Aus der Klinik für Geriatrie und Altersmedizin
der Medizinischen Fakultät Charité – Universitätsmedizin Berlin

DISSERTATION

Impact of Sarcopenia on Clinical Outcome in Old Patients with Cancer

zur Erlangung des akademischen Grades
Doctor rerum medicinalium (Dr. rer. medic.)

vorgelegt der Medizinischen Fakultät
Charité – Universitätsmedizin Berlin

von

Lindsey Otten

aus Prince George, Kanada

Datum der Promotion: 21.06.2020

Table of Contents

Abstract (English)

Introduction and background: Sarcopenia was originally defined as the age-related loss of muscle mass. In addition to primary, or age-related sarcopenia, secondary sarcopenia describes muscle depletion due to physical inactivity, inadequate nutrition or disease. Therefore, particularly older patients with chronic disease, for example cancer, are at an increased risk of developing sarcopenia. In addition to the physiological age-related changes, older patients with cancer are burdened by the physical and metabolic effects of the cancer disease itself as well as its treatment. Loss of muscle mass leads to functional impairment, reduced quality of life and poor clinical outcome. This study aimed to assess the prevalence of sarcopenia in older patients with cancer and its impact on 1-year mortality.

Methods: Sarcopenia was defined as suggested by the European Working Group on Sarcopenia in Older People (EWGSOP) as low skeletal muscle mass index and muscle strength assessed by bioelectric impedance analysis and isometric hand grip strength, respectively. Information on one-year mortality was collected by telephone follow-up or by contacting the local cancer death registry. A step-wise, forward Cox proportional hazards analysis was performed to identify risk factors of 1-year mortality.

Results: Four-hundred thirty-nine older patients with cancer were included in the analysis (60-95 years; 43.5% women), of which 119 (27.1%) were identified as sarcopenic. Sixty-two (52.5%) of the patients with sarcopenia compared to 108 (35.1%) without sarcopenia died within one year of study entry. Patients without sarcopenia had longer survival times (291.2 days, 95% CI: 278.0-304.5 versus 244.0 days, 95% CI: 219.2-268.7, $p<0.001$). Advanced tumour stage IV (HR=1.87; 95% CI: 1.228-2.847; p=0.004), sarcopenia (HR=1.53; 95% CI: 1.034-2.250; p=0.033), number of drugs per day (HR=1.11; 95% CI: 1.057-1.170; $p<0.001$), Karnofsky Index (HR=0.98, 95% CI: 0.963-0.995; p=0.013) and tumour diagnosis (overall p=0.012) were significantly associated with 1-year mortality risk. Sex, age, number of comorbidities and involuntary 6-month weight loss ≥ 5% were not significantly associated with 1-year mortality risk in this study.

Conclusion: Nearly one-third of older patients with cancer were identified as sarcopenic compared to 10% of the healthy, older population worldwide (1). Notably, sarcopenia was nearly as predictive for 1-year mortality as advanced tumour stage IV. This result underscores the importance of the timely identification and monitoring of

sarcopenia in this population and adjustment of therapy accordingly in order to maximise muscle mass preservation.

Abstract (German)

Einleitung: Sarkopenie wurde ursprünglich als alters-assoziierter Verlust der Muskelmasse definiert. Neben der primären, oder alters-assoziierten Sarkopenie, beschreibt die sekundäre Sarkopenie den Verlust an Muskelmasse aufgrund von physischer Inaktivität, unzureichender Nahrungszufuhr oder Krankheit. Insbesondere ältere Patienten mit chronischen Erkrankungen, wie z.B. Tumorerkrankungen, haben dadurch ein erhöhtes Risiko eine Sarkopenie zu entwickeln. Neben den physiologischen altersbedingten Veränderungen sind ältere Patienten mit Tumorerkrankungen auch mit den physischen und metabolischen Auswirkungen der Krebserkrankung sowie deren Behandlung konfrontiert. Der Muskelschwund führt zu funktionellen Beeinträchtigungen, verminderter Lebensqualität sowie schlechtem klinischen Verlauf. Diese Studie untersucht die Prävalenz von Sarkopenie bei älteren Patienten mit Tumorerkrankungen und deren Einfluss auf 1-Jahres Mortalität.

Methoden: Sarkopenie wurde nach den Empfehlungen der *European Working Group on Sarcopenia in Older People* (EWGSOP) definiert. Hierbei wurden die Kriterien verminderter Muskelmassenindex mithilfe der bioelektrischen Impedanzanalyse und verringerter Muskelkraft durch Messung der isometrischen Handkraft mit einem Dynamometer erfasst. Informationen zu 1-Jahres Mortalität wurde bei einem telefonischen Follow-Up oder vom lokalen Krebsregister erhoben. Eine schrittweise, vorwärts Cox-Regression mit proportionalen Hazards wurde durchgeführt, um Risikofaktoren für die 1-Jahresmortalität zu identifizieren.

Ergebnisse: Vierhundert neun-und-dreißig ältere Patienten mit onkologischen Erkrankungen wurden in die Studie eingeschlossen (60-95 Jahre; 43,5% Frauen), davon wiesen 119 (27.1%) eine Sarkopenie auf. Zwei-und-sechzig (52,5%) der Patienten mit Sarkopenie im Vergleich zu 108 (35.1%) ohne Sarkopenie sind innerhalb eines Jahres vom Studieneinschluss verstorben. Patienten ohne Sarkopenie wiesen eine längere Überlebenszeit auf (291,2 Tage, 95% KI: 278,0-304,5 versus 244,0 Tage, 95% KI: 219,2-268,7, p<0,001). Ein fortgeschrittenes Tumorstadium IV (HR=1,87; 95% KI: 1,228-2,847; p=0,004), Sarkopenie (HR=1,53; 95% KI: 1,034-2,250; p=0,033), Anzahl an Medikamenten pro Tag (HR=1,11; 95% KI: 1,057-1,170; p<0,001), Karnofsky Index (HR=0,98, 95% KI: 0,963-0,995; p=0,013) und Tumordiagnose (Gesamt-p=0,012) waren mit einen erhöhten Risiko, nach einem Jahr zu versterben, assoziiert. Geschlecht, Alter, Anzahl an Komorbiditäten sowie unbeabsichtigter

Gewichtsverlust ≥ 5% innerhalb von 6 Monaten waren in dieser Studie nicht mit dem Sterberisiko assoziiert.

