Aus der Klinik für Radiologie und Nuklearmedizin

der Medizinischen Fakultät

der Otto-von-Guericke-Universität Magdeburg

Auswirkung der Körperkomposition auf klinische Ergebnisse bei Patienten mit schwerer Covid-19-Erkrankung

Dissertation

zur Erlangung des Doktorgrades

Dr. med.

(doctor medicinae)

an der Medizinischen Fakultät

der Otto-von-Guericke-Universität Magdeburg

vorgelegt von Hakan Kardas

aus Melikgazi/Türkei

Magdeburg 2023

Angefertigt von April 2021 bis Februar 2023 in der Klinik für Radiologie und Nuklearmedizin.

Klinikdirektor: Herr Professor Dr. med. Maciej Pech

Betreuer: Herr Professor Dr. med. Alexey Surov

Bibliographische Beschreibung:

Kardas, Hakan:
Auswirkung der Körperkomposition auf klinische Ergebnisse bei Patienten mit schwerer Covid-19-Erkrankung

Kurzreferat:

Die Auswirkung der Körperkomposition auf Patienten mit schwerer Covid-19-Erkrankung ist unbekannt. Unser Ziel war es, den Einfluss der Basislinien-Computertomographie (CT-basierten Körperkompositionsparametern [auf T4-Ebene Pectoralis-Muskelfläche, Pectoralis-Muskelindex, Skelettmuskelgauge und auf L3-Ebene Skelettmuskelindex (SMI), Muskeldichte (MD) und Fettgewebemessungen viszeralen Fettgewebes (VAT), subkutanes Fettgewebe (SAT), intramuskuläres Fettgewebe (IMAT), visceral-tosubcutaneous-adipose-tissue-area-ratio (VSR)]) auf klinische Variablen bei erwachsenen Patienten mit bestätigter Covid-19-Infektion, die von März 2020 bis Mai 2021 in sechs europäischen Zentren stationär behandelt wurden, retrospektiv zu analysieren. Des Weiteren wurde der Zusammenhang zwischen der Erkrankung und der Mortalität, der Notwendigkeit einer Intubation (MV) und der Intensivpflichtigkeit innerhalb von 30 Tagen bewertet.

Die Resultate zeigen, dass eine höhere VSR bei Patienten, die wegen einer Covid-19-Infektion ins Krankenhaus eingeliefert wurden, ein entscheidender prognostischer Faktor für die kurzfristige Mortalität ist. Dagegen wurden lediglich schwache Assoziationen mit dem klinischen Verlauf für MD- und Fettgewebemessungen gefunden. Männliches Geschlecht war der stärkste prognostische Faktor für einen ungünstigen klinischen Verlauf. Hinsichtlich der Muskelmasse haben Covid-19-Überlebende im Vergleich zu Nichtüberlebenden größere Areale und einen höheren Index, Gauge und Dichte der Pectoralis-Muskeln.

Schlüsselwörter: Covid-19, Körperkomposition, Computertomographie, *Pectoralis* Muskel, Mortalität, Niedrige Skelettmuskelmasse, Gesamtüberleben, Fettgewebe.

Die vorliegende, kumulative Doktorarbeit basiert auf den folgenden aufgeführten Publikationen:

1) **Hakan Kardas**, Maximilian Thormann, Caroline Bär, Jazan Omari, Andreas Wienke, Maciej Pech, Alexey Surov:
   Impact of Pectoral Muscle Values on Clinical Outcomes in Patients With Severe Covid-19 Disease. In Vivo January 2022, 36 (1) 375-380

2) Alexey Surov, **Hakan Kardas**, Giulia Besutti, Massimo Pellegrini, Marta Ottone, Mehmet Ruhi Onur, Firat Atak, Ahmet Gurkan Erdemir,Elif Hocaoglu, Omer Yildiz,Ercan Inci, Eda Cingoz, Mehmet Cingoz, Memduh Dursun, Inan Korkmaz, Cagri Orhan, Alexandra Strobel, Andreas Wienke, Maciej Pech: Prognostic Role of the Pectoralis Musculature in Patients with COVID-19. A Multicenter Study. Academic Radiology May 15, 2022.

3) Alexey Surov, Maximilian Thormann, **Hakan Kardas**, Mattes Hinnerichs, Jazan Omari, Eda Cingöz, Mehmet Cingöz, Memduh Dursun, Inan Korkmaz, Cagri Orhan, Ömer Yildiz, Elif Hocaoglu, Ercan Inci, Hakan Önder, Hamdullah Erk, Ougkour Chousein, Hadi Sasani, Korcan Aysun Gönen, Maciej Pech, Andreas Wienke: Visceral to subcutaneous fat ratio predicts short term mortality in patients with Covid 19. A multicenter study. The British Journal of Radiology February 6, 2023

Die veröffentlichten Publikationen sind in der Dissertation (unter 6.) aufgeführt.

Inhaltsverzeichnis

Abkürzungen:

CI	
COVID-19	Coronavirus-Krankheit-2019
CT	Computertomographie
HE	
HU	Hounsfield-Einheiten
IMAT	intramuskuläres Fettgewebe
IMV	intensivmedizinische Versorgung
MD	Muskeldichte
MV	maschinelle Beatmung
p	Probabilität
PMA	Pectoralis-Muskelfläche
PMI	Pectoralis-Muskelindex
%	Prozent
OD	Odds Ratio
ROI	Interessenregion
SARS	Schwere akute Atemwegserkrankung
SAT	subkutanes Fettgewebe
SMA	Skelettmuskelfläche
SMG	Skelettmassegauge
SMI	Skelettmasseindex
TAT	Fettgewebeparameter wie Gesamtfettgewebe
VAT	viszerales Fettgewebe
VSR	Verhältnis der viszeralen zum subkutanen Fettgewebearea Fettgewebefläche

1. Einführung

Die Pandemie der Coronavirus-Krankheit 2019 (COVID-19) stellt ein großes Problem für die globale Gesundheit dar. Der klinische Verlauf von COVID-19 ist sehr variabel. Obwohl festgestellt wurde, dass der Verlauf bei den meisten Patienten relativ mild ausfällt, hatten einige eine schnelle Progression mit Mortalität (1,2). Daher ist die Prognose unklarer Ergebnisse von COVID-19 von wesentlicher Bedeutung. Bereits etablierte Prognosefaktoren sind Alter und Geschlecht (3,4). Begleiterkrankungen wie Demenz, Herzinsuffizienz und periphere Gefäßerkrankungen sind ebenfalls Prädiktoren für einen schwierigen Krankheitsverlauf (3,4).

Die Computertomographie (CT) ist das wichtigste bildgebende Verfahren bei COVID-19, insbesondere zum Nachweis von Lungenkonsolidierungen (5-7). Typische Befunde in der CT bei COVID-19 sind bilaterale, peripher dominante Milchglastrübungen mit Unterlappen- und posteriorer Betonung (5-7). Auch extrapulmonale Befunde spielen bei COVID-19 eine entscheidende Rolle (8). Es wurde gezeigt, dass Pleuraerguss, Perikarderguss und mediastinale Lymphadenopathie als Prädiktoren für einen schweren Verlauf von COVID-19 verwendet werden können (6,8). Tatsächlich sind Pleuraerguss und Koronarverkalkungen starke Prädiktoren für die Mortalität bei COVID-19, Odds Ratio (OR) = 4,6 (95 % CI 2,97 - 7,12), $p < 0,00001$ und OR = 2,68 (95 % CI 1,78 - 4,04), $p < 0,00001$ (8).

Es wurde gezeigt, dass Sarkopenie als Risikofaktor für die Dauer des Krankenhausaufenthalts und die Mortalität bei vielen Krankheiten eine wichtige Rolle spielen kann (9-12). Aber bei Patienten mit COVID-19 sind die Ergebnisse weniger eindeutig und daher wird die Körperkomposition als Prognostikfaktor diskutiert. Bisher wurden viele verschiedene Messungen des Muskelbereichs und des Skelettmasseindex (SMI) als Indikator für Sarkopenie auf verschiedenen Muskelebenen sowohl im Pektoral- sowie Psoasbereich durchgeführt und viele widersprüchliche Ergebnisse sind dabei herausgekommen.

1.1. Übersicht der Body-Komposition auf Patienten

Sarkopenie ist definiert als der Verlust von Muskelmasse oder geringe Muskelmasse, geringe Muskelkraft sowie beeinträchtigte Muskelqualität [13]. Ein häufig verwendeter Indikator für Sarkopenie ist der SMI, der anhand von Computertomographie-Scans beurteilt werden kann. Der SMI und die Skelettmuskelfläche (SMA) sind Indikatoren für Sarkopenie und haben sich als Prädiktoren für das Behandlungsergebnis erwiesen [14]. Es wurde auch berichtet, dass die Messungen der Skelettmuskelmasse in Hounsfield-Einheiten (HU) den Lipidinhalt widerspiegeln und damit ein Indikator für die Muskelqualität sein können [15]. Das Skelettmuskelgauge (SMG) entspricht dem Produkt aus SMI und Muskeldichte (MD) und wurde als prognostische Indikator bei Patienten mit Infektionskrankheiten oder Krebs in Verbindung gebracht [16].

Es gibt nur wenige Studien, die den Zusammenhang zwischen standardisierter Körperkompositionsparameter – einschließlich Muskel- und Fettgewebemessungen – und den klinischen Ergebnissen sowie der Mortalität bei COVID-19-Patienten bewerten. Das Ziel dieser Studie war es daher, den Wert verschiedener Körperkompositionsparameter zu bestimmen, um sowohl den Schweregrad von COVID-19 (Risiko einer Aufnahme auf der Intensivstation, invasive Beatmung) als auch die Mortalität innerhalb von 30 Tagen in einer großen multizentrischen Kohorte vorherzusagen.

1.2. Methoden und Patientenselektion

Für die vorliegende Studie wurden Daten aus sechs Zentren in Europa retrospektiv erhoben. Die Patienten wurden von März 2020 bis Dezember 2021 aus elektronischen Krankenhausakten identifiziert. Die Studie wurde jeweils von den lokalen Ethikkommissionen genehmigt.

Einschlusskriterien für alle Zentren:
- PCR bestätigte COVID-19-Erkrankung
- Krankenhausaufenthalt wegen Symptomen oder Komplikationen im Zusammenhang mit der COVID-19-Erkrankung
- Verfügbare Thorax- (für 1. und 2. Studie) und Abdominal- (für 3. Studie) CT-Aufnahmen mit oder ohne Kontrastmittelinjektion
- Verfügbare Daten zu den folgenden Ergebnisvariablen: mechanische Beatmung, Aufnahme auf Intensivstation, Mortalität innerhalb von 30 Tagen nach Aufnahme

Ausschlusskriterien:
- Fehlende klinische Daten
- Krankenhausaufenthalt aus anderen Gründen als COVID-19-Erkrankung
- Für 1. und 2. Studie fehlender CT-Scan des Thorax auf Höhe T4 und für 3. Studie fehlender CT-Scan des Abdomens auf Höhe L3
- Für 1. und 2. Studie CT-Bilder nach intravenöser Kontrastmittelapplikation

Die größte erfasste Patientengruppe (erste multizentrische Studie von CT-Thorax) umfasst 1138 Patienten. Darunter waren547 Frauen (48,1 %) und 591 Männer (51,9 %).

1.3. Messung der Bodykomposition im CT

In allen Fällen wurde der erste opportunistische Thorax-/Abdominal-CT-Scan nach Krankenhausaufnahme verwendet. In allen sechs Zentren wurde die Bildanalyse von erfahrenen Radiologen durchgeführt, die für den klinischen Verlauf der Patienten blind waren. Alle Körperkompositionsmessungen in der ersten sowie zweiten Studie wurden halbautomatisch auf axialen Bildern auf T4-Ebene im Weichteilfenster via Syngovia und Infinitt (1. Studie: Abb. 1) (2. Studie: Abb. 2 und 3) und für die 3. Studie der Mittelteil des dritten Lendenwirbels (L3) im Weichteilfenster (Fenster von 45 bis 250 HE) mit der frei verfügbaren ImageJ Software (Version 1.53, National Institute of Health, USA) (Abb. 4 und 5) durchgeführt. Die Überprüfung der Messungen und notwendigen Korrekturen wurden ebenfalls von erfahrenen Radiologen durchgeführt, die für den klinischen Verlauf der Patienten blind waren.

In der 1. und 2. Studie wurde eine polygonaler Interessenregion (ROI) entlang der Konturen der Mm. pectorales majores et minores auf beiden Seiten gezeichnet (Abb. 1 sowie 2 und 3). Die Pectoralis-Muskelfläche (PMA) wurde als Summe der bilateralen Bereiche der großen und kleinen Brustmuskeln definiert. Darüber hinaus wurde die Pectoralis-Muskeldichte innerhalb der ROIs gemessen. Der Pectoralis-Muskelindex (PMI) wurde als Quotient aus PMA und Körpergröße des Patienten im Quadrat berechnet. Zusätzlich wurde die SMG berechnet, indem der PMI mit der mittleren MD multipliziert wurde, wie zuvor berichtet (17).

In der 3. Studie wurden die folgenden Parameter der Körperkomposition geschätzt: SMA, subkutanes Fettgewebe (SAT), viszerales Fettgewebe (VAT), TAT und intramuskuläres Fettgewebe (IMAT) wurden automatisch von der Software auf Querschnittsbildern gemessen. Die relative Verteilung des abdominalen Körperfetts wurde durch den VSR bewertet, der durch Division von VAT durch SAT berechnet wurde. Der SMI wurde berechnet, indem der SMA durch die Körpergröße des Patienten in Zentimetern im Quadrat dividiert wurde. Der

Fettgewebeindex wurde auf analoge Weise berechnet.

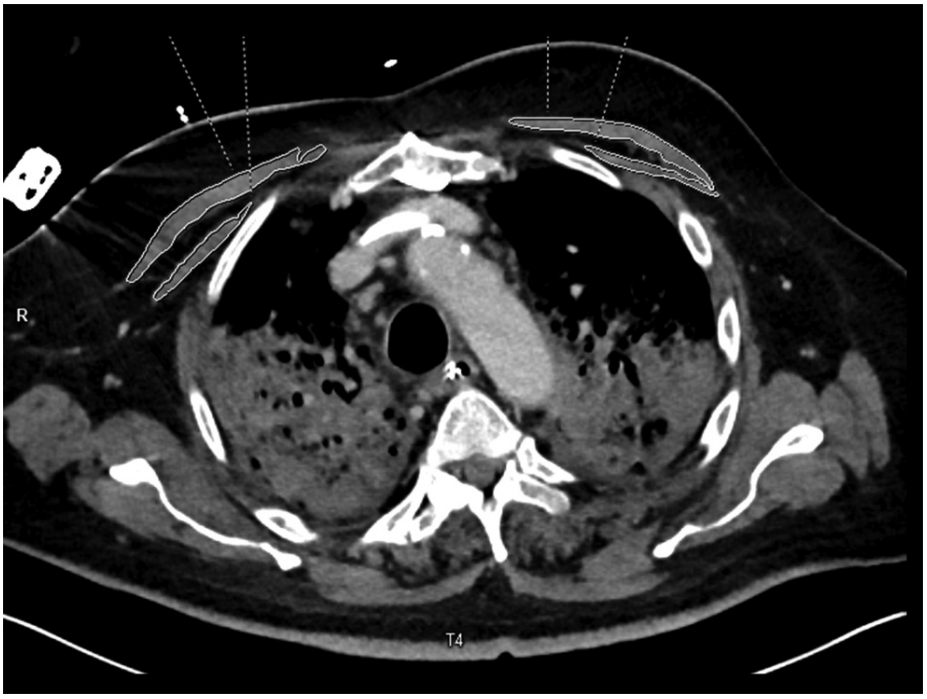


Abb. *1.* Thorax-CT eines 67-jährigen Patienten. Die identifizierten Muskelparameter waren: PMA 18,0 cm^2, PMI 5,8 cm^2/m^2, Muskeldichte 22,5 HU, SMG 132,3. Der Patient starb nach 13 Tagen auf der Intensivstation.

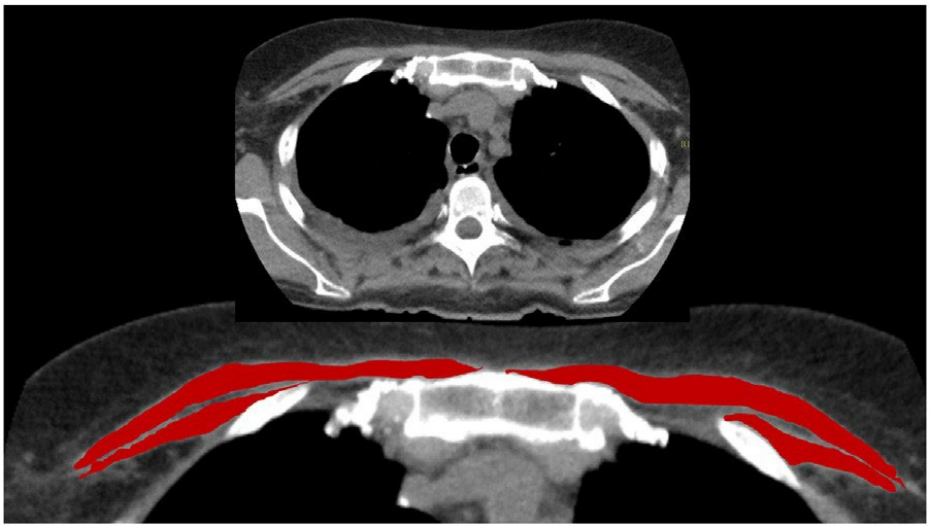


Abb. 2. Thorax-CT einer 55-jährigen Patientin mit COVID-19. Die identifizierten Muskelparameter waren: PMA 14,48 cm^2, Muskeldichte 28 HU, PMI 5,19, SMG 145,3. Die Patientin starb am Tag 19 nach Aufnahme.

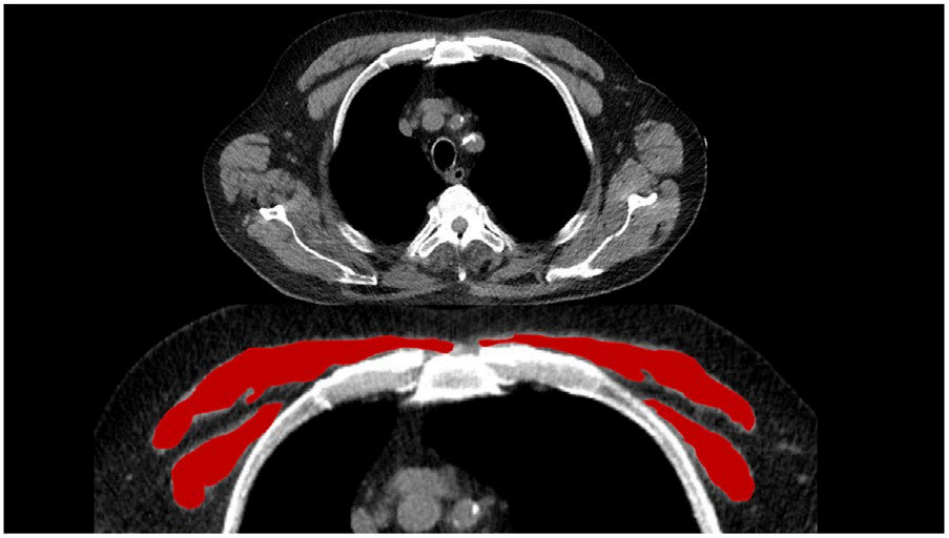


Abb 3. Thorax-CT eines 61-jährigen Patienten mit COVID-19. Die identifizierten Muskelparameter waren: PMA 28,17 cm^2, Muskeldichte 30 HU, PMI 8,69, SMG 260,7. Der Patient wurde im Verlauf gesund entlassen.

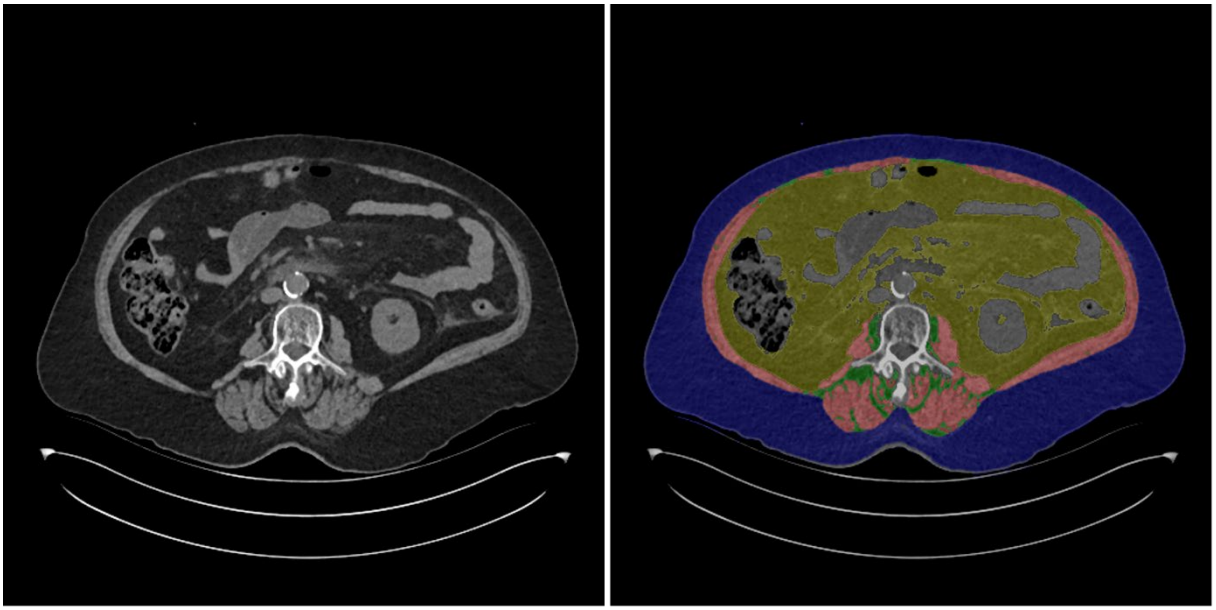


Abb 4. Repräsentative Beispiele für abdominale CT-Scans mit Segmentierung der Skelettmuskulatur: intramuskuläres Fett Gewebe (grün), viszerales Fettgewebe (gelb), subkutan Fettgewebe (blau), Skelettmuskel (rot). Diese Patientin hatte ein SMA von 98,1 cm2, ein SMI von 37,4 kg/cm2, ein VAT von 314,2 cm2 und ein VSR von 0,91.

