol consumption or smoking have also been implicated in the development and progression of sarcopenia¹⁹¹. It is conceivable, that such risk factors were more prevalent in our study population, contributing cumulatively to the high observed rates. Finally, methodological aspects related to sarcopenia assessment may also have influenced the observed prevalence. The structured and systematic application of diagnostic criteria in the present analysis may have facilitated the detection of sarcopenia, particularly in individuals with multifactorial impairment, thereby yielding higher prevalence figures.

Accurately, estimating and comparing the prevalence of sarcopenia across studies may be challenging, not at least because diagnostic algorithms, measurement tools and threshold values differ substantially between research groups⁸⁷. Even when the same underlying criteria are applied, variations in cut-off points for key parameters such as muscle mass, or physical performance can lead to markedly different prevalence estimates. For example, the choice of handgrip strength alone has been shown to influence case assignment: higher cut-offs substantially increase the number of individuals classified as sarcopenic, whereas lower threshold can result in underestimation of the condition in older populations. In this context, Huemer et al. suggested raising the cut-off values for low handgrip strength compared with the EWGSOP2 recommendations¹⁹². This modification could increase the sensitivity of sarcopenia

screening by minimizing early exclusion of patients with clinically relevant impairment during the first step of the diagnostic pathway. In a large cohort from Brazil, adopting higher handgrip strength cut-offs nearly quadrupled the prevalence of probable sarcopenia and doubled that of severe sarcopenia compared with the conventional EWGSOP2 thresholds, without fundamentally altering the pattern of associated risk factors¹⁹³. Similarly, comparative studies have demonstrated that alternative strength criteria, such as chair stand performance or consensus definitions other than EWGSOP2, yield considerably higher prevalence figures, underscoring the impact of methodological choices on sarcopenia identification^{194,195}. Together, these findings highlight that differences in diagnostic criteria and cut-off values substantially contribute to the wide range of sarcopenia prevalence reported in the literature and complicate direct comparisons between studies, even when populations are demographically similar. Implementing higher diagnostic thresholds would likely lead to a further rise in sarcopenia prevalence, underscoring its substantial public health impact and highlighting the urgent need for improved recognition and management strategies^{83,114,196,197}.

In conclusion, there are multiple potential factors that could explain the high prevalence of sarcopenia in our study population, the different definitions and diagnostic steps being an important one. This again highlights the most striking issue in research about sarcopenia: the use of non-uniform definitions and different diagnostic steps and cut-offs leading to results that are hardly comparable. Other studies on geriatric wards revealed a prevalence between 13 and 25%^{198,199}. Therefore, it could also be assumed that due to a previously non-stepwise approach to the diagnosis of sarcopenia, many patients did not receive an adequate diagnosis with many false-negative patients. Further prevalence studies using the procedure according to the EWGSOP2 algorithm are therefore extremely important, even if to date, the question of which sarcopenia definition is the most valid as gold-standard for as well clinical practice and research, has not yet been answered¹⁹⁶. It would thus be of tremendous importance, that at last, a globally accepted definition and subsequent procedure are being established in order to achieve transferable results.

4.4 The value of a consistent and globally used definition of sarcopenia

With the world's population aging, the prevalence of sarcopenia is expected to further increase, leading to significant social and economic implications. As already outlined in the previous chapters, there have been numerous attempts to develop a definition and diagnostic criteria for sarcopenia over the last few decades and interest in research has visibly risen. However, the lack of a global consensus among as well researchers as healthcare professionals has

resulted in a wide range of definitions, leading to significant differences when it comes to study results but also in the handling on clinical grounds. When working through the published articles on sarcopenia of recent years, it is striking how different the used methods and diagnostic tools are. Also, when it comes to cut-off points for muscle mass, strength or function, the used values are not consistent, leading to significant variabilities in the analyzed prevalence. If different definitions are being used in order to diagnose sarcopenia, different patient groups are being compared, leading to poorly comparable results. With no consistent agreement and plan, progress in diagnosis, management, research and treatment are being hindered and the transition of awareness for sarcopenia and its screening in clinical everyday life remains challenging. For precisely these reasons, the Global Leadership Initiative in Sarcopenia (GLIS), an initiative regrouping experts from various fields and countries has recently been formed. The goal is to finally establish a consistent and global definition of sarcopenia and to introduce a diagnostic algorithm in order to improve the accuracy and consistency of diagnosis⁸¹. Once a global conceptual definition of sarcopenia is available and the involved elements, assessments, evidence-based cutoffs, algorithms, and outcome measures are defined, another revolution in the field of sarcopenia can be reached and better clinical outcomes and facilitated research efforts can be expected. The intention is to prioritize sarcopenia in clinical practice, emphasizing the need to educate health professionals on screening, diagnosing and managing both primary and secondary sarcopenia. Most of all, quality of life of older adults worldwide could be improved, as, if detected in early stages, many negative outcomes could still be averted by adapted training and treatment and therefore the condition could be addressed before it results in disability and loss of inherent capacity.

4.5 Limitations and problems along the conduction of the study

This thesis, based on the prospective study „*Vun nix kütt nix*“ and the derived secondary analysis of course have its limitations as well. First, with 110 patients and 97 included into the secondary analysis, the study population was relatively small, although the lost-to-follow-up rate was low. Despite the limited sample size, the cohort was thoroughly characterized and highly phenotyped^{155,156} and multiple results align well with existing evidence from the literature.

Another noteworthy limitation is the relatively short follow-up period of 6 months. This however was predetermined as per the original study design. While this time frame allows the assessment of short- to mid-term outcomes, it may be insufficient to fully capture the long-term trajectory of sarcopenia, particularly with regard to sustained functional decline and mortality. It should be noted, however, that a large proportion of existing sarcopenia research is based

on cross-sectional designs, which do not permit longitudinal outcome assessment at all. In this context, the scarcity of long-term, well-characterized longitudinal studies—especially in acutely ill and hospitalized populations—highlights a significant gap in current knowledge and underscores the need for future investigations with extended follow-up periods to better delineate the long-term consequences of sarcopenia.

Third, the evaluation of sarcopenia and its influence on prognosis was one of many subcategories that were analyzed in the study. The most important aim of the randomized clinical trial was to explore in which way a tailored intersectoral discharge program can influence rehospitalization days, frailty and PROMs. As the idea of inquiring sarcopenia in a more detailed way than only collecting the SARC-F score, was developed only shortly before the start of the study, the BIA-device was not operational for the first included patients. This unfortunately lead to missing body composition values of the first 4 patients, who therefore could not be included in the stepwise subdivision that is based on BIA-based data in the last step and had to be excluded in the secondary analysis. Patients with pacemaker, being a contradiction for the performance of a BIA measurement, lead to further missing values of the body composition of our study sample.

Furthermore, one could argue that the reliability of patient statements in self-answered questionnaires can be a general weakness compared to number-based, standardized examinations. Nevertheless, self-reported and interview-guided questionnaires have wide usage and are well established in geriatric research and can give a solid overview²⁰⁰.

Another limitation is that we performed only one single BIA-measurement on every patient, although multiple (at least 2) measurements over the period of the clinic stay would have given a more detailed overview of the body composition. Also, only BIA-results were used to estimate muscle mass. As BIA-measurement is extremely susceptible to interference and is highly depending on the hydrogenation state, measurement can come with high error rate in patients with altered body composition (for example in patients with edema due to cardiac insufficiency). In case of disturbances in the patient's fluid balance, the measured values in BIA are of very limited use. Accordingly, to use the measured values more reliably, it would be useful to include another diagnostic measure to assess muscle mass, such as DXA, CT or MRI. These, on the other hand, are more expensive and not as quickly and easily accessible and therefore not suitable for a fast, uncomplicated diagnosis.

However, as already mentioned, a general weakness in the scientific setting regarding sarcopenia however is the inconsistency when it comes to definition and diagnostic steps. Despite the publication of definitions that clarify deteriorated muscle function as a condition for

diagnosis, sarcopenia continues to be used synonymously with pure loss of muscle mass in many studies, and different diagnostic tools are in use. This lack of worldwide consensus between widely used definitions is of course still hindering both the field of research and the incorporation of sarcopenia into clinical practice. With the use of the EWGSOP2 criteria for definition and diagnostic of sarcopenia, we used, to our knowledge, the most recent, elaborated and conferrable version.

Finally, if we consider the follow-up data, we unfortunately have no data regarding sarcopenia or its evolution after discharge. It could have been of great interest to gather this information even after the hospitalization, for example by monitoring the SARC-F score by telephone to get a quick overview regarding the patients' current status. Further studies with larger study population, longer and more sarcopenia-focused follow-up therefore seem to be necessary to confirm our findings.

4.6 Conclusion and research outlook

The randomized controlled study "*Vun nix kütt nix*" showed the significant improving effect that TIDP can have both on prognosis, assessed by MPI and mood in advanced age. Within this context, it is important to underline again that the MPI is known to be highly accurate in monitoring overall health trajectories of older patients during hospitalization¹². Together with the reported high prevalence of sarcopenia in deeply phenotyped patients, the present analyses uncovered the clinical relevance of sarcopenia by quantifying using PROMs and of a well-established CGA-based measurement of prognosis and multidimensional frailty. However, further research using the established diagnostic criteria for sarcopenia would be necessary to investigate if additional in-hospital exercise and/or nutritional interventions or rehabilitation programs tailored to the individual, sarcopenia-linked status could have a preventive effect on the further clinical and outpatient outcome. Further research contributing to the development of effective interventions to prevent or treat muscle loss in geriatric patients is of crucial importance and an even better understanding of the underlying mechanisms would help to finally establish a globally accepted definition with clear diagnostic tools and cut-offs. The growing attention that sarcopenia has received in recent years is a positive development suggesting that more progress can be expected in the field in the years to come. This sustained focus on the condition also implies that the efforts to improve early detection are likely to yield positive results soon and the outlook for improving patient outcomes and enhancing quality of life for those affected by sarcopenia is encouraging.