Schlussfolgerung: Nahezu ein Drittel der älteren Patienten mit Tumorerkrankungen wurden im Vergleich zu 10% der gesunden, älteren Population weltweit (1) als sarkopen identifiziert. Beachtenswert ist, dass Sarkopenie fast genauso prädiktiv für die 1-Jahres Mortalität wie ein fortgeschrittenes Tumorstadium war. Diese Ergebnisse unterstreichen die Bedeutung einer frühen Erfassung und kontinuierliche Überwachung der Sarkopenie in dieser Population sowie die entsprechende Anpassung der Therapie, um den Verlust an Muskelmasse zu minimieren.

Introduction

In the late 1980s, it was proposed that the frequently observed decline in lean body mass with increasing age be termed sarcopenia (2). Since then, the topic has taken hold of the literature and various studies have been performed to get a grasp on this change in body composition and clarify its place in age and disease-related processes, including its functional implications and relevance (3). Despite the continuing debate on terminology and diagnostics, low muscle mass has been clearly linked to adverse health outcomes. Patients with chronic disease, particularly cancer, are at an especially high risk of muscle mass depletion which further impedes therapy and reduces prognosis.

The aetiology of muscle loss is multifactorial; two general categories have emerged to differentiate between contributing mechanisms. Primary or age-related sarcopenia comprises changes associated with ageing such as hormonal and neuromuscular changes, mitochondrial dysfunction and reduced postprandial protein synthesis that contribute to a reduction in muscle mass (4). Factors related to lifestyle, including physical inactivity and inadequate dietary intake, as well as disease-related factors, for example inflammation, malignancy, organ failure or endocrine disease and therapy such as an operation or chemotherapy, can also influence muscle maintenance (4). Activity, nutrition or disease-related sarcopenia have been referred to as secondary sarcopenia. However, there is clearly an overlap in the pathophysiology leading to muscle mass decline as, for example, in older individuals with chronic disease.

One main challenge surrounding the topic of sarcopenia has been finding a common clinical definition and diagnostic criteria with which to provide clinicians and researchers common ground on which to base treatment plans and goals as well as study designs with regard to sarcopenia. To this end, working groups have been formed with the goal of establishing consensus, including the Sarcopenia and Frailty Research Special Interest Group (SIG), European Working Group on Sarcopenia in Older People (EWGSOP), International Working Group on Sarcopenia (IWGS) and Asian Working Group for Sarcopenia (AWGS). EWGSOP, for example, published a consensus definition in 2010 and described sarcopenia as “a syndrome characterised by progressive and generalised loss of skeletal muscle mass and strength with a risk of adverse outcomes ...” (5). Accordingly, they recommended the presence of both low muscle mass and function – in

the form of low muscle strength or performance – to diagnose sarcopenia. In addition to distinguishing between primary and secondary sarcopenia, a staging in presarcopenia, sarcopenia and severe sarcopenia serves to reflect the severity of the condition and aid in clinical management. Based on the scientific and clinical evidence gained since 2010, an updated definition, EWGSOP2, was published in October 2018 (6). With the recognition that muscle strength is a better predictor of adverse outcomes than muscle mass, the EWGSOP2 definition regards low muscle strength as the primary diagnostic parameter of sarcopenia. The presence of low muscle quantity or quality should confirm the diagnosis and concomitant low physical performance indicates severity. Lastly, they suggest the identification of sarcopenia as an acute or chronic state (6).

Loss of skeletal muscle is associated with impaired physical function and poor prognosis. Individuals with sarcopenia are less able to perform daily activities (7) and have an increased risk of falls (8, 9). A reduction in muscle mass also influences metabolic processes leading, for example, to insulin resistance and altered myokine production (10-12). Ultimately, sarcopenia leads not only to a reduction in quality of life and increased morbidity but also increased mortality (13, 14). Furthermore, the corresponding increase in health care utilisation and costs, especially in light of the demographic change of an ageing population, cannot be neglected. We recently published a short review providing a summary on the financial impact of sarcopenia in different medical areas (15). Regardless of the diagnostic criteria (low muscle mass alone or with low strength and/or performance) and setting, direct and indirect health care costs were increased for patients with sarcopenia. Thus preventative and early treatment of muscle mass depletion could not only lead to improved clinical outcome but also reduce health care expenditure.

The worldwide prevalence of sarcopenia in healthy adults aged over 60 lies at 10% (1) and increases to 25% and higher in older, hospitalised populations (16, 17), depending on the diagnostic criteria used. Particularly in patients with chronic disease, the presence of sarcopenia poses an increased risk of complications and increases the challenge of determining suitable and effective treatment, especially when sarcopenia is unidentified. Sarcopenia has gained interest in several chronic diseases, in which loss of muscle mass frequently occurs, such as cardiovascular disease (18), renal disease (19), rheumatic disease (14, 20) and cancer (21). In systemic sclerosis, for example, a relatively rare, immune-mediated rheumatic disease characterised by dysfunctional or dysregulated

connective tissue repair (22), we found that nearly every fourth patient had sarcopenia (22.5%)(14). Although the mean age in this study was approximately 60 years, the prevalence is comparable to that found in hospitalised 80-year-old patients (25%)(16). Patients with sarcopenia had lower muscle strength and reported higher impairment in physical function than patients without sarcopenia, adding a considerable burden and challenge to activities in daily life to this already debilitating disease.

Patients with cancer disease are confronted with a number of factors that negatively affect muscle mass and strength, for example a reduction in physical activity and effects of cancer treatment, which frequently exacerbates skeletal muscle mass depletion (23, 24) and negatively affects nutritional intake due to symptoms like nausea and anorexia (25, 26). Furthermore, the biochemical processes involved in cancer cachexia, a complex syndrome characterised by abnormal metabolism and negative energy balance resulting in loss of muscle mass with or without loss of fat mass (27, 28), contribute to a catabolic state. Conversely, low muscle mass in cancer patients negatively impacts therapy tolerance and prognosis. A number of studies have shown an association between low muscle mass and increased risk of dose-limiting toxicities during chemotherapy (29, 30) or increased complications and length of hospital stay after tumour resection (31, 32).

