

The predictive value of CT-assessed sarcopenia for complicated appendicitis in geriatric patients

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Abstract

Purpose

Acute appendicitis is one of the most common surgical pathologies. Geriatric appendicitis patients have more complicated appendicitis, which leads to higher morbidity and mortality rates. Sarcopenia is an emerging concern among geriatric patients and has been shown to have a negative impact on patients undergoing emergency surgery.

Our primary aim in this study is to reveal the predictive value of computerised tomography (CT)-assessed sarcopenia for complicated appendicitis in geriatric patients.

Methods

154 acute appendicitis patients of geriatric age with preoperative contrast-enhanced abdominal CT were analysed. Patients' age, gender, appendicitis status and BMI values were analysed. CT-assessed sarcopenia value, SMI (Skeletal Muscle Index) and related measurements were evaluated by two senior radiologists. Statistical analysis was conducted by descriptive and inferential statistical methods, as applicable.

Results

52% of the patients had complicated (n=80) and 48% had uncomplicated appendicitis (n:74). There was no difference in gender distribution between uncomplicated and complicated cases.

There was a statistically significant difference between uncomplicated and complicated cases in terms of BMI, SMI and muscle area values ($p<0.05$). Moreover, there was a statistically significant difference for subcutaneous fatty tissue area between uncomplicated and complicated cases ($p<0.10$). The cut-off point by ROC analysis was conducted for CT-assessed sarcopenia index and showed 71% sensitivity and 52% specificity ($p=0.042$).

Conclusion

Geriatric patients who have lower BMI, decreased muscle area and CT-detected sarcopenia have an increased risk of complicated appendicitis. Surgeons should be aware of factors leading to complicated appendicitis, which may cause higher morbidity and mortality rates in elderly patients.

Purpose

Acute appendicitis is one of the most common surgical pathologies. The average lifetime risk of having acute appendicitis is 7–8%. Acute appendicitis occurs in 15% of patients above the age of 50 who have acute abdominal pain and 5% of those above the age of 65; hence, it is not an uncommon pathology in the elderly population.

Geriatric patients with acute appendicitis have more risks than younger patients. Firstly, possible comorbidities and frailty can result in diagnostic delays. Secondly, geriatric patients tend to have more complicated appendicitis, as the number presenting with perforation or abscess ranges from 18% to 70%. Hence, they have higher morbidity and mortality rates than younger patient groups (8% for the elderly vs. 0–1% for younger patients) [1–3].

Sarcopenia is the decline in lean skeletal muscle mass and is mostly encountered in advanced age. It has an overall incidence of 10% of men and women worldwide. Moreover, its incidence rises by 15% per decade over the age of 70 [4]. The decreased strength and function of the muscle in sarcopenia is progressive and generalised, so it leads to impaired physical capacity and negatively affects quality of life as well as post-operative mortality. There are several methods to measure sarcopenia, including radiological investigations such as computerised tomography (CT) and magnetic

resonance imaging (MRI), which are amongst the techniques used to evaluate muscle quantity and quality. The psoas muscle is an indicator of the skeletal muscle mass index analysed on CT-assessed sarcopenia [5].

Sarcopenia has shown a negative impact on both elective cancer surgeries and emergency surgeries as regards morbidity and mortality [6]. Recently, therefore, sarcopenia has been used as a prognostic tool to identify those patients who may suffer adverse events after elective or emergency surgery.

The mean age of the general population is increasing, and the rate of emergency surgery for geriatric patients is also higher than previously. Several grading systems have been proposed to reveal possible patient-specific risk factors, but more research is needed as regards high-risk patients undergoing surgery [7].

In this study, our primary aim was to reveal the predictive value of CT-assessed sarcopenia for complicated appendicitis in geriatric patients. We also analysed the predictive value of body mass index (BMI) and the other CT-assessed parameters of muscle area, mesenteric fatty tissue area and single slice total area to diagnose complicated appendicitis.

Methods

Patient data collection

After approval was gained from the local ethical committee (Kutahya Health Sciences University Local Ethical Committee Approval Number: 2021/07-06), 154 acute appendicitis patients of geriatric age (65 or older) who were operated on in our general surgery clinic between January 2018 and October 2020 and had a contrast-enhanced abdominal CT scan prior to surgery were included in this retrospective research. Of 159 patients, five without CT scans were excluded from the study.

Patient demographic and anthropometric data (age, gender, weight and height) were obtained from patient files. BMI was calculated from the patients' weight in kilograms and height in metres squared (kg/m^2). Since the study is retrospective, written informed consent was waived.

CT scan

All CT scans were performed before the surgical operation and were part of the diagnostic routine. The scans were conducted with a 16-slice multidetector CT scanner (Aquilion, Toshiba Medical Systems, Otawara, Japan). Images were contrast-enhanced and acquired at the portal venous phase with a 65-second delay after intravenous contrast material administration in the supine position. When subjects hold their breath, images can be obtained from the heart level to the symphysis pubis. Scanning parameters are 120 kVp, the *mAs* value with automatic tube current modulation, FOV of 370 and section thickness 5mm. Voxel sizes are 0.75x0.75.5 mm.