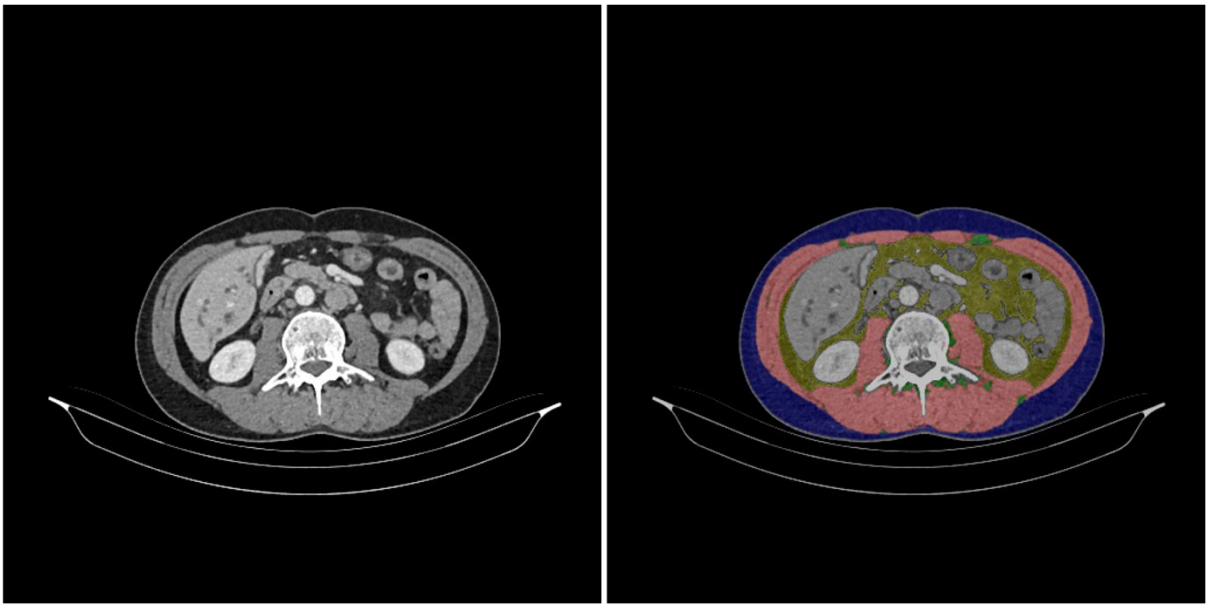


Abb 5. Dieser Patient hatte ein SMA von 140,3 cm2, ein SMI von 46,4 kg/cm2, ein VAT von 72,2 cm2, und ein VSR von 0,72.

1.4. Statistische Analyse

Die statistische Analyse wurde via SPSS Version 25 (IBM SPSS Statistics, NY, USA) durchgeführt. Die Mittel-, Medianwerte sowie Standardabweichungen wurden für kontinuierliche Variablen ausgerechnet. Der Einfluss von Körperkompositionsparametern auf das Risiko einer intensivmedizinischen Versorgung (IMV), einer Aufnahme auf die Intensivstation und der Mortalität wurde mittels logistischer Regression bewertet. Der Vergleich der Pectoralis-Muskelparameter wurde mit Mann-Whitney-U-Tests durchgeführt und die p-Werte wurden für multiples Testen angepasst (Bonferroni-Korrektur). Um den Einfluss der Skelettmuskulatur auf die klinischen Ergebnisse zu bewerten, wurden uni- und multivariable logistische Regressionsmodelle verwendet. Odds Ratios werden zusammen mit 95 % Konfidenzintervallen (95 % KI) dargestellt. Die resultierenden p-Werte wurden im explorativen Sinne interpretiert.

1.5. Zielsetzung der Arbeit

Die vorliegende Arbeit basiert auf einer retrospektiven Datenauswertung von Patienten mit schwerer COVID-19 Erkrankung. Die Daten der Patienten wurden von unserer Klinik und 7 weiteren Kliniken zwischen März 2020 und Dezember 2021 gesammelt. Die über diesen Zeittraum gesammelten Daten unserer Patienten wurden aus dem Klinikinformationssystem MEDICO gebündelt und retrospektiv ausgewertet.

Ziel der Arbeit und der multizentrischen, retrospektiven Analyse war die Beurteilung der Auswirkung von Körperkompositionparametern bei Patienten mit schwerer COVID-19-Erkrankung auf relevante Resultate wie der Mortalität innerhalb von 30 Tagen, der Notwendigkeit einer Intubation oder der Notwendigkeit einer Aufnahme auf die Intensivstation.

Im Detail wurde der Einfluss des PMI auf die klinischen Ergebnisse der Patienten mit schwerer COVID-19-Erkrankung (Orginalarbeit 1 und 2) sowie die Prognose der kurzfristigen Sterblickeit von COVID-19-Patienten anhand viszeraler bis subkutaner Fettgewebemessungen (Orginalarbeit 3) untersucht.

2. Eigene Arbeiten

2.1. Impact of Pectoral Muscle Values on Clinical Outcomes in Patients With Severe COVID-19 Disease.

(Orginalarbeit 1)

Hakan Kardas, Maximilian Thormann, Caroline Bär, Jazan Omari, Andreas Wienke, Maciej Pech, Alexey Surov:
Impact of Pectoral Muscle Values on Clinical Outcomes in Patients With Severe COVID-19 Disease. In Vivo January 2022, 36 (1) 375-380.

Sarkopenie ist eine abnormale Körperkomposition, die als Verlust von Muskelmasse, geringe Muskelkraft und Beeinträchtigung der Muskelqualität definiert ist. Sarkopenie tritt häufig bei Patienten im Alter von ca. 65 Jahren auf und wird mit einem schlechteren klinischen Verlauf, Morbidität und Mortalität in Verbindung gebracht. Thoraxscans mittels Computertomographie (CT) oder Magnetresonanztomographie gelten als Goldstandard für die quantitative Beurteilung der Körperkomposition. Die Auswirkungen von Sarkopenie auf Patienten mit COVID-19 sind noch ebenso unerforscht, wie ob sie durch das schwere akute Atemwegssyndrom (SARS) verursacht wird. Tatsächlich ist die Literatur zur Messung der Skelettmasse uneins. Aus diesem Grund wollten wir den Zusammenhang von CT-basierten Körperkompositionsparametern (PMA, PMI, SMG) und klinischen Variablen bei Patienten mit schwerer COVID-19-Erkrankung untersuchen. Thorax-CT-Scans von erwachsenen Patienten mit bestätigtem COVID-19, die von März 2020 bis Mai 2021 in unserem medizinischen Zentrum (Universitätsklinikum Magdeburg) stationär behandelt wurden, wurden retrospektiv analysiert. PMA, PMI und SMG wurden beim ersten CT-Scan nach der Aufnahme gemessen. Die Parameter der Körperzusammensetzung wurden auf Assoziation mit klinischen Variablen und 30-Tage-Mortalität untersucht. In unserem kleinen Studienkollektiv (46 Patienten) und der retrospektiven Analyse war keine der Körperkompositionen ein Prädiktor für die 30-Tage-Mortalität, die Dauer des Krankenhausaufenthalts, die Dauer der Behandlung auf der Intensivstation oder die Dauer der invasiven mechanischen Beatmung.

2.2. Prognostic Role of the Pectoralis Musculature in Patients with COVID-19. A Multicenter Study.
(Orginalarbeit 2)

Alexey Surov, **Hakan Kardas**, Giulia Besutti, Massimo Pellegrini, Marta Ottone, Mehmet Ruhi Onur, Firat Atak, Ahmet Gurkan Erdemir,Elif Hocaoglu, Omer Yildiz,Ercan Inci, Eda Cingoz, Mehmet Cingoz, Memduh Dursun, Inan Korkmaz, Cagri Orhan, Alexandra Strobel, Andreas Wienke, Maciej Pech:
Prognostic Role of the Pectoralis Musculature in Patients with COVID-19. A Multicenter Study. Academic Radiology May 15, 2022.

Seit Dezember 2019 ist die COVID-19-Pandemie ein großes Problem für die Menschen und die globale Gesundheit. Außerdem hat der klinische Verlauf von COVID-19-Patienten ein sehr breites Spektrum von asymptomatisch bis zur Mortalität. Aus diesem Grund spielen die prognostischen Faktoren bei COVID-19 eine entscheidende Rolle. Bereits etablierte Prognosefaktoren sind Alter und Geschlecht. Komorbiditäten wie Demenz, Herzinsuffizienz und periphere Gefäßerkrankungen sind ebenfalls Prädiktoren für einen ungünstigen Verlauf der Krankheit. Unsere Ziele bestehen in dieser multizentrischen Studie darin, die Auswirkungen einer geringen Skelettmuskelmasse bei Patienten mit COVID-19 auf relevante Ergebnisse wie 30-Tage-Mortalität, Notwendigkeit einer Intubation sowie der Aufnahme auf die Intensivstation zu bewerten.

Für diese Studie wurden Daten aus sechs Zentren erfasst. Die erfasste Stichprobe umfasst 1138 Patienten. Es handelte sich um 547 Frauen (48,1 %) und 591 Männer (51,9 %) mit einem Durchschnittsalter von 54,5 ± 18,8 Jahren (Median: 55 Jahre; Spannweite: 18-84 Jahre). In allen Fällen wurde eine Thorax-CT ohne intravenöse Kontrastmittelgabe durchgeführt. Die folgenden Parameter der Pectoralis-Muskeln wurden geschätzt: Muskelfläche als Summe der bilateralen Flächen der M. pectoralis major und minor, Muskeldichte, Muskelindex (PMI) (Pectoralis-Muskelarea geteilt durch das Quadrat der Körpergröße des Patienten) als Verhältnis der M. pectoralis major und minor geteilt durch die

Körpergröße des Patienten2 und Muskelgauge (PMI x Muskeldichte).

Insgesamt wurden 220 Patienten (19,33 %) auf der Intensivstation aufgenommen. Bei 171 Patienten (15,03 %) wurde eine mechanische Lungenbeatmung durchgeführt. Schließlich starben 154 Patienten (13,53 %) innerhalb der Beobachtungszeit von 30 Tagen. Alle untersuchten Parameter des Brustmuskels waren bei den Patienten mit ungünstigen Covid-19-Verläufen niedriger. Alle Parameter des Pectoralis-Muskels wurden in alters- und geschlechtsbereinigten multivariaten Analysen mit der 30-Tage-Mortalität assoziiert. Die Conclusio unserer Studie: Schlussfolgerung: Bei COVID-19 haben Überlebende im Vergleich zu Nichtüberlebenden größere Flächen und einen höheren Index, Stärke und Dichte der Pectoralis-Muskeln. Die analysierten Muskelparameter können jedoch nicht zur Prognose von Krankheitsverläufen verwendet werden.

2.3. Visceral to subcutaneous fat ratio predicts short term mortality in patients with Covid 19. A multicenter study. (Originalarbeit 3)

Alexey Surov, Maximilian Thormann, **Hakan Kardas**, Mattes Hinnerichs, Jazan Omari, Eda Cingöz, Mehmet Cingöz, Memduh Dursun, Inan Korkmaz, Cagri Orhan, Ömer Yildiz, Elif Hocaoglu, Ercan Inci, Hakan Önder, Hamdullah Erk, Ougkour Chousein, Hadi Sasani, Korcan Aysun Gönen, Maciej Pech, Andreas Wienke: Visceral to subcutaneous fat ratio predicts short term mortality in patients with Covid 19. A multicenter study. The British Journal of Radiology February 6, 2023.

Bei COVID-19 erweisen sich Parameter der Körperkomposition zunehmend als Risikofaktoren für den klinischen Verlauf und die Mortalität. Adipositas und vermehrtes Abdominalfettgewebe sind nachweislich mit einer schweren klinischen Erkrankung und der Mortalität verbunden. Ebenso scheint eine geringe Skelettmuskelmasse, die in der klinischen Routine als Surrogatmarker für Sarkopenie verwendet wird, das Ergebnis der Patienten zu beeinflussen. Die

Daten zur Rolle der Körperkomposition sind jedoch noch vielfältig und stehen mitunter im Widerspruch zueinander, denn verschiedene Studien konnten keinen relevanten Zusammenhang feststellen. Angesichts der anhaltenden Pandemie bleibt die Prognose des klinischen Verlaufs und der Mortalität bei COVID-19-Erkrankungen von entscheidender Bedeutung. Alter und Geschlecht sind bereits etablierte Prognosemarker für COVID-19-Patienten und mit Mortalität assoziiert.

In unserer Studie wurde die Assoziation zwischen den Körperkompositionsparametern und den Ergebnissen bei COVID-19 bewertet. 173 Patienten, die wegen einer COVID-19-Infektion in sechs europäischen Zentren hospitalisiert wurden, bildeten unser Studienkollektiv. Die Messungen wurden auf L3-Ebene durchgeführt und umfassten SMI, MD und Fettgewebemessungen (VAT, SAT, IMAT), VSR). Der Zusammenhang mit der Mortalität, der Notwendigkeit einer maschinellen Beatmung (MV) und einer Aufnahme auf die Intensivstation innerhalb von 30 Tagen wurden bewertet.

Laut der Ergebnisse dieser multizentrischen, retrospektiven Studie scheint eine höhere VSR bei COVID-19-Patienten ein starker prognostischer Faktor für die kurzfristige Mortalität zu sein. Aber es gab lediglich eine schwache Korrelation mit dem klinischen Verlauf für MD- und Fettgewebemessungen. Darüber hinaus war das männliche Geschlecht der stärkste prognostische Faktor für einen ungünstigen klinischen Verlauf. Der SMI hatte keine relevanten Assoziationen mit den anderen Parametern. Die Ergebnisse der Studie zusammenfassend lässt sich sagen, dass die VSR ein prognostischer Biomarker für die 30-Tage-Mortalität bei Patienten ist, die wegen einer COVID-19-Erkrankung ins Krankenhaus eingeliefert worden sind.

3. Diskussion

Die Coronavirus-Krankheit 2019 (COVID-19) ist eine Infektionskrankheit, die durch das schwere akute respiratorische Syndrom Coronavirus 2 (SARS-CoV-2) verursacht wird. Das Virus wurde erstmals im Dezember 2019 in Wuhan beschrieben und verbreitete sich sehr schnell weltweit und ist Ursache der COVID-19-Pandemie, die bis dato weiterhin ein großes Problem für die globale Gesundheit darstellt. Bis zum 18. Oktober 2022 wurden weltweit rund 622 Millionen COVID-Infizierte registriert, es wird aber in vielen Ländern eine hohe Dunkelziffer vermutet (18). Laut einer Schätzung der Weltgesundheitsorganisation (WHO) gab es zwischen Anfang 2020 und Ende 2021 eine weltweite, durch COVID-19 verursachte Übersterblichkeit von 14,83 Millionen Toten (19). Die Infizierung erfolgt durch Tröpfcheninfektion (Bioaerosolen), insbesondere bei längerer Aufenthaltsdauer in geschlossenen und ungenügend gelüfteten Räumen. Der Krankheitsverlauf ist unspezifisch und kann stark variieren. Laut Schätzung des RKI haben 55 bis 85 % der Infizierten spürbare Beschwerden und/oder zeigen erkennbare Anzeichen einer Erkrankung (Symptome) oder typische Symptomkombinationen (Syndrom) einer COVID-19-Erkrankung. Außerdem können die übrigen Infizierten symptomfrei und asymptomatisch erkrankt sein, die aber trotzdem das Virus weiterverbreiten können (20). Rund 81 % der registrierten Patienten haben einen leichten Verlauf mit Fieber oder einer leichten Pneumonie sowie trockenem Husten und Müdigkeit. Bei ca. 14 % der Krankheitsfälle ist der Verlauf schwerer, und in etwa 5 % so schwer, dass eine Intubation des Patienten auf einer Intensivstation erfolgen muss (21). Die höchste Gefährdung, schwer zu erkranken, besteht insbesondere für ältere Menschen und solche mit Vorerkrankungen oder nicht ausreichendem Immunschutz. Die bekannteste Prognosefaktoren sind Alter und Geschlecht (3,4). Begleiterkrankungen wie Demenz, Herzinsuffizienz und periphere Gefäßerkrankungen sind ebenfalls Prädiktoren für einen ungünstigen Krankheitsverlauf (3,4). In unseren Studien wurden die anderen, eventuell prognostischen Faktoren im Hinblick auf den

klinischen Verlauf (30-Tage-Mortalität, Beatmungsbedarf und Aufnahme auf einer Intensivstation) bei hospitalisierten Patienten mit ungünstigem Verlauf bewertet.

In mehreren Studien wurde gezeigt, dass Sarkopenie/abnormale Körperkomposition als Risikofaktor für die Dauer des Krankenhausaufenthalts und die Mortalität bei Schwerkranken und Traumapatienten eine entscheidende Rolle spielen kann (9-12). Aber bei Patienten mit COVID-19 sind die Ergebnisse weniger eindeutig. Bisher wurden Muskelflächemessungen und SMI als Indikator für Sarkopenie auf verschiedenen Muskelebenen durchgeführt, sowohl auf der Thorakal- als auch auf der Pelvikebene, mit widersprüchlichen Ergebnissen.

Bespielsweise war in einer Studie von Schiaffino et al. die geringere Querschnittsfläche der paravertebralen Muskulatur positiv mit der Aufnahme auf die Intensivstation und der Mortalität assoziiert (22), wobei der SMI jedoch nicht berechnet wurde. In einer Kohortenstudie von Feng et al. mit 116 Patienten wurde kein Zusammenhang zwischen dem paraspinalen Muskelindex auf T12-Ebene und den klinischen Ergebnissen gefunden (23). Kim et al. berechneten den SMI auf T12-Niveau und stellten fest, dass Sarkopenie mit verlängertem Krankenhausaufenthalt verbunden war, aber es gab keine Assoziation mit der Mortalität (24) – in ihrer Stichprobe betrug die Aufnahmerate auf die Intensivstation nur 8,3 % und die Sterblichkeit 5,8 %. Die Studie von Hocaoglu et al. zeigte, dass eine höhere MD (gemessen in der Nativ-CT) mit der Mortalität bei Covid-19-Patienten umgekehrt assoziiert war (25). Allerdings waren über 40 % der Kohorte von 217 Patienten ambulante Patienten und der PMI wurde nicht gemessen. Außerdem wurde nur der M. pectoralis major gemessen. Keine relevante Assoziation mit Mortalität wurde für den SMI (unterhalb der Lungenbasis gemessen) in einer Studie von Moctezuma-Velázquez et al. (26) festgestellt. Die Studie von Ufuk et al. stellte einen Zusammenhang zwischen PMA und PMI bei negativen klinischen Ergebnissen wie Intubation, Dauer des Krankenhausaufenthalts und Mortalität her (27). Die Körperkomposition (wie Pectoralmuskelwert, Skelettmuskelmasse/-index, Messungen von paraspinalen, Abdominalwand-, Psoasmuskeln und VAT) kann möglicherweise eine Rolle für das klinische Ergebnis von Patienten mit COVID-19 spielen.

Ingesamt kann die Wirkung der Körperkomposition bei Patienten mit schwerer COVID-19-Erkrankung im Vergleich zu anderen Erkrankungen noch nicht als abschließend erforscht gelten. Deshalb haben wir drei Studien durchgeführt, von denen eine eine Single-Center-Studie war und zwei davon multizentrisch waren. In unserer ersten Single-Center-Studie haben wir 46 Patienten aus unserer Klinik eingeschlossen. Wir erstellten in unseren zwei Multi-Center-Studien einen großeren Pool von 1138 und 173 Patienten.

Die Einschlusskriterien unserer Studien sind sehr breit gefasst, da es das Ziel war, die Auswirkung der Körperkomposition auf klinische Ergebnisse bei Patienten mit schwerer COVID-19-Erkrankung beweisen zu können. Dieses Vorgehen hat ein relativ heterogenes Patientenkollektiv zur Folge, da die Patienten in unterschiedlichem Maße vortherapiert waren und verschiedene Komorbiditäten hatten. Die Behandlung der Patienten hängt natürlich auch von dem behandelten Arzt sowie den verschiedenen verwendeten Therapiemöglichkeiten und COVID-Varianten ab, was das Design einer multizentrischen Studie zusätzlich erschwert.