In the study presented in this work, we aimed to assess the prevalence of sarcopenia, defined as low skeletal mass and muscle strength, and its impact on 1-year mortality in older patients with cancer.

Methods

Study population:

Patients admitted to the Charité University hospital for cancer treatment or staging were included in the study and patients 60 years and older were included for the post hoc analysis. Exclusion criteria included participation in intervention or drug trials, implanted pacemakers or defibrillators, neuromuscular degenerative disease, hemiplegia, severe arthritis of the extremities, cognitive impairment and lack of German language skills. The study was approved by the ethics committee of the Charité University hospital and patients gave written informed consent.

In addition to standard demographic characteristics and clinical data, information on date of tumour diagnosis, location and stage (UICC classification: Union Internationale Contre le Cancer; stages I to IV (advanced)) as well as treatment type were recorded.

The Karnofsky Performance Index was used to evaluate well-being, disease symptoms and functional impairment. On a scale of 0 to 100, low values indicate the need for hospital care and poor prognosis.

Information on one-year mortality was collected by telephone follow-up or by contacting the local cancer death registry, which only transmitted date of death.

Anthropometry and body composition analysis:

Weight (seca 910 portable electronic scale, max. 200 kg ± 100 g, seca GmbH, Hamburg, Germany) and height (telescopic measuring rod, seca 220, seca GmbH, range: 60-200 cm) to the nearest 0.1 kg and 0.1 cm, respectively, were measured in a standardised manner. Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$. Changes in body weight in the previous six months, as reported from the patient, were documented.

Body composition was estimated using bioelectric impedance analysis (BIA) under standard conditions as recommended by the manufacturer. According to the tetrapolar approach, an alternating current of 800 µA at 50 kHz was applied over electrodes on the dorsal side of the hand and foot on the dominant side of the body (Nutriguard M and Ag/AgCl Bianostic AT electrodes, Data-Input GmbH, Darmstadt, Germany). Skeletal muscle mass was calculated using physical (weight and height) and raw impedance parameters (resistance (R) and reactance (Xc)) in the equation from Janssen et al. (33).

Skeletal muscle mass was adjusted for height squared to yield skeletal muscle mass index (kg/m^2).

Muscle strength:

Muscle strength was measured as maximum isometric hand grip strength (kg) in the non-dominant hand (JAMAR® dynamometer, Sammons Preston Roylan, Bolingbrook, Illinois). From a seated position and with the elbow flexed to 90°, forearm and wrist in a neutral position, the highest value of three repetitions was recorded.

Sarcopenia:

The diagnostic criteria and cut-off values recommended by EWGSOP were applied (5). Patients were characterised as sarcopenic when both low skeletal muscle index and low hand grip strength were present. The cut-off values for skeletal muscle index were < 10.75 kg/m^2 for men and < 6.75 kg/m^2 for women, based on a reference group of individuals 60 years and over (34). Sex- and BMI-stratified cut-off values were applied for hand grip strength (35).

Statistical analysis:

The data were analysed using the statistics program IBM SPSS Statistics Version 23. Continuous variables (age, body composition and strength variables, Karnofsky Performance Index, number of drugs and comorbidities) were presented as mean and standard deviation, while nominal variables (presence of sarcopenia, tumour stage and diagnosis category) were presented as percent values.

The student's t-test and the chi-squared test for continuous and nominal variables, respectively, were applied for comparisons between patients with and without sarcopenia. Risk factors of 1-year mortality were evaluated by means of a forward, stepwise Cox proportional hazards regression analysis. Survival time was represented by the number of days from study enrolment to 1-year follow-up; values after one year were censored. The following risk factors were included in the Cox regression: sex (men versus women), age, number of comorbidities, number of drugs per day, Karnofsky Performance Index, weight loss within the previous 6 months (yes versus no), tumour stage (IV versus I-III), tumour category (hematologic, lung, oropharynx, urogenital and other compared to gastrointestinal tumours) and sarcopenia (yes versus no). Data were presented with the hazard ratio (HR) and 95% confidence interval (95% CI).

Kaplan-Meier 1-year survival curves were generated and the log-rank test carried out to test for differences in survival distributions between patients with and without sarcopenia. A significance level < 5% was chosen a priori.

Results

The analysis included 439 older patients (60 – 95 years; 43.5% women) with cancer. One-hundred nineteen (27.1%) patients had both low SMI and hand grip strength and were therefore characterised sarcopenic. More men (68.9% versus 51.9%, p = 0.001) than women were affected and patients with sarcopenia were older (71.7 ± 6.7 versus 68.8 ± 5.8 years, p < 0.001). Patients with sarcopenia had a lower BMI (23.3 ± 3.7 versus 25.6 ± 4.9 kg/m^2, p < 0.001), experienced weight loss more often (81.3% versus 65.9%, p = 0.003) and reported higher weight loss (11.3 ± 7.0% versus 9.2 ± 5.8%, p = 0.008). Furthermore, sarcopenic patients had a higher number of comorbidities (4.4 ± 2.4 versus 3.6 ± 2.3, p < 0.001) and number of drugs per day (6.7 ± 4.2 versus 5.1 ± 3.5, p < 0.001). Average disease duration (date of first diagnosis to study inclusion) was 25.0 ± 40.7 months and 64.8% had an advanced tumour stage IV. Approximately 70% of patients were under active treatment; chemotherapy was the most common (56%). Disease duration, tumour stage and treatment type did not differ between patients with and without sarcopenia.

One-hundred seventy patients (38.7%) died within one year of study inclusion. With regard to tumour diagnosis, most patients who died within one year were in the category other (68.2%) or lung tumours (51.5%) compared to patients who died with gastrointestinal tumours (40.3%, p = 0.004). Overall, more patients with sarcopenia than without (62 (52.5%) versus 108 (35.1%), p = 0.001) died within one year of study entry. Advanced tumour stage IV (HR 1.87, 95% CI: 1.228 – 2.847, p = 0.004), sarcopenia (HR 1.53, 95% CI: 1.034 – 2.250, p = 0.033), number of drugs per day (HR 1.11, 95% CI: 1.057 – 1.170, p < 0.001), Karnofsky Performance Index (HR 0.98, 95% CI: 0.963 – 0.995, p = 0.013) and tumour diagnosis category (overall p = 0.012) emerged as significant risk factors for 1-year mortality.