CT measurements

To evaluate complicated and non-complicated appendicitis, two radiologists separately assessed the existence of 10 previously mentioned CT signs of complicated appendicitis (abscess, extraluminal air, luminal air, extraluminal appendicolith, luminal appendicolith, moderate-to-severe periappendiceal fat stranding, periappendiceal fluid, ileus, ascites and contrast enhancement defects of the appendiceal wall) [8].

Measurements were executed by two radiologists (reader 1 MAG, eight years' experience in radiology; reader 2 ŞA, 10 years' experience in radiology) within the 3D slicer programme [9]. The first reader conducted all 154 patient measurements. Twenty-seven randomly selected patients were re-evaluated by the first reader and evaluated twice by the second reader at an interval of one month to estimate the intraobserver and interobserver reliability.

The voxel size of all patients (0.75x0.75x5 mm) was resampled to 1x1x1 millimetres with the Resample Scalar Volume module. The third lumbar vertebra is detected in the sagittal plane, and volume data is cropped with the crop volume module so that it includes only the third lumbar vertebrae. In the sagittal plane, a single slice located in the middle of the third vertebrae is selected, and all measurements of each patient by all readers are conducted on this axial plane CT slice. The slice is divided into four segments: total cross-sectional area (single slice total area), subcutaneous fatty tissue, muscle tissue and visceral fatty tissue areas (mesenteric fatty tissue area). The total cross-sectional area is used as a mask, and the other three segments are painted in that mask. The total cross-sectional area is segmented with a paint tool. Other segments are painted mainly with semi-automatic flood filling tools. Paint, draw, erase, logical operators, islands and smoothing tools are used for fine adjustment. The area (cm²), maximum, minimum, mean, median and standard deviation values of the Hounsfield unit for each segment are computed with the segment statistics module (Figure 1).

The skeletal muscle index (SMI) was used as the preferred CT-assessed sarcopenia index. It was obtained from the skeletal muscle area (SMA) and adjusted for stature (cm²/m²) on CT images at L3 vertebra level.

Statistical analysis

While evaluating the findings obtained in the study, IBM Statistical Package for the Social Sciences for Windows, Version 20.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis.

Descriptive data on age, gender, BMI and appendicitis status (complicated and uncomplicated appendicitis, as evaluated by CT) were calculated. Furthermore, CT-assessed sarcopenia parameters including SMI, muscle area, mesenteric fatty tissue area and single slice total area were calculated.

The normality of the continuous variables was determined by a Kolmogorov–Smirnov test. Data were shown as mean ± standard deviation or median (min-max), where applicable. The differences between groups were compared by using the independent samples t-test or the Mann–Whitney U-test, where appropriate. Categorical data were analysed by Pearson's chi-square test, where appropriate. The cut-off values of the groups' discrimination parameters were determined using the receiver operating characteristic (ROC) analysis. At each value, the sensitivity and specificity for each outcome under study were plotted, thus generating a ROC curve. A *p*-value of <0.05 and *p*<0.10 was considered statistically significant where applicable.

Results

Of the 154 geriatric patients, 62% were male (n=95), and 38% (n=59) were female; 52% of the patients included in the study were in the complicated (n=80) and 48% (n=74) in the uncomplicated category. There was no difference in gender distribution between uncomplicated and complicated cases. The ratio of male individuals was higher in both categories (Table 1).

Table 2 presents the minimum, maximum, mean and standard deviation values of the age, BMI, sarcopenia index as SMI (cm²/m²), muscle area, subcutaneous fatty tissue area, mesenteric fatty tissue area and single slice total area.

Table 3 presents descriptive values of the variables according to appendicitis status.

There is a statistically significant difference between uncomplicated and complicated cases in terms of BMI, SMI and muscle area values with a margin of error of 0.05. In terms of subcutaneous fatty tissue area value, there is a statistically significant difference with a 0.10 margin of error between uncomplicated and complicated cases. There is

no statistically significant difference between uncomplicated and complicated cases in terms of age, mesenteric fatty tissue area and single slice total area values (Table 4).

The most appropriate cut-off point was applied by ROC analysis to BMI, sarcopenia index and muscle area variables, which had a statistically significant difference with a 0.05 margin of error between uncomplicated and complicated cases.

ROC analysis was performed with data from the sarcopenia index results (Table 5). The cut-off point for the sarcopenia index was determined as $41.62 \text{ cm}^2/\text{m}^2$, with a sensitivity of 71% and a specificity of 52%. The obtained area under the curve (AUC) value was 0.60 ($p=0.042$).

When ROC analysis was performed with the data of the muscle area results, the cut-off point of the muscle area was determined as 115.66 cm^2 with 72% sensitivity and 54% specificity. The AUC value was 0.60 ($p=0.032$).

Finally, when a ROC analysis was performed with the data of BMI results, the cut-off point for BMI was determined as $24.97 \text{ kg}/\text{m}^2$ with 69% sensitivity and 52% specificity. The AUC value was also calculated as 0.62 ($p=0.010$) (Figure 2).

