

The effect of computed tomography parameters on sarcopenia and myosteator assessment: a scoping review

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Abstract

Computed tomography (CT) is a valuable assessment method for muscle pathologies such as sarcopenia, cachexia, and myosteator. However, several key underappreciated scan imaging parameters need consideration for both research and clinical use, specifically CT kilovoltage and the use of contrast material. We conducted a scoping review to assess these effects on CT muscle measures. We reviewed articles from PubMed, Scopus, and Web of Science from 1970 to 2020 on the effect of intravenous contrast material and variation in CT kilovoltage on muscle mass and density. We identified 971 articles on contrast and 277 articles on kilovoltage. The number of articles that met inclusion criteria for contrast and kilovoltage was 11 and 7, respectively. Ten studies evaluated the effect of contrast on muscle density of which nine found that contrast significantly increases CT muscle density (arterial phase 6–23% increase, venous phase 19–57% increase, and delayed phase 23–43% increase). Seven out of 10 studies evaluating the effect of contrast on muscle area found significant increases in area due to contrast ($\leq 2.58\%$). Six studies evaluating kilovoltage on muscle density found that lower kilovoltage resulted in a higher muscle density (14–40% increase). One study reported a significant decrease in muscle area when reducing kilovoltage (2.9%). The use of contrast and kilovoltage variations can have dramatic effects on skeletal muscle analysis and should be considered and reported in CT muscle analysis research. These significant factors in CT skeletal muscle analysis can alter clinical and research outcomes and are therefore a barrier to clinical application unless better appreciated.

Keywords Muscle density; Muscle mass; Contrast enhancement; Kilovoltage; Skeletal muscle analysis

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Introduction

Computed tomography (CT) is an increasingly used method for skeletal muscle area and density analysis due to its high resolution and ability to discern muscle from surrounding tissue.¹ Many patients receive CT scans as part of standard clinical care, which can be used opportunistically to assess muscle health and body composition without additional radiation exposure or cost to the patient.² CT skeletal muscle

analysis has many clinical applications, including evaluating and diagnosing various muscle wasting syndromes and conditions and identifying risk and severity of malnutrition.^{3,4} The number of studies utilizing skeletal muscle analysis has increased in the last 5–10 years,⁵ and many demonstrate strong relationships between survival and muscle density and/or area and in numerous populations, highlighting the potential clinical utility of this approach.^{6–10}

However, several foundational confounding variables exist that are often overlooked when analysing muscle using CT. Notably, the use of contrast material and differing beam energies, in kilovoltage, may increase or decrease measured CT muscle density, affecting the reliability of potential diagnostic cut-off values for identifying myopathic changes in clinical research and clinical care. These variables are starkly underreported, exemplified by Amini *et al.* finding that 94% of studies on CT muscle analyses did not report if contrast material was present or not.¹

Computed tomography skeletal muscle analysis uses computer-assisted or manual techniques to distinguish tissue based on X-ray attenuation and can evaluate both the quantity (area in cm²) and the relative density of muscle in Hounsfield units (HU or CT number). X-rays are more attenuated by denser tissues with a higher atomic number, such as bone (HU range +300 to 400), and less attenuated by less dense tissues, like adipose and muscle (HU ranges: −190 to −30 and −29 to +150 HU, respectively).¹¹ Muscle density can be viewed as a surrogate measure of muscle quality, which encompasses adipose infiltration in muscle tissue, or myosteatosis, which leads to decreases in muscle tissue density and strength.¹² Muscle quality is included in sarcopenia definitions^{13,14} and is inversely associated with consequential health outcomes, such as immobility, hospital length of stay, and mortality.^{15,16}

Intravenously administered contrast material (also called contrast agents or contrast media) is utilized clinically to increase the diagnostic power of CT scans. The high atomic number of contrast material increases the visual brightness of perfused tissue to distinguish areas of clinical interest, that is, contrast enhancement.¹⁷ However, contrast material also affects skeletal muscle density, a fact that has been underappreciated in the skeletal muscle research community.¹

The effects of contrast material are dependent on the perfusion of contrast-enhanced blood through tissue. Hence, the amount of contrast enhancement is highly dependent on when the image was taken in relation to contrast injection, the haemodynamics of the patient, and the vascularization of the tissue.¹⁸ Radiologists use three specific time phases of perfusion in diagnostic imaging—the arterial, venous, and delayed phases. However, the exact timing of these phases can differ between CT protocols.

Timing the phase of contrast to initiate the exam can be performed either by tracking the amount of time that has elapsed since contrast injection or by tracking when the bolus of contrast material reaches a location of interest with serial CT images of one axial slice.^{18,19} For the *arterial phase*, the contrast bolus is tracked until it reaches a threshold of 100–150 HU in the thoracic aorta or up to 35 s after injection.^{20,21} For the *venous phase* (also called portal or parenchymal phase), the contrast bolus is tracked by liver enhancement, which is about 60–90 s after injection.²⁰ The *delayed phase* is denoted 3–5 min after injection.²⁰

Another variable that can have a dramatic impact on CT muscle measures is the voltage applied to the X-ray tube. The X-rays in a CT scan originate from the energy applied to the X-ray tube, measured in kilovoltage.¹⁹ Higher kilovoltage allows for greater X-ray penetration through tissues, leading to lower attenuation and thus lower HU, which is often necessary to modulate to account for patient size. This variation alters CT muscle characteristics, but the magnitude this effect of remains ambiguous, especially in conjunction with contrast agents. This is becoming increasingly important as lower kilovoltage scans are explored to reduce patient radiation exposure.²⁰

To establish clinically useful cut points of healthy muscle, the effects of contrast material and beam energy must be understood. Our specific research objective is to review the current literature to determine the effect of contrast, kilovoltage variations, and other potential confounders (e.g. manufacturer, body position, and slice thickness) on CT skeletal muscle area and density measures. Our goal is to encourage future research to better acknowledge potential confounders, so CT skeletal muscle analysis may have a clear path towards clinical implementation to improve patient care and outcomes.

Methods

Research question

There is a lack of understanding regarding the effect contrast and kilovoltage have on measures of muscle density and area. As a result, we aimed to synthesize the existing literature on these topics. Our specific research question was: to what extent do potential confounding CT variables/parameters impact CT muscle measures?

We chose variables of interest from reviewing literature and consulting with an expert clinical CT physicist (T. P. S.), and they include presence of intravenous (IV) contrast and contrast timing, kilovoltage, vertical patient position/gantry position, CT device make/model, and CT slice thickness. CT skeletal muscle measures include muscle attenuation and area. Possible nomenclature for each of these variables and measures is not consistent and therefore was thoroughly explored in our search terms (*Figure 1*). We included virtual monoenergetic images and dual-energy CT (DECT) in search results, which mathematically estimate kilovoltage variations. Virtual non-contrast (VNC) studies via DECT were also present in the literature, but none of the retrieved studies compared VNC with contrast images and so were omitted. We chose not to include reconstruction kernel/filter in our analysis. For the larger regions of interest used to characterize muscle, it is well known that changes to reconstruction kernel/filter do not affect CT number. For small objects, which may be

1) CT terms:

(Hounsfield [text word] OR "CT attenuation"[Text Word] OR "Tomography, X-Ray Computed"[MeSH Terms] OR "Computed Tomography" [Text Word] OR "x-ray tomography" [Text Word])

2) Confounding variable terms:

Contrast:

("iodin*" [Text Word] OR "contrast material" [Text Word] OR "contrast media" [Text Word] OR "contrast media" [MeSH] OR "contrast enhance*" [Text Word] OR "with contrast" [Text Word] OR "parenchymal" [Text Word] OR "parenchymal phase" [Text Word] OR "CTA" [Text Word] OR "arterial phase" [Text Word] OR "delayed phase" [Text Word] OR "delayed series" [Text Word] OR "angiography" [Text Word] OR "Angiography" [MeSH])