The survival distributions were significantly different between patients with and without sarcopenia (X^2 = 12.879, p < 0.001). Patients without sarcopenia had longer survival times (291.2 days; 95% CI: 278.0 – 304.5 versus 244.0 days; 95% CI: 219.2 –268.7).

Discussion

Using a definition for age-related sarcopenia, we found that nearly 30% of our study population of older patients with cancer were sarcopenic. This is comparable to the prevalence reported in mixed, older, hospitalised populations using the same diagnostic criteria (16, 17). Patients identified as sarcopenic were older, more often male, had a lower BMI and had experienced higher and more often weight loss. They also reported higher functional impairment, more comorbidities and a higher number of medications. Notably, the presence of sarcopenia was nearly as strong a predictor of 1-year mortality as advanced disease stage.

Older patients with cancer are particularly vulnerable to a loss in muscle mass. In addition to the increased risk of muscle depletion due to age-related processes, the cancer and cancer treatment-related processes described above further increase this risk and accelerate the loss of muscle (23, 24). This, in turn, contributes to poor therapy tolerance (29, 30), increased complications and increased length of hospital stay (31, 32). Thus, older patients with cancer experience a double blow on tissue maintenance with age-related sarcopenia on the one side and cancer cachexia on the other.

However, it is virtually impossible to disentangle the effects of age-related sarcopenia versus cachexia especially when looking at older patients with cancer (36). As with sarcopenia, the definition and diagnostic criteria for cachexia have evolved over the years and include a combination of significant weight loss, low BMI, and low muscle mass (37). Thus, the criteria overlap with those for sarcopenia such that patients with cachexia are often also sarcopenic (5, 37).

The overlap of sarcopenia and cancer cachexia can be seen in our results. On the one hand, our population was 60 to 95 years old and patients with sarcopenia were older than those without (71.7 ± 6.7 versus 68.8 ± 5.8 years, $p < 0.001$). On the other hand, weight loss was more common in sarcopenic than non-sarcopenic patients (81.3% versus 65.9%, $p = 0.003$) and sarcopenic patients lost more weight than non-sarcopenic patients (11.3 ± 7.0% versus 9.2 ± 5.8%, $p = 0.008$). However, the number of patients with stage IV disease was comparable between sarcopenic and non-sarcopenic patients (63.9% vs. 65.2%) and tumour as well as treatment type did not differ between patients with and without sarcopenia.

It is arguable that whether the loss of muscle mass is due to sarcopenia or cancer-cachexia has implications on treatment and treatment success. Unfortunately, in this study population, with the knowledge we have at this point in time, it is not possible to determine the aetiology of muscle loss on an individual basis. Therefore, a holistic approach including individualised cancer treatment as well as physical and nutritional therapy must be applied (38).

While all existing definitions and criteria include some combination of the three characteristics muscle mass, muscle strength and physical performance, discussion remains on which method and which cut-off values to use. Various established methods enable the quantification of these parameters and various cut-off values from different populations have been developed and proposed. The most common methods to assess muscle mass and strength are briefly discussed below.

Muscle mass is typically assessed as total body skeletal muscle mass, appendicular skeletal muscle mass or cross-sectional area of specific muscle groups or body locations. The accurate, precise and clinically feasible quantification of muscle mass remains a challenge. Computer tomography (CT) and magnetic resonance imaging (MRI) are known as gold standard imaging techniques that can be used for body composition analysis (39). The cross-sectional muscle area at the third lumbar vertebra or of the mid-thigh muscle with CT or MRI have been shown to correlate with whole-body muscle (40, 41). In cancer patients, where CT is used to image tumours, images are commonly also used to evaluate body composition; however, high costs for equipment and trained personnel as well as radiation exposure limit their use for whole-body measures in routine clinical practice. Currently, CT and MRI for the quantification of muscle mass are still limited to areas in which they are part of standard treatment or to research studies but they may play a larger role in the future with regard to sarcopenia diagnosis (39). Dual energy X-ray absorptiometry (DXA) is considered a good alternative for low-radiation whole-body scans (39). However, in contrast to CT and MRI, intramuscular fat as a measure of muscle quality cannot be accessed by DXA (39). Furthermore, the lack of portability and requirement of trained personnel also limit widespread use. For use in hospitals, a safe and inexpensive bedside method is required to allow large scale screening and assessment. Bioimpedance analysis (BIA) represents an inexpensive and easy to use alternative with the strong advantage of being transportable, thus making it suitable as a bedside method in the clinic as well as community setting. Practicality has

contributed to its widespread use (6). BIA indirectly estimates lean body muscle mass based on whole-body resistance to an applied alternating current. The total resistance, or impedance, arises from the combination of ohmic resistance (R) and reactance (Xc). These raw values are put into BIA prediction equations to determine body composition parameters. BIA estimations of lean body mass have been validated with MRI and DXA measures of lean mass (33, 42).

Potential future methods to assess muscle mass but which still require adjustment for use in clinical settings and/or validation include creatine dilution test and ultrasound as well as the use of biomarkers to identify individuals at-risk and aid in monitoring (6).

While hand grip strength and knee extension strength are both used to measure muscle strength, the most common and applicable method is maximum isometric hand grip strength (39). With the use of a dynamometer, this method is inexpensive, portable and easy to use and therefore well-suited for routine clinical practice and community healthcare. Under standard conditions, low hand grip strength has been shown to predict poor outcome such as increased hospital stays and functional limitations, low quality of life and mortality (43). As with measures of muscle mass, appropriate reference values are critical in the evaluation of hand grip strength.

In conclusion, this age and disease-related phenotype of low muscle mass and strength strongly increased the risk of mortality in this population of older patients with cancer. In light of the detrimental effects of muscle mass depletion on prognosis in these patients, continued assessment in the changing course of the disease is necessary in order to provide the best support and treatment. Incorporating screening tools for low muscle mass and strength will identify patients at risk and, importantly, the identification of low muscle mass and strength is possible with simple, cost-effective bedside methods.