In conclusion, this work highlights that sarcopenia is strongly linked to multidimensional prognostic indicators, patient-reported outcomes, and adverse clinical events, underscoring its relevance as a prognostic factor in older hospitalized patients. Recognizing sarcopenia in routine practice may therefore support informed, shared decision-making and individualized care planning. Given the high and rising prevalence of sarcopenia among older adults, coupled with its frequent underdiagnosis^{148,201}, the implementation of standardized diagnostic criteria—such as those recently established—offers an essential framework for early detection and systematic management of this disabling condition. While global consensus on diagnostic thresholds and assessment methods is still evolving, the present findings contribute to a growing body of evidence that can guide future research and help develop more effective strategies to preserve function, independence, and quality of life in this vulnerable population. Even if there is still a certain way to go to achieve a global consensus, new avenues of research have been opened and with a more comprehensive understanding of the condition, better management strategies can be found.

5. References

1. Betty Friedan Quotes. . (n.d.). <https://allauthor.com/quote/7628/>.
 2. Rainer R. Lebenserwartung in Deutschland bei Geburt nach Geschlecht. 2022. <https://de.statista.com/statistik/daten/studie/273406/umfrage/entwicklung-der-lebenserwartung-bei-geburt-in-deutschland-nach-geschlecht/> (accessed 02.01.2023 2023).
 3. (2020) EU. Health at glance, 2020.
 4. Steves CJ, Spector TD, Jackson SHD. Ageing, genes, environment and epigenetics: what twin studies tell us now, and in the future. *Age and Ageing* 2012; **41**(5): 581-6.
 5. Rose MR, Flatt T, Graves JL, et al. What is aging? *Frontiers in genetics* 2012; **3**: 134.
 6. Booth Lauren N, Brunet A. The Aging Epigenome. *Molecular Cell* 2016; **62**(5): 728-44.
 7. Bardenheier BH, Lin J, Zhuo X, et al. Disability-free life-years lost among adults aged ≥ 50 years with and without diabetes. *Diabetes care* 2016; **39**(7): 1222-9.
 8. Nolte E, Knai C, Saltman R. Assessing chronic disease management in European health systems. Concepts and approaches. 2014.
 9. Wieland D, Hirth V. Comprehensive Geriatric Assessment. *Cancer Control* 2003; **10**(6): 454-62.
 10. Polidori MC. Comprehensive geriatric assessment in patients with cognitive decline. *Comprehensive geriatric assessment* 2018: 159-67.
 11. Ellis G, Whitehead MA, Robinson D, O'Neill D, Langhorne P. Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. *Bmj* 2011; **343**.
 12. Meyer AM, Becker I, Siri G, et al. New associations of the Multidimensional Prognostic Index. *Zeitschrift für Gerontologie und Geriatrie* 2019; **52**(5): 460-7.
 13. Giantin V, Valentini E, Iasevoli M, et al. Does the Multidimensional Prognostic Index (MPI), based on a Comprehensive Geriatric Assessment (CGA), predict mortality in cancer patients? Results of a prospective observational trial. *Journal of geriatric oncology* 2013; **4**(3): 208-17.
 14. Cammalleri V, Bonanni M, Buetti FM, et al. Multidimensional Prognostic Index (MPI) in elderly patients with acute myocardial infarction. *Aging Clinical and Experimental Research* 2021; **33**(7): 1875-83.
 15. Bureau M-L, Liuu E, Christiaens L, et al. Using a multidimensional prognostic index (MPI) based on comprehensive geriatric assessment (CGA) to predict mortality in elderly undergoing transcatheter aortic valve implantation. *International journal of cardiology* 2017; **236**: 381-6.
 16. Pilotto A, Panza F, Sancarlo D, Paroni G, Maggi S, Ferrucci L. Usefulness of the multidimensional prognostic index (MPI) in the management of older patients with chronic kidney disease. *J Nephrol* 2012; **25**(Suppl 19): S79-S84.
 17. Evert J, Lawler E, Bogan H, Perls T. Morbidity Profiles of Centenarians: Survivors, Delayers, and Escapers. *The Journals of Gerontology: Series A* 2003; **58**(3): M232-M7.
 18. Ritch A. History of geriatric medicine: from Hippocrates to Marjory Warren. *JR Coll Physicians Edinb* 2012; **42**(4): 368-74.
 19. Nascher J. Geriatrics. *NY Med J*; **1909**; **90**: 358-359.
 20. Warren MW. Care of chronic sick. *British Medical Journal* 1943; **2**(4329): 822.
 21. Warren MW. Rehabilitation of the elderly patient. *Ann Phys Med* 1960; **5**: 170-81.
 22. St. John PD, Hogan DB. The relevance of Marjory Warren's writings today. *The Gerontologist* 2014; **54**(1): 21-9.
 23. Institute of Medicine Committee on Quality of Health Care in A. Crossing the Quality Chasm: A New Health System for the 21st Century. Washington (DC): National Academies Press (US)
- Copyright 2001 by the National Academy of Sciences. All rights reserved.; 2001.
24. Wolfe A. Institute of Medicine Report: Crossing the Quality Chasm: A New Health Care System for the 21st Century. *Policy, Politics, & Nursing Practice* 2001; **2**(3): 233-5.

25. Guyatt G, Montori V, Devereaux P, Schunemann H, Bhandari M. Patients at the center: in our practice, and in our use of language. *ACP journal club* 2004; **140**(1): A11.
26. Rathert C, Wyrwich MD, Boren SA. Patient-centered care and outcomes: a systematic review of the literature. *Medical Care Research and Review* 2013; **70**(4): 351-79.
27. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. *The Lancet* 2019; **394**(10206): 1365-75.
28. Zampino M, Polidori MC, Ferrucci L, et al. Biomarkers of aging in real life: three questions on aging and the comprehensive geriatric assessment. *GeroScience* 2022; **44**(6): 2611-22.
29. Morley JE, Haren MT, Rolland Y, Kim MJ. Frailty. *Medical Clinics* 2006; **90**(5): 837-47.
30. Fried LP, Tangen CM, Walston J, et al. Frailty in Older Adults: Evidence for a Phenotype. *The Journals of Gerontology: Series A* 2001; **56**(3): M146-M57.
31. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *The lancet* 2013; **381**(9868): 752-62.
32. Pilotto A, Custodero C, Maggi S, Polidori MC, Veronese N, Ferrucci L. A multidimensional approach to frailty in older people. *Ageing Research Reviews* 2020; **60**: 101047.
33. Wleklik M, Uchmanowicz I, Jankowska EA, et al. Multidimensional Approach to Frailty. *Frontiers in Psychology* 2020; **11**.
34. Rockwood K, Mitnitski A. Frailty in Relation to the Accumulation of Deficits. *The Journals of Gerontology: Series A* 2007; **62**(7): 722-7.
35. Gill TM, Gahbauer EA, Allore HG, Han L. Transitions Between Frailty States Among Community-Living Older Persons. *Archives of Internal Medicine* 2006; **166**(4): 418-23.
36. Handforth C, Clegg A, Young C, et al. The prevalence and outcomes of frailty in older cancer patients: a systematic review. *Annals of oncology* 2015; **26**(6): 1091-101.
37. Kojima G, Iliffe S, Walters K. Frailty index as a predictor of mortality: a systematic review and meta-analysis. *Age and ageing* 2018; **47**(2): 193-200.
38. Kim S-w, Han H-S, Jung H-w, et al. Multidimensional frailty score for the prediction of postoperative mortality risk. *JAMA surgery* 2014; **149**(7): 633-40.
39. Kojima G. Frailty as a predictor of future falls among community-dwelling older people: a systematic review and meta-analysis. *Journal of the American Medical Directors Association* 2015; **16**(12): 1027-33.
40. At J, Bryce R, Prina M, et al. Frailty and the prediction of dependence and mortality in low- and middle-income countries: a 10/66 population-based cohort study. *BMC medicine* 2015; **13**(1): 1-12.
41. Kojima G. Frailty as a predictor of disabilities among community-dwelling older people: a systematic review and meta-analysis. *Disability and rehabilitation* 2017; **39**(19): 1897-908.
42. Soysal P, Veronese N, Thompson T, et al. Relationship between depression and frailty in older adults: a systematic review and meta-analysis. *Ageing research reviews* 2017; **36**: 78-87.
43. Hoogendijk EO, Suanet B, Dent E, Deeg DJ, Aartsen MJ. Adverse effects of frailty on social functioning in older adults: Results from the Longitudinal Aging Study Amsterdam. *Maturitas* 2016; **83**: 45-50.
44. Kojima G. Frailty as a predictor of hospitalisation among community-dwelling older people: a systematic review and meta-analysis. *J Epidemiol Community Health* 2016; **70**(7): 722-9.
45. Morley JE. Frailty and sarcopenia: the new geriatric giants. *Revista de investigacion clinica* 2016; **68**(2): 59-67.
46. Bernabei R, Martone AM, Vetrano DL, Calvani R, Landi F, Marzetti E. Frailty, physical frailty, sarcopenia: a new conceptual model. *Active Ageing and Healthy Living* 2014: 78-84.
47. Cesari M, Landi F, Vellas B, Bernabei R, Marzetti E. Sarcopenia and physical frailty: two sides of the same coin. *Frontiers in aging neuroscience* 2014; **6**: 192.
48. Jiang S, Li P. Current Development in Elderly Comprehensive Assessment and Research Methods. *BioMed Research International* 2016; **2016**: 3528248.
49. Rodin MB, Mohile SG. A practical approach to geriatric assessment in oncology. *Journal of Clinical Oncology* 2007; **25**(14): 1936-44.