4. Zusammenfassung

Sarkopenie/abnormale Körperkomposition stellt einen relevanten Risikofaktor für die Dauer des Krankenhausaufenthalts und die Mortalität bei Schwerkranken und Traumapatienten dar. Aber die Ergebnisse bei Patienten mit COVID-19 Erkrankung waren bisher widersprüchlich und nicht sehr eindeutig.

Bei unserer ersten Single-Center-Studie wurden insgesamt 46 Patienten (19 Frauen und 27 Männer) mit einem Durchschnittalter von 64,5 Jahren eingeschlossen. Das Ergebnis dieser Studie war, dass kein Aspekt der Körperkomposition (Baseline-Charakteristika der Patienten, PMA, PMI, SMG und Dichte/PMA sind in Table I zusammengefasst) ein Prädiktor für die 30-Tage-Mortalität, die Dauer des Krankenhausaufenthalts, die Dauer der Behandlung auf der Intensivstation oder die Dauer der invasiven mechanischen Beatmung war (Assoziation zwischen Muskelparametern und klinischen Ergebnissen in Table II).

Um zuverlässigere Ergebnisse zu erhalten, wurden insgesamt 1138 Patienten (547 Frauen, 591 Männer mit einem Durchschnittsalter von 55 Jahren) aus sechs europäischen Zentren in unsere multizentrische Studie einbezogen. 220 dieser Patienten (19,33 %) wurden auf die Intensivstation aufgenommen. Darüber hinaus wurde bei 171 Patienten (15,03 %) eine MV durchgeführt. Schließlich starben 154 Patienten (13,53 %) innerhalb der Beobachtungszeit von 30 Tagen.

Bei den Patienten mit ungünstigen COVID-19-Verläufen waren alle untersuchten Muskelwerte bzw. Parameter der Pectoralis-Muskulatur laut unserer Studienergebnisse niedriger (Table III). Regressionsanalysen zeigten, dass alle Pectoralis-Muskelparameter mit ungünstigen Verläufen assoziiert waren (Tabelle 2). Alters- und geschlechtsadjustiert waren auch alle Pectoralis-Muskelparameter mit ungünstigen Verläufen assoziiert (Table IV). Das heißt, dass die überlebenden Patienten auch in größeren Patientengruppen im Vergleich zu Nichtüberlebenden stärkere und dichtere Pektoralmuskeln hatten bzw. diese eine größere Fläche und einen höheren Index aufwiesen. Aber die analysierten Muskelparameter können nicht zur Vorhersage von Krankheitsverläufen herangezogen werden.

Bei unserer letzten multizentralisierten Studie umfasste die analysierte Bedarfsstichprobe 173 Patienten (80 weiblich und 93 männlich mit einem Durchschnittsalter von 61 Jahren). Von den eingeschlossenen Patienten wurden 52 auf die Intensivstation aufgenommen. 46 Patienten benötigten eine MV und 33 Patienten starben innerhalb des 30-tägigen Beobachtungszeitraums. Unsere Werte haben uns gezeigt, dass eine höhere SAT-Dichte mit einem größeren MV-Risiko verbunden war und eine höhere VAT mit der Aufnahme auf die Intensivstation verbunden war. Darüber hinaus war eine höhere MD ein Schutzfaktor gegen die Aufnahme auf die Intensivstation sowie gegen die MV. Besonders stark betroffen vom Risiko einer Verlegung auf die Intensivstation und einer MV zeigte sich das männliche Geschlecht. Der SMI war keinem der Parameter zugeordnet. Eine Erkenntnis unserer Studie war, dass die VSR ein prognostischer Biomarker für die 30-Tage-Mortalität bei Patienten ist, die wegen einer COVID-19-Erkrankung ins Krankenhaus eingeliefert wurden. (Table V und VI)

Table I. *Patient characteristics (n=46).*

Characteristic		Value
Age, years	Median (range)	64.5 (41-92)
Gender, n (%)	Male	27 (58.7%
	Female	19 (41.3%)
BMI, kg/m^2	Median (range)	27.3 (20.6-58.5)
Length of hospital stay, days	Median (range)	19 (1-53)
ICU stay	Yes, n (%)	37 (80.4%)
	Median duration (range), days	11.5 (2-53)
IMV needed	Yes, n (%)	33 (71.7%)
	Median duration (range), h	228.5 (46-1268)
Mortality, n (%)	30-Day	19 (41.3%)
PMA, cm^2	Median (range)	22.8 (9.0-64.0)
PMI, cm^2/m^2	Median (range)	7.7 (3.1-20.9)
Muscle density, HU	Median (range)	27.0 (4.0-53.5)
SMG, cm^2 HU/m^2	Median (range)	188.8 (16.5-612.0)
Muscle density/PMA, HU/cm^2	Median (range)	1.3 (0.3-2.9)

Table II. *Association of pectoralis muscle composition parameters with 30-day mortality.*

Value	OR	95% CI	*p*-Value
Age	0.996	0.951-1.042	0.853
Gender (male)	1.371	0.412-4.563	0.607
BMI	0.990	0.922-1.064	0.790
PMA	1.068	0.992-1.150	0.079
PMI	1.145	0.906-1.447	0.257
Muscle density	0.998	0.951-1.047	0.942
SMG	1.002	0.998-1.006	0.309
Muscle density/PMA	0.689	0.250-1.903	0.472

TABLE III. Comparison of the Pectoralis Muscle Parameters in Patients With COVID-19

a. Pectoralis Muscle Values and Need for ICU Admission			
Muscle Parameters	No ICU Admission	ICU Admission	*p* Values
Pectoralis muscle area, cm^2	29.80 § 14.17	25.20 § 10.09	<0.001
Pectoralis muscle density, HU	37.29 § 12.98	28.03 § 14.56	<0.001
Pectoralis muscle index, cm^2/m^2	11.03 § 4.60	9.23 § 3.54	<0.001
Pectoralis muscle gauge	436.77 § 252.03	274.55 § 206.89	<0.001
b. Pectoralis Muscle Values and Need for Mechanical Ventilation			
Muscle Parameters	No Mechanical Ventilation	Mechanical Ventilation	*p* Values
Pectoralis muscle area, cm^2	29.754 § 13.95	24.156 § 10.16	<0.001
Pectoralis muscle density, HU	36.916 § 13.06	27.484 § 15.06	<0.001
Pectoralis muscle index, cm^2/m^2	11.242 § 4.53	8.866 § 3.57	<0.001
Pectoralis muscle gauge	429.678 § 250.47	257.508 § 206.24	<0.001
c. Pectoralis Muscle Values and 30-day Mortality			
Muscle Parameters	Survivors	Nonsurvivors	*p* Values
Pectoralis muscle area, cm^2	30.189 § 13.74	20.757 § 9.13	<0.001
Pectoralis muscle density, HU	36.841 § 13.15	26.929 § 14.71	<0.001
Pectoralis muscle index, cm^2/m^2	11.277 § 4.49	8.0365 § 3.15	<0.001
Pectoralis muscle gauge	428.305 § 250.02	223.505 § 182.80	<0.001

TABLE IV. Associations Between Pectoralis Muscle Values and Unfavorable Outcomes in COVID-19 (Multivariate Analysis)

Muscle Parameters	OR	CI95%	*p* Values
a. Associations Between Pectoralis Muscle Values and Need for Intensive Care Admission			
Pectoralis muscle area, cm^2	0.99	(0.98, 1.007)	0.391
Pectoralis muscle density, HU	0.96	(0.95, 0.97)	<0.001
Pectoralis muscle index, cm^2/m^2	0.94	(0.90, 0.99)	<0.001
Pectoralis muscle gauge	0.998	(0.997, 0.999)	<0.001
b. Associations Between Pectoralis Muscle Values and Need for Mechanical Ventilation			
Pectoralis muscle area, cm^2	0.98	(0.97, 0.99)	0.033
Pectoralis muscle density, HU	0.96	(0.94, 0.97)	<0.001
Pectoralis muscle index, cm^2/m^2	0.87	(0.87, 0.96)	<0.001
Pectoralis muscle gauge	0.997	(0.996, 0.999)	<0.001
c. Associations Between Pectoralis Muscle Values and 30-day Mortality			
Pectoralis muscle area, cm^2	0.96	(0.94, 0.98)	<0.001
Pectoralis muscle density, HU	0.96	(0.95, 0.98)	<0.001
Pectoralis muscle index, cm^2/m^2	0.86	(0.80, 0.91)	<0.001
Pectoralis muscle gauge	0.996	(0.995, 0.998)	<0.001

Table V. Regression analysis for 30-day mortality

	Univariable			Multivariable		
Variables	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Continuous values						
Age (years)	1.034	(1.008; 1.060)	0.010	1.015	(0.979; 1.053)	0.408
Sex (male *vs* female)	2.300	(1.020; 5.186)	0.045	2.891	(0.915; 9.132)	0.070
BMI, (kg/m^2)	1.013	(0.936; 1.096)	0.749	1.030	(0.941; 1.128)	0.521
SMA (cm^2)	0.997	(0.986; 1.008)	0.611			
SMI (kg/cm^2)	0.995	(0.958; 1.032)	0.777			
Muscle density (HU)	0.935	(0.901; 0.971)	<0.001			
VAT (cm^2)	1.001	(0.997; 1.005)	0.642			
SAT (cm^2)	0.996	(0.992; 1.000)	0.035			
TAT (cm^2)	0.999	(0.997; 1.001)	0.321			
IMAT (cm^2)	1.042	(1.011; 1.073)	0.008	1.083	(1.035; 1.133)	<0.001
VSR	1.918	(1.114; 3.305)	0.019	2.147	(1.022; 4.512)	0.044
VATI (cm^2/m^2)	1.004	(0.993; 1.015)	0.534			
SATI (cm^2/m^2)	0.990	(0.980; 1.000)	0.054			
TATI (cm^2/m^2)	0.998	(0.992; 1.003)	0.416			
IMATI (cm^2/m^2)	1.109	(1.023; 1.203)	0.012			
VAT density (HU)	1.038	(1.008; 1.068)	0.011	1.090	(1.046; 1.136)	<0.001
SAT density (HU)	1.049	(1.018; 1.081)	0.002			
IMAT density (HU)	1.069	(1.005; 1.138)	0.034			
SMI/TAT	3.296	(0.06; 173.83)	0.556			
SMA/TAT	1.448	(0.365; 5.743)	0.598			
SMA/VAT	0.864	(0.567; 1.318)	0.498			
FFM (kg)	0.990	(0.955; 1.028)	0.611			
FM (kg)	0.975	(0.927; 1.025)	0.321			
Dichotomized values						
SMI (low *vs* high)	0.647	(0.260; 1.605)	0.347	0.299	(0.089; 1.008)	0.051
VAT (high *vs* low)	1.013	(0.401; 2.560)	0.978			
SAT (high *vs* low)	0.344	(0.136; 0.869)	0.024			
VSR (high *vs* low)	2.196	(1.014; 4.755)	0.046			

Table VI. Regression analysis for need for intubation

	Univariable			Multivariable		
Variables	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Continuous values						
Age (years)	1.032	(1.010; 1.055)	0.005	0.995	(0.961; 1.031)	0.788
Sex (male *vs* female)	1.679	(0.840; 3.356)	0.142	4.138	(1.610; 10.63)	0.003
BMI, (kg/m^2)	1.081	(1.006; 1.161)	0.033	1.117	(1.011; 1.233)	0.029
SMA (cm^2)	0.996	(0.986; 1.006)	0.384			
SMI (kg/cm^2)	0.991	(0.958; 1.024)	0.584			
Muscle density (HU)	0.925	(0.894; 0.958)	<0.001	0.914	(0.870; 0.960)	<0.001
VAT (cm^2)	1.002	(0.998; 1.005)	0.346			
SAT (cm^2)	0.998	(0.995; 1.001)	0.155			
TAT (cm^2)	1.000	(0.998; 1.002)	0.766			
IMAT (cm^2)	1.038	(1.009; 1.067)	0.009			
VSR	1.760	(1.053; 2.943)	0.019			
VATI (cm^2/m^2)	1.006	(0.996; 1.016)	0.246			
SATI (cm^2/m^2)	0.996	(0.988; 1.004)	0.274			
TATI (cm^2/m^2)	1.000	(0.995; 1.005)	0.992			
IMATI (cm^2/m^2)	1.106	(1.025; 1.193)	0.009			
VAT density (HU)	1.038	(1.011; 1.066)	0.005			
SAT density (HU)	1.059	(1.029; 1.091)	<0.001	1.071	(1.034; 1.110)	<0.001
IMAT density (HU)	1.087	(1.026; 1.151)	0.004			
SMI/TAT	0.753	(0.015; 39.03)	0.888			
SMA/TAT	0.856	(0.218; 3.360)	0.824			
SMA/VAT	0.811	(0.527; 1.247)	0.339			
FFM (kg/m^2)	0.985	(0.954; 1.018)	0.384			
FM (kg)	0.994	(0.952; 1.037)	0.766			
Dichotomized values						
SMI (low *vs* high)	0.754	(0.326; 1.744)	0.510			
VAT (high *vs* low)	1.163	(0.502; 2.695)	0.725			
SAT (high *vs* low)	0.482	(0.199; 1.167)	0.106			
VSR (high *vs* low)	1.802	(0.898; 3.613)	0.097			

5. Literaturverzeichnis

1. Abate SM, Ahmed Ali S, Mantfardo B, et al. Rate of Intensive Care Unit admission and outcomes among patients with coronavirus: a systematic review and Meta-analysis. PLoS One 2020; 15:e0235653.
2. Hu Y, Sun J, Dai Z, et al. Prevalence and severity of corona virus disease 2019 (COVID-19): a systematic review and meta-analysis. J Clin Virol 2020; 127:104371.
3. Liu B, Spokes P, He W, et al. High risk groups for severe COVID-19 in a whole of population cohort in Australia. BMC Infect Dis 2021; 21:685.
4. Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: a systematic literature review and meta-analysis. J Infect 2020; 81:e16–e25.
5. Besutti G, Ottone M, Fasano T, et al. The value of computed tomography in assessing the risk of death in COVID-19 patients presenting to the emergency room. Eur Radiol 2021: 1–12.
6. Koch V, Gruenewald LD, Albrecht MH, et al. Lung opacity and coronary artery calcium score: a combined tool for risk stratification and outcome prediction in COVID-19 patients. Acad Radiol 2022; 29:861–870.
7. Salehi S, Abedi A, Balakrishnan S, et al. Coronavirus Disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. AJR Am J Roentgenol 2020; 215:87–93.
8. Meyer HJ, Wienke A, Surov A. Extrapulmonary CT findings predict in- hospital mortality in COVID-19. A systematic review and meta-analysis. Acad Radiol 2022; 29:17–30.
9. DeAndrade J, Pedersen M, Garcia L and Nau P: Sarcopenia is a risk factor for complications and an independent predictor of hospital length of stay in trauma patients. J Surg Res 221: 161-166, 2018. PMID: 29229123. DOI: 10.1016/j.jss.2017.08.018
10. Ji Y, Cheng B, Xu Z, Ye H, Lu W, Luo X, Fu S and Fang X:Impact of sarcopenic obesity on 30-day mortality in critically ill patients with intra-abdominal sepsis. J Crit Care 46: 50-54, 2018. PMID: 29677586. DOI: 10.1016/j.jcrc.2018.03.019
11. Joyce PR, O'Dempsey R, Kirby G and Anstey C: A retrospective observational study of sarcopenia and outcomes in critically ill patients. Anaesth Intensive Care 48(3): 229-235, 2020. PMID:32486830. DOI: 10.1177/0310057X20922234
12. Kou HW, Yeh CH, Tsai HI, Hsu CC, Hsieh YC, Chen WT, Cheng HT, Yu MC and Lee CW: Sarcopenia is an effective predictor of difficult-to-wean and mortality among critically ill surgical patients. PLoS One 14(8): e0220699, 2019. PMID: 31393937. DOI: 10.1371/journal.pone.0220699
13. Cruz-Jentoft AJ, Bahat G, Bauer J et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019; 48: 16–31
14. Gu DH, Kim MY, Seo YS et al. Clinical usefulness of psoas muscle thickness for the diagnosis of sarcopenia in patients with liver cirrhosis. Clin Mol Hepatol 2018; 24: 319–330
15. Bak SH, Kwon SO, Han SS et al. Computed tomography-derived area and density of pectoralis muscle associated disease severity and longitudinal changes in chronic obstructive pulmonary disease: a case control study. Respir Res 2019; 20: 226
16. Shachar SS, Deal AM, Weinberg M et al. Body Composition as a Predictor of Toxicity in Patients Receiving Anthracycline and Taxane-Based Chemotherapy for Early-Stage Breast Cancer. Clin Cancer Res 2017; 23: 3537– 3543
17. Weinberg MS, Shachar SS, Muss HB, Deal AM, Popuri K, Yu H, Nyrop KA, Alston SM and Williams GR: Beyond sarcopenia:Characterization and integration of skeletal muscle quantity and radiodensity in a curable breast cancer population. Breast J 24(3): 278-284, 2018. PMID: 29139618. DOI: 10.1111/tbj.12952

18. WHO Coronavirus Disease (COVID-19) Dashboard. Auf:covid19.who.int, Stand:18. Oktober 2022
19. William Msemburi et al.: The WHO estimates of excess mortality associated with the COVID-19 pandemic. In: Nature. Online-Veröffentlichung vom 14. Dezember 2022, doi:10.1038/s41586-022-05522-2.
20. D. Baud, X. Qi, K. Nielsen-Saines et al.: Real estimates of mortality following COVID-19 infection. In: The Lancet. Band 20, 12. März 2020, S. 773,
21. Zunyou Wu, Jennifer M. McGoogan, CCDC: Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China. In: Journal of the American Medical Association. 24. Februar 2020, doi:10.1001/jama.2020.2648
22. Schiaffino S, Albano D, Cozzi A, Messina C, Arioli R, Bnà C, Bruno A, Carbonaro LA, Carriero A, Carriero S, Danna PSC, D'Ascoli E, De Berardinis C, Della Pepa G, Falaschi Z, Gitto S, Malavazos AE, Mauri G, Monfardini L, Paschè A, Rizzati R, Secchi F, Vanzulli A, Tombini V, Vicentin I, Zagaria D, Sardanelli F and Sconfienza LM: CT-derived chest muscle metrics for outcome prediction in patients with COVID-19. Radiology 300(2): E328-E336, 2021. PMID: 33724065. DOI: 10.1148/radiol.2021204141
23. Feng Z, Zhao H, Kang W, Liu Q, Wu J, Bragazzi NL, Ma X, Wang W and Rong P: Association of paraspinal muscle measurements on chest computed tomography with clinical outcomes in patients with severe Coronavirus disease 2019. Gerontol A Biol Sci Med Sci 76(3): e78-e84, 2021. PMID: 33355656. DOI: 10.1093/gerona/glaa317
24. Kim JW, Yoon JS, Kim EJ, Hong HL, Kwon HH, Jung CY, Kim KC, Sung YS, Park SH, Kim SK and Choe JY: Prognostic implication of baseline sarcopenia for length of hospital stay and survival in patients with Coronavirus disease 2019. J Gerontol A Biol Sci Med Sci 76(8): e110-e116, 2021. PMID: 33780535. DOI: 10.1093/gerona/glab085
25. Hocaoglu E, Ors S, Yildiz O and Inci E: Correlation of pectoralismuscle volume and density with severity of COVID-19
pneumonia in adults. Acad Radiol 28(2): 166-172, 2021. PMID: 33281041. DOI: 10.1016/j.acra.2020.11.017
26. Moctezuma-Velázquez P, Miranda-Zazueta G, Ortiz-Brizuela E, González-Lara MF, Tamez-Torres KM, Román-Montes CM, Díaz-Mejía BA, Pérez-García E, Villanueva-Reza M, Tovar-Méndez VH, Medrano-Borromeo C, Martínez-Valenzuela A, Jandete-Medina MÁ, Martínez-Guerra BA, Uscanga-Domínguez L, Sifuentes-Osornio J, Ponce-de-León A, Olivas-Martinez A and Moctezuma-Velázquez C: Low thoracic skeletal muscle area is not associated with negative outcomes in patients with COVID-19. Am J Phys Med Rehabil 100(5): 413-418, 2021. PMID: 33587451. DOI:10.1097/PHM.0000000000001716
27. Ufuk F, Demirci M, Sagtas E, Akbudak IH, Ugurlu E and Sari T: The prognostic value of pneumonia severity score and pectoralis muscle Area on chest CT in adult COVID-19 patients. Eur J Radiol 131: 109271, 2020. PMID: 32942198. DOI: 10.1016/j.ejrad.2020.109271

6. Veröffentlichungen

1) **Hakan Kardas**, Maximilian Thormann, Caroline Bär, Jazan Omari, Andreas Wienke, Maciej Pech, Alexey Surov:
Impact of Pectoral Muscle Values on Clinical Outcomes in Patients With Severe Covid-19 Disease. In Vivo January 2022, 36 (1) 375-380

2) Alexey Surov, **Hakan Kardas**, Giulia Besutti, Massimo Pellegrini, Marta Ottone, Mehmet Ruhi Onur, Firat Atak, Ahmet Gurkan Erdemir,Elif Hocaoglu, Omer Yildiz,Ercan Inci, Eda Cingoz, Mehmet Cingoz, Memduh Dursun, Inan Korkmaz, Cagri Orhan, Alexandra Strobel, Andreas Wienke, Maciej Pech: Prognostic Role of the Pectoralis Musculature in Patients with COVID-19. A Multicenter Study. Academic Radiology May 15, 2022.