Cancer-specific as well as nutritional and physical therapy should all be considered to conserve muscle mass and strength in order to achieve optimum outcome.

References

1. 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. J Diabetes Metab Disord. 2017;16:21.
2. Rosenberg IH. Sarcopenia: origins and clinical relevance. The Journal of nutrition. 1997;127(5 Suppl):990S-1S.
3. Morley JE, Anker SD, von Haehling S. Prevalence, incidence, and clinical impact of sarcopenia: facts, numbers, and epidemiology-update 2014. Journal of cachexia, sarcopenia and muscle. 2014;5(4):253-9.
4. Rolland Y, Czerwinski S, Abellan Van Kan G, Morley JE, Cesari M, Onder G, Woo J, Baumgartner R, Pillard F, Boirie Y, Chumlea WMC, Vellas B. Sarcopenia: its assessment, etiology, pathogenesis, consequences and future perspectives. The journal of nutrition, health & aging. 2008;12(7):433-50.
5. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinkova E, Vandewoude M, Zamboni M. 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.
6. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber C, Topinkova E, Vandewoude M, Visser M, Zamboni M. Sarcopenia: revised European consensus on definition and diagnosis. Age and ageing. 2018.
7. 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.
8. Bischoff-Ferrari HA, Orav JE, Kanis JA, Rizzoli R, Schlogl M, Staehelin HB, Willet WC, Dawson-Hughes B. Comparative performance of current definitions of sarcopenia against the prospective incidence of falls among community-dwelling seniors age 65 and older. Osteoporos Int. 2015;26(12):2793-802.
9. Schaap LA, van Schoor NM, Lips P, Visser M. Associations of Sarcopenia Definitions, and Their Components, With the Incidence of Recurrent Falling and Fractures: The Longitudinal Aging Study Amsterdam. The journals of gerontology Series A, Biological sciences and medical sciences. 2018;73(9):1199-204.

10. Karakelides H, Nair KS. Sarcopenia of aging and its metabolic impact. Curr Top Dev Biol. 2005;68:123-48.
11. Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, Abellan van Kan G, Andrieu S, Bauer J, Breuille D, Cederholm T, Chandler J, De Meynard C, Donini L, Harris T, Kannt A, Keime Guibert F, Onder G, Papanicolaou D, Rolland Y, Rooks D, Sieber C, Souhami E, Verlaan S, Zamboni M. 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.
12. Lee MJ, Kim EH, Bae SJ, Choe J, Jung CH, Lee WJ, Kim HK. Protective role of skeletal muscle mass against progression from metabolically healthy to unhealthy phenotype. Clinical endocrinology. 2019;90(1):102-13.
13. Brown JC, Harhay MO, Harhay MN. Sarcopenia and mortality among a population-based sample of community-dwelling older adults. Journal of cachexia, sarcopenia and muscle. 2016;7(3):290-8.
14. Siegert E, March C, Otten L, Makowka A, Preis E, Buttgereit F, Riemekasten G, Muller-Werdan U, Norman K. Prevalence of sarcopenia in systemic sclerosis: Assessing body composition and functional disability in patients with systemic sclerosis. Nutrition. 2018;55-56:51-5.
15. Norman K, Otten L. Financial impact of sarcopenia or low muscle mass - A short review. Clinical nutrition. 2018.
16. 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.
17. Martone AM, Bianchi L, Abete P, Bellelli G, Bo M, Cherubini A, Corica F, Di Bari M, Maggio M, Manca GM, Marzetti E, Rizzo MR, Rossi A, Volpato S, Landi F. The incidence of sarcopenia among hospitalized older patients: results from the Glisten study. Journal of cachexia, sarcopenia and muscle. 2017;8(6):907-14.
18. Fulster S, Tacke M, Sandek A, Ebner N, Tschope C, Doehner W, Anker SD, von Haehling S. Muscle wasting in patients with chronic heart failure: results from the studies investigating co-morbidities aggravating heart failure (SICA-HF). European heart journal. 2013;34(7):512-9.
19. Souza VA, Oliveira D, Barbosa SR, Correa J, Colugnati FAB, Mansur HN, Fernandes Nmds, Bastos MG. Sarcopenia in patients with chronic kidney disease

not yet on dialysis: Analysis of the prevalence and associated factors. PloS one. 2017;12(4):e0176230.

20. Teixeira Vde O, Filippin LI, Xavier RM. Mechanisms of muscle wasting in sarcopenia. Rev Bras Reumatol. 2012;52(2):252-9.
21. Chindapasirt J. Sarcopenia in Cancer Patients. Asian Pac J Cancer Prev. 2015;16(18):8075-7.
22. Denton CP, Khanna D. Systemic sclerosis. Lancet. 2017;390(10103):1685-99.
23. Grossberg AJ, Chamchod S, Fuller CD, Mohamed AS, Heukelom J, Eichelberger H, Kantor ME, Hutcheson KA, Gunn GB, Garden AS, Frank S, Phan J, Beadle B, Skinner HD, Morrison WH, Rosenthal DI. Association of Body Composition With Survival and Locoregional Control of Radiotherapy-Treated Head and Neck Squamous Cell Carcinoma. JAMA Oncol. 2016;2(6):782-9.
24. Awad S, Tan BH, Cui H, Bhalla A, Fearon KC, Parsons SL, Catton JA, Lobo DN. Marked changes in body composition following neoadjuvant chemotherapy for oesophagogastric cancer. Clinical nutrition. 2012;31(1):74-7.
25. Eriksson S, Nilsson JH, Strandberg Holka P, Eberhard J, Keussen I, Sturesson C. The impact of neoadjuvant chemotherapy on skeletal muscle depletion and preoperative sarcopenia in patients with resectable colorectal liver metastases. HPB (Oxford). 2017;19(4):331-7.
26. Farhangfar A, Makarewicz M, Ghosh S, Jha N, Scrimger R, Gramlich L, Baracos V. Nutrition impact symptoms in a population cohort of head and neck cancer patients: multivariate regression analysis of symptoms on oral intake, weight loss and survival. Oral Oncol. 2014;50(9):877-83.
27. Argiles JM, Busquets S, Stemmler B, Lopez-Soriano FJ. Cachexia and sarcopenia: mechanisms and potential targets for intervention. Current opinion in pharmacology. 2015;22:100-6.
28. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, Jatoi A, Loprinzi C, MacDonald N, Mantovani G, Davis M, Muscaritoli M, Ottery F, Radbruch L, Ravasco P, Walsh D, Wilcock A, Kaasa S, Baracos VE. Definition and classification of cancer cachexia: an international consensus. The Lancet Oncology. 2011;12(5):489-95.
29. Mir O, Coriat R, Blanchet B, Durand JP, Boudou-Rouquette P, Michels J, Ropert S, Vidal M, Pol S, Chaussade S, Goldwasser F. Sarcopenia predicts early dose-