50. Rubenstein LZ, Stuck AE, Siu AL, Wieland D. Impacts of Geriatric Evaluation and Management Programs on Defined Outcomes: Overview of the Evidence. *Journal of the American Geriatrics Society* 1991; **39**(S1): 8S-16S.
51. Ellis G, Gardner M, Tsiachristas A, et al. Comprehensive geriatric assessment for older adults admitted to hospital. *Cochrane Database of Systematic Reviews* 2017; (9).
52. Pilotto A, Martin FC. Comprehensive geriatric assessment: Springer; 2017.
53. Ward KT, Reuben DB. Comprehensive geriatric assessment. *UpToDate2013* <http://www.uptodate.com/contents/comprehensive-geriatric-assessment> 2016.
54. Kuo H-K, Scandrett KG, Dave J, Mitchell SL. The influence of outpatient comprehensive geriatric assessment on survival: a meta-analysis. *Archives of gerontology and geriatrics* 2004; **39**(3): 245-54.
55. Stuck AE, Siu AL, Wieland GD, Rubenstein L, Adams J. Comprehensive geriatric assessment: a meta-analysis of controlled trials. *The Lancet* 1993; **342**(8878): 1032-6.
56. Pilotto A, Ferrucci L, Franceschi M, et al. Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. *Rejuvenation research* 2008; **11**(1): 151-61.
57. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *The gerontologist* 1970; **10**(1_Part_1): 20-30.
58. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *The gerontologist* 1969; **9**(3_Part_1): 179-86.
59. Linn BS, Linn MW, Gurel L. Cumulative illness rating scale. *Journal of the American Geriatrics Society* 1968; **16**(5): 622-6.
60. Bliss MR, McLaren R, Exton-Smith AN. Mattresses for preventing pressure sores in geriatric patients. *Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service* 1966; **25**: 238-68.
61. Sancarlo D, D'Onofrio G, Franceschi M, et al. Validation of a Modified-Multidimensional Prognostic Index (m-MPI) including the Mini Nutritional Assessment Short-Form (MNA-SF) for the prediction of one-year mortality in hospitalized elderly patients. *The journal of nutrition, health & aging* 2011; **15**(3): 169-73.
62. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *Journal of the American Geriatrics Society* 1975; **23**(10): 433-41.
63. Pilotto A, Rengo F, Marchionni N, et al. Comparing the prognostic accuracy for all-cause mortality of frailty instruments: a multicentre 1-year follow-up in hospitalized older patients. *PloS one* 2012; **7**(1): e29090.
64. Brunello A, Fontana A, Zafferri V, et al. Development of an oncological-multidimensional prognostic index (Onco-MPI) for mortality prediction in older cancer patients. *Journal of cancer research and clinical oncology* 2016; **142**(5): 1069-77.
65. Lai S, Amabile MI, Mazzaferro S, et al. Association between multidimensional prognostic index and hospitalization and mortality among older adults with chronic kidney disease on conservative or on replacement therapy. *Journal of Clinical Medicine* 2020; **9**(12): 3965.
66. Bielecki K, Kamiński P, Klukowski M. Large bowel perforation: morbidity and mortality. *Techniques in coloproctology* 2002; **6**(3): 177-82.
67. Morley JE, Malmstrom TK, Rodriguez-Mañas L, Sinclair AJ. Frailty, sarcopenia and diabetes. *Journal of the American Medical Directors Association* 2014; **15**(12): 853-9.
68. Kinney JM. Nutritional frailty, sarcopenia and falls in the elderly. *Current Opinion in Clinical Nutrition & Metabolic Care* 2004; **7**(1): 15-20.
69. Aging Nlo. National Institute on Aging: Department of Health, Education, and Welfare, Public Health Service ...; 1978.
70. Rosenberg IH. Sarcopenia: origins and clinical relevance. *J Nutr* 1997; **127**(5 Suppl): 990s-1s.
71. Muscaritoli M, Anker S, Argilés J, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups (SIG) "cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics". *Clinical nutrition* 2010; **29**(2): 154-9.

72. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis. Report of the European Working Group on Sarcopenia in Older People. *Age and ageing* 2010; **39**(4): 412-23.
73. Chen L-K, Liu L-K, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. *Journal of the American Medical Directors Association* 2014; **15**(2): 95-101.
74. Goodpaster BH, Park SW, Harris TB, et al. The Loss of Skeletal Muscle Strength, Mass, and Quality in Older Adults: The Health, Aging and Body Composition Study. *The Journals of Gerontology: Series A* 2006; **61**(10): 1059-64.
75. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age and Ageing* 2010; **39**(4): 412-23.
76. Fielding RA, Vellas B, Evans WJ, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *Journal of the American Medical Directors Association* 2011; **12**(4): 249-56.
77. Morley JE, Abbatecola AM, Argiles JM, et al. Sarcopenia with limited mobility: an international consensus. *Journal of the American Medical Directors Association* 2011; **12**(6): 403-9.
78. Hillienhof A. Sarkopenie: Neuer Diagnoseschlüssel für altersbedingten Muskelabbau. *Dtsch Arztebl International* 2018; **115**(8): 352.
79. Anker SD, Morley JE, von Haehling S. Welcome to the ICD-10 code for sarcopenia. *J Cachexia Sarcopenia Muscle* 2016; **7**(5): 512-4.
80. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age and ageing* 2019; **48**(1): 16-31.
81. Global Leadership Initiative in Sarcopenia - GLIS.
<https://www.eugms.org/news/read/article/661.html>.
82. Sayer AA, Cruz-Jentoft A. Sarcopenia definition, diagnosis and treatment: consensus is growing. *Age Ageing* 2022; **51**(10).
83. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *The Lancet* 2019; **393**(10191): 2636-46.
84. Berger MJ, Doherty TJ. Sarcopenia: prevalence, mechanisms, and functional consequences. *Body composition and aging* 2010; **37**: 94-114.
85. Starr KNP, McDonald SR, Bales CW. Obesity and Physical Frailty in Older Adults: A Scoping Review of Lifestyle Intervention Trials. *Journal of the American Medical Directors Association* 2014; **15**(4): 240-50.
86. Shafiee G, Keshtkar A, Soltani A, Ahadi Z, Larijani B, Heshmat R. Prevalence of sarcopenia in the world: a systematic review and meta-analysis of general population studies. *Journal of Diabetes & Metabolic Disorders* 2017; **16**(1): 1-10.
87. Von Haehling S, Morley JE, Anker SD. An overview of sarcopenia: facts and numbers on prevalence and clinical impact. *Journal of cachexia, sarcopenia and muscle* 2010; **1**(2): 129-33.
88. Phillips A, Strobl R, Vogt S, Ladwig K-H, Thorand B, Grill E. Sarcopenia is associated with disability status—results from the KORA-Age study. *Osteoporosis International* 2017; **28**(7): 2069-79.
89. Cruz-Jentoft AJ, Landi F, Schneider SM, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age and Ageing* 2014; **43**(6): 748-59.
90. Yazar T, Yazar HO. Prevalance of sarcopenia according to decade. *Clinical nutrition ESPEN* 2019; **29**: 137-41.
91. Shafiee G, Heshmat R, Ostovar A, et al. Comparison of EWGSOP-1 and EWGSOP-2 diagnostic criteria on prevalence of and risk factors for sarcopenia among Iranian older people: the Bushehr Elderly Health (BEH) program. *Journal of Diabetes & Metabolic Disorders* 2020; **19**(2): 727-34.
92. Gariballa S, Alessa A. Sarcopenia: prevalence and prognostic significance in hospitalized patients. *Clinical nutrition* 2013; **32**(5): 772-6.
93. Papadopoulou S, Tsintavis P, Potsaki G, Papandreou D. Differences in the prevalence of sarcopenia in community-dwelling, nursing home and hospitalized individuals. A systematic review and meta-analysis. *The journal of nutrition, health & aging* 2020; **24**(1): 83-90.

94. Rodríguez-Rejón AI, Ruiz-López MD, Wanden-Berghe C, Artacho R. Prevalence and diagnosis of sarcopenia in residential facilities: a systematic review. *Advances in Nutrition* 2019; **10**(1): 51-8.
95. Reiss J, Iglseider B, Alzner R, et al. Consequences of applying the new EWGSOP2 guideline instead of the former EWGSOP guideline for sarcopenia case finding in older patients. *Age and ageing* 2019; **48**(5): 719-24.
96. Stangl MK, Böcker W, Chubanov V, et al. Sarcopenia—endocrinological and neurological aspects. *Experimental and Clinical Endocrinology & Diabetes* 2019; **6**(01): 8-22.
97. III LJM, Khosla S, Crowson CS, O'Connor MK, O'Fallon WM, Riggs BL. Epidemiology of sarcopenia. *Journal of the American Geriatrics Society* 2000; **48**(6): 625-30.
98. Vandervoort AA. Aging of the human neuromuscular system. *Muscle Nerve* 2002; **25**(1): 17-25.
99. Lexell J, Taylor CC, Sjöström M. What is the cause of the ageing atrophy?: Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15-to 83-year-old men. *Journal of the neurological sciences* 1988; **84**(2-3): 275-94.
100. Fleg JL, Lakatta EG. Role of muscle loss in the age-associated reduction in VO₂ max. *Journal of applied physiology* 1988; **65**(3): 1147-51.
101. Janssen I, Heymsfield SB, Wang Z, Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. *Journal of applied physiology* 2000.
102. Buford TW, Anton SD, Judge AR, et al. Models of accelerated sarcopenia: critical pieces for solving the puzzle of age-related muscle atrophy. *Ageing research reviews* 2010; **9**(4): 369-83.
103. Nilwik R, Snijders T, Leenders M, et al. The decline in skeletal muscle mass with aging is mainly attributed to a reduction in type II muscle fiber size. *Experimental gerontology* 2013; **48**(5): 492-8.
104. Johnston AP, De Lisio M, Parise G. Resistance training, sarcopenia, and the mitochondrial theory of aging. *Applied physiology, nutrition, and metabolism* 2008; **33**(1): 191-9.
105. Marzetti E, Calvani R, Bernabei R, Leeuwenburgh C. Apoptosis in skeletal myocytes: a potential target for interventions against sarcopenia and physical frailty—a mini-review. *Gerontology* 2012; **58**(2): 99-106.
106. Degens H, Alway SE. Control of muscle size during disuse, disease, and aging. *International journal of sports medicine* 2006; **27**(02): 94-9.
107. Dickinson JM, Volpi E, Rasmussen BB. Exercise and Nutrition to Target Protein Synthesis Impairments in Aging Skeletal Muscle. *Exercise and Sport Sciences Reviews* 2013; **41**(4).
108. Burd NA, Gorissen SH, Van Loon LJ. Anabolic resistance of muscle protein synthesis with aging. *Exercise and sport sciences reviews* 2013; **41**(3): 169-73.
109. Ferrucci L, Penninx BWJH, Volpato S, et al. Change in Muscle Strength Explains Accelerated Decline of Physical Function in Older Women With High Interleukin-6 Serum Levels. *Journal of the American Geriatrics Society* 2002; **50**(12): 1947-54.
110. Tuttle CSL, Thang LAN, Maier AB. Markers of inflammation and their association with muscle strength and mass: A systematic review and meta-analysis. *Ageing Research Reviews* 2020; **64**: 101185.
111. Dayanidhi S, Lieber RL. Skeletal muscle satellite cells: mediators of muscle growth during development and implications for developmental disorders. *Muscle Nerve* 2014; **50**(5): 723-32.
112. McKay BR, Ogborn DI, Baker JM, Toth KG, Tarnopolsky MA, Parise G. Elevated SOCS3 and altered IL-6 signaling is associated with age-related human muscle stem cell dysfunction. *American Journal of Physiology-Cell Physiology* 2013; **304**(8): C717-C28.
113. Borja-Gonzalez M, Casas-Martinez JC, McDonagh B, Goljanek-Whysall K. Inflamma-miR-21 Negatively Regulates Myogenesis during Ageing. *Antioxidants* 2020; **9**(4): 345.
114. Bauer J, Morley JE, Schols AMWJ, et al. Sarcopenia: A Time for Action. An SCWD Position Paper. *Journal of Cachexia, Sarcopenia and Muscle* 2019; **10**(5): 956-61.
115. Narici MV, Maffulli N. Sarcopenia: characteristics, mechanisms and functional significance. *British Medical Bulletin* 2010; **95**(1): 139-59.