KV:

"kV" [Text Word] OR "kilovoltage" [Text Word] OR "keV" [Text Word] OR "kilolectron" [Text Word] OR "voltage" [Text Word] OR "beam energy" [Text Word] OR "tube voltage" [Text Word] OR ("spectr*" [Text Word] AND "CT" [Text Word]) OR ("spectr*" [Text Word] AND "tube" [Text Word]) OR ("spectr*" [Text Word] AND "anode" [Text Word]) OR ("spectr*" [Text Word] AND "generator" [Text Word]) OR ("tube" [Text Word] AND ("potential" [Text Word] OR "energy" [Text Word])) OR ("generator" [Text Word] AND ("potential" [Text Word] OR "energy" [Text Word])) OR ("Anode" [Text Word] AND ("potential" [Text Word] OR "energy" [Text Word]))

3) Muscle terms:

("cachexia" [MeSH Terms] OR "cachex*" [Text Word] OR "sarcopenia" [MeSH Terms] OR "sarcopen*" [Text Word] OR "myosteat*" [Text Word] OR "myopen*" [Text Word] OR ("Muscle, Skeletal" [MeSH Terms] AND "frailty" [MeSH Terms]) OR

("paresis" [MeSH Terms] AND "muscle, skeletal" [MeSH Terms]) OR ("paresis" [Text Word] AND "muscle*" [Text Word]) OR ("paresis" [Text Word] AND "muscular" [Text Word]) OR "muscle weakness" [MeSH Terms] OR "muscle weakness" [Text Word] OR "muscular weakness" [Text Word] OR

"muscular atrophy" [MeSH Terms] OR "muscle atrophy" [Text Word] OR "muscular atrophy" [Text Word] OR "muscle wasting" [Text Word] OR "muscular wasting" [Text Word] OR "muscle function" [Text Word] OR "muscular function" [Text Word]

OR "muscle quantity" [Text Word] OR "muscular quantity" [Text Word] OR "Body Composition" [MeSH Terms] OR "body composition" [Text Word] OR "muscle quality" [Text Word] OR "muscular quality" [Text Word] OR

("Muscle, Skeletal" [MeSH Terms] AND "adiposity" [MeSH Terms]) OR ("muscle" [Text Word] AND "adiposity" [Text Word]) OR ("muscle" [Text Word] AND "frailty" [Text Word]) OR ("fatty infiltration" [Text Word] AND "skeletal muscle" [Text Word]) OR ("fat infiltration" [Text Word] AND "skeletal muscle" [Text Word]) OR ("fatty infiltration" [Text Word] AND "Muscle, Skeletal" [MeSH Terms]) OR ("fat infiltration" [Text Word] AND "Muscle, Skeletal" [MeSH Terms]) OR ("lipid infiltration" [Text Word] AND "muscle, skeletal" [MeSH Terms]) OR ("lipid infiltration" [Text Word] AND "muscle, skeletal" [Text Word]) OR ("adipose infiltration" [Text Word] AND "Muscle, Skeletal" [MeSH Terms]) OR ("adipose infiltration" [Text Word] AND "skeletal muscle" [Text Word]) OR ("fat infiltration" [Text Word] AND "muscle" [Text Word]) OR ("fatty infiltration" [Text Word] AND "muscle" [Text Word]) OR ("lipid infiltration" [Text Word] AND "muscle" [Text Word]) OR ("adipose infiltration" [Text Word] AND "muscle" [Text Word]) OR

((("muscle" [Text Word] OR "muscles" [Text Word] OR "muscles" [MeSH Terms]) AND ("density" [Text Word] OR "densities" [Text Word] OR "radiodense" [Text Word] OR "radiodensity" [Text Word] OR "radiodensities" [Text Word])) OR

((("muscle" [Text Word] OR "muscles" [Text Word] OR "muscular" [Text Word] OR "muscle, skeletal" [MeSH Terms]) AND ("roi" [Text Word] OR "region of interest" [Text Word])) OR

((("muscle" [Text Word] OR "muscles" [Text Word] OR "muscular" [Text Word] OR "muscle, skeletal" [MeSH Terms]) AND ("mass" [Text Word])) NOT ("neoplasms" [MeSH terms] OR "cancer" [Text Word] OR "carcinoma" [Text Word] OR "sarcoma" [Text Word] OR "tumor" [Text Word] OR "tumour" [Text Word]) OR

((("muscle" [Text Word] OR "muscles" [Text Word] OR "muscular" [Text Word] OR "Muscle, Skeletal" [MeSH Terms]) AND ("segmentation" [Text Word])) OR (((("muscle" [Text Word] OR "muscles" [Text Word] OR "muscular" [Text Word] OR "Muscle, Skeletal" [MeSH Terms]) AND ("area" [Text Word])) NOT ("neoplasms" [MeSH terms] OR "cancer" [Text Word] OR "carcinoma" [Text Word] OR "sarcoma" [Text Word] OR "tumor" [Text Word] OR "tumour" [Text Word]))

Figure 1 Example systematic search terms for PubMed. Search terms were translated to site-specific syntax for Scopus and Web of Science. Only one confounding variable term group was included per search (2). '*' indicates that any suffix may be used for word. CT, computed tomography; kV, kilovoltage; MeSH, Medical Subject Headings terms.

'smoothed' until their intensity profiles are lowered, changes in reconstruction kernel/filters will cause changes to CT number.²¹

Identifying relevant studies

We used PubMed, Scopus, and Web of Science to identify literature. Search strategy was developed with the assistance of three University of Wisconsin–Madison Science & Engineering Librarians who serve as subject liaisons to the Department of Nutritional Sciences. We placed search terms in three groups, with each term within the group combined with a Boolean 'OR' and each group combined with a Boolean 'AND'. Groups were CT terms, confounding variable terms (one per search), and muscle terms. The Boolean operator 'NOT' was used to omit combining cancer-related

articles with 'muscle' + 'mass' and 'muscle' + 'area' terms due to a high amount of retrieval noise in this subcategory. Manuscripts were included if they specifically discussed the chosen variables and CT muscle measures. Studies were excluded if they were non-human studies, cell studies, reviews or editorials, case studies, non-English papers, and cadaver studies or occurred prior to 1970. Example search terms for PubMed are shown in *Figure 1*, and the search terms were translated to Scopus and Web of Science with site-specific syntax.

Study selection

Two independent reviewers (J. L. and G. G.) screened articles with the assistance of Covidence (<https://www.covidence.com>), detailed in *Figure 2*. The first round of screening omitted articles