limiting toxicities and pharmacokinetics of sorafenib in patients with hepatocellular carcinoma. PloS one. 2012;7(5):e37563.

30. Palmela C, Velho S, Agostinho L, Branco F, Santos M, Santos MP, Oliveira MH, Strecht J, Maio R, Cravo M, Baracos VE. Body Composition as a Prognostic Factor of Neoadjuvant Chemotherapy Toxicity and Outcome in Patients with Locally Advanced Gastric Cancer. J Gastric Cancer. 2017;17(1):74-87.
31. Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. Br J Cancer. 2012;107(6):931-6.
32. van Vugt JL, Braam HJ, van Oudheusden TR, Vestering A, Bollen TL, Wiezer MJ, de Hingh IH, van Ramshorst B, Boerma D. Skeletal Muscle Depletion is Associated with Severe Postoperative Complications in Patients Undergoing Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis of Colorectal Cancer. Ann Surg Oncol. 2015;22(11):3625-31.
33. Janssen I, Heymsfield SB, Baumgartner RN, Ross R. Estimation of skeletal muscle mass by bioelectrical impedance analysis. Journal of applied physiology. 2000;89(2):465-71.
34. Janssen I, Baumgartner RN, Ross R, Rosenberg IH, Roubenoff R. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. American journal of epidemiology. 2004;159(4):413-21.
35. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA. Frailty in older adults: evidence for a phenotype. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(3):M146-56.
36. Muscaritoli M, Anker SD, Argiles J, Aversa Z, Bauer JM, Biolo G, Boirie Y, Bosaeus I, Cederholm T, Costelli P, Fearon KC, Laviano A, Maggio M, Rossi Fanelli F, Schneider SM, Schols A, Sieber CC. 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.
37. Sadeghi M, Keshavarz-Fathi M, Baracos V, Arends J, Mahmoudi M, Rezaei N. Cancer cachexia: Diagnosis, assessment, and treatment. Crit Rev Oncol Hematol. 2018;127:91-104.

38. Peterson SJ, Mozer M. Differentiating Sarcopenia and Cachexia Among Patients With Cancer. Nutr Clin Pract. 2017;32(1):30-9.
39. Beaudart C, McCloskey E, Bruyere O, Cesari M, Rolland Y, Rizzoli R, Araujo de Carvalho I, Amuthavalli Thiyagarajan J, Bautmans I, Bertiere MC, Brandi ML, Al-Daghri NM, Burlet N, Cavalier E, Cerreta F, Cherubini A, Fielding R, Gielen E, Landi F, Petermans J, Reginster JY, Visser M, Kanis J, Cooper C. Sarcopenia in daily practice: assessment and management. BMC geriatrics. 2016;16(1):170.
40. Schweitzer L, Geisler C, Pourhassan M, Braun W, Gluer CC, Bosy-Westphal A, Muller MJ. What is the best reference site for a single MRI slice to assess whole-body skeletal muscle and adipose tissue volumes in healthy adults? The American journal of clinical nutrition. 2015;102(1):58-65.
41. Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme. 2008;33(5):997-1006.
42. 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. Clinical nutrition. 2015;34(4):667-73.
43. Norman K, Stobaus N, Gonzalez MC, Schulzke JD, Pirlich M. Hand grip strength: outcome predictor and marker of nutritional status. Clinical nutrition. 2011;30(2):135-42.

Eidesstattliche Versicherung

„Ich, Lindsey Otten, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: „Impact of Sarcopenia on Clinical Outcome in Old Patients with Cancer" selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.
Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren beruhen, sind als solche in korrekter Zitierung kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen werden von mir verantwortet.

Meine Anteile an etwaigen Publikationen zu dieser Dissertation entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Betreuer/in, angegeben sind. Für sämtliche im Rahmen der Dissertation entstandenen Publikationen wurden die Richtlinien des ICMJE (International Committee of Medical Journal Editors; www.icmje.og) zur Autorenschaft eingehalten. Ich erkläre ferner, dass mir die Satzung der Charité – Universitätsmedizin Berlin zur Sicherung Guter Wissenschaftlicher Praxis bekannt ist und ich mich zur Einhaltung dieser Satzung verpflichte.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§156,161 des Strafgesetzbuches) sind mir bekannt und bewusst.“

_____ _____

Datum Unterschrift

Anteilserklärung an der erfolgten Publikation

Otten, L., N. Stobäus, K. Franz, L. Genton, U. Müller-Werdan, R. Wirth, K. Norman. Impact of Sarcopenia on 1-year Mortality in Older Patients with Cancer. Age Ageing. 2019 Jan 4. doi: 10.1093/ageing/afy212. [Epub ahead of print]

Lindsey Otten contributed to the development of the research question, performed the data analyses, including the selection of variables and calculation of new variables and all statistical analyses as well as interpretation of the results, drafted, wrote and submitted the first manuscript. Lastly, Lindsey Otten revised the manuscript according to the comments of the peer reviewers with the support of K. Norman.