116. Sasaki K-i, Fukumoto Y. Sarcopenia as a comorbidity of cardiovascular disease. *Journal of Cardiology* 2022; **79**(5): 596-604.
117. Montero-Errasquín B, Cruz-Jentoft AJ. Acute Sarcopenia. *Gerontology* 2023; **69**(5): 519-25.
118. Dent E, Morley JE, Cruz-Jentoft AJ, et al. International Clinical Practice Guidelines for Sarcopenia (ICFSR): Screening, Diagnosis and Management. *The journal of nutrition, health & aging* 2018; **22**(10): 1148-61.
119. Malmstrom TK, Morley JE. SARC-F: a simple questionnaire to rapidly diagnose sarcopenia. *Journal of the American Medical Directors Association* 2013; **14**(8): 531-2.
120. Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. *Journal of cachexia, sarcopenia and muscle* 2016; **7**(1): 28-36.
121. Woo J, Leung J, Morley J. Defining sarcopenia in terms of incident adverse outcomes. *Journal of the American Medical Directors Association* 2015; **16**(3): 247-52.
122. Sacar DE, Kilic C, Karan M, Bahat G. Ability of SARC-F to find probable sarcopenia cases in older adults. *The journal of nutrition, health & aging* 2021; **25**(6): 757-61.
123. Bahat G, Yilmaz O, Kiliç C, Oren M, Karan M. Performance of SARC-F in regard to sarcopenia definitions, muscle mass and functional measures. *The journal of nutrition, health & aging* 2018; **22**(8): 898-903.
124. Bahat G, Yilmaz O, Oren MM, et al. Cross-cultural adaptation and validation of the SARC-F to assess sarcopenia: methodological report from European Union Geriatric Medicine Society Sarcopenia Special Interest Group. *European Geriatric Medicine* 2018; **9**(1): 23-8.
125. Drey M, Ferrari U, Schraml M, et al. German Version of SARC-F: Translation, Adaption, and Validation. *J Am Med Dir Assoc* 2020; **21**(6): 747-51.e1.
126. McGrath R, Johnson N, Klawitter L, et al. What are the association patterns between handgrip strength and adverse health conditions? A topical review. *SAGE Open Medicine* 2020; **8**: 2050312120910358.
127. Gopinath B, Kifley A, Liew G, Mitchell P. Handgrip strength and its association with functional independence, depressive symptoms and quality of life in older adults. *Maturitas* 2017; **106**: 92-4.
128. Buchman AS, Wilson RS, Boyle PA, Bienias JL, Bennett DA. Grip strength and the risk of incident Alzheimer's disease. *Neuroepidemiology* 2007; **29**(1-2): 66-73.
129. Leong DP, Teo KK, Rangarajan S, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *The Lancet* 2015; **386**(9990): 266-73.
130. McGrath RP, Kraemer WJ, Snih SA, Peterson MD. Handgrip strength and health in aging adults. *Sports medicine* 2018; **48**(9): 1993-2000.
131. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Research quarterly for exercise and sport* 1999; **70**(2): 113-9.
132. Tomczak J. Körperanalysen: Die bioelektrische Impedanzanalyse BIA. *FIT Wissenschaftsmagazin der Deutschen Sporthochschule Köln* 2003; **1**: 34-40.
133. Graf CE, Herrmann FR, Genton L. Relation of Disease with Standardized Phase Angle Among Older Patients. *The journal of nutrition, health & aging* 2018; **22**(5): 601-7.
134. Kushner RF, Gudivaka R, Schoeller DA. Clinical characteristics influencing bioelectrical impedance analysis measurements. *The American journal of clinical nutrition* 1996; **64**(3): 423S-7S.
135. Liang M, Norris S. Effects of skin blood flow and temperature on bioelectric impedance after exercise. *Medicine and science in sports and exercise* 1993; **25**(11): 1231-9.
136. Beaudart C, Rolland Y, Cruz-Jentoft AJ, et al. Assessment of muscle function and physical performance in daily clinical practice. *Calcified tissue international* 2019; **105**(1): 1-14.
137. Herman T, Giladi N, Hausdorff JM. Properties of the 'timed up and go' test: more than meets the eye. *Gerontology* 2011; **57**(3): 203-10.
138. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *Journal of the American geriatrics Society* 1991; **39**(2): 142-8.
139. Dodds RM, Syddall HE, Cooper R, et al. Grip strength across the life course: normative data from twelve British studies. *PloS one* 2014; **9**(12): e113637.

140. Gould H, Brennan SL, Kotowicz MA, Nicholson GC, Pasco JA. Total and appendicular lean mass reference ranges for Australian men and women: the Geelong osteoporosis study. *Calcified tissue international* 2014; **94**(4): 363-72.
141. Bischoff HA, Stähelin HB, Monsch AU, et al. Identifying a cut-off point for normal mobility: a comparison of the timed 'up and go' test in community-dwelling and institutionalised elderly women. *Age and ageing* 2003; **32**(3): 315-20.
142. Liebendörfer A. DGIM 2017 - Altersproblem Muskelabbau wird oft unterschätzt. 2017.
143. Bruyère O, Beaudart C, Ethgen O, Reginster J-Y, Locquet M. The health economics burden of sarcopenia: a systematic review. *Maturitas* 2019; **119**: 61-9.
144. Beaudart C, Rizzoli R, Bruyère O, Reginster J-Y, Biver E. Sarcopenia: burden and challenges for public health. *Archives of Public Health* 2014; **72**(1): 1-8.
145. Yeung SS, Reijnierse EM, Pham VK, et al. Sarcopenia and its association with falls and fractures in older adults: a systematic review and meta-analysis. *Journal of cachexia, sarcopenia and muscle* 2019; **10**(3): 485-500.
146. Landi F, Liperoti R, Russo A, et al. Sarcopenia as a risk factor for falls in elderly individuals: results from the iSIRENTE study. *Clinical nutrition* 2012; **31**(5): 652-8.
147. Dos Santos L, Cyrino ES, Antunes M, Santos DA, Sardinha LB. Sarcopenia and physical independence in older adults: the independent and synergic role of muscle mass and muscle function. *Journal of cachexia, sarcopenia and muscle* 2017; **8**(2): 245-50.
148. Beaudart C, Zaaria M, Pasleau F, Reginster J-Y, Bruyère O. Health outcomes of sarcopenia: a systematic review and meta-analysis. *PloS one* 2017; **12**(1): e0169548.
149. Mijnders D, Luiking Y, Halfens R, et al. Muscle, health and costs: a glance at their relationship. *The journal of nutrition, health & aging* 2018; **22**(7): 766-73.
150. Janssen I, Shepard DS, Katzmarzyk PT, Roubenoff R. The healthcare costs of sarcopenia in the United States. *Journal of the American Geriatrics Society* 2004; **52**(1): 80-5.
151. Joglekar S, Nau PN, Mezhr JJ. The impact of sarcopenia on survival and complications in surgical oncology: a review of the current literature. *Journal of surgical oncology* 2015; **112**(5): 503-9.
152. Wong L, Duque G, McMahon LP. Sarcopenia and frailty: challenges in mainstream nephrology practice. *Kidney International Reports* 2021; **6**(10): 2554-64.
153. Hollingworth TW, Oke SM, Patel H, Smith TR. Getting to grips with sarcopenia: Recent advances and practical management for the gastroenterologist. *Frontline Gastroenterology* 2021; **12**(1): 53-61.
154. Bruyère O, Beaudart C, Reginster J-Y, et al. Assessment of muscle mass, muscle strength and physical performance in clinical practice: an international survey. *European Geriatric Medicine* 2016; **7**(3): 243-6.
155. Ferring A, Mück L, Stegemann J, et al. Prognostic features of sarcopenia in older hospitalized patients: a 6-month follow-up study. *Journal of Clinical Medicine* 2024; **13**(11): 3116.
156. Meyer AM, Bartram MP, Antczak P, Becker I, Benzing T, Polidori MC. A Tailored Discharge Program Improves Frailty and Mood in Patients Undergoing Usual Rehabilitative Care: A Randomized Controlled Trial. *Journal of the American Medical Directors Association* 2022; **23**(12): 1962. e1-. e13.
157. Yang M, Liu Y, Zuo Y, Tang H. Sarcopenia for predicting falls and hospitalization in community-dwelling older adults: EWGSOP versus EWGSOP2. *Scientific reports* 2019; **9**(1): 17636.
158. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. *The Lancet* 2019; **394**(10206): 1376-86.
159. Nordin E, Lindelöf N, Rosendahl E, Jensen J, Lundin-olsson L. Prognostic validity of the Timed Up-and-Go test, a modified Get-Up-and-Go test, staff's global judgement and fall history in evaluating fall risk in residential care facilities. *Age and Ageing* 2008; **37**(4): 442-8.
160. Bhatt T, Espy D, Yang F, Pai Y-C. Dynamic Gait Stability, Clinical Correlates, and Prognosis of Falls Among Community-Dwelling Older Adults. *Archives of Physical Medicine and Rehabilitation* 2011; **92**(5): 799-805.