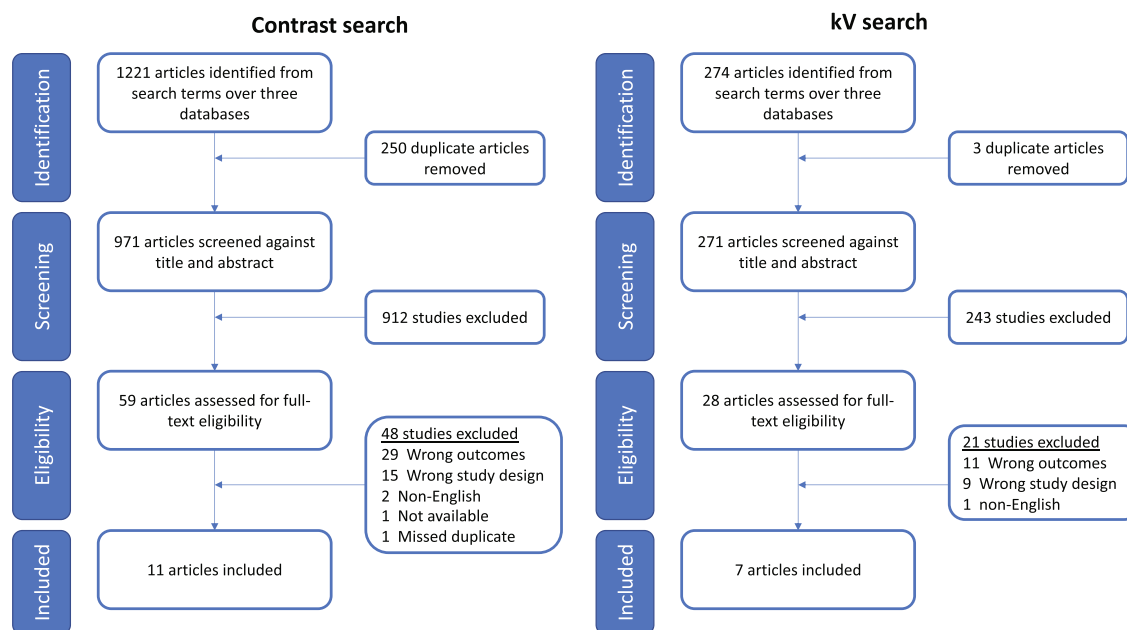


Figure 2 PRISMA flow chart of article identification, screening, and eligibility process.

based on titles and abstracts, and in the second round of screening, articles were reviewed in entirety. In both stages, the two reviewers met at the beginning, midpoint, and final stages during the process to discuss challenges. If there were disagreements at any stage, A. J. K. or T. P. S. determined the final inclusion of articles. Both reviewing authors (J. L. and G. G.) had a consensus on the final article inclusion.

Charting the data

J. L. developed an extraction form based on the most relevant study details and best practice guidelines.²² J. L. completed data extraction for the included studies on contrast, and G. G. completed data extraction for the included studies on kilovoltage.

Collating, summarizing, and reporting the results

We conducted systematic reviews on contrast and kilovoltage variable terms. The results of these are presented in *Tables 1–3*. We discuss articles narratively in the results, with selected studies chosen because they are representative of the collective data, highlight interesting results, or present conflicting data.

We attempted systematic searches of other confounding variables including CT make/model, patient positioning, and slice thickness. However, we determined that it was not feasible at this time to conduct a systematic search on these CT variables because of the lack of existing research and the high

amount of noise in these searches required to retrieve a low number of target articles. Instead, brief narrative reviews were written on these variables based on searches conducted with the same three-bucket methods as the systematic searches.

Results

Our first search yielded 971 articles on contrast and CT muscle measures after removing duplicates. After two screening stages, 11 articles were chosen for final inclusion: 9 regarding HU and area, 1 regarding HU only, and 1 regarding area only (*Figure 2*). The second search on kilovoltage and muscle measures yielded 271 articles after removing duplicates. After screening, seven articles were chosen for final inclusion: six regarding HU and one regarding area (*Figure 2*).

Of those eliminated from full-text screening, the majority either did not report muscle measures in usable outcomes such as HU or area (wrong outcomes) or did not design the study so that the effect of contrast or kilovoltage could be related to muscle measures (wrong study design).

Effect of contrast on computed tomography muscle density

Our search yielded 10 studies evaluating the effect of contrast on muscle HU. Of the 10, 8 studies evaluated muscle HU from an axial image at the third lumbar vertebra (L3)

Table 1 The effect of contrast media on CT muscle density

Author, year	Tissue/image location	Baseline non-contrast mean HU	Arterial phase HU increase (% change)	Venous phase HU increase (% change)	Delayed phase HU increase (% change)	Sig.
Boutin, 2016	L4 psoas and paraspinal ROIs	45.2 psoas 31.3 paraspinal	4.8 (11%) psoas 4.6 (15%) paraspinal	11.1 (25%) psoas 11.8 (28%) paraspinal	12.8 (28%) psoas 13.3 (43%) paraspinal	$P < 0.001$
Zhang, 2021	Psoas muscle at umbilicus	34.3	3.2 (9.2%)	6.4 (18.6%)	8.7 (25.3%)	$P < 0.001$
Rollins, 2017	L3 skeletal muscle	29.4	3.0 (10%)	5.5 (19%)	–	$P < 0.0001$
van Vugt, 2018	L3 skeletal muscle	30.9	7.1 (23%)	7.8 (25%)	–	$P < 0.001$
Paris, 2018	L3 skeletal muscle	37.2	6.3 (17.2%)	–	8.7 (23.4%)	$P < 0.001$
Morsbach, 2019	L3 skeletal muscle	30	5.0 (17%)	6.0 (20%) early venous	–	$P < 0.001$
Fuchs, 2018	L3 skeletal muscle	–	1.4 (5.9%)	–	–	$P < 0.0001$
Perez, 2021	L3 skeletal muscle	32.7	–	18.8 (57%)	–	$P < 0.001$
Feng, 2019	L3 skeletal muscle	37	5.5 (14.8%)	8.0 (21.6%)	–	$P < 0.001$
van der Werf, 2018	L3 skeletal muscle	33.3 (median)	6.7 HU (20.1%)	–	–	n.s.

CT, computed tomography; GE, GE Healthcare, Milwaukee, WI, USA; HU, Hounsfield units; kV, tube kilovoltage; L3, third lumbar vertebra; L4, fourth lumbar vertebra; n.s., not significant; Philips, Philips Healthcare, Best, the Netherlands; ROIs, regions of interest; Siemens, Siemens Healthcare, Forchheim, Germany; Sig., significance. Missing data indicated with a '–'.

Table 1 (continued)

Author, year	kV	N	Population	Contrast	Bolus tracking/timing	Scanner(s)
Boutin, 2016	120	201	Mixed diagnoses	125 mL iohexol	Arterial phase bolus tracked. Venous 40 s after arterial. Delayed 90 s after arterial	Siemens: SOMATOM Definition, Definition AS Plus, and Sensation; GE Lightspeed VCT Siemens Force
Zhang, 2021	120	45	Pancreatic cancer patients	100 mL iopromide	Arterial phase bolus tracked. Venous phase 30 s after arterial. Delayed 120 s after arterial	GE Optima CT660 and Philips Ingenuity 128
Rollins, 2017	–	111	Mixed diagnoses	100 mL iopamidol	Arterial phase bolus tracked. Venous at 65 s after injection	–
van Vugt, 2018	–	50	Cancer or liver transplant evaluation	120–150 mL Visipaque per body weight	Arterial phase bolus tracked. Venous at 70 s after injection	–
Paris, 2018	120	45	Clear cell renal carcinoma patients	–	Arterial phase timing N/A. Delayed set 3 min after injection	–
Morsbach, 2019	80	20	Suspected hepatocellular carcinoma	60 mL iomeron	Arterial phase bolus tracked. Venous 52–54 s after tracking	Siemens SOMATOM Definition Flash
Fuchs, 2018	120	72	Mixed diagnoses	90 mL iopamidol	Arterial phase bolus tracked	Siemens Biograph 64
Perez, 2021	120	1211	Healthy kidney donors	Non-ionic split dose	–	GE (model not listed)
Feng, 2019	120	316	Healthy kidney donors	Omnipace 350, 1.5 mL/kg up to 120 mL	Arterial phase bolus tracked. Venous phase 28 s after tracking	Philips Brilliance 64
van der Werf, 2018	120	21	Healthy kidney donors	140–145 mL (300 mg iodine/mL)	–	Siemens Sensation 64

CT, computed tomography; GE, GE Healthcare, Milwaukee, WI, USA; HU, Hounsfield units; kV, tube kilovoltage; L3, third lumbar vertebra; L4, fourth lumbar vertebra; n.s., not significant; Philips, Philips Healthcare, Best, the Netherlands; ROIs, regions of interest; Siemens, Siemens Healthcare, Forchheim, Germany; Sig., significance. Missing data indicated with a '–'.