3) Alexey Surov, Maximilian Thormann, **Hakan Kardas**, Mattes Hinnerichs, Jazan Omari, Eda Cingöz, Mehmet Cingöz, Memduh Dursun, Inan Korkmaz, Cagri Orhan, Ömer Yildiz, Elif Hocaoglu, Ercan Inci, Hakan Önder, Hamdullah Erk, Ougkour Chousein, Hadi Sasani, Korcan Aysun Gönen, Maciej Pech, Andreas Wienke: Visceral to subcutaneous fat ratio predicts short term mortality in patients with Covid 19. A multicenter study. The British Journal of Radiology February 6, 2023

in vivo *36*: 375-380 (2022)
doi:10.21873/invivo.12713

Impact of Pectoral Muscle Values on Clinical Outcomes in Patients With Severe Covid-19 Disease

HAKAN KARDAS[1*], MAXIMILIAN THORMANN[1*], CAROLINE BÄR[1], JAZAN OMARI[1], ANDREAS WIENKE[2], MACIEJ PECH[1] and ALEXEY SUROV[1]

[1]*University Clinic for Radiology and Nuclear Medicine, University Hospital Magdeburg, Magdeburg, Germany;*
[2]*Institute of Medical Epidemiology, Biometry, and Informatics, Martin Luther University, Halle-Wittenberg, Germany*

Abstract. *Background/Aim: The effect of sarcopenia on patients with severe Covid-19 disease is unknown. We aimed to assess the influence of baseline computed tomography (CT)-based body composition parameters (pectoralis muscle area, pectoralis muscle index, skeletal muscle gauge) on clinical variables in patients with severe Covid-19 disease. Patients and Methods: Chest CT scans of adult patients with confirmed Covid-19 who were hospitalized from March 2020 to May 2021 at a level-one medical center in Germany were retrospectively analyzed. Pectoralis muscle area, pectoralis muscle index and skeletal muscle gauge were measured on the first CT scan after admission. Body composition parameters were assessed for association with clinical variables and 30-day mortality. Results: A total of 46 patients were included. None of the body composition parameters was a predictor for 30-day mortality, duration of hospital stay, duration of intensive care unit treatment, or duration of invasive mechanical ventilation. Conclusion: Pectoralis muscle composition parameters in CT chest scans did not predict outcomes in adult patients with severe Covid-19 infection.*

Sarcopenia is an abnormal body composition defined as the loss of muscle mass, low muscle strength, and impaired muscle quality (1). Screening measures include clinical parameters as well as image-based techniques (1, 2). Sarcopenia is common in patients aged 65 years and older and has been related to worse clinical outcome, disability, and mortality (3-7). Chest scans with either computed tomography (CT) or magnetic resonance imaging are considered the gold-standard for quantitative evaluation of body composition (1). Measurements such as skeletal muscle mass or density can be used as a surrogate marker for sarcopenia and muscle quality (8-10).

The etiology of sarcopenia is manifold and includes nutritional, environmental, behavioral, and medical factors. Sarcopenia is associated with malnutrition, metabolic dysregulation and chronic inflammation, increasing vulnerability of affected adults to various diseases (9, 11). Suboptimal protein intake has been associated with sarcopenia, but the diagnosis does not depend on body weight and body mass index (12).

The *pectoralis* muscle index (PMI) and the *pectoralis* muscle area (PMA) have been shown to be indicators of sarcopenia and predictors of clinical variables such as length of hospital stay and mortality for multiple diseases (7, 9, 13-17). In addition, measurements of muscle density on CT scans are regarded as an indicator of muscle quality, reflecting lipid content (10). The skeletal muscle gauge (SMG) integrates both the PMI and muscle density and has been shown to be associated with outcomes in patients with cancer (18, 19).

The effect of sarcopenia on patients suffering from Coronavirus 2019 disease (Covid-19) caused by severe acute respiratory syndrome coronavirus 2 is yet unknown. The disease affects mostly elderly people at highest risk for sarcopenia, with age being an independent risk factor for worse outcome (20, 21).

Some authors have described that certain body composition parameters can identify unfavorable outcome in patients with Covid-19. For example, a higher level of adipose tissue has been associated with higher rates of hospitalization and mechanical ventilation (22-24). In another study, higher visceral fat area and higher abdominal circumference measured at the lumbar level were correlated with higher rates of transfer to the Intensive Care Unit (ICU) and mechanical ventilation, but mortality was not investigated (25).

*These Authors contributed equally to this study.

Correspondence to: Dr. med. Maximilian Thormann, M.A., Clinic for Radiology and Nuclear Medicine, University of Magdeburg, Leipziger Str. 44, 39112 Magdeburg, Germany. E-mail: maximilian.thormann@med.ovgu.de

Key Words: Covid-19, body composition, computed tomography, *pectoralis* muscle, mortality.

Regarding measurement of skeletal mass, however, the literature results are controversial. For example, in one study, PMI and PMA were associated with length of hospital stay and death in Covid-19 patients (26). However, no strong association between skeletal muscle index (SMI) and clinical variables or mortality was found in another study (27). Density of the pectoralis muscle has been associated with the risk of death in symptomatic patients with Covid-19 (28). Yet no effect of the paraspinal muscle index at the T12 level with clinical outcomes was found in a Chinese cohort of patients hospitalized with Covid-19 disease (29). The literature is still preliminary and shows some variation regarding the muscle region measured and the level where muscle mass is assessed (9, 30). However, if an association between muscle mass and clinical outcomes of patients with Covid-19 existed, it might be an important means of triage at hospital admission.

The purpose of the present study was to analyze the effect of *pectoralis* muscle composition, as measured by PMA, PMI and SMG on CT chest scans, on clinical variables. Length of hospital stay, length of ICU stay, length of invasive mechanical ventilation, and mortality at 30 days were assessed in patients hospitalized with severe Covid-19 infection.

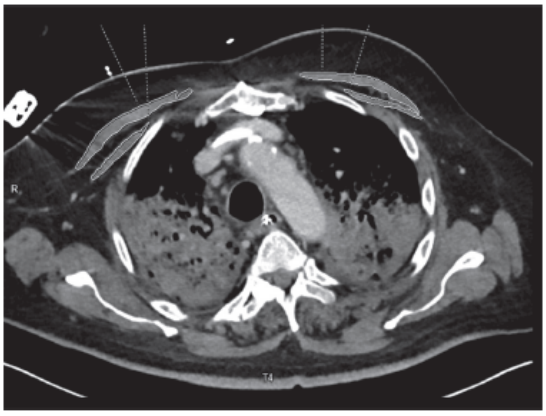


Figure 1. *Computed tomography of the thorax of a 67-year-old male patient after contrast injection. The identified muscle parameters were: pectoralis muscle area 18.0 cm^2, pectoralis muscle index 5.8 cm^2/m^2, muscle density 22.5 HU, skeletal muscle gauge 132.3 AU. The patient died after 13 days on Intensive Care Unit.*

Patients and Methods

Study population. We retrospectively analyzed a sample of patients admitted to a level-one medical center in Germany with polymerase chain reaction-confirmed symptomatic Covid-19 infection between March 2020 and May 2021. Patients that had undergone a CT chest scan after admission to our clinic were included. Patients were followed-up until discharge or death. The patient cohort included both primary admissions and referrals from other hospitals to the ICU unit. Scans with strong motion artifacts were excluded. For all patients, the length of overall hospital stay, length of ICU stay, length of invasive mechanical ventilation, and mortality at 30 days were noted. Data on clinical variables and mortality were obtained from the hospital system.

Image analysis. All CT scans were obtained on a multidetector CT scanner (Siemens Somatom Definition AS+; Siemens Healthcare, Germany). During the Covid-19 pandemic the scanner was set aside for suspected or confirmed cases. Patients were positioned in supine position. The CT protocol was as follows: Acquisition slice thickness 1 mm with 5 mm reconstructions, tube voltage 120 kV, automatic tube current modulation, pitch factor 1.2, and collimation 0.6 mm.

We used the first CT scan of patients after hospital admission. All images were assessed in consensus by two experienced radiologists (HK and AS) who were blinded to the clinical course of the patients. Measurements were performed on axial images at the T4 level in the soft tissue window (window of 45 to 250 HU) on a dedicated workstation (Infinitt PACS, Version 3.0; Infinitt Healthcare, Seoul, Republic of Korea). A line was drawn along the contours of the *pectoralis* major and minor muscles on both sides and the bilateral areas as determined by the software were added to obtain the PMA (Figure 1). Muscle density was measured for each side on all contrast scans and the mean was calculated. The PMI was calculated by dividing the PMA by the patient's height. SMG was calculated multiplying the PMI by the mean muscle density as reported previously (18). SMG units are cm^2 HU/m^2 but are reported as arbitrary units (AU) for simplicity. A further variable was calculated dividing the mean density by the PMA.

Statistical analysis. Mean and standard deviation as well as median and interquartile range (IQR) were calculated for continuous variables. To assess the impact of *pectoralis* muscle composition on clinical variables and mortality, we used a multivariable logistic regression model. Odds ratios are presented together with 95% confidence intervals (95% CI). The resulting *p*-values were interpreted in an exploratory sense.

Results

Included patients and muscle mass analysis. Of the 74 patients screened, 46 underwent a chest CT scan at admission and were included in the analysis. There were 19 female and 27 male patients. The median age was 64.5 years and median body mass index was 27.3 kg/m^2. Baseline characteristics of patients, PMA, PMI, SMG and density/PMA are summarized in Table I.

Association between muscle parameters and clinical outcomes (Table II). Nineteen patients died within 30 days after admission (41.3%). Neither PMI nor PMA were strongly associated with 30-day mortality. Likewise, SMG, muscle density and density divided by PMA showed no significant association with mortality. Moreover, neither age nor sex were predictors of death at 30 days in our cohort.

Table I. *Patient characteristics (n=46).*

Characteristic		Value
Age, years	Median (range)	64.5 (41-92)
Gender, n (%)	Male	27 (58.7%
	Female	19 (41.3%)
BMI, kg/m^2	Median (range)	27.3 (20.6-58.5)
Length of hospital stay, days	Median (range)	19 (1-53)
ICU stay	Yes, n (%)	37 (80.4%)
	Median duration (range), days	11.5 (2-53)
IMV needed	Yes, n (%)	33 (71.7%)
	Median duration (range), h	228.5 (46-1268)
Mortality, n (%)	30-Day	19 (41.3%)
PMA, cm^2	Median (range)	22.8 (9.0-64.0)
PMI, cm^2/m^2	Median (range)	7.7 (3.1-20.9)
Muscle density, HU	Median (range)	27.0 (4.0-53.5)
SMG, cm^2 HU/m^2	Median (range)	188.8 (16.5-612.0)
Muscle density/PMA, HU/cm^2	Median (range)	1.3 (0.3-2.9)

BMI: Body mass index; IMV: invasive mechanical ventilation; PMA: pectoralis muscle area; PMI: pectoralis muscle index; SMG: skeletal muscle gauge.

Table II. *Association of pectoralis muscle composition parameters with 30-day mortality.*

Value	OR	95% CI	*p*-Value
Age	0.996	0.951-1.042	0.853
Gender (male)	1.371	0.412-4.563	0.607
BMI	0.990	0.922-1.064	0.790
PMA	1.068	0.992-1.150	0.079
PMI	1.145	0.906-1.447	0.257
Muscle density	0.998	0.951-1.047	0.942
SMG	1.002	0.998-1.006	0.309
Muscle density/PMA	0.689	0.250-1.903	0.472

BMI: Body mass index; CI: confidence interval; IMV: invasive mechanical ventilation; OR: odds ratio; PMA: pectoralis muscle area; PMI: pectoralis muscle index; SMG: skeletal muscle gauge.

The median length of hospital stay was 19.0 days, with 37 patients (80.4%) being admitted to the ICU for a median of 11.5 days. A total of 33 patients (71.7%) received invasive mechanical ventilation for a median duration of 228.5 hours. No association was found between PMA, PMI, SMG or density/PMI for length of hospital stay nor length of ICU stay. No association was found between either variable and length of invasive mechanical ventilation (Table III).

Discussion

We aimed to evaluate whether muscle-based body composition parameters as measured on chest CT scans were prognostic factors for mortality and clinical variables such as length of hospital stay and length of invasive mechanical ventilation in hospitalized patients with severe Covid-19 disease. Our study is a comprehensive analysis, associating multiple sarcopenia measures including PMA, PMI, muscle density, and SMG with clinical variables for patients hospitalized with Covid-19. We were not able to find an association between any variable and clinical outcomes nor 30-day mortality in our cohort.

It has been shown that sarcopenia can serve as a predictor of length of hospital stay and mortality in critically ill and trauma patients (16, 31-34). In patients with Covid-19, the results are less clear. Muscle area measurements and skeletal mass indices as an indicator for sarcopenia have been conducted at different muscle levels, both at the thoracic and the pelvic level, with conflicting results. In a study by Schiaffino *et al.*, lower cross-sectional area of paravertebral muscles were positively associated with ICU admission and mortality (30). Skeletal muscle indices were not calculated. In a cohort with 116 patients by Feng *et al.*, no association between paraspinal muscle index at the T12 level and clinical outcomes was found (29). Higher muscle attenuation was associated with reduced critical illness or death, yet only for female patients. Kim *et al.* calculated the SMI at the T12 level and found that sarcopenia was associated with prolonged hospital stay but not mortality in patients with Covid-19 (35). In their sample, the ICU admission rate was only 8.3% and mortality was 5.8%. Hocaoglu *et al.* showed that higher muscle density as measured in non-contrast CT was inversely associated with death in patients with Covid-19 (28). However, over 40% of the cohort of 217 patients were outpatients and PMI was not measured. Furthermore, only major *pectoralis* muscle was measured. No association with mortality was found for SMI measured below the lung base in a study by Moctezuma-Velázquez *et al.* (27). Ufuk *et al.* presented an association between PMA and PMI on negative clinical outcomes such as intubation, length of hospital stay, and mortality (26).

Our cohort differs strongly from those analyzed previously and our patients were more severely affected than in other samples. The median age for our cohort was 65 years, with no patient being younger than 41 years, which is older than the cohort analyzed by Ufuk *et al.* (median age of 48 years) (26). This may have introduced selection bias, explaining why neither age nor sex were a significant predictor of mortality in our cohort. Overall 30-day mortality was 41%, while it ranged between 5.8% and 31.8% in other studies (26, 28, 35). This is mirrored in the high proportion of our patients treated in the ICU (80.4%) and requiring mechanical ventilation (71.7%). In the sample by Kim *et al.*, the ICU admission rate was only 8.3% (35). The percentage of patients receiving mechanical ventilation were 6.6%, 11.5%

Table III. *Association of pectoralis muscle composition parameters with clinical variables (univariable model).*

	Length of hospital stay			Length of ICU stay			Duration of IMV		
Parameter	β	95% CI	*p*-Value	β	95% CI	*p*-Value	β	95% CI	*p*-Value
Age	−0.009	−0.301-0.283	0.953	−0.241	−0.529-0.048	0.099	−4.918	−11.891-2.054	0.162
Gender (male)	0.242	−7.392-7.875	0.949	3.559	−4.134-11.253	0.356	112.450	−70.758-295.659	0.223
BMI	0.003	−0.449-0.455	0.989	0.300	−0.151-0.751	0.187	8.289	−2.460-19.038	0.127
PMA	−0.165	−0.547-0.216	0.387	0.246	−0.139-0.631	0.204	7.323	−1.814-16.460	0.113
PMI	−0.792	−2.222-0.639	0.271	0.610	−0.855-2.075	0.406	17.603	−17.406-52.612	0.316
Density	−0.100	−0.406-0.205	0.511	0.003	−0.310-0.315	0.987	0.269	−7.220-7.758	0.943
SMG	−0.019	−0.043-0.005	0.116	−0.001	−0.026-0.025	0.963	0.033	−0.573-0.640	0.912
Density/PMA	2.879	−3.408-9.165	0.361	−2.542	−8.955-3.872	0.429	−77.385	−230.534-75.765	0.314

BMI: Body mass index; CI: confidence interval; ICU: Intensive Care Unit; IMV: invasive mechanical ventilation; PMA: pectoralis muscle area; PMI: pectoralis muscle index; SMG: skeletal muscle gauge.

and 21.4% in the study by Kim *et al.*, Ufuk *et al.*, and Besutti *et al.*, respectively (22, 26, 35). The study by Moctezuma-Velázquez had a patient cohort with characteristics closer to ours, with an ICU admission rate of 40% and a mortality of 25%, revealing no association with clinical outcomes (27). A large proportion of our patients (73.9%) had a hospital stay of more than 10 days, with a median of 19 days, compared with 18.5% and 7 days for the sample by Ufuk *et al.* (26). Density values in our sample were measured in contrast CT scans, with other studies using non-contrast images (28, 29). Hocaoglu *et al.* measured the *pectoralis* muscle density in non-contrast scans, finding cut-off values of 34.1 HU for men and 15.9 HU for women for association with increased mortality (28). Muscle density values are typically higher when measured in the venous phase (36). Nevertheless, our mean density was lower than the cut-off determined by Hocaoglu *et al.* for the male group, indicating a more critical disease stage.

Sarcopenia may potentially play a role in clinical outcome of patients with Covid-19. Yet we were not able to find such association in patients with severe disease. A possible explanation for this may be found in the nature of the disease, which causes multisystem inflammation and organ failure and subsequent mortality (27). In a cohort already severely affected by the disease in a progressed state, muscle mass at admission may no longer be a good predictor for outcome, as muscle loss is already advanced (37, 38).

Our study has several limitations. Firstly, it was a single-center study with a small cohort. Not all symptomatic patients with Covid-19 at our center underwent a chest CT scan at admission. Only those with respiratory distress or infiltrates on chest X-ray were further evaluated at the discretion of the attending physician. Thus, patients with symptomatic but mild disease were not analyzed. In the follow-up, only mortality at 30 days was noted. As we evaluated *pectoralis* muscle composition as a proxy indicator for sarcopenia, the effect of muscle mass at other levels remains unknown. We did not associate our muscle indices with comorbidities.

In conclusion, in patients severely affected by Covid-19, *pectoralis* muscle composition parameters were not associated with length of hospital or ICU stay, length of mechanical invasive ventilation, or 30-day mortality. Further research is warranted to determine whether muscle indices predict clinical outcome in patients with a less advanced stage of disease.

Conflicts of Interest

None declared.

Authors' Contributions

HK: Data analysis, validation and writing original draft. MT: Supervision, validation, investigation, data analysis and writing original draft. CB: Review and editing. JO: validation, review and editing. AW: statistical analysis, review and editing. MP: supervision and writing original draft. AS: supervision, data analysis, review and editing.