161. Hofheinz M, Mibs M. The prognostic validity of the timed up and go test with a dual task for predicting the risk of falls in the elderly. *Gerontology and geriatric medicine* 2016; **2**: 2333721416637798.
162. Cruz-Jentoft AJ, Kiesswetter E, Drey M, Sieber CC. Nutrition, frailty, and sarcopenia. *Aging Clin Exp Res* 2017; **29**(1): 43-8.
163. Robinson SM, Reginster J-Y, Rizzoli R, et al. Does nutrition play a role in the prevention and management of sarcopenia? *Clinical Nutrition* 2018; **37**(4): 1121-32.
164. Bahat G, Tufan A, Kilic C, Karan MA, Cruz-Jentoft AJ. Prevalence of sarcopenia and its components in community-dwelling outpatient older adults and their relation with functionality. *The Aging Male* 2020; **23**(5): 424-30.
165. Tanimoto Y, Watanabe M, Sun W, et al. Association of sarcopenia with functional decline in community-dwelling elderly subjects in Japan. *Geriatrics & gerontology international* 2013; **13**(4): 958-63.
166. Wang DX, Yao J, Zirek Y, Reijnierse EM, Maier AB. Muscle mass, strength, and physical performance predicting activities of daily living: a meta-analysis. *Journal of cachexia, sarcopenia and muscle* 2020; **11**(1): 3-25.
167. Janssen I, Heymsfield SB, Ross R. Low Relative Skeletal Muscle Mass (Sarcopenia) in Older Persons Is Associated with Functional Impairment and Physical Disability. *Journal of the American Geriatrics Society* 2002; **50**(5): 889-96.
168. Rantanen T. Muscle strength, disability and mortality. *Scandinavian journal of medicine & science in sports* 2003; **13**(1): 3-8.
169. Janssen I. Influence of Sarcopenia on the Development of Physical Disability: The Cardiovascular Health Study. *Journal of the American Geriatrics Society* 2006; **54**(1): 56-62.
170. Hirani V, Blyth F, Naganathan V, et al. Sarcopenia is associated with incident disability, institutionalization, and mortality in community-dwelling older men: the concord health and ageing in men project. *Journal of the American Medical Directors Association* 2015; **16**(7): 607-13.
171. Xu J, Wan CS, Ktoris K, Reijnierse EM, Maier AB. Sarcopenia is associated with mortality in adults: a systematic review and meta-analysis. *Gerontology* 2022; **68**(4): 361-76.
172. Bijlsma AY, Pasma JH, Lambers D, et al. Muscle strength rather than muscle mass is associated with standing balance in elderly outpatients. *Journal of the American Medical Directors Association* 2013; **14**(7): 493-8.
173. Muir SW, Berg K, Chesworth B, Klar N, Speechley M. Quantifying the magnitude of risk for balance impairment on falls in community-dwelling older adults: a systematic review and meta-analysis. *Journal of clinical epidemiology* 2010; **63**(4): 389-406.
174. Bianchi L, Maietti E, Abete P, et al. Comparing EWGSOP2 and FNIH Sarcopenia Definitions: Agreement and 3-Year Survival Prognostic Value in Older Hospitalized Adults: The GLISTEN Study. *The Journals of Gerontology: Series A* 2019; **75**(7): 1331-7.
175. Malafarina V, Malafarina C, Baiñ Ugarte A, Martinez JA, Abete Goñi I, Zulet MA. Factors Associated with Sarcopenia and 7-Year Mortality in Very Old Patients with Hip Fracture Admitted to Rehabilitation Units: A Pragmatic Study. *Nutrients* 2019; **11**(9): 2243.
176. Suzan V, Kanat BB, Yavuzer H. Association of sarcopenia with geriatric syndromes and neutrophil/lymphocyte ratio. *Medicine* 2022; **11**(2): 645-50.
177. Ates Bulut E, Soysal P, Isik AT. Frequency and coincidence of geriatric syndromes according to age groups: single-center experience in Turkey between 2013 and 2017. *Clin Interv Aging* 2018; **13**: 1899-905.
178. Bennett A, Gnjdjic D, Gillett M, et al. Prevalence and impact of fall-risk-increasing drugs, polypharmacy, and drug-drug interactions in robust versus frail hospitalised falls patients: a prospective cohort study. *Drugs & aging* 2014; **31**(3): 225-32.
179. Baake. Begutachtungsverfahren NBA - Pflegegrad bei Erwachsenen In: Fachverlag W, ed.: Baake C.; 2017.
180. Meyer AM, Becker I, Siri G, et al. The prognostic significance of geriatric syndromes and resources. *Aging Clinical and Experimental Research* 2020; **32**(1): 115-24.

181. Lee S-Y, Tung H-H, Peng L-N, Chen L-K, Hsu C-I, Huang Y-L. Resilience among older cardiovascular disease patients with probable sarcopenia. *Archives of gerontology and geriatrics* 2020; **86**: 103939.
182. Li Z, Tong X, Ma Y, Bao T, Yue J. Prevalence of depression in patients with sarcopenia and correlation between the two diseases: systematic review and meta-analysis. *Journal of cachexia, sarcopenia and muscle* 2022; **13**(1): 128-44.
183. Tsekoura M, Kastrinis A, Katsoulaki M, Billis E, Gliatis J. Sarcopenia and its impact on quality of life. *GeNeDis 2016: Genetics and Neurodegeneration* 2017: 213-8.
184. Guerrero-Escobedo P, Tamez-Rivera O, Amieva H, Avila-Funes JA. Frailty is associated with low self-esteem in elderly adults. *Journal of the American Geriatrics Society* 2014; **62**(2): 396-8.
185. Heppner H. Soft skills: somewhat different doping. *Zeitschrift für Gerontologie und Geriatrie* 2018; **51**: 160-4.
186. Beswick AD, Rees K, Dieppe P, et al. Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis. *The Lancet* 2008; **371**(9614): 725-35.
187. Mercer S, Furler J, Moffat K, Fischbacher-Smith D, Sanci L. Multimorbidity: technical series on safer primary care: World Health Organization; 2016.
188. Brugliera L, Giordani A, D'Angelo G, et al. Prevalence of Sarcopenia in Older Patients in Rehabilitation Wards. *Journal of Personalized Medicine* 2023; **13**(6): 960.
189. Mesinovic J, Zengin A, De Courten B, Ebeling PR, Scott D. Sarcopenia and type 2 diabetes mellitus: a bidirectional relationship. *Diabetes, metabolic syndrome and obesity: targets and therapy* 2019: 1057-72.
190. Kim Y, Han B-D, Han K, et al. Optimal cutoffs for low skeletal muscle mass related to cardiovascular risk in adults: The Korea National Health and Nutrition Examination Survey 2009–2010. *Endocrine* 2015; **50**: 424-33.
191. Rom O, Kaisari S, Aizenbud D, Reznick AZ. Lifestyle and sarcopenia—etiology, prevention, and treatment. *Rambam Maimonides medical journal* 2012; **3**(4).
192. Huemer M-T, Kluttig A, Fischer B, et al. Grip strength values and cut-off points based on over 200,000 adults of the German National Cohort - a comparison to the EWGSOP2 cut-off points. *Age and Ageing* 2023; **52**(1).
193. Lima SS, Máximo RO, Luiz MM, et al. How does the cut-off point for grip strength affect the prevalence of sarcopenia and associated factors? Findings from the ELSI-Brazil Study. *Cad Saude Publica* 2025; **41**(5): e00155624.
194. Hanna-Deschamps E, Herrmann FR, Chirouzes D, et al. Sarcopenia in Hospitalized Older Adults: A Cross-Sectional Study Comparing Diagnostic Thresholds and Handgrip Strength Measurement Tools. *Geriatrics (Basel)* 2026; **11**(1).
195. Pedauyú-Rueda B, García-Fernández P, Maicas-Pérez L, Maté-Muñoz JL, Hernández-Lougedo J. Different Diagnostic Criteria for Determining the Prevalence of Sarcopenia in Older Adults: A Systematic Review. *Journal of Clinical Medicine* 2024; **13**(9): 2520.
196. Stuck AK, Basile G, Freystaetter G, de Godoi Rezende Costa Molino C, Lang W, Bischoff-Ferrari HA. Predictive validity of current sarcopenia definitions (EWGSOP2, SDOC, and AWGS2) for clinical outcomes: A scoping review. *Journal of cachexia, sarcopenia and muscle* 2023; **14**(1): 71-83.
197. Bernabei R, Landi F, Calvani R, et al. Multicomponent intervention to prevent mobility disability in frail older adults: randomised controlled trial (SPRINTT project). *Bmj* 2022; **377**: e068788.
198. Smoliner C, Sieber CC, Wirth R. Prevalence of sarcopenia in geriatric hospitalized patients. *Journal of the American Medical Directors Association* 2014; **15**(4): 267-72.
199. Reiss J, Iglseider B, Alzner R, et al. Sarcopenia and osteoporosis are interrelated in geriatric inpatients. *Zeitschrift für Gerontologie und Geriatrie* 2019; **52**(7): 688.
200. Schofield P. The Assessment of Pain in Older People: UK National Guidelines. *Age and Ageing* 2018; **47**(suppl_1): i1-i22.
201. Coletta G, Phillips SM. An elusive consensus definition of sarcopenia impedes research and clinical treatment: A narrative review. *Ageing Research Reviews* 2023; **86**: 101883.

6. Supplements

List of figures

- Figure 1: SARC-F questionnaire used in the study
- Figure 2: Diagnostic algorithm of the EWGSOP2 consensus
- Figure 3: Cut-off points for sarcopenia on the basis of EWGSOP2 consensus, by Cruz-Jentoft et al.

Publications (as first author)

- 05/2021 Ferring, A., Stegemann, J., Meyer, A.M. ANCA-assozierte Vaskulitis beim älteren Patienten. Zeitschrift für Gerontologie und Geriatrie, März 2021.

Publications (Data collection)

- 11/2021 Meyer AM, Polidori MC. Ratgeber Altern: Leitfaden für Gesundheit und Wohlbefinden im Alter: Elsevier Health Sciences; 2021.
- 12/2022 Meyer AM, Bartram MP, Antczak P, Becker I, Benzing T, Polidori MC. A Tailored Discharge Program Improves Frailty and Mood in Patients Undergoing Usual Rehabilitative Care: A Randomized Controlled Trial. J Am Med Dir Assoc 2022.