Table 2 The effect of contrast media on CT muscle area

Author, year	Tissue/image location	Baseline non-contrast area	Arterial phase area change	Venous phase area change	Delayed phase area increase	Sig.
Zhang, 2021	Psoas area index	6.905 cm ² /m ²	-0.019 cm ² /m ²	0.018 cm ² /m ²	-0.039 cm ² /m ²	P = 0.09
Rollins, 2017	L3 skeletal muscle index	47.1 cm ² /m ²	0.0 cm ² /m ²	0.1 cm ² /m ²	-	n.s.
van Vugt, 2018	L3 skeletal muscle index	42.5 cm ² /m ²	0.3 cm ² /m ²	1.1 cm ² /m ²	-	P < 0.05
Paris, 2018	L3 skeletal muscle index	54.3 cm ² /m ²	0.6 cm ² /m ²	-	0.8 cm ² /m ²	P < 0.05
Morsbach, 2019	L3 skeletal muscle index	50.1 cm ² /m ²	0.3 cm ² /m ²	0.4 cm ² /m ²	-	P < 0.001
Fuchs, 2018	L3 skeletal muscle area	-	2.33 cm ²	-	-	P < 0.0001
Perez, 2021	L3 skeletal muscle area	141.0 mm ²	-	2.8 mm ²	-	P < 0.001
Feng, 2019	L3 skeletal muscle index	46.8 cm ² /m ²	0.4 cm ² /m ²	0.8 cm ² /m ²	-	P < 0.001
van der Werf, 2018	L3 skeletal muscle area	118.0 cm ² (median)	2.3 cm ²	-	-	n.s.
Derstine, 2018	L3 skeletal muscle area	M: 179.6 cm ² F: 117.5 cm ²	M: -8.03 cm ² F: -4.8 cm ²	-	-	P < 0.001

CT, computed tomography; GE, GE Healthcare, Milwaukee, WI, USA; HU, Hounsfield units; L3, third lumbar vertebra; n.s., not significant; Philips, Philips Healthcare, Best, the Netherlands; Siemens, Siemens Healthcare, Forchheim, Germany; Sig., significance.

Missing data indicated with a '-'. F: female; M: male.

Table 2 (continued)

Author, year	kV	N	Population	Contrast	Bolus tracking/timing	Scanner(s)
Zhang, 2021	120	45	Pancreatic cancer patients	100 mL iopromide	Arterial phase bolus tracked. Venous phase 30 s after arterial. Delayed 120 s after arterial	Siemens Force
Rollins, 2017	-	111	Mixed diagnoses	100 mL iopamidol	Arterial bolus tracked. Venous at 65 s after injection	GE Optima CT660 and Philips Ingenuity 128
van Vugt, 2018	-	50	Cancer or liver transplant evaluation	120–150 mL Visipaque per body weight	Arterial bolus tracked. Venous at 70 s after injection	-
Paris, 2018	120	45	Renal carcinoma patients	-	Arterial timing not specified. Delayed set 3 min after injection	-
Morsbach, 2019	80	20	Suspected hepatocellular carcinoma	60 mL iomeron	Arterial bolus tracked. Venous 52–54 s after tracking	Siemens SOMATOM Definition Flash
Fuchs, 2018	120	72	Mixed diagnoses	90 mL iopamidol	-	Siemens Biograph 64
Perez, 2021	120	1211	Healthy kidney donors	Non-ionic split dose Omnipaque 350, 1.5 mL/kg up to 120 mL	Arterial phase bolus tracked. Venous phase 28 s after tracking	GE (model not listed)
Feng, 2019	120	316	Healthy kidney donors	140–145 mL (300 mg iodine/mL)	-	Philips Brilliance 64
van der Werf, 2018	120	21	Healthy kidney donors	-	Arterial phase bolus tracked	Siemens Sensation 64
Derstine, 2018	120	604	Healthy kidney donors	-	-	GE Discovery and GE Lightspeed

CT, computed tomography; GE, GE Healthcare, Milwaukee, WI, USA; HU, Hounsfield units; L3, third lumbar vertebra; n.s., not significant; Philips, Philips Healthcare, Best, the Netherlands; Siemens, Siemens Healthcare, Forchheim, Germany; Sig., significance.

Missing data indicated with a '-'. F: female; M: male.

Table 3 The effect of kV on CT muscle density

Author, year	Tissue/image location	kV 1	kV 2	kV 1 HU	kV 2 HU (% change)	Sig.	N	Population	Scanner(s)
Ippolito, 2021	Averaged ROIs in the chest, abdominal, and paraspinal muscles	120	100	45.5	67.8 (40.0%)	$P < 0.001$	125	Mixed oncological patients	Philips iCT Brilliance (120 kV) and Philips iCT Elite (100 kV)
Morsbach, 2018	L3 skeletal muscle	140	80	41.0	48.0 (17.0%)	$P < 0.01$	17	Mixed diagnoses	Siemens SOMATOM Definition Flash
Bunch, 2021	ROI of the SCM	70	40	57.0 (median)	67.0 (17.5%)	$P < 0.001$	20	Parathyroid lesion patients	GE Revolution Apex
Georgiev, 2019	ROIs in the psoas, iliac, and quadriceps muscles	120	80	58.1	70.2 (20.8%)	$P < 0.001$	200	Mixed diagnoses	GE Lightspeed VCT 64
Hérin, 2015	ROI in lumbar muscle	120	100	55.4	ASIR: 63.0 (13.7%) MBIR: 63.7 (14.9%)	$P = 0.0017$	40	Lymphoma patients	GE Discovery HD 750 and GE Lightspeed VCT
Lennartz, 2019	ROI in paraspinal muscle	120	40	45.4	50.6 (11.5%)	$P < 0.001$	40	Skeletal muscle metastatic disease patients	Philips IQon

ASIR, advanced statistical iterative reconstruction; CT, computed tomography; GE, GE Healthcare, Milwaukee, WI, USA; HU, Hounsfield units; kV, tube kilovoltage; L3, third lumbar vertebra; MBIR, model-based iterative reconstruction; Philips, Philips Healthcare, Best, the Netherlands; ROI, region of interest; SCM, sternocleidomastoid muscle; Siemens, Siemens Healthcare, Forchheim, Germany; Sig., significance.

level, and 7 of these found that contrast significantly increased muscle density (Table 1). Additionally, two studies evaluated the effect of contrast on muscle in specific muscle groups (psoas and paraspinal muscles) and found significant increases in HU with contrast application.^{23,24}

Boutin *et al.* examined regions of interest in the psoas and paraspinal muscles in a fourth lumbar vertebra (L4) slice of 201 patients with mixed diagnoses using 125 mL of iohexol.²³ They compared all three phases with bolus tracking in the arterial phase and the venous and delayed phases 40 and 90 s after the arterial phase, respectively. They found a 4.8 and 4.6 HU increase in the psoas and paraspinal muscles in the arterial phase, respectively (11% and 15%), an 11.1 and 11.8 HU increase in the psoas and paraspinal muscles in the venous phase (25% and 38%), and a 12.8 and 13.3 HU increase in the psoas and paraspinal muscles in the delayed phase (28% and 43%). Notably, a variety of different scanner makes and models were used for this study, which may introduce significant variation.²⁵ However, these results were corroborated more recently by Zhang *et al.* in the psoas muscles.²⁴

Several studies also found increases in HU at various phases in the combined abdominal skeletal muscles in axial L3 scans of patients. In all cases, skeletal muscle was analysed within the standard range of -29 (or -30) to 150 HU. Rollins *et al.* evaluated L3 skeletal muscle in 111 mixed diagnosis hospital patients injected with 100 mL of iopamidol.²⁶ The arterial phase was bolus tracked, and the venous phase was set to 65 s after injection. They found a 3.0 HU increase (10%) over baseline in the arterial phase and a 5.5 HU increase (19%) at the venous phase. Similar effects were found in other clinical populations,²⁷⁻³⁰ with HU increases ranging from 6% to 23% in the arterial phase, from 19% to 57% in the venous phase, and from 23% to 43% in the delayed phase across all studies.