References

1 Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M and Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2: Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing *48(1)*: 16-31, 2019. PMID: 30312372. DOI: 10.1093/ageing/afy169

2 Liguori I, Russo G, Aran L, Bulli G, Curcio F, Della-Morte D, Gargiulo G, Testa G, Cacciatore F, Bonaduce D and Abete P: Sarcopenia: assessment of disease burden and strategies to improve outcomes. Clin Interv Aging *13*: 913-927, 2018. PMID: 29785098. DOI: 10.2147/CIA.S149232

3 Iannuzzi-Sucich M, Prestwood KM and Kenny AM: Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women. J Gerontol A Biol Sci Med Sci *57(12)*: M772-M777, 2002. PMID: 12456735. DOI: 10.1093/gerona/57.12.m772

4 Shachar SS, Williams GR, Muss HB and Nishijima TF: Prognostic value of sarcopenia in adults with solid tumours: A meta-analysis and systematic review. Eur J Cancer *57*: 58-67, 2016. PMID: 26882087. DOI: 10.1016/j.ejca.2015.12.030

5 Rossi S, Di Noia V, Tonetti L, Strippoli A, Basso M, Schinzari G, Cassano A, Leone A, Barone C and D'Argento E: Does sarcopenia affect outcome in patients with non-small-cell lung cancer harboring EGFR mutations? Future Oncol *14(10)*: 919-926, 2018. PMID: 29528255. DOI: 10.2217/fon-2017-0499

6 Janssen I: Influence of sarcopenia on the development of physical disability: the Cardiovascular Health Study. J Am Geriatr Soc *54(1)*: 56-62, 2006. PMID: 16420198. DOI: 10.1111/j.1532-5415.2005.00540.x

7 Surov A and Wienke A: Sarcopenia predicts overall survival in patients with malignant hematological diseases: A meta-analysis. Clin Nutr *40(3)*: 1155-1160, 2021. PMID: 32768316. DOI: 10.1016/j.clnu.2020.07.023

8 Hemke R, Buckless C and Torriani M: Quantitative imaging of body composition. Semin Musculoskelet Radiol *24(4)*: 375-385, 2020. PMID: 32992366. DOI: 10.1055/s-0040-1708824

9 Ali AM and Kunugi H: Screening for sarcopenia (physical frailty) in the COVID-19 era. Int J Endocrinol *2021*: 5563960, 2021. PMID: 34113379. DOI: 10.1155/2021/5563960

10 Bak SH, Kwon SO, Han SS and Kim WJ: Computed tomography-derived area and density of pectoralis muscle associated disease severity and longitudinal changes in chronic obstructive pulmonary disease: a case control study. Respir Res *20(1)*: 226, 2019. PMID: 31638996. DOI: 10.1186/s12931-019-1191-y

11 Welch AA, Hayhoe RPG and Cameron D: The relationships between sarcopenic skeletal muscle loss during ageing and macronutrient metabolism, obesity and onset of diabetes. Proc Nutr Soc *79(1)*: 158-169, 2020. PMID: 31685055. DOI: 10.1017/S0029665119001150

12 Wannamethee SG and Atkins JL: Muscle loss and obesity: the health implications of sarcopenia and sarcopenic obesity. Proc Nutr Soc *74(4)*: 405-412, 2015. PMID: 25913270. DOI: 10.1017/S002966511500169X

13 Diaz AA, Martinez CH, Harmouche R, Young TP, McDonald ML, Ross JC, Han ML, Bowler R, Make B, Regan EA, Silverman EK, Crapo J, Boriek AM, Kinney GL, Hokanson JE, Estepar RSJ and Washko GR: Pectoralis muscle area and mortality in smokers without airflow obstruction. Respir Res *19(1)*: 62, 2018. PMID: 29636050. DOI: 10.1186/s12931-018-0771-6

14 Kinsey CM, San José Estépar R, van der Velden J, Cole BF, Christiani DC and Washko GR: Lower pectoralis muscle area is associated with a worse overall survival in non-small cell lung cancer. Cancer Epidemiol Biomarkers Prev *26(1)*: 38-43, 2017. PMID: 27197281. DOI: 10.1158/1055-9965.EPI-15-1067

15 Oh J, Song IK, Nam JS, Lee SW, Lee EH and Choi IC: Sarcopenia as a prognostic factor for outcomes after isolated tricuspid valve surgery. J Cardiol *76(6)*: 585-592, 2020. PMID: 32736904. DOI: 10.1016/j.jjcc.2020.07.010

16 DeAndrade J, Pedersen M, Garcia L and Nau P: Sarcopenia is a risk factor for complications and an independent predictor of hospital length of stay in trauma patients. J Surg Res *221*: 161-166, 2018. PMID: 29229123. DOI: 10.1016/j.jss.2017.08.018

17 Surov A and Wienke A: Low skeletal muscle mass predicts relevant clinical outcomes in head and neck squamous cell carcinoma. A meta analysis. Ther Adv Med Oncol *13*: 17588359211008844, 2021. PMID: 34035838. DOI: 10.1177/17588359211008844

18 Weinberg MS, Shachar SS, Muss HB, Deal AM, Popuri K, Yu H, Nyrop KA, Alston SM and Williams GR: Beyond sarcopenia: Characterization and integration of skeletal muscle quantity and radiodensity in a curable breast cancer population. Breast J *24(3)*: 278-284, 2018. PMID: 29139618. DOI: 10.1111/tbj.12952

19 Shachar SS, Deal AM, Weinberg M, Nyrop KA, Williams GR, Nishijima TF, Benbow JM and Muss HB: Skeletal muscle measures as predictors of toxicity, hospitalization, and survival in patients with metastatic breast cancer receiving taxane-based chemotherapy. Clin Cancer Res *23(3)*: 658-665, 2017. PMID: 27489287. DOI: 10.1158/1078-0432.CCR-16-0940

20 Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, Curtis HJ, Mehrkar A, Evans D, Inglesby P, Cockburn J, McDonald HI, MacKenna B, Tomlinson L, Douglas IJ, Rentsch CT, Mathur R, Wong AYS, Grieve R, Harrison D, Forbes H, Schultze A, Croker R, Parry J, Hester F, Harper S, Perera R, Evans SJW, Smeeth L and Goldacre B: Factors associated with COVID-19-related death using OpenSAFELY. Nature *584(7821)*: 430-436, 2020. PMID: 32640463. DOI: 10.1038/s41586-020-2521-4

21 Risk for COVID-19 infection, hospitalization, and death by age group | CDC. Available at: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-age.html [Last accessed on June 14th, 2021]

22 Besutti G, Pellegrini M, Ottone M, Cantini M, Milic J, Bonelli E, Dolci G, Cassone G, Ligabue G, Spaggiari L, Pattacini P, Fasano T, Canovi S, Massari M, Salvarani C, Guaraldi G, Rossi PG and Reggio Emilia COVID-19 Working Group: The impact of chest CT body composition parameters on clinical outcomes in COVID-19 patients. PLoS One *16(5)*: e0251768, 2021. PMID: 33989341. DOI: 10.1371/journal.pone.0251768

23 Viddeleer AR, Raaphorst J, Min M, Beenen LFM, Scheerder MJ, Vlaar APJ, Amsterdam UMC COVID-19 Biobank, Beudel M and Hemke R: Intramuscular adipose tissue at level Th12 is associated with survival in COVID-19. J Cachexia Sarcopenia Muscle *12(3)*: 823-827, 2021. PMID: 33939338. DOI: 10.1002/jcsm.12696

24 Watanabe M, Caruso D, Tuccinardi D, Risi R, Zerunian M, Polici M, Pucciarelli F, Tarallo M, Strigari L, Manfrini S, Mariani S, Basciani S, Lubrano C, Laghi A and Gnessi L: Visceral fat shows the strongest association with the need of intensive care in patients with COVID-19. Metabolism *111*: 154319, 2020. PMID: 32712222. DOI: 10.1016/j.metabol.2020.154319

25 Petersen A, Bressem K, Albrecht J, Thieß HM, Vahldiek J, Hamm B, Makowski MR, Niehues A, Niehues SM and Adams LC: The role of visceral adiposity in the severity of COVID-19: Highlights from a unicenter cross-sectional pilot study in Germany. Metabolism *110*: 154317, 2020. PMID: 32673651. DOI: 10.1016/j.metabol.2020.154317

26 Ufuk F, Demirci M, Sagtas E, Akbudak IH, Ugurlu E and Sari T: The prognostic value of pneumonia severity score and pectoralis muscle Area on chest CT in adult COVID-19 patients.

Eur J Radiol *131*: 109271, 2020. PMID: 32942198. DOI: 10.1016/j.ejrad.2020.109271

27 Moctezuma-Velázquez P, Miranda-Zazueta G, Ortiz-Brizuela E, González-Lara MF, Tamez-Torres KM, Román-Montes CM, Díaz-Mejía BA, Pérez-García E, Villanueva-Reza M, Tovar-Méndez VH, Medrano-Borromeo C, Martínez-Valenzuela A, Jandete-Medina MÁ, Martínez-Guerra BA, Uscanga-Domínguez L, Sifuentes-Osornio J, Ponce-de-León A, Olivas-Martinez A and Moctezuma-Velázquez C: Low thoracic skeletal muscle area is not associated with negative outcomes in patients with COVID-19. Am J Phys Med Rehabil *100(5)*: 413-418, 2021. PMID: 33587451. DOI: 10.1097/PHM.0000000000001716

28 Hocaoglu E, Ors S, Yildiz O and Inci E: Correlation of pectoralis muscle volume and density with severity of COVID-19 pneumonia in adults. Acad Radiol *28(2)*: 166-172, 2021. PMID: 33281041. DOI: 10.1016/j.acra.2020.11.017

29 Feng Z, Zhao H, Kang W, Liu Q, Wu J, Bragazzi NL, Ma X, Wang W and Rong P: Association of paraspinal muscle measurements on chest computed tomography with clinical outcomes in patients with severe Coronavirus disease 2019. J Gerontol A Biol Sci Med Sci *76(3)*: e78-e84, 2021. PMID: 33355656. DOI: 10.1093/gerona/glaa317

30 Schiaffino S, Albano D, Cozzi A, Messina C, Arioli R, Bnà C, Bruno A, Carbonaro LA, Carriero A, Carriero S, Danna PSC, D'Ascoli E, De Berardinis C, Della Pepa G, Falaschi Z, Gitto S, Malavazos AE, Mauri G, Monfardini L, Paschè A, Rizzati R, Secchi F, Vanzulli A, Tombini V, Vicentin I, Zagaria D, Sardanelli F and Sconfienza LM: CT-derived chest muscle metrics for outcome prediction in patients with COVID-19. Radiology *300(2)*: E328-E336, 2021. PMID: 33724065. DOI: 10.1148/radiol.2021204141

31 Ji Y, Cheng B, Xu Z, Ye H, Lu W, Luo X, Fu S and Fang X: Impact of sarcopenic obesity on 30-day mortality in critically ill patients with intra-abdominal sepsis. J Crit Care *46*: 50-54, 2018. PMID: 29677586. DOI: 10.1016/j.jcrc.2018.03.019

32 Joyce PR, O'Dempsey R, Kirby G and Anstey C: A retrospective observational study of sarcopenia and outcomes in critically ill patients. Anaesth Intensive Care *48(3)*: 229-235, 2020. PMID: 32486830. DOI: 10.1177/0310057X20922234

33 Kou HW, Yeh CH, Tsai HI, Hsu CC, Hsieh YC, Chen WT, Cheng HT, Yu MC and Lee CW: Sarcopenia is an effective predictor of difficult-to-wean and mortality among critically ill surgical patients. PLoS One *14(8)*: e0220699, 2019. PMID: 31393937. DOI: 10.1371/journal.pone.0220699

34 Ng CC, Lee ZY, Chan WY, Jamaluddin MF, Tan LJ, Sitaram PN, Ruslan SR and Hasan MS: Low muscularity as assessed by abdominal computed tomography on intensive care unit admission is associated with mortality in a critically ill Asian population. JPEN J Parenter Enteral Nutr *44(3)*: 425-433, 2020. PMID: 31173666. DOI: 10.1002/jpen.1666

35 Kim JW, Yoon JS, Kim EJ, Hong HL, Kwon HH, Jung CY, Kim KC, Sung YS, Park SH, Kim SK and Choe JY: Prognostic implication of baseline sarcopenia for length of hospital stay and survival in patients with Coronavirus disease 2019. J Gerontol A Biol Sci Med Sci *76(8)*: e110-e116, 2021. PMID: 33780535. DOI: 10.1093/gerona/glab085

36 van Vugt JLA, Coebergh van den Braak RRJ, Schippers HJW, Veen KM, Levolger S, de Bruin RWF, Koek M, Niessen WJ, IJzermans JNM and Willemsen FEJA: Contrast-enhancement influences skeletal muscle density, but not skeletal muscle mass, measurements on computed tomography. Clin Nutr *37(5)*: 1707-1714, 2018. PMID: 28743427. DOI: 10.1016/j.clnu.2017.07.007

37 Baggerman MR, van Dijk DPJ, Winkens B, van Gassel RJJ, Bol ME, Schnabel RM, Bakers FC, Olde Damink SWM and van de Poll MCG: Muscle wasting associated co-morbidities, rather than sarcopenia are risk factors for hospital mortality in critical illness. J Crit Care *56*: 31-36, 2020. PMID: 31805466. DOI: 10.1016/j.jcrc.2019.11.016

38 Ju S, Choi SM, Park YS, Lee CH, Lee SM, Yoo CG, Kim YW, Han SK and Lee J: Rapid muscle loss negatively impacts survival in critically ill patients with cirrhosis. J Intensive Care Med *35(7)*: 663-671, 2020. PMID: 29742956. DOI: 10.1177/0885066618775706

Received September 21, 2021
Revised October 31, 2021
Accepted November 13, 2021

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Original Investigation

Prognostic Role of the Pectoralis Musculature in Patients with COVID-19. A Multicenter Study

Alexey Surov, MD, Hakan Kardas, MD, Giulia Besutti, MD, Massimo Pellegrini, MD, Marta Ottone, MD, Mehmet Ruhi Onur, MD, Firat Atak, MD, Ahmet Gurkan Erdemir, MD, Elif Hocaoglu, MD, Ömer Yıldız, MD, Ercan Inci, MD, Eda Cingöz, MD, Mehmet Cingöz, MD, Memduh Dursun, MD, İnan Korkmaz, MD, Çağrı Orhan, MD, Alexandra Strobel, MD, Andreas Wienke, MD, Maciej Pech, MD

Rationale and Objectives: To evaluate the impact of low skeletal muscle mass in patients with COVID-19 on relevant outcomes like 30-day mortality, need for intubation and need for intensive care unit admission.

Materials and Methods: For this study, data from six centers were acquired. The acquired sample comprises 1138 patients. There were 547 women (48.1%) and 591 men (51.9%) with a mean age of 54.5 ± 18.8 years; median age, 55 years; range, 18–84 years). In every case, thoracic CT without intravenous application of contrast medium was performed. The following parameters of the pectoralis muscles were estimated: muscle area as a sum of the bilateral areas of the pectoralis major and minor muscles, muscle density, muscle index (PMI) (pectoralis muscle area divided by the patient's body height square) as a ratio pectoralis major and minor muscles divided by the patient's body height^2, and muscle gauge as PMI x muscle density.

Results: Overall, 220 patients (19.33%) were admitted to the intensive care unit. In 171 patients (15.03%), mechanical lung ventilation was performed. Finally, 154 patients (13.53%) died within the observation time of 30-day. All investigated parameters of pectoralis muscle were lower in the patients with unfavorable courses of Covid-19. All pectoralis muscle parameters were associated with 30-day mortality in multivariate analyses adjusted for age and sex: pectoralis muscle area, HR = 0.93 CI 95% (0.91–0.95) $p < 0.001$; pectoralis muscle density, HR = 0.94 CI 95% (0.93–0.96) $p < 0.001$; pectoralis muscle index, HR = 0.79 CI 95% (0.75–0.85) $p < 0.001$, pectoralis muscle gauge, HR = 0.995 CI 95% (0.99–0.996) $p < 0.001$.

Conclusion: in COVID-19, survivors have larger areas and higher index, gauge and density of the pectoralis muscles in comparison to nonsurvivors. However, the analyzed muscle parameters cannot be used for prediction of disease courses.

Key Words: COVID-19; sarcopenia; survival.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic represents a great problem for the global health. The clinical course of COVID-19 is very variable. In fact, although it has been identified that most patients had a relatively mild course, some patients still had a rapid progression with fatal outcome (1,2). However, some patients had a rapid progression of disease with fatal outcome (1,2).

Therefore, prediction of unfavorable outcomes of COVID-19 is essential. Already established prognostic factors are age and sex (3,4). Comorbidities, such as dementia, heart failure and peripheral vascular diseases are also predictors of an unfavorable course of the disease (3,4).

Computed tomography (CT) is the imaging modality of choice in COVID-19, especially for detection of pulmonary consolidations (5–7). Typical imaging findings in COVID-19 are bilateral, peripheral dominant ground-glass opacities with lower lobe and posterior predilection (5–7).

Acad Radiol 2023; 30:77–82

From the Department of Radiology and Nuclear Medicine, Otto-von-Guericke University Magdeburg (A.S., H.K., M.P.) (A.S., H.K., M.P.); Radiology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy (G.B., M.P., M.O.) (G.B., M.P., M.O.); Department of Radiology, University of Hacettepe School of Medicine, Ankara, Turkey (M.R.O., F.A., A.G.E.) (M.R.O., F.A., A.G.E.); Department of Radiology, University of Health Sciences, Bakirkoy Dr. Sadi Konuk Research and Training Hospital, Radiology (E.H., O.Y., E.I.) (E.H., Ö.Y., E.I.); İstanbul Medical Faculty Radiology Department, Istanbul Turkey (E.C., M.C., M.D.) (E.C., M.C., M.D.); Basaksehir Cam and Sakura City Hospital Radiology Department (M.C.) (M.C.); Hatay Mustafa Kemal University, Faculty of Medicine, Department of Radiology, Antakya, Hatay, Turkey (I.K., C.O.) (I.K., Ç.O.); Institute of Medical Epidemiology, Biostatistics, and Informatics, Profile Area Clinical Studies & Biostatistics, Martin-Luther-University Halle-Wittenberg, Halle, Germany (A.S., A.W.) (A.S., A.W.). Received April 27, 2022; revised May 4, 2022; accepted May 5, 2022. **Address correspondence to:** A.S. e-mail: alexey.surov@med.ovgu.de

https://doi.org/10.1016/j.acra.2022.05.003

Also, extrapulmonary findings play an important role in COVID-19 (8). It has been shown that pleural effusion, pericardial effusion and mediastinal lymphadenopathy can be used as predictors of severe course of COVID-19 (6,8). In fact, pleural effusion and coronary calcifications are strong predictors of mortality in COVID-19, odds ratio (OR) = 4.6 (95% CI 2.97−7.12), $p < 0.00001$, and OR = 2.68 (95% CI 1.78−4.04), $p < 0.00001$, respectively (8).

Similarly, low skeletal muscle mass (LSMM) measured on CT can also predict unfavourable courses of COVID-19 (9).

The purpose of the present multi-center study was to evaluate the impact of LSMM in COVID-19 patients on relevant outcomes like 30-day mortality, need for intubation and need for intensive care.

METHODS

Data Acquisition and Patients

This retrospective study was approved by our institutional review board (Medical Faculty, Otto-von-Guericke-University Magdeburg, number 145-21).

This study comprises data from six centers:

- Radiology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy;
- Department of Radiology, University of Hacettepe School of Medicine, Ankara, Turkey;
- Department of Radiology and Nuclear Medicine, Otto-von-Guericke University Magdeburg;
- Department of Radiology, University of Health Sciences, Bakirkoy Dr. Sadi Konuk Research and Training Hospital, Radiology;
- Department of Radiology, Mustafa-Kemal-University, Antakya, Turkey;
- Department of Radiology, Istanbul University, Istanbul, Turkey.
- In the centers, the data were acquired retrospectively. Inclusion criteria were as follows:
- diagnosis of COVID-19 confirmed by PCR;
- available thoracic CT images without intravenous administration of contrast medium;
- available data regarding the following clinical outcomes: 30-day mortality, need for mechanical ventilation, and admission on an intensive care unit.
- Exclusion criteria were as follows:
  - cases with missing data regarding the previously-mentioned outcomes;
  - CT images after intravenous application of contrast medium;
  - missing confirmation of COVID-19 infection by PCR.

The acquired sample comprises 1138 patients. There were 547 women (48.1%) and 591 men (51.9%) with a mean age of 54.5 ± 18.8 years; median age, 55 years; range, 18−84 years). In every case, thoracic CT without intravenous application of contrast medium was performed on different clinical CT scanners or on each center's CT units.

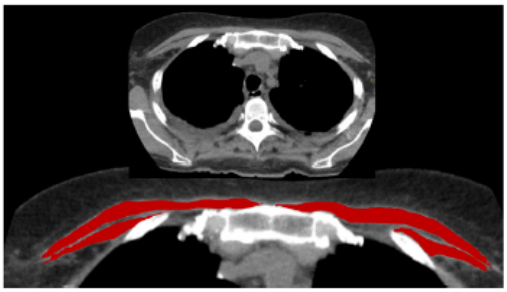


Figure 1. Imaging findings in a 55- year-old woman with COVID-19. Pectoralis muscle area = 14,48 cm^2, pectoralis muscle density = 28 HU, pectoralis muscle index = 5.19, pectoralis muscle gauge = 145.3. The patient died on the day 19 after admission. (Color version of figure is available online.)

Measure of the Pectoralis Musculature on CT

In every case, the first CT scan of patients after hospital admission was used. In all six centers, measurements were performed by experienced radiologists blinded to the clinical course of patients. The measurements were performed on axial images at the T4 level in the soft tissue window on dedicated workstations. A polygonal region of interest (ROI) was drawn along the contours of the pectoralis major and minor muscles on both sides (Figs 1 and 2). Pectoralis muscle area (PMA) was defined as a sum of the bilateral areas of the pectoralis major and minor muscles. Furthermore, pectoralis muscle density was measured within the ROIs. Pectoralis muscle index (PMI) was calculated as a ratio PMA divided by the patient's body height square. Additionally, skeletal muscle gauge (SMG) was calculated by multiplying PMI with mean muscle density as reported previously (10).

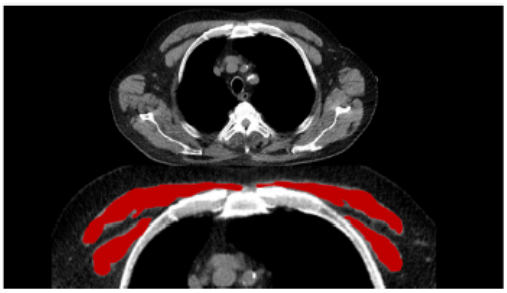


Figure 2. Imaging findings in a 61- year-old old man with COVID-19. Pectoralis muscle area = 28.17 cm^2, pectoralis muscle density = 30 HU, pectoralis muscle index = 8.69, pectoralis muscle gauge = 260.7. The patient was discharged in good health. (Color version of figure is available online.)