Poster presentations (as first author)

- 10/2020 Instabilität und reduzierte Alltagskompetenz bei ANCA-assoziierter Vaskulitis - ein Fallbericht aus der Altersmedizin. Ferring, A., Stegemann, J., Meyer, A.M., Benzing, T., Bartram, M.P., Polidori, M.C.
i.R. der 12. Jahrestagung der Deutschen Gesellschaft für Nephrologie DGfN, Onlinekongress 2020
- 09/2021 Verlauf von Depressionssymptomen und Selbstwirksamkeit älterer Patienten während der COVID-Pandemie. L. Mück, A. Ferring, J. Stegemann, L. Wiebe, M. C. Polidori Nelles, A. M. Meyer.
i.R. des 33. Jahreskongress der deutschen Gesellschaft für Geriatrie, Onlinekongress
- 06/2022 Verlauf von Depressionssymptomen und Selbstwirksamkeit älterer Patienten während der COVID-Pandemie. L. Mück, A. Ferring, J. Stegemann, L. Wiebe, M. C. Polidori Nelles, A. M. Meyer.

i.R. des 5th Cologne Symposium on Ageing Medicine 2022, Köln, Deutschland
04/2024 Prognostic features of sarcopenia according to the EWGSOP2 algorithm in older hospitalised patients: A 6-month follow-up study. Ferring A., Meyer AM., Mück L., Stegemann J., Wieber L., Becker I., Benzing T., Polidori MC.
i.R. des 131. Kongress der Deutschen Gesellschaft für Innere Medizin 2024, Wiesbaden, Deutschland.

Supplementary Material

Supplementary 1

Liebe Kolleginnen und Kollegen,
aufgrund der Pandemie können wir das Poster leider nicht
persönlich vor Ort präsentieren. Wir freuen uns aber über Ihr
Interesse und werden jede Rückmeldung gerne beantworten.
Zum **ZEITUM** für eine **Live-Präsentation** können Sie die Autorinnen
über **Zoom** für eine **Live-Präsentation** erreichen. Bitte scannen
Sie dazu den QR Code. Falls Sie Zoom noch nicht verwendet
haben, werden Sie aufgefordert, zunächst die kostenlose App zu
installieren.

Vielen Dank und bitte bleiben Sie gesund!
Während der Postersession erreichen Sie uns hier

 **Passwort: 123**

 **E-Mail Kontakt**

Einleitung

Bei Vaskuliden handelt es sich um Autoimmunerkrankungen, die sich in verschiedenen Organsystemen manifestieren können. Typischerweise sind im Falle einer ANCA-Vaskulitis aneuphorie zykloplasmatische Antikörper im Blut nachzuweisen. Aufgrund des inhomogenen Erscheinungsbildes einer ANCA-Vaskulitis wird die Diagnose bei älteren Patienten häufig erst nach längerem Krankheitsverlauf gestellt und die Therapie dementsprechend spät eingeleitet, oft erst nach der Entstehung erheblicher Folgeschäden. Dies kann gerade den funktionellen Status und die Alltagskompetenz älterer Patienten schwer beeinträchtigen.

Patientenvorstellung

Ein 80-Jähriger Patient wird nach rezidivierenden Episoden akuten Nierenversagens, hydropischer Dekompensation, Blutungen, Infekten, Verschlechterung des Allgemeinzustandes und der Alltagskompetenz zur Dialyseeinleitung in die universitäre Altersmedizin aufgenommen. Zuvor hat er 8 Monate mit wenigen Unterbrechungen fast durchgehend in diversen Krankenhäusern verbracht.

Klinik bei Aufnahme:

- o Urämische Enzephalopathie mit kognitiver Verschlechterung und Verwirrung
- o Chronisch blutig, borkige Sinusitis, Hämoptysen, Hämatochezie und Purpura
- o Milchglasinfiltrate im CT-Thorax
- o Verschlechterung der Alltagskompetenz (Barthel-Index 25) und Lebensqualität (EQ-5D-5L 0,225)
- o Multidimensional Prognostischer Index (MPI) 0,75 (hohes Risiko)
- o Steigende Retentionsparameter (Kreatinin 6,48 mg/dl)
- o Steigende Entzündungswerte (CRP 199,6 mg/l)
- o Diffuse Blutungen mit schwerer Anämie (Hb 7,1 g/dl)

Geriatrische Syndrome bei Aufnahme

Polypharmazie – Inkontinenz – Immobilität – Irritabilität/ Depression
– irritables Kolon – Flüssigkeits- und Elektrolystörungen – Inkontinenz/ Delirium

Instabilität und reduzierte Alltagskompetenz bei ANCA-assoziiierter Vaskulitis - ein Fallbericht aus der Altersmedizin

Anne Ferring¹, Jil Slegemann¹, Anna Maria Meyer¹, Thomas Bending^{1,2}, Malte P. Bartram¹

¹ Department II of Internal Medicine and Center for Molecular Medicine Cologne, University of Cologne ² Cologne Cluster of Excellence in Aging-associated Diseases, University of Cologne

*Equal first authors

Fallbericht

Verlauf: Bei Verdacht auf ANCA-Vaskulitis wird eine erweiterte rheumatologische Diagnostik abgenommen. Es können cANCA Subtyp PR3 nachgewiesen werden, welche eine hohe Spezifität für die Granulomatose mit Polyangiitis aufweisen. Die im Verlauf erfolgte Nierenbiopsie zeigt eine frisch nekrotisierende und extrakapillär proliferative Glomerulonephritis vom Pauciform-Typ mit bereits beginnender Atrophie und schwerem Tubulusschaden.

Diagnosestellung: Granulomatose mit Polyangiitis mit pulmonalem Syndrom

Therapie: Es erfolgt eine Induktionstherapie mit initialer Steroiddosis von 80mg Prednisolon p.o., sowie 1g Rituximab. Anschließend erfolgen 2 weitere Rituximab-Gaben, die der Patient gut verträgt. Ein Demerskatheter wird zur weiteren Dialyse gelegt.

Follow-Up: Initial waren häufiger Bluttransfusionen notwendig, eine nosokomiale Pneumonie wurde zudem antibiotisch therapiert. Unter pedanginösen Beschwerden und respiratorischer Insuffizienz befand sich der Patient für 4 Tage auf der Intensivstation. Unter der Therapie war die Infektion, das klinische Bild, sowie die Anämie rückläufig. Der initial bettlägerige Patient verbessert sich unter der geriatrischen Komplexbehandlung innerhalb von 3 Wochen funktionell deutlich (Barthel-Index 65 EQ-5D-5L 0,872). Der MPI betrug bei Entlassung 0,50 (mittleres Risiko). Es erfolgte eine Anschlussheilbehandlung und nach zwei weiteren Monaten ist der Patient wieder in der Lage selbstständig Treppen zu steigen. Nach Einleitung der Induktionstherapie stabilisiert und bessert sich im Verlauf die Nierenfunktion, eine Fortführung der Dialyse war erforderlichweise nicht mehr notwendig. Der Patient lebt nach 6 Monaten im häuslichen Umfeld mit seiner Ehefrau.

Diskussion

Der vorliegende Fallbericht zeigt, dass auch bei älteren Patienten mit geriatrischen Syndromen die somatische Abklärung der Beschwerden entscheidend ist, um damit vor allem bei gebrechlichen Patienten den sogenannten „Drehlühreffekt“ und eine frühzeitige Therapieeinstellung zu verhindern. Eine funktionelle, altersmedizinische Behandlung, gerade auch bei schweren akuten Erkrankungen wie der ANCA-Vaskulitis, kann, wenn unmittelbar durchgeführt, die Alltagskompetenz und damit auch die Prognose und Lebensqualität älterer Patienten deutlich verbessern.

Literatur

¹ Borczyk-Kucio B, Andrzejewski S, Pawlowski M, Dinculescu Z, Vetrovici B, Niciu M. Prolonged infection associated with anti-neutrophil cytoplasmic antibodies specific to proteinase 3 and myeloperoxidase: diagnostic and therapeutic challenge. Clin Rheumatol. 2010 Aug;29(8):953-964.

² Jansen J, R. ANCA-associated vasculitis in elderly people. Med Lett. 2019;72(8):111591-1598. PMID: 3156895

³ Schmitt J, H. Avel, P.M. de Groot, K. et al. S1-Leitlinie Diagnostik und Therapie der ANCA-assoziierten Vaskuliden. Z Rheumatol 76, 77-104 (2017)

Kontakt: anna.meyer@uk-koeln.de

Z Gerontol Geriat 2021 · 54:451–453
<https://doi.org/10.1007/s00391-021-01913-8>
 Eingegangen: 31. März 2021
 Angenommen: 27. April 2021
 Online publiziert: 11. Juni 2021
 © Springer Medizin Verlag GmbH, ein Teil von Springer Nature 2021



Anne Ferring · Jill Stegemann · Anna Maria Meyer

Klinik II für Innere Medizin und Zentrum für Molekulare Medizin Köln, Medizinische Fakultät und Universitätsklinik Köln, Universität zu Köln, Köln, Deutschland

ANCA-assoziierte Vaskulitis beim älteren Patienten

Anamnese

Ein 80-jähriger Patient wurde bei Verschlechterung des Allgemeinzustandes, steigenden Entzündungswerten (CRP 199,6 mg/l) und sich verschlechternden Retentionsparametern in die universitäre Altersmedizin übernommen. In den vorherigen Monaten fanden mehrfach stationäre Aufenthalte in externen Krankenhäusern aufgrund von wiederholten Episoden mit einem Anstieg der Retentionsparameter mit Ausschluss einer postrenalen Genese, Blutungsereignissen und rezidivierenden pulmonalen Infekten statt. Bei Aufnahme bestanden Instabilität, Immobilität, Inkontinenz sowie ein Delir.

Vorerkrankungen: 2-Gefäß-Koronare Herzkrankheit mit Myokardinfarkten 2012, Trikuspidal- und Mitralklappeninsuffizienz, Aortenklappenstenose, Adenokarzinom des Colon descendens mit erweiterter Hemikolektomie links, paroxysmales Vorhofflimmern, ICD-Implantation, Hypothyreose, Knie-Totalendoprothese links.