Several L3 muscle studies have also been conducted in healthy subjects thanks to data from kidney donors. Feng *et al.* evaluated 316 subjects injected with a weight-adjusted dose of Omnipaque.³¹ The arterial phase was bolus tracked, and the venous phase was set at 28 s after the bolus tracking threshold was reached. They found that the arterial phase increased by 5.5 HU (14.8%) and the venous phase increased by 8.0 HU (21.6%). A similar study in kidney donors by van der Werf *et al.* found an increase of 6.7 HU (20.1%) in the arterial phase but did not find this to be significant.³² However, this study may have been underpowered with only 21 subjects. Most recently, Perez *et al.* evaluated the effect of contrast on the venous phase of healthy kidney donors and found a staggering 18.8 HU increase (57%) in L3 skeletal muscle.³³ These data were uniquely analysed with automated muscle segmentation software, making it possible to include 1211 subjects.

Effect of contrast on computed tomography muscle quantity

Our review found 10 studies that evaluated the effect of contrast material on CT muscle area, and 7 of those found significantly different area measurements from baseline to one or more contrast phases (Table 2). However, the magnitude of this effect is relatively small and likely represents a clinically irrelevant amount. All seven studies found a significant effect of contrast, but the greatest change in area in all of these was 2.58% (range 0–2.58%).

For example, van Vugt *et al.* evaluated L3 axial skeletal muscle (indexed to height, muscle range from –30 to 150 HU) in 50 cancer or liver transplant patients injected with 120–150 mL Visipaque based on body weight.²⁷ The arterial phase was bolus tracked, and the venous phase was set at 70 s after injection. They found baseline skeletal muscle index to be 42.5 cm²/m². Arterial contrast enhancement increased area by 0.3 cm²/m² (0.7%), and venous contrast enhancement increased area by 1.1 cm²/m² (2.58%). This was corroborated by other studies mentioned in this review (Table 2).^{24,28–30,33}

Interestingly, another study looked at L3 axial skeletal muscle while using several different muscle HU ranges to examine if contrast material affected them differently, because no consensus range exists. Derstine *et al.* conducted this research in 604 healthy kidney donors with the contrast bolus tracked to the arterial phase.³⁴ They found that when using a muscle HU range of 0–100 to assess skeletal muscle area, a significant difference between non-contrast and contrast measurements existed because of a portion of muscle area being enhanced above the 100 HU limit. However, when using a muscle HU range of –29 to 150, there was no significant difference in skeletal muscle area between non-contrast and contrast scans. This is evidence that the effect of confounding variables on CT muscle area can be mitigated when using a muscle range of –29 to 150 HU.

Effect of kilovoltage on computed tomography muscle density

Several studies have assessed the effects of kilovoltage on muscle attenuation. Our review obtained six studies evaluating this, all of which found significant increases in attenuation with reduced kilovoltage dose (Table 3) across various anatomical locations.

In 2018, Morsbach *et al.* found reduced kilovoltage dose to increase L3 axial muscle attenuation by 7 HU (17%).³⁵ The study was conducted on 17 hospital patients with a single scanner, with the low dose set at 80 kV and the high dose at 120 kV. Georgiev *et al.* corroborated these findings in 200 patients, averaging muscle regions of interest in the psoas, iliac, and quadriceps muscles.³⁶ They found that

the average muscle density in the 120 kV group was 58.1 HU and the 80 kV group was 70.2 HU (17% increase). Bunch *et al.* found similar results in the sternocleidomastoid muscle at 70 and 40 kV.³⁷ They examined 20 patients with parathyroid lesions and found that the 70 kV group had an average muscle density of 57 HU and the 40 kV group increased to 67 HU (15%). Similar studies can be found in Table 3.^{38–40}

Out of necessity to narrow search terms due to a large amount of article retrieval noise, a few relevant studies were incidentally omitted from our systematic search. Gill *et al.* evaluated paraspinal muscles in CT pulmonary angiography scans with contrast on 66 patients with suspected pulmonary embolism.⁴¹ Voltage was varied, and 33 patients received 100 kV while the other 33 patients received 120 kV. They found that HU was elevated in the 100 kV protocol from 35.7 to 49.6 (38.9%). Likewise, May *et al.* evaluated patients with a head and neck CT.⁴² An automated analysis of a localizer suggested 100 kV scans for 62 patients and 120 kV scans for 37 patients. In the 100 kV scan, sternocleidomastoid muscle attenuation was higher by 7 HU (10.6%).

Effect of kilovoltage on computed tomography muscle quantity

Our review only found one study that examined the effect of kilovoltage on muscle quantity. Morsbach *et al.* utilized DECT on 17 patients who simultaneously received imaging from 80 and 140 kV single-slice scans at the L3 level.³⁵ This study found lower kilovoltage to reduce skeletal muscle index from 42.2 to 40.1 cm²/m² (2.9%). Furthermore, they found that myosteatotic muscle area, or muscle at the lower end of the muscle HU range (from –29 to 30 HU), was significantly reduced from 35 to 31 cm² (12.9%).

Other potential confounders

Computed tomography make and model

Although the research on skeletal muscle analysis on different CT scanners is limited, some studies have found considerable variation in HU numbers when using different CT scanning devices. Lamba *et al.* overviewed 47 patients in their radiology database that had undergone CT scans of the psoas muscles on both a Volume CT (GE Healthcare, Milwaukee, WI, USA) and a Definition AS Plus (Siemens Healthcare, Forchheim, Germany) within 12 months of each other.⁴³ They found the right psoas on average to be 3.3 HU higher (7.4%) and the left psoas 5.4 HU higher (12.3%) in the Volume CT than the Definition AS Plus. The intraclass correlation coefficient for the right psoas muscle was 0.454 and the left psoas muscle 0.485. Birnbaum

et al. tested five different CT scanners, while minimizing variation in CT protocols, with a rectus abdominis muscle tissue-equivalent phantom, simulating the abdominal axial anatomy.²⁵ They found the mean attenuation of the rectus abdominis muscle to range between all five scanners measured from 63.9 to 91.0 HU. Similar intrascanner variability has also been found in CT studies that use a phantom to simulate human tissue.^{44,45}

Patient positioning

To our knowledge, no studies have evaluated the effect of vertical patient positioning/table height on muscle specifically. However, altering patient positioning will dis-align a CT scanner's bowtie filter to the patient. A bowtie filter is beam filtration device that assumes the patient is centred within the scanner. One study on an anthropomorphic thorax phantom found that table heights 4 or 6 cm above centre significantly lowered HU, in some cases by more than 20 HU.⁴⁶ This study also assessed correct positioning of hospital patients and found that out of 20 316 patients, 1.9% were positioned >4 cm off-centre, and 0.3% were positioned >6 cm off-centre.

Slice thickness

Two-dimensional CT images have a depth representing the thickness of the cross section, and changing this thickness may affect muscle measures. Morsbach *et al.* evaluated 20 patients with suspected hepatocellular carcinoma.²⁹ These patients had upper abdomen perfusion CTs that were analysed at the L3 level. Slices of 2, 3, 4, 5, and 10 mm were created and analysed from the unenhanced phase for each patient. While there were no significant differences in muscle attenuation ($P = 0.07$), myosteatotic muscle area (HU range from -29 to 30) increased by $\leq 3.3\%$ when increasing slice thickness from 2 to 10 mm ($P = 0.02$). In another study, Fuchs *et al.* collected 34 positron emission tomography–CT examinations without IV contrast from a departmental database, and a total of 102 images were ultimately analysed.³⁰ L3 level non-contrast scans were compared with a slice thickness of 2 and 5 mm within the same patient. Skeletal muscle cross-sectional area was found to have increased by 1.11% in 5 mm slices compared with 2 mm, while skeletal muscle density decreased by 11.64% ($P < 0.0001$). The inconsistent results of slice thickness acting on attenuation call for more research to be conducted in this emerging field.