Statistical Analysis

Statistical analysis was performed using the SPSS package (IBM SPSS Statistics for Windows, version 225.0, Armonk, NY: IBM corporation). Continuous variables were described by mean value, median and standard deviation. Categorical variables were given as relative frequencies. The comparison of pectoralis muscle parameters was performed by Mann-Whitney-U tests and the *p*-values were adjusted for multiple testing (Bonferroni correction). To assess the impact of the pectoralis musculature on clinical outcomes, uni- and multivariable logistic regression models were used to assess the impact of pectoralis muscle on clinical outcomes. Odds ratios are presented together with 95 % confidence intervals (95 % CI). In all instances, *p*values < 0.05 were taken to indicate statistical significance.

RESULTS

The estimated values (Mean ± SD) of the pectoralis muscles were as follows: pectoralis muscle area, 28.91 ± 13.60 cm^2; skeletal muscle index, 10.85 ± 4.47 cm^2/m^2; pectoralis muscle density, 35.50 ± 13.77 HU; pectoralis muscle gauge, 401.30 ± 251.87.

Overall, 220 patients (19.33%) were admitted to intensive care unit. Furthermore, in 171 patients (15.03%), mechanical lung ventilation was performed. Finally, 154 patients (13.53%) died within the observation time of 30-day. All investigated muscle values or parameters of pectoralis muscles were lower in the patients with unfavorable courses of COVID-19 (Table 1).

Regression analysis identified that all pectoralis muscle parameters were associated with unfavorable courses (Table 2). Also, all pectoralis muscle parameters were associated with unfavorable courses after adjusting for age and sex (Table 3).

DISCUSSION

The present study showed at the first time the prognostic role of the pectoralis musculature in COVID-19 based on a large sample in a multicenter setting.

According to the literature, parameters of body composition measured on cross sectional imaging techniques like CT play an important clinical role and are strong predictors for several relevant outcomes in different disorders (11–15). Importantly, muscle measurement is a by-product of cross-sectional imaging and does not need additional investigations. So far, in patients with abdominal trauma, low skeletal muscle mass on CT is significantly associated with longer hospitalization, longer intensive care length of stay, higher cost, higher frequency of mechanical ventilation, longer duration of vasopressor use, and higher incidence of massive transfusion and transfusion-related complications (11). Furthermore, in trauma patients, LSMM increases risk of 30-day mortality, RR = 1.60 CI 95% (1.21–2.13) and risk of 1-year mortality, RR = 3.11 CI 95% (1.94–4.96) (12).

There are numerous large meta-analyses suggesting that LSMM is an essential biomarker in oncology. In short, in lung cancer, LSMM is associated with a shorter overall survival HR = 2.23 CI 95% (1.68–2.94) (13). In head and neck cancer, LSMM is associated with occurrence of severe postoperative complications, OR = 4.79, CI 95% (2.52–9.11), and predicts disease free survival HR = 1.64, CI 95% (1.33–2.03), as well as overall survival, HR = 1.87, CI 95% (1.53–2.29) (14). Finally, LSMM predicts worse overall survival in gastric cancer, HR = 2.12, CI 95% (1.89–2.38) (15). Similar findings are known for pancreatic cancer, colorectal cancer, esophageal cancer, prostatic cancer, and malignant hematological diseases (16–20). In intensive care units, LSMM predicts short-term mortality, HR = 2.78 CI 95% (2.05–3.75) (21).

TABLE 1. Comparison of the Pectoralis Muscle Parameters in Patients With COVID-19

a. Pectoralis Muscle Values and Need for ICU Admission			
Muscle Parameters	No ICU Admission	ICU Admission	*p* Values
Pectoralis muscle area, cm^2	29.80 ± 14.17	25.20 ± 10.09	<0.001
Pectoralis muscle density, HU	37.29 ± 12.98	28.03 ± 14.56	<0.001
Pectoralis muscle index, cm^2/m^2	11.03 ± 4.60	9.23 ± 3.54	<0.001
Pectoralis muscle gauge	436.77 ± 252.03	274.55 ± 206.89	<0.001
b. Pectoralis Muscle Values and Need for Mechanical Ventilation			
Muscle Parameters	No Mechanical Ventilation	Mechanical Ventilation	*p* Values
Pectoralis muscle area, cm^2	29.754 ± 13.95	24.156 ± 10.16	<0.001
Pectoralis muscle density, HU	36.916 ± 13.06	27.484 ± 15.06	<0.001
Pectoralis muscle index, cm^2/m^2	11.242 ± 4.53	8.866 ± 3.57	<0.001
Pectoralis muscle gauge	429.678 ± 250.47	257.508 ± 206.24	<0.001
c. Pectoralis Muscle Values and 30-day Mortality			
Muscle Parameters	Survivors	Nonsurvivors	*p* Values
Pectoralis muscle area, cm^2	30.189 ± 13.74	20.757 ± 9.13	<0.001
Pectoralis muscle density, HU	36.841 ± 13.15	26.929 ± 14.71	<0.001
Pectoralis muscle index, cm^2/m^2	11.277 ± 4.49	8.0365 ± 3.15	<0.001
Pectoralis muscle gauge	428.305 ± 250.02	223.505 ± 182.80	<0.001

TABLE 2. Associations Between Pectoralis Muscle Values and Unfavorable Outcomes in COVID-19 (Univariate Analysis)

Muscle Parameters	OR	CI95%	*p* Values
a. Associations Between Pectoralis Muscle Values and Need for Intensive Care Admission			
Pectoralis muscle area, cm^2	0.97	(0.96, 0.98)	<0.001
Pectoralis muscle density, HU	0.95	(0.93, 0.96)	<0.001
Pectoralis muscle index, cm^2/m^2	0.88	(0.85, 0.92)	<0.001
Pectoralis muscle gauge	0.996	(0.996, 0.997)	<0.001
b. Associations Between Pectoralis Muscle Values and Need for Mechanical Ventilation			
Pectoralis muscle area, cm^2	0.97	(0.95, 0.98)	<0.001
Pectoralis muscle density, HU	0.95	(0.93, 0.96)	<0.001
Pectoralis muscle index, cm^2/m^2	0.86	(0.82, 0.90)	<0.001
Pectoralis muscle gauge	0.996	(0.995, 0.997)	<0.001
c. Associations Between Pectoralis Muscle Values and 30-day Mortality			
Pectoralis muscle area, cm^2	0.93	(0.91, 0.95)	<0.001
Pectoralis muscle density, HU	0.94	(0.93, 0.96)	<0.001
Pectoralis muscle index, cm^2/m^2	0.79	(0.75, 0.85)	<0.001
Pectoralis muscle gauge	0.995	(0.993, 0.996)	<0.001

In COVID-19, data concerning the role of LSMM are mixed (9,22–25). So far, Schiaffino et al. indicates that LSMM is strongly associated with either ICU admission, OR = 4.8, CI 95% (2.7–8.5), $p < 0.001$ and mortality, OR = 2.3, CI 95% (1.0–2.9), $p < 0.027$ (9). Kim et al. reports that LSMM is associated with prolonged hospital stay in patients with COVID-19 but not with mortality (22). However, other authors do not report significant relationships between LSMM and relevant outcomes in patients with COVID-19 (24,25). For example, according to Moctezuma-Velázquez et al., skeletal muscle index is not associated with negative outcomes, such as in-hospital mortality, need of invasive mechanical ventilation, and intensive care unit admission, in hospitalized patients with COVID-19 (24).

Our results based on the largest cohort to date show that all pectoralis muscle values including muscle area, index, density and gauge are statistically significant higher in survivors vs nonsurvivors. It indicates that patients with more metabolic reserve and predominance of anabolic processes may have a better prognosis. However, according to the regression analysis, the investigated pectoralis muscle parameters cannot discriminate patients with favorable vs unfavorable disease courses. This finding suggests that the status of the pectoralis musculature cannot be used for patients stratifying in COVID-19.

Associations between LSMM and unfavorable courses of COVID-19 are multifactorial. The presence of LSMM may reflect a state of malnutrition and/or catabolism. It is also known that anemia and hypoalbuminemia are associated with low muscle density (26). Furthermore, there are significant interactions between the skeletal musculature and immune system. So far, skeletal muscles release numerous myokines with autocrine, paracrine, and immune effects (27). For instance, interleukin (IL)-15 is a myokine that stimulates proliferation and activation of natural killer cells and CD8+

TABLE 3. Associations Between Pectoralis Muscle Values and Unfavorable Outcomes in COVID-19 (Multivariate Analysis)

Muscle Parameters	OR	CI95%	*p* Values
a. Associations Between Pectoralis Muscle Values and Need for Intensive Care Admission			
Pectoralis muscle area, cm^2	0.99	(0.98, 1.007)	0.391
Pectoralis muscle density, HU	0.96	(0.95, 0.97)	<0.001
Pectoralis muscle index, cm^2/m^2	0.94	(0.90, 0.99)	<0.001
Pectoralis muscle gauge	0.998	(0.997, 0.999)	<0.001
b. Associations Between Pectoralis Muscle Values and Need for Mechanical Ventilation			
Pectoralis muscle area, cm^2	0.98	(0.97, 0.99)	0.033
Pectoralis muscle density, HU	0.96	(0.94, 0.97)	<0.001
Pectoralis muscle index, cm^2/m^2	0.87	(0.87, 0.96)	<0.001
Pectoralis muscle gauge	0.997	(0.996, 0.999)	<0.001
c. Associations Between Pectoralis Muscle Values and 30-day Mortality			
Pectoralis muscle area, cm^2	0.96	(0.94, 0.98)	<0.001
Pectoralis muscle density, HU	0.96	(0.95, 0.98)	<0.001
Pectoralis muscle index, cm^2/m^2	0.86	(0.80, 0.91)	<0.001
Pectoralis muscle gauge	0.996	(0.995, 0.998)	<0.001

T lymphocytes (28). These cells play an essential role in antiviral immune defense (28). Furthermore, IL 15 induces activation and phagocytosis of neutrophils (29). IL 15 also delays human neutrophil apoptosis (30). Presumably, in patients with reduced muscle quantity and/or quality a smaller number of myokines is produced.

Notably, different measurements and values for estimation of LSMM in patients with COVID-19 are used. According to the literature, SMI estimation on CT at the level of the third lumbar vertebra (L3) represents a standardized method to quantify the skeletal musculature (31). In patients with COVID-19, often only thoracic CT investigations for the analysis of pulmonary damage are performed. Therefore, the estimation of the standardized SMI values at the L3 level is impossible. Hence, in the previous studies, other vertebral levels for the quantification of the skeletal musculature are proposed, such as thoracic vertebra 5 (32), thoracic vertebra 12 (22,24,33), or lumbar vertebra 1 (34).The pectoralis muscles as surrogate marker is also used (35,36).

The present study has several limitations. Firstly, it is based on retrospective cohorts. Secondly, only patients, who underwent CT investigations without intravenous administration of contrast medium, were included. Thirdly, we did not analyze virus subtypes in our patients. It is well known that several viruses provoke different disease severity. However, to date, it is the largest multicenter cohort and our results represent evidence based data regarding associations between skeletal musculature and clinical outcomes in COVID-19.

In conclusion, in COVID-19, survivors have larger areas and higher index, gauge and density of the pectoralis muscles in comparison to nonsurvivors. However, the analyzed muscle parameters cannot be used for prediction of disease courses.

FUNDING

None.

ACKNOWLEDGMENT

This research was supported by the German Federal Ministry of Education and Research (BMBF) as part of the University Medicine Network (Project RACOON, 01KX2021).

REFERENCES

1. Abate SM, Ahmed Ali S, Mantfardo B, et al. Rate of Intensive Care Unit admission and outcomes among patients with coronavirus: a systematic review and Meta-analysis. PLoS One 2020; 15:e0235653.
2. Hu Y, Sun J, Dai Z, et al. Prevalence and severity of corona virus disease 2019 (COVID-19): a systematic review and meta-analysis. J Clin Virol 2020; 127:104371.
3. Liu B, Spokes P, He W, et al. High risk groups for severe COVID-19 in a whole of population cohort in Australia. BMC Infect Dis 2021; 21:685.
4. Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: a systematic literature review and meta-analysis. J Infect 2020; 81:e16–e25.
5. Besutti G, Ottone M, Fasano T, et al. The value of computed tomography in assessing the risk of death in COVID-19 patients presenting to the emergency room. Eur Radiol 2021: 1–12.
6. Koch V, Gruenewald LD, Albrecht MH, et al. Lung opacity and coronary artery calcium score: a combined tool for risk stratification and outcome prediction in COVID-19 patients. Acad Radiol 2022; 29:861–870.
7. Salehi S, Abedi A, Balakrishnan S, et al. Coronavirus Disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. AJR Am J Roentgenol 2020; 215:87–93.
8. Meyer HJ, Wienke A, Surov A. Extrapulmonary CT findings predict in-hospital mortality in COVID-19. A systematic review and meta-analysis. Acad Radiol 2022; 29:17–30.
9. Schiaffino S, Albano D, Cozzi A, et al. CT-derived chest muscle metrics for outcome prediction in patients with COVID-19. Radiology 2021; 300: E328–E336.
10. Kardas H, Thormann M, Bär C, et al. Impact of pectoral muscle values on clinical outcomes in patients with severe Covid-19 disease. In Vivo 2022; 36:375–380.
11. Xi F, Tan S, Gao T, Ding W, Sun J, Wei C, Li W, Yu W. Low skeletal muscle mass predicts poor clinical outcomes in patients with abdominal trauma. Nutrition 2021; 89:111229. doi:10.1016/j.nut.2021.111229.
12. Xia W, Barazanchi AWH, MacFater WS, Hill AG. The impact of computed tomography-assessed sarcopenia on outcomes for trauma patients - a systematic review and meta-analysis. Injury 2019; 50:1565–1576.
13. Yang M, Shen Y, Tan L, Li W. Prognostic value of sarcopenia in lung cancer: a systematic review and meta-analysis. Chest 2019; 156:101–111.
14. Surov A, Wienke A. Low skeletal muscle mass predicts relevant clinical outcomes in head and neck squamous cell carcinoma. A meta analysis. Ther Adv Med Oncol 2021; 13:17588359211008844.
15. Kamarajah SK, Bundred J, Tan BHL. Body composition assessment and sarcopenia in patients with gastric cancer: a systematic review and meta-analysis. Gastric Cancer 2019; 22:10–22.
16. Meyer HJ, Wienke A, Surov A. CT-defined low-skeletal muscle mass as a prognostic marker for survival in prostate cancer: a systematic review and meta-analysis. Urol Oncol 2022; 40:103.e9–103.e16. S1078-1439(21)00368-9.
17. Deng HY, Zha P, Peng L, Hou L, Huang KL, Li XY. Preoperative sarcopenia is a predictor of poor prognosis of esophageal cancer after esophagectomy: a comprehensive systematic review and meta-analysis. Dis Esophagus 2019; 32. doi:10.1093/dote/doy115.
18. Trejo-Avila M, Bozada-Gutiérrez K, Valenzuela-Salazar C, Herrera-Esquivel J, Moreno-Portillo M. Sarcopenia predicts worse postoperative outcomes and decreased survival rates in patients with colorectal cancer: a systematic review and meta-analysis. Int J Colorectal Dis 2021; 36:1077–1096.
19. Bundred J, Kamarajah SK, Roberts KJ. Body composition assessment and sarcopenia in patients with pancreatic cancer: a systematic review and meta-analysis. HPB (Oxford) 2019; 21:1603–1612.
20. Surov A, Wienke A. Sarcopenia predicts overall survival in patients with malignant hematological diseases: a meta-analysis. Clin Nutr 2021; 40:1155–1160.
21. Meyer HJ, Wienke A, Surov A. Computed tomography-defined low skeletal muscle mass as a prognostic marker for short-term mortality in critically ill patients: a systematic review and meta-analysis. Nutrition 2021; 91-92:111417.
22. Kim JW, Yoon JS, Kim EJ, et al. Prognostic implication of baseline sarcopenia for length of hospital stay and survival in patients with coronavirus Disease2019. J Gerontol A Biol Sci Med Sci 2021; 76:e110–e116.
23. Viddeleer AR, Raaphorst J, Min M, et al. Intramuscular adipose tissue at level Th12 is associated with survival in COVID-19. J Cachexia Sarcopenia Muscle 2021; 12:823–827.
24. Moctezuma-Velázquez P, Miranda-Zazueta G, Ortiz-Brizuela E, et al. Low Thoracic Skeletal Muscle Area Is Not Associated With Negative Outcomes in Patients With COVID-19. Am J Phys Med Rehabil 2021; 100:413–418.
25. Molwitz I, Ozga AK, Gerdes L, et al. Prediction of abdominal CT body composition parameters by thoracic measurements as a new approach to detect sarcopenia in a COVID-19 cohort. Sci Rep 2022; 12:6443.
26. Fragala MS, Kenny AM, Kuchel GA. Muscle quality in aging: a multidimensional approach to muscle functioning with applications for treatment. Sport Med 2015; 45:641–658.
27. Nelke C, Dziewas R, Minnerup J, et al. Skeletal muscle as potential central link between sarcopenia and immune senescence. EBioMedicine 2019; 49:381–388.

28. Conlon KC, Lugli E, Welles HC, et al. Redistribution, hyperproliferation, activation of natural killer cells and CD8 T cells, and cytokine production during first-in-human clinical trial of recombinant human interleukin-15 in patients with cancer. J Clin Oncol 2015; 33:74–82.
29. Girard D, Paquet ME, Paquin R, et al. Differential effects of interleukin-15 (IL-15) and IL-2 on human neutrophils: modulation of phagocytosis, cytoskeleton rearrangement, gene expression, and apoptosis by IL-15. Blood 1996; 88:3176–3184.
30. Bouchard A, Ratthé C, Girard D. Interleukin-15 delays human neutrophil apoptosis by intracellular events and not via extracellular factors: role of Mcl-1 and decreased activity of caspase-3 and caspase-8. J Leukoc Biol 2004; 75:893–900.
31. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019; 48:601.
32. Poros B, Becker-Pennrich AS, Sabel B, et al. Anthropometric analysis of body habitus and outcomes in critically ill COVID-19 patients. Obes Med 2021; 25:100358.
33. Feng Z, Zhao H, Kang W, et al. Association of paraspinal muscle measurements on chest computed tomography with clinical outcomes in patients with severe coronavirus disease 2019. J Gerontol A Biol Sci Med Sci 2021; 76:e78–e84.
34. Petersen A, Bressem K, Albrecht J, et al. The role of visceral adiposity in the severity of COVID-19: Highlights from a unicenter cross-sectional pilot study in Germany. Metabolism 2020; 110:154317.
35. Hocaoglu E, Ors S, Yildiz O, Inci E. Correlation of pectoralis muscle volume and density with severity of COVID-19 pneumonia in adults. Acad Radiol 2021; 28:166–172.
36. Ufuk F, Demirci M, Sagtas E, et al. The prognostic value of pneumonia severity score and pectoralis muscle Area on chest CT in adult COVID-19 patients. Eur J Radiol 2020; 131:109271.

BJR https://doi.org/10.1259/bjr.20220869

Received: 12 September 2022 | Accepted: 18 January 2023 | Published online: 22 February 2023

Cite this article as:
Surov A, Thormann M, Kardas H, Hinnerichs M, Omari J, Cingöz E, et al. Visceral to subcutaneous fat ratio predicts short-term mortality in patients with Covid 19. A multicenter study. *Br J Radiol* (2023) 10.1259/bjr.20220869.