Befunde

Bei Aufnahme bestanden Einschränkungen der Alltagskompetenz (Barthel-Index 25) und Lebensqualität, (EQ-5D-5L 0,225), Hinweise auf Depression (Geriatrische Depressionsskala [Yesavage, GDS 5]) sowie Mangelernährung (Mini Nutritional Index - Short Form, MNA-SF 4). Der Comprehensive Geria-

tric Assessment (CGA)-basierte Multidimensionale Prognostische Index (MPI) wies mit 0,75 eine erhöhte Vulnerabilität mit hohem Risiko für Mortalität und Rehospitalisierung im Folgejahr auf [1]. Die erhobenen Parameter deuteten auf eine ausgeprägte Frailty hin [2], trotz bestehender Ressourcen (sozial, intellektuell, motivational und spirituell).

Aufgrund der erhöhten Entzündungswerte erfolgte eine weiterführende Abklärung. Die Urindiagnostik zeigte mit einer Leukozyturie und Bakteriurie einen Harnwegsinfekt mit *Enterococcus faecium* und *Klebsiella pneumoniae*, der resistogrammgerecht mit Meropenem behandelt wurde. Zusätzlich wies das Röntgen Thorax fleckig-konfluierende Transparenzminderungen im rechten Unterfeld, möglicherweise pneumonischen Infiltraten entsprechend auf.

Bei Anämie (Hb 7,1 g/dl) und Hämatocryzen waren mehrfach Bluttransfusionen notwendig.

Aufgrund der Nierenschädigung (Kreatinin 6,48 mg/dl, Harnstoff 333 mg/dl) erfolgte eine umfangreiche nephrologische Abklärung. Bei urämischer Symptomatik (Pruritus, Delir) wurde eine Hämodialyse erforderlich. Aufgrund einer auch nach Reduktion der urämischen Symptome fortbestehenden Agitiertheit erfolgte zur Delirbehandlung eine Melperontherapie für 5 Tage, worunter sich das Delir rückläufig zeigte. Im Urinsediment zeigte sich ein nephritisches Sediment mit Mikrohämaturie. Eine erweiterte immunologische Diagnostik bestätigte einen hochtitrigen cANCA (cytoplasmatischer Anti-Neutrophile cytoplasmatische Antikörper 1:640, Subtyp PR3 388,1 RE/ml). Nachträglich wurde vom Patienten über blutig-borkige Si-

nusitis, Hämoptysen und Purpura berichtet, sodass der Verdacht auf eine ANCA-assoziierte Vaskulitis (AAV) gestellt wurde. Auch die beschriebenen pneumonischen Infiltrate können eine mögliche Manifestation der Erkrankung sein. Zur Diagnosesicherung und zur prognostischen Einschätzung wurde eine Nierenbiopsie durchgeführt, in der sich eine frisch nekrotisierende und extrakapillär proliferative Glomerulonephritis vom Pauci-Immun-Typ zeigte.

Diagnose

Zusammenfassend wurde die Diagnose einer Granulomatose mit Polyangiitis (GPA) gestellt. Der Patient erhielt eine Induktionstherapie mit Prednisolon sowie Rituximab, anschließend erfolgte eine Rituximaberhaltungstherapie. Trotz der umgehend eingeleiteten Therapie mit gutem Ansprechen der immunologischen Parameter zeigte sich der Patient aufgrund des bereits langen Verlaufs der Nierenschädigung zunächst weiter dialysepflichtig.

Infobox 1 Granulomatose mit Polyangiitis

Die Granulomatose mit Polyangiitis (GPA, früher: M. Wegener) ist eine Kleingefäßvaskulitis mit Assoziation zu cANCA. Gekennzeichnet durch eine nekrotisierende granulomatöse Entzündung sind oftmals die oberen und unteren Atemwege sowie die Nieren, Gelenke und Haut befallen. Grundsätzlich kann jedes Organsystem betroffen sein, sodass ein inhomogenes Erscheinungsbild die Diagnose besonders bei älteren Patienten erschwert.

Die Autoren A. Ferring und J. Stegemann haben zu gleichen Teilen zum Manuskript beigetragen. Teile des Falls wurden als Poster bei der 12. Jahrestagung der Deutschen Gesellschaft für Nephrologie (Oktober 2020) gezeigt.



Abb. 1 ▲ Verlauf des Kreatinin-Werts parallel zum Barthel-Index während der Hospitalisierung

Therapie und Verlauf

Unter der immunsuppressiven Therapie entwickelte der Patient in den nächsten Tagen eine nosokomiale Pneumonie mit respiratorischer Insuffizienz, sodass eine kurzzeitige intensivmedizinische Therapie notwendig wurde.

Während des gesamten Aufenthaltes war der Patient durch seine Krankheitssituation depressiv verstimmt, sodass erfolgreich eine Therapie mit Mirtazapin begonnen wurde (GDS bei Entlassung 2 Punkte).

Unter der beschriebenen Therapie und der parallel durchgeführten Komplexbehandlung verbesserte sich der Patient bei Entlassung insgesamt deutlich (Barthel-Index 65, EQ-5D-5L 0,872). Der MPI lag bei Entlassung nur noch bei 0,50, entsprechend einem mittleren Risiko.

Der Patient konnte nach 33-tägigem Krankenhausaufenthalt in die Anschlussheilbehandlung entlassen werden (Abb. 1). Zwei Monate nach Entlassung aus der Altersmedizin war unter Fortführung der Therapie eine sich stetig bessernde Nierenfunktion zu verzeichnen, sodass eine Fortführung der Dialyse erfreulicherweise nicht mehr notwendig war. Laborchemisch waren zuletzt eine stabile Nierenfunktion (Kreatinin

1,86 mg/dl) und ein stabiler Hb-Wert (13,1 mg/dl) zu verzeichnen; die AAV war in Remission. Auch subjektiv stellte sich eine Besserung ein: Der Patient gab eine deutliche Zunahme der Belastbarkeit und des Appetits an. Er lebt weiter im häuslichen Umfeld mit seiner Ehefrau und kann das Haus selbstständig verlassen.

Diskussion

Aufgrund des inhomogenen Erscheinungsbildes einer AAV kommt es häufig erst nach längerem Krankheitsverlauf zur Diagnosestellung, wenn bereits organische und funktionelle Folgeschäden eingetreten sind. Gerade bei älteren, multimorbiden Patienten zeigen sich oft diffuse Beschwerdebilder mit teils atypischen Symptomen – oft werden diese zusätzlich von geriatrischen Syndromen überlagert, was die Diagnosefindung erschwert. Studien konnten zeigen, dass eine AAV bei älteren Patienten häufiger mit einer erhöhten Mortalität einhergeht [3, 4].

Der vorliegende Fallbericht zeigt die Wichtigkeit einer genauen somatischen Abklärung von Beschwerden auch im höheren Alter und bei Gebrechlichkeit, um den „Drehtüreffekt“ und eine frühzeitige Therapielimitierung zu vermeiden sowie

eine gewisse funktionelle Reserve und Resilienz wiederherzustellen.

Denn durch eine leitliniengerechte immunsuppressive Therapie ist auch bei älteren Patienten eine effektive Remission mit Verringerung der Mortalität und Morbidität möglich [5]. Dennoch sollte auf das erhöhte Risiko für Infektionen (z. B. Herpes-zoster-Infektionen und Pneumonien) unter einer immunsuppressiven Therapie geachtet werden [6].

Eine multidimensionale und interdisziplinäre Behandlung älterer Patienten kann gerade bei schweren akuten Erkrankungen wie der AAV die funktionellen Outcomes älterer Patienten deutlich verbessern.

Korrespondenzadresse



Dr. Anna Maria Meyer
Klinik II für Innere Medizin
und Zentrum für Molekulare
Medizin Köln, Medizinische
Fakultät und Universitätsklinik
Köln, Universität zu Köln
Kerpener Straße 62,
50937 Köln, Deutschland
anna.meyer@uk-koeln.de

Danksagung. Wir möchten uns ganz besonders bei dem Patienten, bei Prof. Thomas Benzing, Prof. M. Cristina Polidori und Dr. Malte P. Bartram für die

große Unterstützung zur Erstellung dieses Fallberichtes bedanken.

Einhaltung ethischer Richtlinien

Interessenkonflikt. A. Ferring, J. Stegemann und A.M. Meyer geben an, dass kein Interessenkonflikt besteht.

Für diesen Beitrag wurden von den Autoren keine Studien an Menschen oder Tieren durchgeführt. Für die aufgeführten Studien gelten die jeweils dort angegebenen ethischen Richtlinien. Für Bildmaterial oder anderweitige Angaben innerhalb des Manuskripts, über die Patienten zu identifizieren sind, liegt von ihnen und/oder ihren gesetzlichen Vertretern eine schriftliche Einwilligung vor.

for clinical practice and public health. *Lancet* 394(10206):1365–1375

3. Hoganson DD, From AM, Michet CJ (2008) ANCA vasculitis in the elderly. *J Clin Rheumatol* 14(2):78–81
4. McVay G, McGeoch L, Chalmers GW (2018) ANCA-associated vasculitis (AAV) in the elderly: clinical presentation, treatment and outcomes. *Eur Geriatr Med* 9(5):725–728
5. Weiner M, Goh SM, Mohammad AJ, Hruskova Z, Tanna A, Bruchfeld A et al (2015) Outcome and treatment of elderly patients with ANCA-associated vasculitis. *Clin J Am Soc Nephrol* 10(7):1128–1135
6. Timlin H, Lee SM, Manno RL, Seo P, Geetha D (2015) Rituximab for remission induction in elderly patients with ANCA-associated vasculitis. *Semin Arthritis Rheum* 45(1):67–69

Literatur

1. Pickert L, Meyer AM, Becker I, Heess A, Noetzel N, Brinkkötter P et al (2021) Role of a multidimensional prognosis in-hospital monitoring for older patients with prolonged stay. *Int J Clin Pract* 2021 May;75(5):e13989. <https://doi.org/10.1111/ijcp.13989>
2. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP (2019) Frailty: implications



Neue S1-Leitlinie Post-COVID – die wichtigsten Eckpunkte im Webinar



Dr. med. Erik Heintz
Chefredakteur SpringerMedizin.de

Prof. Dr. med. A. Rembert Koczulla
Professor für Pneumologische Rehabilitation an der Philipps-Universität Marburg
Chefred. Fachzentrum Pneumologie Südlich Rheingebiet Land
Lehrstuhl für die Philipps-Universität Marburg und Philipps-Universität