Discussion

Our scoping review on the effects of contrast and kilovoltage on CT muscle measures discovered several peer-reviewed articles with clear trends observed within these studies. All 10 studies examining the effect of contrast on muscle attenuation demonstrated an increase in muscle HU with contrast administration, with all but one of these showing a significant

change. The six studies on kilovoltage and muscle attenuation all showed significant increases in muscle HU with lower kilovoltage. Studies on muscle area and either contrast or kilovoltage variations showed conflicting results. However, the degree of change from either contrast or kilovoltage is relatively minor and likely represents a clinically insignificant amount.

Differences in CT protocols make comparison of contrast phases problematic. In our retrieved articles, the arterial phase was commonly bolus tracked, but did not always have tracking details, or the location and threshold of the bolus tracking varied between studies. The venous phase ranged from 28 to 54 s after the arterial phase or from 65 to 70 s after injection (Table 1). The delayed phase had little consensus between studies, ranging from 90 to 120 s after arterial or 3 min after injection. Several studies were lacking many key details about contrast timing. Despite these challenges, we see a consensus that contrast generally increases CT muscle HU.

To further speculate, there appears to be an increase in contrast enhancement from early phases to later phases, yet when the enhancement plateaus is unknown. Only a few studies conducted statistical tests between phases, with mixed results.^{23,24,26–28} The plateau of contrast enhancement is shown in excellent temporal detail by Morsbach *et al.* who tracked contrast enhancement in L3 muscle at 2 s intervals from early arterial to early venous phases and shows an increase and plateau as attenuation in the aorta decreases from 500 to 150 HU.²⁹ Yet identifying the correct scan timing may pose issues as well, as even for sites following weight-based contrast with bolus tracking, large deviations around 50 HU can occur in the liver simply due to underlying patient diseases and limitations with administering enough contrast volume for large patients.⁴⁷ More work needs to be performed to achieve a consensus of contrast timing and how contrast timing affects the magnitude of deviation in muscle.

Similar to contrast, the articles we retrieved on kilovoltage tested different comparisons of kilovoltage levels, making it difficult to establish a consensus on the effect of each level on HU. The upper limit ranged from 70 to 140 kV, with three at 120 kV. The lower limit ranged from 40 to 100 kV. The difference between the upper and lower limits ranged from 20 to 60 kV. All decreases in kilovoltage led to an increase in muscle HU. Surprisingly, the smallest decreases from 120 to 100 kV showed a large discrepancy in two different studies—a 13.7% increase and a 40% increase in muscle HU.^{39,40}

Unlike density, changes in area due to contrast or kilovoltage variations are likely not clinically significant. The greatest change in area from contrast was 2.58% and from kilovoltage was 2.9%. Notably, alterations in muscle density and area measures are not independent. As factors modulate attenuation, changes in muscle quantity are commonly observed because of the ranges used to designate muscle

Table 4 Reporting recommendations for CT muscle studies

Parameter	Example	Implications on muscle density/quantity
CT acquisition parameters		
Make/model	GE Discovery HD 750	Systematic biases exist between scanner makes and models
Beam energy (kV)	120 kV	Large effect on density; increasing effect for higher atomic number materials
Slice thickness	3.75 mm	Density and quantity accuracy may be affected for small volumes or structures
Slice interval	2 mm	
Reconstruction kernel/algorithm	Bone, detail, lung, etc.	
CTDIvol	8 mGy	Not related to density or quantity but determines quality of data (noise)
CT contrast details (IV only)		
Concentration	350 mg/mL	Density increases linearly with iodine concentration
Dose (specify prescription if weight adjusted)	80 mL or 1.7 mL/kg	If not weight adjusted, iodine enhancement decreases with patient weight
Phase/scan time after contrast	Early arterial, arterial, venous phase, etc. if fixed delay, state time in seconds after injection (e.g. 60–80 s after injection)	Iodine enhancement of density measurements is phase dependent
Timing method (bolus tracking or timed)	Bolus tracked, fixed delay	Fixed delays do not account for patient-specific haemodynamics and will have more iodine enhancement variability
Enhancement threshold (bolus tracking only)		Injection delivery parameters will influence iodine enhancement in non-trivial ways
Enhancement threshold ROI location (bolus tracking only)	100 HU	
Injection location	Liver, thoracic aorta, etc.	
Injection rate/duration	Antecubital vein	
Saline flush	3 mL/s 50 mL	

CT, computed tomography; CTDIvol, computed tomography dose index volume; HU, Hounsfield units; IV, intravenous; ROI, region of interest.

specific HU (−29 to 150 HU).¹ Therefore, increasing the attenuation with added contrast or reduced kilovoltage raises the HU for additional tissue to be included in muscle that was previously below the threshold or for existing tissue to now be above the threshold when it was previously included.

The interaction of contrast and kilovoltage may lead to unpredictable variations in muscle measures. Contrast material and tube voltage increases have opposing effects on HU, making it difficult to account for a combination of the two. This may be relevant as protocols attempt to reduce radiation dose with the use of contrast or reduce contrast dose by modulating kilovoltage.⁴⁸ In a 2018 study, van der Werf *et al.* analysed muscle area and attenuation measurements in 41 paired contrast and non-contrast scans.³² Scans were conducted at 100 or 120 kV prior to contrast injection and 120 kV after injection. When scan kilovoltage was 100 kV before and 120 kV after, they found no difference in mean muscle attenuation of contrast and non-contrast scans, presumably due to the opposite effects on HU, that is, the increase in tube voltage counteracts the increase in attenuation of the contrast. Conversely, when scan kilovoltage matched, non-contrast and contrast scans had a mean difference of 6.7 (±3.2) HU. Skeletal muscle area was also affected by kilovoltage, but in an opposite direction. Contrast scans with different tube voltage had increased area than non-contrast scans by 7.0 (±7.5) HU, and scans with the same tube voltage were higher than non-contrast scans by only 2.3 (±1.7) HU.

Variations in area and density due to CT protocols are important to consider when diagnosing muscle wasting conditions, such as sarcopenia. Sarcopenia is diagnosed by establishing cut-off values of healthy muscle at 2 SDs below the mean reference value.^{13,14,49} It is likely that altering muscle area or HU would shift individuals to either side of the cut-off point, especially those that are near the delineation. Based on the studies in our review, HU is more sensitive than area to contrast or kilovoltage variations and, therefore, has the potential to be more prone to incorrect classifications. Taking variations in kilovoltage or use of contrast into account when establishing cut-off points or comparing individuals against established cut-off points is critical.

Several studies have created regression equations based on the association of data between non-contrast and contrast scans.^{23,26,33} This is helpful in working towards a correction factor that may allow integration of data between the two types of scans, which may facilitate development of healthy muscle cut points and allow skeletal muscle analyses to be conducted regardless of scan type. Future research should work towards establishing correction models or a protocol for institutions to create their own correction models based on their specific equipment.