_____

Unterschrift, Datum und Stempel des betreuenden Hochschullehrers/der betreuenden Hochschullehrerin

_____

Unterschrift des Doktoranden/der Doktorandin

Journal Summary List

Accessed January 30, 2019 through the Charité Medical Library from https://intranet.charite.de/medbib/impact_faktoren_2017_fuer_zeitschriften_nach_fachgebieten/

Category: Geriatrics and Gerontology. Ranked 11/53

Journal Data Filtered By: **Selected JCR Year: 2017** Selected Editions: SCIE,SSCI Selected Categories: **"GERIATRICS and GERONTOLOGY"** Selected Category Scheme: WoS

Gesamtanzahl: 53 Journale

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
1	Journal of Cachexia Sarcopenia and Muscle	2,207	12.511	0.005180
2	AGEING RESEARCH REVIEWS	5,297	8.973	0.012030
3	AGING CELL	8,067	7.627	0.018910
4	Journal of the American Medical Directors Association	6,905	5.325	0.018230
5	Aging-US	4,410	5.179	0.010910
6	Aging and Disease	1,386	5.058	0.003230
7	JOURNALS OF GERONTOLOGY SERIES A-BIOLOGICAL SCIENCES AND MEDICAL SCIENCES	17,809	4.902	0.023940
8	NEUROBIOLOGY OF AGING	21,914	4.454	0.044830
9	JOURNAL OF THE AMERICAN GERIATRICS SOCIETY	29,943	4.155	0.036360
10	Immunity & Ageing	749	4.019	0.001580
11	AGE AND AGEING	10,751	4.013	0.014720
12	MECHANISMS OF AGEING AND DEVELOPMENT	5,523	3.739	0.004380
13	BIOGERONTOLOGY	2,135	3.702	0.003510
14	Frontiers in Aging Neuroscience	4,995	3.582	0.016550

Publication

Otten L, Stobäus N, Franz K, Genton L, Müller-Werdan U, Wirth R, Norman K. Impact of Sarcopenia on 1-year Mortality in Older Patients with Cancer.

Age Ageing. 2019 Jan 4. doi: 10.1093/ageing/afy212. [Epub ahead of print]

Impact Factor 2017: 4.013; 5-Year Impact Factor: 4.715

https://doi.org/10.1093/ageing/afy212

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

Complete List of Publications

Publications

Original article

Otten L, Stobäus N, Franz K, Genton L, Müller-Werdan U, Wirth R, Norman K.

Impact of Sarcopenia on 1-year Mortality in Older Patients with Cancer.

Age Ageing. 2019 Jan 4. doi: 10.1093/ageing/afy212. [Epub ahead of print]

IF: 4.013 (2017)

Original article

Franz K, Ost M, **Otten L**, Herpich C, Coleman V, Endres A-S, Klaus S, Müller-Werdan U, Norman K.

Higher Serum Levels of Fibroblast Growth Factor 21 in Old Patients with Cachexia.

Nutrition, 2019, doi: 10.1016/j.nut.2018.11.004, in press.

IF: 3.734 (2017)

Original article

Siegert E, March C, **Otten L**, Makowka A, Preis E, Buttgereit F, Riemekasten G, Müller-Werdan U, Norman K.

Prevalence of Sarcopenia in Systemic Sclerosis: assessing body composition and functional disability in patients with Systemic Sclerosis.

Nutrition. 2018;55-56:51-5. Epub 2018/07/01. doi: 10.1016/j.nut.2018.03.046.

IF: 3.734 (2017)

Review

Financial impact of sarcopenia or low muscle mass - A short review.

Norman K*, **Otten L*.**

Clin Nutr. 2018 Sep 27

IF: 5.496 (2017)

* both authors contributed equally

Original article

Otten L, Bosy-Westphal A, Ordemann J, Rothkegel E, Stobäus N, Elbelt U, Norman K.

Abdominal fat distribution differently affects muscle strength of the upper and lower extremities in women.
Eur J Clin Nutr. 2017;71(3):372-6.
IF: 3.06

Original article
Nikolov J, Spira D, Aleksandrova K, **Otten L**, Meyer A, Demuth I, Steinhagen-Thiessen E, Eckardt R, Norman K.
Adherence to a Mediterranean-Style Diet and Appendicular Lean Mass in Community-Dwelling Older People: Results From the Berlin Aging Study II.
J Gerontol A-Biol. 2016;71(10):1315-21.
IF: 5.96

Conference proceedings

The Gerontological Society of America (GSA) Annual Scientific Meeting, Boston, USA, November 2018 - Poster presentation
Otten L, Franz K, Herpich C, Kiselev J, Müller-Werdan U, Norman K. Functional Limitations, Frailty and Quality of Life in Malnourished, Geriatric Patients at Hospital Discharge. Innovation in Aging. 2018; 2(1): 718-719.

Gerontology and Geriatrics (DGG-DGGG) Annual Congress, Cologne, Germany September 2018 - Symposium oral presentation
Otten L, Franz K, Herpich C, Kiselev J, Müller-Werdan U, Norman K. Funktionelle Einschränkungen, Frailty und Lebensqualität bei mangelernährten, geriatrischen Patienten zum Zeitpunkt der Krankenhausentlassung. Z Gerontol Geriat 2018 · 51 (Suppl 1):S1–S162.

40th ESPEN Congress on Clinical Nutrition and Metabolism, Madrid, Spain, September 2018 - Poster presentation
Otten L, Franz K, Herpich C, Kiselev J, Müller-Werdan U, Norman K. Functional Limitations, Frailty and Quality of Life in Malnourished, Geriatric Patients at Hospital Discharge. Clin Nutr 2018; 37(1):63.
* Travel Award 2018 from Danone GmbH Germany

Nutrition 2018, 17th Three Nations Conference of DGEM, AKE and GESKES, Kassel, Germany, June 2018 - Oral presentation
Otten L, Franz K, Herpich C, Kiselev J, Müller-Werdan U, Norman K. Funktionelle Einschränkungen, Frailty und Lebensqualität bei mangelernährten, geriatrischen Patienten zum Zeitpunkt der Krankenhausentlassung. Aktuel Ernahrungsmed 2018; 43(03): 215-216.

International Conference on Frailty and Sarcopenia Research (ICFSR), Philadelphia, USA, April 2016 - Poster presentation
Otten L, Franz K, Kiselev J, Steinhagen-Thiessen E, Müller-Werdan U, Eckardt R, Spira D, Norman K. Effect of a three month post-hospital nutritional intervention on functional parameters in frail and malnourished older adults – a randomized controlled study. JFA, Vol 5, Supplement 1, 2016; P147.