Webinar mit Prof. Dr. med. A. Rembert Koczulla (Koordinator der S1-Leitlinie „Post-COVID“)

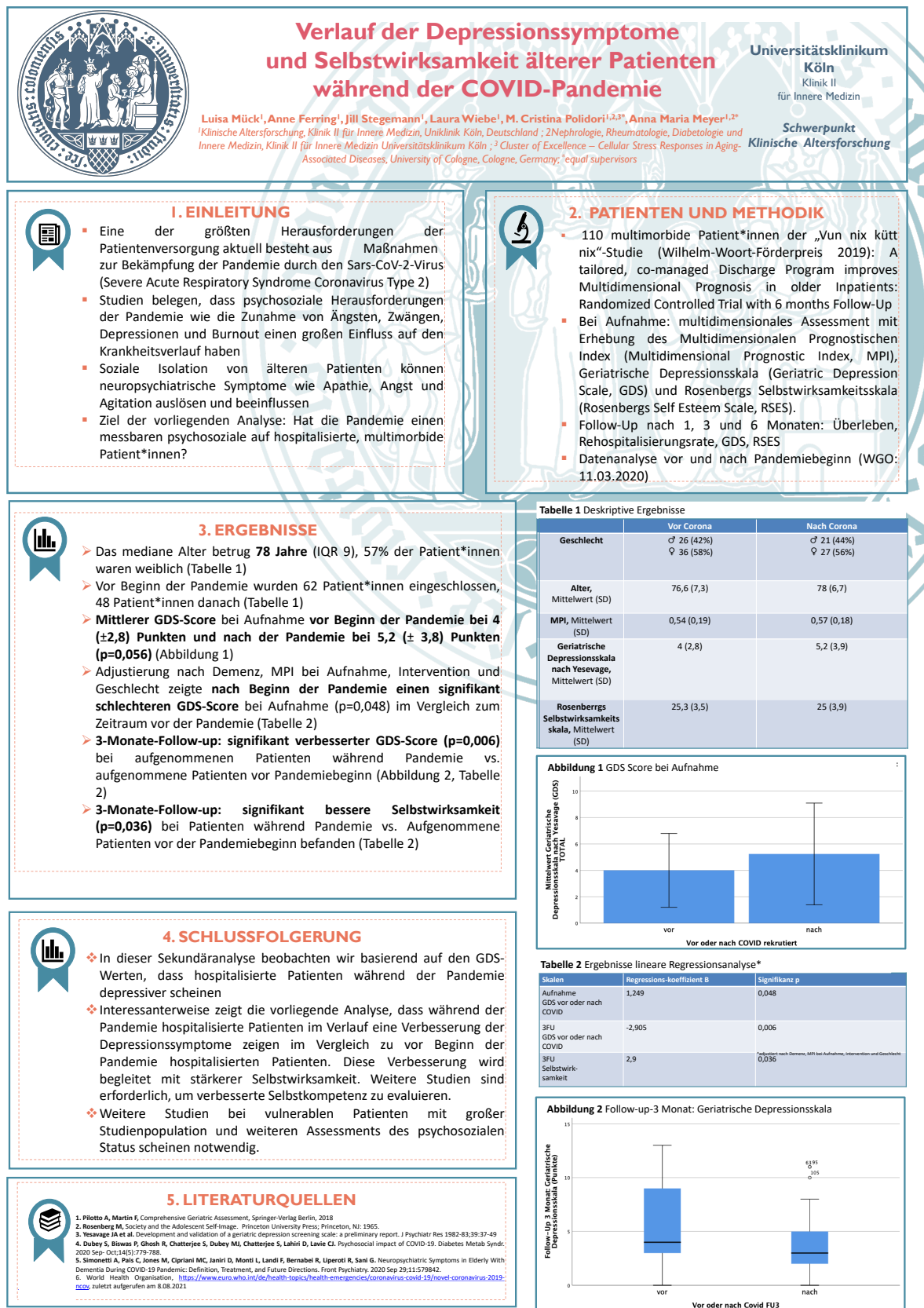
Im Webinar beleuchtet der Koordinator der S1-Leitlinie „Post-COVID“, Prof. Rembert Koczulla, wichtige Eckpunkte der S1-Leitlinie „Post-COVID“

Hier geht es zum Webinar vom 30. Juni 2021:



Die Leitlinie und weitere Informationen finden Sie unter <https://go.sn.pub/UI8zs1> oder über den QR-Code.

Supplementary 3



Supplementary 4



Uniklinik Köln
Klinik II für Innere Medizin

Schwerpunkt Klinische
Altersforschung

Prognostic features of sarcopenia according to the EWGSOP2 algorithm in older hospitalised patients: A 6-month follow-up study

Ferring A¹, Meyer AM¹, Mück L¹, Stegemann J¹, Wiebe L¹, Becker I², Benzing T^{1,3}, and Polidori MC^{1,3}

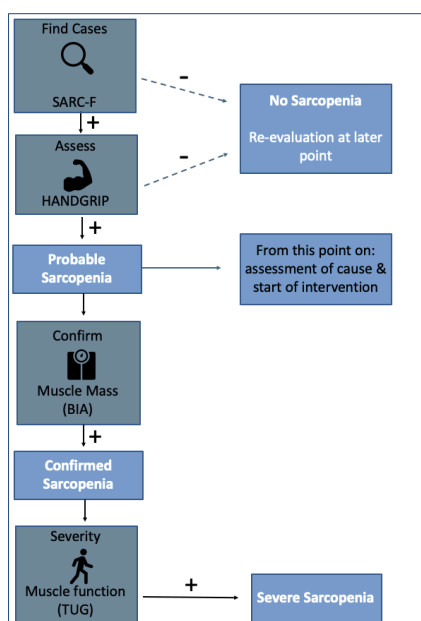
¹University of Cologne, Faculty of Medicine and University Hospital Cologne, Aging Clinical Research, Department II of Internal Medicine, Cologne, Germany; ²Institute of Medical Statistics and Computational Biology, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany; ³Cluster of Excellence – Cellular Stress Responses in Aging-Associated Diseases, University of Cologne, Cologne, Germany

I. Introduction

Sarcopenia, defined as a generalised and progressive age-related decline in muscle mass, strength and function [1], is extremely common in older people and is known to be associated with adverse health outcomes [2]. However, sarcopenia has long been underdiagnosed and undertreated in routine clinical practice due to the lack of universally accepted diagnostic algorithms. The aim of this analysis was to assess the prevalence and prognostic signature of sarcopenia in older adults at risk of functional decline during hospitalisation in an acute hospital setting jointly managed by internists and geriatricians.

II. Methods

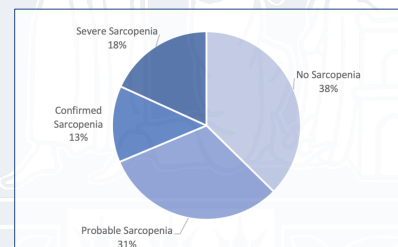
Sarcopenia was assessed using the European Working Group on Sarcopenia in Older People (EWGSOP2) algorithm [3], including the SARC-F (Strength, Assistance with walking, Rising from a chair, Climbing stairs and Falls) score, handgrip strength, bioelectrical impedance analysis (BIA) and the Timed Up and Go (TUG) test in 97 older multimorbid inpatients. A Comprehensive Geriatric Assessment (CGA) including assessment of geriatric syndromes (GS) and resources (GR) and prognostic calculation using the CGA-based Multidimensional Prognostic Index (MPI), European Quality of Life-5 Dimensions (EQ-5D-5L), Rosenberg Self-Esteem Scale (RSES) and Geriatric Depression Scale (GDS). Information on survival and rehospitalisation was collected 1, 3 and 6 months after discharge.



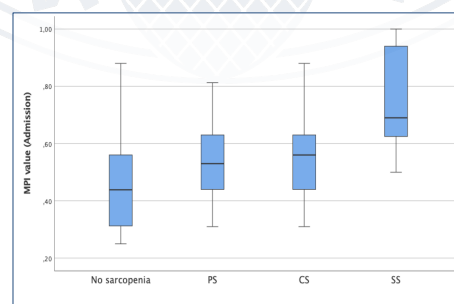
Diagnostic algorithm based on the EWGSOP2-guideline by Cruz-Jentoft et al. [3]

III. Results

The mean age of the study population was 76.5 ($\pm$ 6.8) years and 55% were female. Sarcopenia was present in 63% (95% CI: 54-72%) of patients and was categorised as probable (31%), confirmed (13%) and severe sarcopenia (18%).



Sarcopenic patients had significantly higher median MPI scores ($p < 0.001$), more GS ($p = 0.033$), less GR ($p = 0.003$), lower EQ-5D-5L ($p < 0.001$) and lower RSES ($p = 0.025$) than non-sarcopenic patients. Sarcopenic patients also had significantly more falls in the previous year ($p = 0.008$).



Six months after discharge, being sarcopenic at baseline was predictive of falls ($p = 0.027$) and quality of life ($p = 0.043$), independent of age, gender and MPI.

IV. Discussion

Sarcopenia, as defined by EWGSOP2, is highly prevalent in hospitalised elderly multimorbid patients, and for the first time a significant association between sarcopenia, as structured by the EWGSOP2 algorithm, multidimensional prognosis and frailty as measured by the MPI, and health outcomes at different time points has been demonstrated. As sarcopenia is an independent strong predictor of poor outcomes after discharge, older patients should be systematically assessed for sarcopenia and receive ad hoc counselling and treatment.

V. Literature

- [1] Cruz-Jentoft AJ, Sayer AA; Sarcopenia. *The Lancet* 2019;393(10191):2636-2646
- [2] Yeung SS, Reijnierse EM, Pham VK, et al.; Sarcopenia and its association with falls and fractures in older adults: a systematic review and meta-analysis. *Journal of cachexia, sarcopenia and muscle* 2019;10(3):485-500
- [3] Cruz-Jentoft AJ, Bahat G, Bauer J, et al.; Sarcopenia: revised European consensus on definition and diagnosis. *Age and ageing* 2019;48(1):16-31