It is possible that other sources of variability exist beyond those mentioned in this review that currently have a lack of data or new sources that may arise because of

changes in CT technology. Within contrast alone, there are many potentially confounding variables, for example, contrast dose and patient weight contribute to a different concentration of contrast in the body. Additionally, the timing method of the scan, contrast injection flow rate, contrast injection access location, and cardiac output/vascular status can cause contrast discrepancies between patients.¹⁸ New software such as image reconstruction algorithms, or new CT scanners or hardware may introduce future sources of variation. Similarly, inter-rater and intra-rater variability may be present when analysing muscle, although minimal. Inter-rater and intra-rater correlation coefficients from CT muscle measurements range from 0.97 to 0.99 and from 0.95 to 0.99, respectively ($P < 0.0001$),⁵⁰ and a Bland–Altman analysis between the two most popular CT muscle measurement programs (Slice-O-Matic and OsiriX) shows excellent agreement (≥ 0.954 , $P < 0.001$).⁵¹ It may be impossible to account for all sources of variation in CT muscle analysis, but our goal in this review was (and the goal of future research should be) to identify the most egregious sources and account for them.

Our study was limited by a high amount of noise in our search results. This restricted us from utilizing general muscle terms in our systematic search, as the specific terms we used were not always present in the study if muscle was not a main focus, and other terms are used such as ‘soft tissue’, or the specific muscle group is named, that is, *Erector spinae*. Additionally, our narrative reviews on CT make/model, patient position, and slice thickness may be able to be conducted systematically in the future when more research has been performed in these areas.

Conclusions

Computed tomography skeletal muscle analysis is a promising technique for the fields of sarcopenia, cachexia, frailty, nutrition, and beyond. CT provides a wealth of information that may save resources, improve health outcomes, and save lives. However, to use CT data effectively, evidenced-based clinical cut points and ranges must be developed to delineate healthy tissue accurately and precisely. Furthermore, the development and usage of these cut points or ranges is inappropriate when variables that may obscure them are not fully appreciated. Overall, we found enough of a consensus on the effects of contrast and kilovoltage on CT skeletal muscle analysis to demonstrate a clear challenge for the burgeoning field of CT skeletal muscle research.

We hope that establishing confounding variables for CT skeletal muscle analysis will lead to their consideration in future research. As Amini *et al.* established, few studies report

methods on all pertinent CT variables.¹ It is important that all CT skeletal muscle studies carefully detail their methods including the use of contrast and specific contrast parameters, kilovoltage, scanner make and model, slice thickness, errors in patient positioning, and any other pertinent scan protocol details that may arise in the future. Additionally, the effect of contrast variation at different phases and different kilovoltage levels on muscle measures should be studied further to attempt to develop a correction factor that allows the comparison of data with discrepancies.

Therefore, we suggest that researchers should consider the following fundamental recommendations in future studies:

- Recognize that contrast and kilovoltage can have a significant impact on CT muscle measures and pertinent CT parameters should always be reported in study methods (Table 4).
- Avoid using data with contrast and kilovoltage variations interchangeably without accounting for them.

These recommendations aim to harmonize results across studies to align data for the development of accurate muscle reference values. This is the first step towards having congruence in measures and the ability to incorporate those data into an accurate model of muscle health.

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Conflict of interest

S.B.H. is on the Medical Advisory Board of the Taniya Corporation. T.P.S. receives research support and is on an advisory board to GE Healthcare and is a consultant to AstroCT LLC, ALARA Medical, AiDoc, and FlowHow.ai. J.L., G.G., B.R., and A.J.K. declare no conflicts of interest.

References

- Amini B, Boyle SP, Boutin RD, Lenchik L. Approaches to assessment of muscle mass and myosteatosis on computed tomography: a systematic review. *J Gerontol A Biol Sci Med Sci* 2019;**74**:1671–1678. Available from: <https://academic.oup.com/biomedgerontology/article/74/10/1671/5308117>
- Bruce RJ, Binkley N. Opportunistic screening for osteoporosis using abdominal computed tomography scans obtained for other indications. *Ann Intern Med* 2013;**158**:588–595.
- Heymsfield SB, Gonzalez MC, Lu J, Jia G, Zheng J. Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. *Proc Nutr Soc* 2015;**74**:355–366.
- Heymsfield SB, Olafson RP, Kutner MH, Nixon DW. A radiographic method of quantifying protein-calorie undernutrition. *Am J Clin Nutr* 1979;**32**:693–702.
- Goodpaster BH, Thaete FL, Kelley DE. Thigh adipose tissue distribution is associated with insulin resistance in obesity and in type 2 diabetes mellitus. *Am J Clin Nutr* 2000;**71**:885–892.
- Looijaard WGP, Dekker IM, Stapel SN, Girbes ARJ, Twisk JWR, Oudemans-van Straaten HM, et al. Skeletal muscle quality as assessed by CT-derived skeletal muscle density is associated with 6-month mortality in mechanically ventilated critically ill patients. *Crit Care* 2016;**20**:386.
- Cho YH, Do KH, Chae EJ, Choi SH, Jo KW, Lee SO, et al. Association of chest CT-based quantitative measures of muscle and fat with post-lung transplant survival and morbidity: a single institutional retrospective cohort study in Korean population. *Korean J Radiol* 2019;**20**:522–530. Available from: <https://pubmed.ncbi.nlm.nih.gov/30799584/>
- van Vugt JLA, Levolver S, de Bruin RWF, van Rosmalen J, Metselaar HJ, IJzermans JNM. Systematic review and meta-analysis of the impact of computed tomography-assessed skeletal muscle mass on outcome in patients awaiting or undergoing liver transplantation. *Am J Transplant* 2016;**16**:2277–2292.
- von Haehling S, Garfias Macedo T, Valentova M, Anker MS, Ebner N, Bekfani T, et al. Muscle wasting as an independent predictor of survival in patients with chronic heart failure. *J Cachexia Sarcopenia Muscle* 2020;**11**:1242–1249.
- Cogswell R, Trachtenberg B, Murray T, Schultz J, Teigen L, Allen T, et al. A novel model incorporating pectoralis muscle measures to predict mortality after ventricular assist device implantation. *J Heart Lung Transplant* 2019;**38**:308–315.
- Seeram E. Computed tomography: a technical review. *Radiol Technol* 2018;**89**:279CT–302CT.
- Goodpaster BH, Kelley DE, Thaete FL, He J, Ross R. Skeletal muscle attenuation determined by computed tomography is associated with skeletal muscle lipid content. *J Appl Physiol* 2000;**89**:104–110.
- Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;**48**:601.
- Bhasin S, Travison TG, Manini TM, Patel S, Pencina KM, Fielding RA, et al. Sarcopenia definition: the position statements of the Sarcopenia Definition and Outcomes Consortium. *J Am Geriatr Soc* 2020;**68**:1410–1418.
- Correa-de-Araujo R, Addison O, Miljkovic I, Goodpaster BH, Bergman BC, Clark R, et al. Myosteatosis in the context of skeletal muscle function deficit: an interdisciplinary workshop at the National Institute on Aging. *Front Physiol* 2020;**11**:963.
- Fuggle N, Shaw S, Dennison E, Cooper C. Sarcopenia. *Best Pract Res Clin Rheumatol* 2017;**31**:218–242. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29224698>
- Koç MM, Aslan N, Kao AP, Barber AH. Evaluation of X-ray tomography contrast agents: a review of production, protocols, and biological applications. *Microsc Res Tech* 2019;**82**:812–848.
- Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. *Radiology* 2010;**256**:32–61.
- Szczykutowicz TP. *The CT Handbook*. Medical Physics Publishing; 2020.
- Kulkarni NM, Fung A, Kambadakone AR, Yeh BM. Computed tomography techniques, protocols, advancements, and future directions in liver diseases. *Magn Reson Imaging Clin N Am* 2021;**29**:305–320.
- Dougherty G, Newman D. Measurement of thickness and density of thin structures by computed tomography: a simulation study. *Med Phys* 1999;**26**:1341–1348.
- Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;**8**:19–32.
- Boutin RD, Kaptuch JM, Bateni CP, Chalfant JS, Yao L. Influence of IV contrast administration on CT measures of muscle and bone attenuation: implications for sarcopenia and osteoporosis evaluation. *Am J Roentgenol* 2016;**207**:1046–1054.
- Zhang Y, Liu J, Li F, Cao F, Li A. Contrast-enhanced computed tomography does not provide more information about sarcopenia than unenhanced computed tomography in patients with pancreatic cancer. *Contrast Media Mol Imaging* 2021;**2021**:5546030.
- Birnbaum BA, Hindman N, Lee J, Babb JS. Multi-detector row CT attenuation measurements: assessment of intra- and interscanner variability with an anthropomorphic body CT phantom. *Radiology* 2007;**242**:109–119.
- Rollins KE, Javanmard-Emamghissi H, Awwad A, Macdonald IA, Fearon KCH, Lobo DN. Body composition measurement using computed tomography: does the phase of the scan matter? *Nutrition* 2017;**41**:37–44.
- van Vugt JLA, Coebergh van den Braak RRJ, Schippers HJW, Veen KM, Levolver S, de Bruin RWF, et al. Contrast-enhancement influences skeletal muscle density, but not skeletal muscle mass, measurements on computed tomography. *Clin Nutr* 2018;**37**:1707–1714.
- Paris MT, Furberg HF, Petruzella S, Akin O, Hötker AM, Mourtzakis M. Influence of contrast administration on computed tomography-based analysis of visceral adipose and skeletal muscle tissue in clear cell renal cell carcinoma. *J Parenter Enteral Nutr* 2018;**42**:1148–1155. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29350403>
- Morsbach F, Zhang YH, Martin L, Lindqvist C, Brismar T. Body composition evaluation with computed tomography: contrast media and slice thickness cause methodological errors. *Nutrition* 2019;**59**:50–55.
- Fuchs G, Chretien YR, Mario J, Do S, Eikermann M, Liu B, et al. Quantifying the effect of slice thickness, intravenous contrast and tube current on muscle segmentation: implications for body composition analysis. *Eur Radiol* 2018;**28**:2455–2463.
- Feng Z, Rong P, Luo M, Sun X, Wang W. Influence of methods used to establish sarcopenia cutoff values for skeletal muscle measures using unenhanced and contrast-enhanced computed tomography images. *J Parenter Enteral Nutr* 2019;**43**:1028–1036.
- van der Werf A, Dekker IM, Meijerink MR, Wierdsma NJ, de van der Schueren MAE, Langius JAE. Skeletal muscle analyses: agreement between non-contrast and contrast CT scan measurements of skeletal muscle area and mean muscle attenuation. *Clin Physiol Funct Imaging* 2018;**38**:366–372.
- Perez AA, Pickhardt PJ, Elton DC, Sandfort V, Summers RM. Fully automated CT imaging biomarkers of bone, muscle, and fat: correcting for the effect of intravenous contrast. *Abdom Radiol* 2021;**46**:1229–1235.
- Derstine BA, Holcombe SA, Goulson RL, Ross BE, Wang NC, Sullivan JA, et al. Quantifying sarcopenia reference values using lumbar and thoracic muscle areas in a healthy population. *J Nutr Health Aging* 2018;**22**:180–185.
- Morsbach F, Zhang YH, Nowik P, Martin L, Lindqvist C, Svensson A, et al. Influence of tube potential on CT body composition analysis. *Nutrition* 2018;**53**:9–13.
- Georgiev E, Radeva R, Naseva E, Kirova-Nedyalkova G. Comparison of radiation dose and image quality in CTA of the peripheral arteries. *Radiat Prot Dosimetry* 2019;**186**:437–442.
- Bunch PM, Pavlina AA, Lipford ME, Sachs JR. Dual-energy parathyroid 4D-CT: im-