FULL PAPER

Visceral to subcutaneous fat ratio predicts short-term mortality in patients with Covid 19. A multicenter study

[1]ALEXEY SUROV, MD, [2]MAXIMILIAN THORMANN, MD, [2]HAKAN KARDAS, MD, [2]MATTES HINNERICHS, MD, [2]JAZAN OMARI, MD, [3]EDA CINGÖZ, MD, [4]MEHMET CINGÖZ, MD, [3]MEMDUH DURSUN, MD, [5]İNAN KORMAZ, MD, [5]ÇAĞRI ORHAN, MD, [6]ÖMER YILDIZ, MD, [6]ELIF HOCAOĞLU, MD, [6]ERCAN INCI, MD, [7]HAKAN ÖNDER, MD, [7]HAMDULLAH ERK, MD, [8]OUGKOUR CHOUSEIN, MD, [8]HADI SASANI, MD, [8]KORCAN AYSUN GÖNEN, MD, [2]MACIEJ PECH, MD and [9]ANDREAS WIENKE, PhD

[1]Department of Radiology,, Neuroradiology and Nuclear Medicine, Johannes Wesling University Hospital, Ruhr University Bochum, Bochum, Germany
[2]Clinic for Radiology and Nuclear Medicine, University Hospital Magdeburg, Magdeburg, Germany
[3]Istanbul Medical Faculty Radiology Department, Istanbul University, Istanbul, Turkey
[4]Department of Radiology, Istanbul Cam and Sakura City Hospital, Istanbul, Turkey
[5]Department of Radiology, Hatay Mustafa Kemal University, Antakya, Hatay, Turkey
[6]Radiology Department, University of Health Sciences, Bakirkoy Dr. Sadi Konuk Research and Training Hospital, Bakirkoy, Istanbul, Turkey
[7]Radiology Department, Health Science University, Prof. Dr. Cemil Tascioğlu City Hospital, Istanbul, Turkey
[8]Department of Radiology, Tekirdag Namik Kemal University, Tekirdag, Turkey
[9]Institute of Medical Epidemiology, Biometry, and Informatics, Martin- Luther- University, Halle-Wittenberg, Germany

Address correspondence to: Maximilian Thormann
E-mail: *maximilian.thormann@med.ovgu.de*

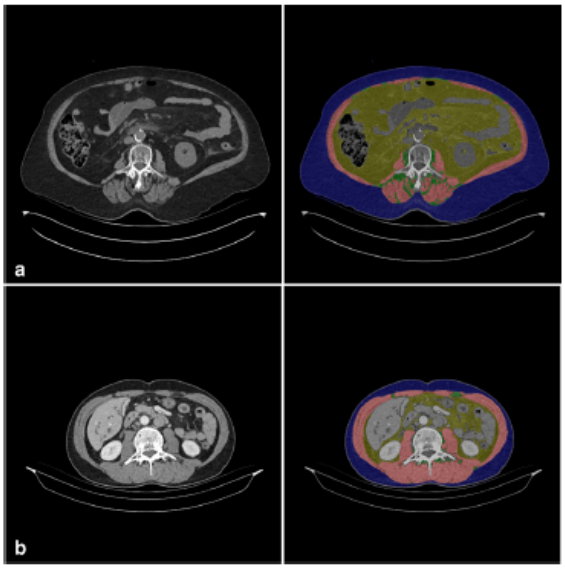
Objective: To evaluate the association of body composition parameters with outcomes in Covid-19.
Methods: 173 patients hospitalized for Covid-19 infection in 6 European centers were included in this retrospective study. Measurements were performed at L3-level and comprised skeletal muscle index (SMI), muscle density (MD), and adipose tissue measurements [visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), intramuscular adipose tissue (IMAT), visceral-to-subcutaneous-adipose-tissue-area-ratio (VSR)]. The association with mortality, the need for intubation (MV), and the need for admission to ICU within 30 days were evaluated.
Results: Higher SAT density was associated with a greater risk of MV (OR = 1.071, 95%CI=(1.034;1.110), $p < 0.001$). Higher VAT density was associated with admission to ICU (OR = 1.068, 95%CI=(1.029;1.109), $p < 0.001$). Higher MD was a protective factor for MV and ICU admission (OR = 0.914, 95%CI=(0.870;0.960), $p < 0.001$; OR = 0.882, 95%CI=(0.832;0.934), $p = 0.028$). Higher VSR was associated with mortality (OR = 2.147, 95%CI=(1.022;4.512), $p = 0.044$). Male sex showed the strongest influence on the risk of ICU admission and MV. SMI was not associated with either parameter.
Conclusion: In patients hospitalized for Covid-19 infection, higher VSR seems to be a strong prognostic factor of short-term mortality. Weak associations with clinical course were found for MD and adipose tissue measurements. Male sex was the strongest prognostic factor of adverse clinical course.
Advances in knowledge: VSR is a prognostic biomarker for 30-day mortality in patients hospitalized for Covid-19 disease.

INTRODUCTION

In coronavirus 2019 disease (Covid-19), body composition parameters are increasingly emerging as risk factors for clinical course and mortality.[1–4] Obesity and increased abdominal adipose tissue have been shown to be associated with severe clinical disease and mortality.[1,5] Likewise, low skeletal muscle mass, in clinical routine used as a surrogate marker for sarcopenia, seems to influence patient outcome.[6,7] However, the data on the role of body composition are still mixed and results are contradictory, with other studies not finding a relevant association.[8–10]

Given the ongoing nature of the pandemic, prognosis of clinical course and mortality in Covid-19 disease remains essential. Age and sex are already established prognostic markers for Covid-19 patients and associated with mortality.[11,12] At the same time, standardized parameters that allow for better stratification are warranted. The use of CT-derived measurements of skeletal muscle and

Figure 1. Representative examples of abdominal CT scans with segmentation of skeletal muscle: intramuscular adipose tissue (green), visceral adipose tissue (yellow), subcutaneous adipose tissue (blue), skeletal muscle (red). (A) Patient 1 (female) had an SMA of 98.1 cm^2, an SMI of 37.4 kg/cm^2, a VAT of 314.2 cm^2, and a VSR of 0.91 (1a). (B) Patient 2 (male) had a SMA of 140.3 cm^2, an SMI of 46.4 kg/cm^2, a VAT of 72.2 cm^2, and a VSR of 0.72 (1b). SMA, skeletal muscle area; SMI, skeletal muscle index; VAT, visceral adipose tissue; VSR, visceral-to-subcutaneous adipose tissue area ratio.



abdominal fat tissue allows quantification of different body composition parameters in routine clinical use. For skeletal muscle mass, measurements of paraspinal, abdominal wall, and psoas muscles are usually performed at the L3 level.[7] For visceral adipose tissue measurements, the optimal level of measurement is not yet standardized.[13] Published studies have used different levels, both below and above the L3 level.

As fat depots are not distributed equally across the body and pose various cardiometabolic risks, different kind of fat tissues are usually evaluated. Fat tissue parameters like total adipose tissue (TAT), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and intramuscular adipose tissue (IMAT) have been associated with clinical course in different diseases.[13–15] Recently, it was shown that excess VAT, as expressed by the visceral-to-subcutaneous adipose tissue area ratio (VSR) was associated with the risk of ICU admission in Covid-19 patients.[16]

There is a paucity of studies assessing the association between a detailed set of standardized abdominal body composition parameters—including both muscle and adipose tissue measurements—and clinical outcomes and mortality in Covid-19 patients. The purpose of this study was therefore to determine the value of different body composition parameters to predict both Covid-19 severity (risk of ICU admission, invasive ventilation) and mortality within 30 days in a large multicenter cohort.

METHODS

For the present study, data from the following six centers in Europe were retrospectively analyzed:

- Clinic for Radiology and Nuclear Medicine, University Hospital Magdeburg, Magdeburg, Germany ($n = 25$).
- Istanbul Medical Faculty Radiology Department, Istanbul University, Istanbul, Turkey ($n = 47$).
- Hatay Mustafa Kemal University, Faculty of Medicine, Department of Radiology, Antakya, Hatay, Turkey ($n = 12$).
- Radiology Department, University of Health Sciences, Bakirkoy Dr Sadi Konuk Research and Training Hospital, Bakirkoy, Istanbul, Turkey ($n = 23$).
- Radiology Department, Health Science University, Prof Dr Cemil Tascioğlu City Hospital, Istanbul, Turkey ($n = 47$).
- Department of Radiology, Tekirdag Namik Kemal University, Tekirdag, Turkey ($n = 19$).

Patients were identified from electronic hospital records from March 2020 to December 2021. The study was approved by the local ethic committees.

Inclusion criteria across all centers were:

- PCR confirmed Covid-19 disease.
- Hospitalization for symptoms or complications associated with Covid-19 disease.
- Available abdominal CT images with or without contrast medium injection.
- Available data regarding the following outcome variables: mechanical ventilation, admission to ICU, mortality within 30 days of admission.

Exclusion criteria were

- Missing clinical data.
- Hospitalization for other causes than Covid-19 disease.
- Missing abdominal CT scan on L3 level

The analyzed convenience sample comprised 173 patients, with 93 males and 80 females. Median age was 61 years (range 17–91).

Measurement of body composition parameters

In all cases, the first opportunistic abdominal CT scan after hospital admission was used. Image analysis was standardized across all six centers. All body composition measurements were performed by two trained residents (with 2 and 3 years of experience, respectively) semi-automatically on axial images at the midsection of the third lumbar vertebra level (L3) in the soft tissue window (window of 45–250 HU) with the freely available ImageJ Software (v. 1.53, National Institute of Health, Bethesda, Maryland, USA) (Figure 1). Review of measurements and necessary corrections were performed by one experienced radiologist (MH, with 4 years of experience in muscle and fat demarcation) blinded to the clinical course of the patients. All measurements were performed on non-contrast images. The following parameters of body composition were estimated: skeletal muscle area (SMA), SAT, VAT, TAT, and IMAT were measured on cross-sectional images automatically by the software. The relative distribution of abdominal body fat was assessed by the VSR, which was calculated by dividing VAT by SAT. The skeletal muscle index (SMI) was calculated by dividing the SMA by the

patient's height squared in cm. Adipose tissue indices were calculated in an analogous manner. Low skeletal muscle mass (LSMM) was defined as SMI <52.4 cm^2/m^2 for males and <38.5 cm^2/m^2 for females.[17] High VAT and high SAT were defined as an area >100 cm^2. High VSR was defined as >1.1. Additionally, radiodensity of the analyzed body compartments was measured. Finally, fat-free mass (FFM) and fat mass (FM) were calculated using the following formulae[18]:

FFM (kg) = 0.30×[muscle L3 cross-sectional area] + 6.06;

FM (kg) = 0.042×[fat L3 cross-sectional area] + 11.2.

Statistical analysis

SPSS v. 25 was used for statistical analysis (IBM SPSS Statistics, NY). Mean and standard deviation as well as median and interquartile range (IQR) were calculated for continuous variables. Influence of body composition parameters on the risk of IMV, ICU admission, and mortality was assessed using logistic regression. Odds ratios are presented together with 95% confidence intervals (95% CI). The resulting *p*-values were interpreted in an exploratory sense.

RESULTS

Of the included patients, 52 were admitted to ICU, 46 required mechanical ventilation, and 33 patients died within the 30 day observation period.

Patients baseline characteristics and measurements of body composition parameters are summarized in Table 1.

30-day mortality

In univariable analysis, several body composition parameters were associated with mortality (Table 2). In multivariable analysis, IMAT, VSR, and VAT density showed a relevant influence on mortality. There was no association between SMI and mortality (Table 2).

Mechanical ventilation

Muscle density, SAT density, and BMI showed a relevant association with the risk of intubation. Male sex was also strongly associated with the risk of intubation. Neither adipose tissue parameter nor skeletal muscle parameter showed a relevant influence on the risk of intubation (Table 3).

ICU admission

In univariable analysis, numerous values of body compositions showed an influence on the risk of ICU admission (Table 4).

In multivariable analysis, muscle density, VAT density, SAT, and BMI were associated with the risk of ICU admission. Sex also showed a relevant influence (OR = 3.423, 95%CI=(1.294; 9.054), $p = 0.013$) (Table 4).

DISCUSSION

Our study indicates that higher VSR, IMAT and VAT density are prognostic factors of higher 30-day mortality when assessed on abdominal CT scans among patients hospitalized for Covid-19 infection. This association is independent of other known prognostic factors, such as age, sex, and BMI. VSR may therefore be used as a marker for adverse outcome.

Decreased muscle density, increased SAT density and BMI showed a weak association with the risk of intubation. Decreased muscle density and increased VAT density were also weakly associated with the risk of ICU admission, as was decreased SAT. However, none of these biomarkers may be used as a prognostic factor of clinical course. The strongest influence for

Table 1. Baseline characteristics of included patients

Variables	Total $N = 173$
Age, (range)	61 (17-91)
Male / female, n	93, 80
BMI	27.4 kg/m^2
SMA	118.2 cm^2
SAT	207.3 cm^2
IMAT	15.6 cm^2
VAT	180.6 cm^2
Muscle density	27.2 HU
SAT density	−100.1 HU
IMAT density	−61.5 HU
VAT density	−90.1 HU
TAT	419.6 cm^2
SMI	40.1 kg/cm^2
SATI	71.7 cm^2/m^2
IMATI	5.4 cm^2/m^2
VATI	59.2 cm^2/m^2
TATI	141.3 cm^2/m^2
VSR	0.81
FFM	41.5 kg
FM	28.8 kg
Low SMI, n	110 (63.6 %)
High VAT, n	136 (78.6 %)
High SAT, n	148 (85.5 %)
High VSR, n	48 (27.7 %)
30-day mortality, n	33 (19.1 %)
30-day IMV, n	46 (26.6 %)
30-day ICU, n	52 (30.1 %)

BMI, body mass index; FFM, fat free mass; FM, fat mass; HU, Hounsfield unit; IMAT, intramuscular adipose tissue; IMATI, intramuscular adipose tissue index; SAT, subcutaneous adipose tissue ; SATI, subcutaneous adipose index; SMA, skeletal muscle area; SMI, skeletal muscle index; TAT, total adipose tissue; TATI, total adipose tissue index; VAT, visceral adipose tissue; VATI, visceral adipose tissue indeX; VSR, visceral-to-adipose-tissue ratio.
Values are median, unless otherwise indicated.

Table 2. Regression analysis for 30-day mortality

	Univariable			Multivariable		
Variables	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Continuous values						
Age (years)	1.034	(1.008; 1.060)	0.010	1.015	(0.979; 1.053)	0.408
Sex (male *vs* female)	2.300	(1.020; 5.186)	0.045	2.891	(0.915; 9.132)	0.070
BMI, (kg/m^2)	1.013	(0.936; 1.096)	0.749	1.030	(0.941; 1.128)	0.521
SMA (cm^2)	0.997	(0.986; 1.008)	0.611			
SMI (kg/cm^2)	0.995	(0.958; 1.032)	0.777			
Muscle density (HU)	0.935	(0.901; 0.971)	<0.001			
VAT (cm^2)	1.001	(0.997; 1.005)	0.642			
SAT (cm^2)	0.996	(0.992; 1.000)	0.035			
TAT (cm^2)	0.999	(0.997; 1.001)	0.321			
IMAT (cm^2)	1.042	(1.011; 1.073)	0.008	1.083	(1.035; 1.133)	<0.001
VSR	1.918	(1.114; 3.305)	0.019	2.147	(1.022; 4.512)	0.044
VATI (cm^2/m^2)	1.004	(0.993; 1.015)	0.534			
SATI (cm^2/m^2)	0.990	(0.980; 1.000)	0.054			
TATI (cm^2/m^2)	0.998	(0.992; 1.003)	0.416			
IMATI (cm^2/m^2)	1.109	(1.023; 1.203)	0.012			
VAT density (HU)	1.038	(1.008; 1.068)	0.011	1.090	(1.046; 1.136)	<0.001
SAT density (HU)	1.049	(1.018; 1.081)	0.002			
IMAT density (HU)	1.069	(1.005; 1.138)	0.034			
SMI/TAT	3.296	(0.06; 173.83)	0.556			
SMA/TAT	1.448	(0.365; 5.743)	0.598			
SMA/VAT	0.864	(0.567; 1.318)	0.498			
FFM (kg)	0.990	(0.955; 1.028)	0.611			
FM (kg)	0.975	(0.927; 1.025)	0.321			
Dichotomized values						
SMI (low *vs* high)	0.647	(0.260; 1.605)	0.347	0.299	(0.089; 1.008)	0.051
VAT (high *vs* low)	1.013	(0.401; 2.560)	0.978			
SAT (high *vs* low)	0.344	(0.136; 0.869)	0.024			
VSR (high *vs* low)	2.196	(1.014; 4.755)	0.046			

BMI, body mass index; FFM, fat free mass; FM, fat mass; HU, Hounsfield unit; IMAT, intramuscular adipose tissue; IMATI, intramuscular adipose tissue index; SAT, subcutaneous adipose tissue; SATI, subcutaneous adipose index; SMA, skeletal muscle area; SMI, skeletal muscle index; TAT, total adipose tissue; TATI, total adipose tissue index; VAT, visceral adipose tissue; VATI, visceral adipose tissue index; VSR, visceral-to-adipose-tissue ratio.

both outcomes was found for sex. To our knowledge, this is to date the largest study performing a comprehensive analysis of both adipose tissue and musculature parameters on different outcomes in patients hospitalized for Covid-19 disease.

Several studies have shown an influence of different body composition parameters on outcomes in Covid-19 disease. In a small cohort with 51 patients, Chandarana et al showed that patients requiring hospitalization for Covid-19 disease had a higher VAT at the L3 level than those who did not require hospitalization.[19] Similarly, higher VAT was associated with the risk of ICU admission in an Italian cohort.[20] Higher VAT was predictive of the cumulative outcome of severe disease or death in a large American cohort.[21] Similarly, visceral fat area was associated with higher risk of ICU admission and 30 day mortality in a UK cohort.[22] The studies did not investigate other parameters such as adipose tissue densities, IMAT, or VSR. Molwitz et al did not find an influence of either adipose tissue parameter and muscle density on clinical outcomes in a German cohort.[23] The study by Viddeleer et al showed an association between increased IMAT and 21-day mortality.[24] A recent meta-analysis found an influence of LSMM and high VAT on in-hospital mortality.[25]

Table 3. Regression analysis for need for intubation

	Univariable			Multivariable		
Variables	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Continuous values						
Age (years)	1.032	(1.010; 1.055)	0.005	0.995	(0.961; 1.031)	0.788
Sex (male *vs* female)	1.679	(0.840; 3.356)	0.142	4.138	(1.610; 10.63)	0.003
BMI, (kg/m^2)	1.081	(1.006; 1.161)	0.033	1.117	(1.011; 1.233)	0.029
SMA (cm^2)	0.996	(0.986; 1.006)	0.384			
SMI (kg/cm^2)	0.991	(0.958; 1.024)	0.584			
Muscle density (HU)	0.925	(0.894; 0.958)	<0.001	0.914	(0.870; 0.960)	<0.001
VAT (cm^2)	1.002	(0.998; 1.005)	0.346			
SAT (cm^2)	0.998	(0.995; 1.001)	0.155			
TAT (cm^2)	1.000	(0.998; 1.002)	0.766			
IMAT (cm^2)	1.038	(1.009; 1.067)	0.009			
VSR	1.760	(1.053; 2.943)	0.019			
VATI (cm^2/m^2)	1.006	(0.996; 1.016)	0.246			
SATI (cm^2/m^2)	0.996	(0.988; 1.004)	0.274			
TATI (cm^2/m^2)	1.000	(0.995; 1.005)	0.992			
IMATI (cm^2/m^2)	1.106	(1.025; 1.193)	0.009			
VAT density (HU)	1.038	(1.011; 1.066)	0.005			
SAT density (HU)	1.059	(1.029; 1.091)	<0.001	1.071	(1.034; 1.110)	<0.001
IMAT density (HU)	1.087	(1.026; 1.151)	0.004			
SMI/TAT	0.753	(0.015; 39.03)	0.888			
SMA/TAT	0.856	(0.218; 3.360)	0.824			
SMA/VAT	0.811	(0.527; 1.247)	0.339			
FFM (kg/m^2)	0.985	(0.954; 1.018)	0.384			
FM (kg)	0.994	(0.952; 1.037)	0.766			
Dichotomized values						
SMI (low *vs* high)	0.754	(0.326; 1.744)	0.510			
VAT (high *vs* low)	1.163	(0.502; 2.695)	0.725			
SAT (high *vs* low)	0.482	(0.199; 1.167)	0.106			
VSR (high *vs* low)	1.802	(0.898; 3.613)	0.097			

BMI, body mass index; FFM, fat free mass; FM, fat mass; HU, Hounsfield unit; IMAT, intramuscular adipose tissue; IMATI, intramuscular adipose tissue index; SAT, subcutaneous adipose tissue; SATI, subcutaneous adipose index; SMA, skeletal muscle area; SMI, skeletal muscle index; TAT, total adipose tissue; TATI, total adipose tissue index; VAT, visceral adipose tissue; VATI, visceral adipose tissue index; VSR, visceral-to-adipose-tissue ratio.

Regarding VSR, the available data are yet sparse. In an American cohort with 124 patients by Bunnell et al, a higher VAT/SAT ratio was associated with the composite outcome of ICU admission or death.[1] Measurements were carried out at the mid-portion of the L4 level. Battisti et al showed that higher VAT/SAT ratio, measured at the L2 level, was a predictor of ICU admission.[16] In a Chinese cohort with 143 patients, high VAT/SAT ratio and low muscle density were independent risk factors for ICU admission or mechanical ventilation, yet no association with mortality was found.[26] Inversing the ratio, Favre et al found that the subcutaneous to visceral fat ratio was lower in patients with severe Covid-19.[2] In contrast, Nobel et al were not able to find a relevant influence of an increased VAT/SAT ratio on clinical outcomes.[10]

In our cohort, VSR showed a relevant influence on 30-day mortality. This supports the hypothesis that fat distribution rather than total abdominal fat tissue may be a more appropriate risk parameter for outcomes in patients with Covid-19 disease. When controlled for other body composition parameters, we did not find a significant association between VSR and either the risk of intubation or ICU admission. The associations between adipose tissue and unfavorable course in Covid-19 disease is manifold.