Nutrition 2016, 15th Three Nations Conference of DGEM, AKE and GESKES, Dresden, Germany, June 2016 - Oral presentation
Otten L, Kiselev J, Franz K, Steinhagen-Thiessen E, Müller-Werdan U, Eckardt R, Spira D, Norman K. Einflussfaktoren für die Verbesserung des Ernährungszustandes bei gebrechlichen älteren Menschen nach dem Krankenhausaufenthalt. Aktuel Ernährungsmed 2016; 41 – V23.

Nutrition 2016, 15th Three Nations Conference of DGEM, AKE and GESKES, Dresden, Germany, June 2016 - Oral presentation
Otten L, Franz K, Kiselev J, Steinhagen-Thiessen E, Müller-Werdan U, Eckardt R, Spira D, Norman K. Der Einfluss einer 3-monatigen poststationären Ernährungsintervention auf funktionelle Parameter bei älteren Menschen mit Frailty – eine randomisierte kontrollierte Studie. Aktuel Ernahrungsmed 2016; 41 – V20
*DGEM best poster 2016

39th ESPEN Congress on Clinical Nutrition and Metabolism, Copenhagen, Denmark, 2016 - Poster presentation
Otten L, Franz K, Kiselev J, Müller-Werdan U, Eckardt R, Spira D, Norman K. Improving Nutritional Status in the Frail Old after Hospital Discharge – Influence Factors. Clin Nutr. 2016; 35, S161

39th ESPEN Congress on Clinical Nutrition and Metabolism, Copenhagen, Denmark, 2016 - Poster presentation
Otten L, Kiselev J, Franz K, Steinhagen-Thiessen E, Müller-Werdan U, Eckardt R, Spira D, Norman K. Effect of a three month Post-Hospital Nutritional Intervention on Functional Performance in Frail and Malnourished Older Adults – A Randomized Controlled Study. Clin Nutr. 2016; 35, S161

The International Association of Gerontology and Geriatrics European Region (IAGG-ER) 8th Congress, Dublin, Ireland, April 2015 - Poster presentation
Otten L, Stobäus N, Wirth R, Neubauer M, Norman K. Impact of Sarcopenia on 1-year Mortality in Old Patients with Cancer. Irish Ageing studies Review, Volume 6, Issue 1, 2015

38th ESPEN Congress on Clinical Nutrition and Metabolism, Lisbon, Portugal, September 2015 - Poster presentation
Otten L, Elbelt U, Ordemann J, Rothkegel E, Stobaeus N, Norman K. Influence of Abdominal Fat Distribution on the Muscle Strength of the Upper and Lower Extremities in Obese Patients. Clin Nutr. 2015; 34, S212

38th ESPEN Congress on Clinical Nutrition and Metabolism, Lisbon, Portugal, September 2015- Poster presentation
Otten L, Ott K-M, Eckardt R, Steinhagen-Thiessen E, Demuth I, Norman K. Influence of Body Composition Phenotype on Mobility and Grip Strength in the Community-Dwelling Old. Clin Nutr. 2015; 34, S189

Nutrition 2015, 15th Three Nations Conference of DGEM, AKE and GESKES, Bregenz, Austria, May 2015 - Oral presentation
Otten L, Stobäus N, Wirth R, Neubauer M, Norman K. Impact of Sarcopenia on 1-year Mortality in Old Patients with Cancer. Aktuel Ernahrungsmed 2015; 40 - O2_6.

Nutrition 2015, 15th Three Nations Conference of DGEM, AKE and GESKES, Bregenz, Austria, May 2015 - Oral presentation

Otten L, Elbelt U, Ordemann J, Rothkegel E, Stobäus N, Norman K. Einfluss der abdominalen Fettverteilung auf die Muskelkraft der oberen und unteren Extremitäten bei adipösen Patienten. Aktuel Ernahrungsmed 2015; 40: 179-201

36th ESPEN Congress on Clinical Nutrition and Metabolism, Leipzig, Germany, September 2013 - Poster presentation
Otten L, Boschmann M, Pfeiffer E, Haas V. Bioimpedance Vector Analysis (BIVA) in Adolescents with Anorexia Nervosa. Clin Nutr. 2013; 32, S84-S85

36th ESPEN Congress on Clinical Nutrition and Metabolism, Leipzig, Germany, September 2013 - Poster presentation
Otten L, Freudenreich M, Stobaus N, Paffhausen S, Norman K. Cancer and the Use of Nutritional Supplements. Clin Nutr. 2013; 32, S158-S159

Further abstracts as co-author.

Book chapters

Otten, L., Norman, K.
Diets and Diet Therapy: Oral Nutritional Supplements. In: Ferranti, P., Berry, E.M., Anderson, J.R. (Eds.), Encyclopedia of Food Security and Sustainability, vol. 2, pp. 113–118. Elsevier. 2019

Acknowledgements

I would like to express my gratitude to my supervisor, mentor and ‘Doktormutter’, Prof. Dr. Kristina Norman. Thank you for giving me the opportunity to work in your department and for all of the opportunities that have come with that. I sincerely appreciate your guidance and support, which always come in the right amount at the right time.

I would like to thank the co-authors with whom I’ve had the opportunity to work with and learn from, especially A. Bosy-Westphal, K. Franz, L. Genton, U. Müller-Werdan, J. Ockenga, N. Stobäus and R. Wirth to name a few.

Furthermore, I would like to thank the Academic Grants' Committee of the Charité – Universitätsmedizin Berlin for the Scholarship for Postgraduate Thesis Projects (Promotionsstipendium I).

The past 5 years would not have been as enjoyable and fulfilling if not for the many wonderful colleagues who have accompanied and supported me on different levels. N. Stobäus and M. Neubauer, thank you for the warm welcome and continued support and friendship. A special thanks goes to K. Franz who has provided tremendous support, especially during my pregnancy and maternity leave, and with whom I’m thankful to share an office. To K. Kessler and S. Pevny, thanks for listening and for the advice.

Last but not least, I thank my family including my parents, parents-in-law and especially my husband for their support.