- proved discrimination of parathyroid lesions from thyroid tissue using noncontrast 40-keV virtual monoenergetic images. *Am J Neuroradiol* 2021;**42**:2001–2008.
38. Lennartz S, Große Hokamp N, Abdullayev N, le Blanc M, Iuga A-I, Bratke G, et al. Diagnostic value of spectral reconstructions in detecting incidental skeletal muscle metastases in CT staging examinations. *Cancer Imaging: Off Publ Int Cancer Imaging Soc* 2019;**19**:50.
 39. Ippolito D, Maino C, Pecorelli A, Salemi I, Gandola D, Riva L, et al. Application of low-dose CT combined with model-based iterative reconstruction algorithm in oncologic patients during follow-up: dose reduction and image quality. *Br J Radiol* 2021;**94**:20201223.
 40. Hérin E, Gardavaud F, Chiaradia M, Beaussart P, Richard P, Cavet M, et al. Use of Model-Based Iterative Reconstruction (MBIR) in reduced-dose CT for routine follow-up of patients with malignant lymphoma: dose savings, image quality and phantom study. *Eur Radiol* 2015;**25**:2362–2370.
 41. Gill MK, Vijayanathan A, Kumar G, Jayarani K, Ng K-H, Sun Z. Use of 100 kV versus 120 kV in computed tomography pulmonary angiography in the detection of pulmonary embolism: effect on radiation dose and image quality. *Quant Imaging Med Surg* 2015;**5**:524–533. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26435916> <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4559980>
 42. May MS, Kramer MR, Eller A, Wuest W, Scharf M, Brand M, et al. Automated tube voltage adaptation in head and neck computed tomography between 120 and 100 kV: effects on image quality and radiation dose. *Neuroradiology* 2014;**56**:797–803.
 43. Lamba R, McGahan JP, Corwin MT, Li CS, Tran T, Seibert JA, et al. CT Hounsfield numbers of soft tissues on unenhanced abdominal CT scans: variability between two different manufacturers' MDCT scanners. *Am J Roentgenol* 2014;**203**:1013–1020. Available from: <https://www.ajronline.org>
 44. Kim DW, Ha J, Ko Y, Kim KW, Park T, Lee J, et al. Reliability of skeletal muscle area measurement on CT with different parameters: a phantom study. *Korean J Radiol* 2021;**22**:624–633.
 45. Mackin D, Fave X, Zhang L, Fried D, Yang J, Taylor B, et al. Measuring CT scanner variability of radiomics features. *Invest Radiol* 2015;**50**:757.
 46. Szczutkiewicz TP, DuPlissis A, Pickhardt PJ. Variation in CT number and image noise uniformity according to patient positioning in MDCT. *Am J Roentgenol* 2017;**208**:1064–1072. Available from: <https://www.ajronline.org>
 47. Szczutkiewicz TP, Viggiano B, Rose S, Pickhardt PJ, Lubner MG. A metric for quantification of iodine contrast enhancement (Q-ICE) in computed tomography. *J Comput Assist Tomogr* 2021;**45**:870–876. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/34469906>
 48. Aschoff AJ, Catalano C, Kirchin MA, Krix M, Albrecht T. Low radiation dose in computed tomography: the role of iodine. *Br J Radiol* 2017;**90**:20170079.
 49. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol* 2011;**12**:489–495.
 50. Kuchnia AJ, Lortie J, Osterbauer K, Hess T, Stabo N, Tsuchiya N, et al. Computed tomography measured tissue density of pectoral muscle and liver predicts outcomes in heart transplant recipients. *JCSM Rapid Commun* 2022;**5**:171–181.
 51. Barbalho ER, da Rocha IMG, de Medeiros GOC, Friedman R, Fayh APT. Agreement between software programmes of body composition analyses on abdominal computed tomography scans of obese adults. *Arch Endocrinol Metab* 2020;**64**:24–29.
 52. von Haehling S, Morley JE, Coats AJS, Anker SD. Ethical guidelines for publishing in the Journal of Cachexia, Sarcopenia and Muscle: update 2021. *J Cachexia Sarcopenia Muscle* 2021;**12**:2259–2261.