Table 4. Regression analysis for need for admission to ICU

	Univariable			Multivariable		
Variables	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Continuous values						
Age (years)	1.032	(1.010; 1.054)	0.004	0.975	(0.939; 1.012)	0.183
Sex (male *vs* female)	1.574	(0.811; 3.053)	0.180	3.423	(1.294; 9.054)	0.013
BMI, (kg/m^2)	1.069	(0.997; 1.145)	0.061	1.199	(1.070; 1.344)	0.002
SMA (cm^2)	0.994	(0.985; 1.004)	0.226			
SMI (kg/cm^2)	0.985	(0.954; 1.018)	0.371			
Muscle density (HU)	0.928	(0.897; 0.959)	<0.001	0.882	(0.832; 0.934)	<0.001
VAT (cm^2)	1.001	(0.997; 1.004)	0.761			
SAT (cm^2)	0.997	(0.994; 1.000)	0.049	0.993	(0.987; 0.999)	0.028
TAT (cm^2)	0.999	(0.997; 1.001)	0.311			
IMAT (cm^2)	1.030	(1.003; 1.058)	0.029			
VSR	1.665	(1.007; 2.755)	0.047			
VATI (cm^2/m^2)	1.003	(0.993; 1.012)	0.597			
SATI (cm^2/m^2)	0.994	(0.986; 1.002)	0.113			
TATI (cm^2/m^2)	0.998	(0.994; 1.003)	0.513			
IMATI (cm^2/m^2)	1.085	(1.009; 1.168)	0.028			
VAT density (HU)	1.050	(1.022; 1.078)	<0.001	1.068	(1.029; 1.109)	<0.001
SAT density (HU)	1.068	(1.036; 1.101)	<0.001			
IMAT density (HU)	1.095	(1.036; 1.159)	0.001			
SMI/TAT	4.818	(0.14; 164.76)	0.383			
SMA/TAT	1.523	(0.449; 5.161)	0.500			
SMA/VAT	1.038	(0.960; 1.123)	0.350			
FFM (kg)	0.980	(0.950; 1.012)	0.226			
FM (kg)	0.978	(0.938; 1.021)	0.311			
Dichotomized values						
SMI (low *vs* high)	0.933	(0.407; 2.141)	0.871			
VAT (high *vs* low)	1.020	(0.461; 2.258)	0.961			
SAT (high *vs* low)	0.330	(0.139; 0.785)	0.012			
VSR (high *vs* low)	1.731	(0.882; 3.398)	0.111			

BMI, body mass index; FFM, fat free mass; FM, fat mass; HU, Hounsfield unit; ICU, intensive care unit ; IMAT, intramuscular adipose tissue; IMATI, intramuscular adipose tissue index; SAT, subcutaneous adipose tissue; SATI, subcutaneous adipose index; SMA, skeletal muscle area; SMI, skeletal muscle index; TAT, total adipose tissue; TAT, total adipose tissue; TATI, total adipose tissue index ; VAT, visceral adipose tissue; VATI, visceral adipose tissue index; VSR, visceral-to-adipose-tissue ratio.

The inverse relation between SAT and clinical outcomes has been described in the literature. Studies have shown that visceral and subcutaneous fat have different metabolic and endocrine characteristics.[27] Visceral fat is metabolically active and releases pro-inflammatory cytokines such as IL-6 and is linked with various diseases.[28] Subcutaneous fat excretes anti-inflammatory cytokines such as adiponectin.[29,30] Disproportionate visceral adipose tissue might modify metabolism and cell-mediated immune response, by increasing macrophage accumulation and decreasing adiponectin.[29,31,32]

Interestingly, neither skeletal muscle parameter showed a relevant association with either outcome in our cohort. This is somewhat contradictory to the literature published so far. Schiaffino et al have indicated that LSMM is associated with higher risk of ICU admission and increased mortality.[4] Measurements of paravertebral muscle area were not performed on the L3 level, but on T5 and T12, different to our cohort. Measuring on T12, Kim et al found an association between LSMM and prolonged hospital stay, but not with mortality.[33] Other authors did not find any relationship between muscle parameters and clinical outcomes.[8,23]

Furthermore, most of the literature concentrated either on the musculature or adipose tissue parameters. There are only few studies that analyze both. The novelty of our study is therefore a comprehensive comparative analysis of the influence of different kinds of body composition measurements. For both ICU admission and intubation, higher muscle density and higher SAT seem to be protective in hospitalized Covid-19 patients. Muscle density is considered to be a proxy for muscle lipid content and representative of muscle quality and capacity.[31,34] However, their influence is too weak to be routinely applied as relevant biomarkers in clinical routine. It seems that, when controlled for different parameters, male sex is still the best-established risk factor for adverse clinical course, but not for mortality.

Body composition parameters can be assessed on opportunistic CT scans in clinical routine. Compared to X-ray absorptiometry and body impedance assessment, CT scans are more objective and easy to acquire.[35] CT scans are frequently performed in hospitalized patients and measurements can be performed as a byproduct of radiological diagnostics. The literature on CT-based body composition parameters is large. For the musculature, most studies use the level L3, where the highest correlation of the skeletal muscle with body muscle volume has been described.[36] For MRI measurements, there is a good correlation between L3 cross-sectional adipose tissue and total tissue volume.[37] We therefore chose to perform our measurements on the same level to achieve standardization. Our data suggest that semi-automated CT body composition measurements should be included into clinical routine to identify patients at risk and provide best nutritional and physical therapy to patients with changes in muscle and adipose tissue density.

Our study has several limitations. It was a retrospective cohort analysis and only patients that underwent an abdominal CT scan at the discretion of the treating physician were included. We did not consider the impact of different virus subtypes on clinical course in our analysis. We did not control for comorbidities. However, this is to date the largest multicenter cohort investigating the spectrum of body composition parameters on outcomes in Covid-19 patients with a standardized measurement level at L3.

In conclusion, VSR is a prognostic biomarker for 30-day mortality in patients hospitalized for Covid-19 disease. Sex is more strongly associated with the risk of intubation and ICU admission than adipose tissue variables. Increased muscle density is a protective factor for adverse clinical course. There was no impact of musculature parameters on either outcome.

ACKNOWLEDGEMENTS

This research was supported by the German Federal Ministry of Education and Research (BMBF) as part of the University Medicine Network (Project RACOON, 01KX2021).

AUTHOR CONTRIBUTIONS

AS, MT: study design, data acquisition, data analysis drafting and revision, final approval; HK, MH, JO: data acquisition, data analysis, revision; EC, MC, MD, IK, CO, ÖY, EH, EI, HÖ, HE, OC, HS, KAG: data acquisition and interpretation, revision; MP: data analysis and interpretation; AW: study conception and design, data interpretation, drafting and revision.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

FUNDING

Open Access funding enabled and organized by Projekt DEAL.

REFERENCES

1. Bunnell KM, Thaweethai T, Buckless C, Shinnick DJ, Torriani M, Foulkes AS, et al. Body composition predictors of outcome in patients with COVID-19. *International Journal of Obesity (2005)* 2021; **45**: 2238–43. doi: https://doi.org/10.1038/s41366-021-00907-1
2. Favre G, Legueult K, Pradier C, Raffaelli C, Ichai C, Iannelli A, et al. Visceral fat is associated to the severity of COVID-19. *Metabolism: Clinical and Experiment*2021; **115**: 154440. https://doi.org/10.1016/j.metabol.2020.154440
3. Watanabe M, Caruso D, Tuccinardi D, Risi R, Zerunian M, Polici M, et al. Visceral fat shows the strongest association with the need of intensive care in patients with COVID-19. *Metabolism: Clinical and Experiment* 2020; **111**: 154319. https://doi.org/10.1016/j.metabol.2020.154319
4. Schiaffino S, Albano D, Cozzi A, Messina C, Arioli R, Bnà C, et al. CT-derived chest muscle metrics for outcome prediction in patients with COVID-19. *Radiology* 2021; **300**: E328–E336. https://doi.org/10.1148/radiol.2021204141
5. Huang Y, Lu Y, Huang YM, Wang M, Ling W, Sui Y, et al. Obesity in patients with COVID-19: a systematic review and meta-analysis. *Metabolism: Clinical and Experiment* 2020; **113**: 154378. https://doi.org/10.1016/j.metabol.2020.154378
6. Pinto FCS, Andrade MF, Gatti da Silva GH, Faiad JZ, Barrére APN, Gonçalves R de C, et al. Function over mass: a meta-analysis on the importance of skeletal muscle quality in COVID-19 patients. *Front Nutr* 2022; **9**. https://doi.org/10.3389/fnut.2022.837719
7. Zopfs D, Theurich S, Große Hokamp N, Knuever J, Gerecht L, Borggrefe J, et al. Single-slice CT measurements allow for accurate assessment of sarcopenia and body composition. *Eur Radiol* 2020; **30**: 1701–1708. https://doi.org/10.1007/s00330-019-06526-9
8. Moctezuma-Velázquez P, Miranda-Zazueta G, Ortiz-Brizuela E, González-Lara MF, Tamez-Torres KM, Román-Montes CM, et al. Low thoracic skeletal muscle area is not associated with negative outcomes in patients with COVID-19. *Am J Phys Med Rehabil* 2021; **100**: 413–18. https://doi.org/10.1097/PHM.0000000000001716
9. Surov A, Kardas H, Besutti G, Pellegrini M, Ottone M, Onur MR, et al. Prognostic role of the pectoralis musculature in patients with COVID-19. A multicenter study. *Acad Radiol* 2023; **30**: 77–82. https://doi.org/10.1016/j.acra.2022.05.003

10. Nobel YR, Su SH, Anderson MR, Luk L, Small-Saunders JL, Reyes-Soffer G, et al. Relationship between body composition and death in patients with COVID-19 differs based on the presence of gastrointestinal symptoms. *Dig Dis Sci* 2021; **1** : 1–8. https://doi.org/10.1007/s10620-021-07324-4
11. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: a comparison with young and middle-aged patients. *J Infect* 2020; **80**: e14–18. https://doi.org/10.1016/j.jinf.2020.03.005
12. Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. Risk factors of critical & mortal COVID-19 cases: a systematic literature review and meta-analysis. *Journal of Infection* 2020; **81**: e16–25. https://doi.org/10.1016/j.jinf.2020.04.021
13. Irlbeck T, Janitza S, Poros B, Golebiewski M, Frey L, Paprottka PM, et al. Quantification of adipose tissue and muscle mass based on computed tomography scans: comparison of eight planimetric and diametric techniques including a step-by-step guide. *Eur Surg Res* 2018; **59**: 23–34. https://doi.org/10.1159/000486173
14. Dunne RF, Loh KP, Williams GR, Jatoi A, Mustian KM, Mohile SG. Cachexia and sarcopenia in older adults with cancer: a comprehensive review. *Cancers* 2019; **11**: 1861. https://doi.org/10.3390/cancers11121861
15. Waters DL (2019) Intermuscular Adipose Tissue: A Brief Review of Etiology, Association With Physical Function and Weight Loss in Older Adults. Annals of geriatric medicine and research 23:3–8
16. Battisti S, Pedone C, Napoli N, Russo E, Agnoletti V, Nigra SG, et al. Computed tomography highlights increased visceral adiposity associated with critical illness in COVID-19. *Diabetes Care* 2020; **43**: e129–30. https://doi.org/10.2337/dc20-1333
17. Prado CMM, Baracos VE, McCargar LJ, Reiman T, Mourtzakis M, Tonkin K, et al. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. *Clin Cancer Res* 2009; **15**: 2920–26. https://doi.org/10.1158/1078-0432.CCR-08-2242
18. Mourtzakis M, Prado CMM, 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. *Appl Physiol Nutr Metab* 2008; **33**: 997–1006. https://doi.org/10.1139/H08-075
19. Chandarana H, Dane B, Mikheev A, Taffel MT, Feng Y, Rusinek H. Visceral adipose tissue in patients with COVID-19: risk stratification for severity. *Abdom Radiol (NY)* 2021; **46**: 818–25. https://doi.org/10.1007/s00261-020-02693-2
20. Pediconi F, Rizzo V, Schiaffino S, Cozzi A, Della Pepa G, Galati F, et al. Visceral adipose tissue area predicts intensive care unit admission in COVID-19 patients. *Obes Res Clin Pract* 2021; **15**: 89–92. https://doi.org/10.1016/j.orcp.2020.12.002
21. Goehler A, Hsu T-M, Seiglie JA, Siedner MJ, Lo J, Triant V, et al. Visceral adiposity and severe COVID-19 disease: application of an artificial intelligence algorithm to improve clinical risk prediction. *Open Forum Infect Dis* 2021; **8**(7). https://doi.org/10.1093/ofid/ofab275
22. McGovern J, Dolan R, Richards C, Laird BJ, McMillan DC, Maguire D. Relation between body composition, systemic inflammatory response, and clinical outcomes in patients admitted to an urban teaching hospital with COVID-19. *J Nutr* 2021; **151**: 2236–44. https://doi.org/10.1093/jn/nxab142
23. Molwitz I, Othman A, Brendlin A, Afat S, Barkhausen J, Reinartz SD. Digital teaching with, during and after COVID-19. *Radiologe* 2021; **61**: 64–66. https://doi.org/10.1007/s00117-020-00794-z
24. Viddeleer AR, Raaphorst J, Min M, Beenen LFM, Scheerder MJ, Vlaar APJ, et al. Intramuscular adipose tissue at level th12 is associated with survival in COVID-19. *J Cachexia Sarcopenia Muscle* 2021; **12**: 823–27. https://doi.org/10.1002/jcsm.12696
25. Meyer HJ, Wienke A, Surov A. Computed tomography-defined body composition as prognostic markers for unfavourable outcomes and in-hospital mortality in coronavirus disease 2019. *J Cachexia Sarcopenia Muscle* 2022; **13**: 159–68. https://doi.org/10.1002/jcsm.12868
26. Yang Y, Ding L, Zou X, Shen Y, Hu D, Hu X, et al. Visceral adiposity and high intramuscular fat deposition independently predict critical illness in patients with SARS-cov-2. *Obesity (Silver Spring)* 2020; **28**: 2040–48. https://doi.org/10.1002/oby.22971
27. Ghazarian M, Luck H, Revelo XS, Winer S, Winer DA. Immunopathology of adipose tissue during metabolic syndrome. *Turk Patoloji Derg* 2015; **31 Suppl 1**: 172–80. https://doi.org/10.5146/tjpath.2015.01323
28. Chau Y-Y, Bandiera R, Serrels A, Martínez-Estrada OM, Qing W, Lee M, et al. Visceral and subcutaneous fat have different origins and evidence supports a mesothelial source. *Nat Cell Biol* 2014; **16**: 367–75. https://doi.org/10.1038/ncb2922
29. Chait A, den Hartigh LJ. Adipose tissue distribution, inflammation and its metabolic consequences, including diabetes and cardiovascular disease. *Front Cardiovasc Med* 2020; **7**: 22. https://doi.org/10.3389/fcvm.2020.00022
30. Barchetta I, Cimini FA, Ciccarelli G, Baroni MG, Cavallo MG. Sick fat: the good and the bad of old and new circulating markers of adipose tissue inflammation. *J Endocrinol Invest* 2019; **42**: 1257–72. https://doi.org/10.1007/s40618-019-01052-3
31. Yang Y, Ding L, Zou X, Shen Y, Hu D, Hu X, et al. Visceral adiposity and high intramuscular fat deposition independently predict critical illness in patients with SARS-cov-2. *Obesity (Silver Spring)* 2020; **28**: 2040–48. https://doi.org/10.1002/oby.22971
32. Malavazos AE, Corsi Romanelli MM, Bandera F, Iacobellis G. Targeting the adipose tissue in COVID-19. *Obesity (Silver Spring)* 2020; **28**: 1178–79. https://doi.org/10.1002/oby.22844
33. Kim J-W, Yoon JS, Kim EJ, Hong H-L, Kwon HH, Jung CY, et al. Prognostic implication of baseline sarcopenia for length of hospital stay and survival in patients with coronavirus disease 2019. *J Gerontol A Biol Sci Med Sci* 2021; **76**: e110–16. https://doi.org/10.1093/gerona/glab085
34. Tanaka M, Okada H, Hashimoto Y, Kumagai M, Nishimura H, Oda Y, et al. Relationship between nonalcoholic fatty liver disease and muscle quality as well as quantity evaluated by computed tomography. *Liver Int* 2020; **40**: 120–30. https://doi.org/10.1111/liv.14253
35. Thompson DL, Thompson WR, Prestridge TJ, Bailey JG, Bean MH, Brown SP, et al. Effects of hydration and dehydration on body composition analysis: a comparative study of bioelectric impedance analysis and hydrodensitometry. *J Sports Med Phys Fitness* 1991; **31**: 565–70.
36. Shen W, Punyanitya M, Wang Z, Gallagher D, St-Onge M-P, Albu J, et al. Total body skeletal muscle and adipose tissue volumes: estimation from a single abdominal cross-sectional image. *J Appl Physiol (1985)* 2004; **97**: 2333–38. https://doi.org/10.1152/japplphysiol.00744.2004
37. Schweitzer L, Geisler C, Pourhassan M, Braun W, Glüer CC, Bosy-Westphal A, et al. What is the best reference site for a single MRI slice to assess whole-body skeletal muscle and adipose tissue volumes in healthy adults? *Am J Clin Nutr* 2015; **102**: 58–65. https://doi.org/10.3945/ajcn.115.111203

7. Appendix

7.1. Danksagung

Meine Dankbarkeit gilt dem Klinikdirektor der diagnostischen und interventionellen Radiologie des Universitätsklinikums Magdeburg Herrn Prof. Dr. M. Pech für die Unterstützung und den offenen Dialog über diverse wissenschaftliche Themengebiete inklusive einer kumulativen Promotion.

Besonderer Dank gebührt meinem Doktorvater bzw. Betreuer Herrn Prof. Dr. A. Surov, der zu jeder Zeit hilfsbereit und in unterschiedlichsten Belangen ansprechbar war. Außerdem stellte er nach einer offenen Diskussion das Thema zur Verfügung.

Mein ausdrücklicher Dank gilt ebenfalls meinen Freunden für die moralische, verständnisvolle und auch anderweitig währende Unterstützung. Damit haben sie sicherlich zum Gelingen dieser Arbeit viel beigetragen. Im gleichen Zuge möchte ich Herrn PD Dr. J. Omari danken, welcher mir immer ein Vorbild war und mich zu dieser Arbeit inspirierte.

Ganz besonders möchte ich mich bei meinen Eltern Serpil und Ergül Kardas bedanken. Speziell bin ich für ihre Geduld, Rücksichtnahme und für die unaufhörliche Unterstützung in aller Hinsicht dankbar. Dieser Beistand war mir immer sehr wichtig, vor allem im Verlauf dieser Dissertation.

An letzter, doch eigentlich an erster Stelle möchte ich meiner Ehefrau Olca Oguz-Kardas danken. Vornehmlich bin ich ihr für ihr unermüdliches, geduldiges Zuhören, ihre Hilfe in Wort und Tat, für ihre Rücksichtnahme und uneingeschränkten Aufmunterungen sowie für jede einzelne Umarmung in der schwierigen Endphase dieser Dissertation dankbar.

7.2. Ehrenerklärung

Ich erkläre, dass ich die der Medizinischen Fakultät der Otto-von-Guericke Universität zur Promotion eingereichte Dissertation mit dem Titel

Auswirkung der Körper-Komposition auf klinische Ergebnisse
bei Patienten mit schwerer Covid-19-Erkrankung

in der Klinik für Radiologie und Nuklearmedizin der Medizinischen Fakultät der Otto- von-Guericke-Universität Magdeburg

mit Unterstützung durch Herrn Prof. Dr. med. A. Surov

ohne sonstige Hilfe durchgeführt und bei der Abfassung der Dissertation keine anderen als die dort aufgeführten Hilfsmittel benutzt habe.

Bei der Abfassung der Dissertation sind Rechte Dritter nicht verletzt worden.

Ich habe diese Dissertation bisher an keiner in- oder ausländischen Hochschule zur Promotion eingereicht. Ich übertrage der Medizinischen Fakultät das Recht, weitere Kopien meiner Dissertation herzustellen und zu vertreiben.

Magdeburg, 1.3.2023

Unterschrift

7.3. Erklärung zur strafrechtlichen Verurteilung

Ich erkläre hiermit, nicht wegen einer Straftat verurteilt worden zu sein, die Wissenschaftsbezug hat.

Magdeburg, 01.03.2023

Unterschrift

8. Anhang

Lebenslauf

Hakan Kardas

Geboren: Am 13.06.1993 in Melikgazi/Türkei

Weiterbildung:	**Radiologie:**
(01/2021 – aktuell)	Assistenzarzt am Uniklinikum Magdeburg Rotationen: CT, Röntgen, MRT, 24h Bereitschaftsdienste seit September 2021
(02/2019 – 12/2020)	**Psychiatrie und Psychotherapie:** Assistenzarzt am AMEOS Klinikum Heiligenhafen Rotationen: Akut Psychiatrie, Abhängigkeits-erkrankungen, 24h Bereitschaftsdienste seit Begin
	Klinische Erfahrung:
Hospitation:	
(01/2019 – 02/2019)	Psychiatrie bei Klinikum AMEOS Heiligenhafen
(02/2018 – 11/2018)	Psychiatrie bei LNK Dr. Spernau Bad Salzuflen
(07/2017 – 08/2017)	Gefäßchirurgie bei Klinikum Nürnberg

Studium:

Studium der Humanmedizin:	Medizinische Fakultät Istanbul,
(09/2011 – 06/2017)	Istanbul Universität, Türkei

Praktikum:

08/2014	Neurochirurgie bei Hospital General Regional De Leon, Mexiko
07/2013	Ophtalmologie bei Ekaterinburg Regional Krankenhaus 1, Jaketerinburg, Russland
2/2013	Orthopädie bei Landeskrankenhaus Murtal, Stolzalpe Österreich

Austauschprogramm:

03/2013	Universität Groningen, Holland
07/2012	Internationale Sommerschule mit Schwerpunkt Vaccinologie, Universität Antwerpen, Belgien
04/2012	Universität Nova de Lisboa, Lissabon, Portugal

Mitgliedschaften:

(05/2017 – aktuell)	Mitglied von Leo Clubs-Lions Clubs International