Discussion

Our study presents the first analysis of the predictive value of CT-assessed sarcopenia for complicated appendicitis in the literature. Accordingly, CT-assessed sarcopenia index SMI, muscle volume and BMI can predict complicated appendicitis in geriatric patients.

Geriatric age is amongst the factors associated with complicated appendicitis [10]. Co-morbidities such as anaemia, cardiac disease and chronic renal disease in geriatric patients are also associated with complicated appendicitis [11].

Higher rates of complicated appendicitis in geriatric patients are attributed to risk factors such as vascular sclerosis, fibrotic narrowing of the lumen and fat infiltration on the muscular layer of the appendix, so complications such as perforation tend to occur more easily [12]. There might also be a diagnostic delay related to an inability to sense pain and laboratory abnormalities of co-morbidities in advanced age [13, 14]. Fifty-two percent of the patients included in this study were in the complicated appendicitis category. The patient population in our study was of geriatric age, so the complicated appendicitis ratio was higher than that seen in the general population.

The term 'sarcopenia' has been previously used to describe the loss of muscle with increased age; however, according to new definitions, physical performance and muscle strength are equally important as a decrease in muscle volume. Its pathogenesis is multifactorial and includes chronic metabolic changes, low BMI and reduced activity and protein intake. The factors usually combine, resulting in dysfunction of muscle mass function and strength.

Different research groups' evolving terminology and definitions of sarcopenia have seen different criteria proposed, including numeric cut-off values that may differ across countries and ethnic groups [15]. Consequently, it may be better interpreted as a syndrome that may be presented in different degrees in different patient cohorts [16]. As the degree of muscle volume decreases, adverse events seem to be more highly related to decreased muscle strength or function [17].

There are several validated methods to measure sarcopenia, such as dual X-ray absorptiometry, bioelectric impedance analysis, MRI and CT scanning. Of these techniques, CT is considered the gold standard method to diagnose sarcopenia with a range of minimal errors (1% to 4%) [18,19]. Although it is more expensive than anthropometric methods and poses a greater radiation exposure than the other techniques, it provides high accuracy and reproducible results. It also enables the evaluation of lean body mass and visceral and subcutaneous fat tissues at the same time [20].

In our retrospective study, we chose SMI as a CT-assessed sarcopenia index. In this technique, the psoas muscle at L3 vertebra level on cross-section imaging was analysed as a representative of the total body muscle mass which gave information about muscle quantity and quality. The distinction among different tissues such as muscle and fat was assessed by Hounsfield units [17].

In general, CT has been widely used in geriatric patients presenting with emergency abdominal pain, especially in differential diagnosis. CT results in the elderly might be highly influential on the direction of the therapeutic process [21]. Thus, analysing the sarcopenia at the same time during an index CT might have several benefits, such as predicting complicated appendicitis. In our study, we used the preoperative contrast-enhanced abdominal CT to differentiate appendicitis status and analyse the sarcopenia as SMI.

Recently, sarcopenia has been analysed on the surgical outcomes of patients who have undergone elective cancer surgery or emergency abdominal surgery. In general, CT-assessed sarcopenia has been shown to be a risk factor in the short- and long-term outcomes of gastrointestinal oncology patients. In geriatric patients with colorectal cancer, sarcopenia has been not only associated with postoperative complications and long-term outcomes but can also predict preoperative nutritional risks. Therefore, it can guide treatment and follow-up strategies. Studies have shown that among patients undergoing exploratory laparotomy, sarcopenia has been associated with higher morbidity, mortality and length of stay as well as undesirable discharge rates [22]. It is also associated with higher mortality rates during the one-year postoperative follow-up period in geriatric patients who underwent emergency abdominal surgery [23].

Our study result is compatible with the literature and shows the significance of sarcopenia in predicting complicated appendicitis.

In our patient cohort, the mean BMI of geriatric patients with complicated appendicitis was 25,28 kg/m², while with uncomplicated cases it was 27,29 kg/m². Although there is statistical significance between the mean BMI levels of the two groups, it might not be interpreted as clinical significance. A BMI level between 25 kg/m² and 29.9 kg/m² is accepted as overweight, according to National Institute of Health (NIH) and World Health Organisation (WHO) classifications. BMI is a statistical index for estimating body fat in both genders and is commonly used. However, due to individual and geographical variations, it is still insufficient to classify a person as obese or malnourished [24]. Furthermore, it does not differentiate between body lean mass and body fat mass. It is an easily obtainable metric, but it does not correlate solely with a patient's morbidity and mortality, considering many variables including genetic and environmental confounders [25]. In the literature, BMI as an indicator of nutritional status is associated with different surgical outcomes in different patient cohorts. Geriatric obese patients who have undergone emergency surgery have higher morbidity and lower mortality rates than their normal-BMI counterparts [26]. In another study, patients who underwent emergency diverting esophagectomy and who had lower BMI tended to have more anastomotic leaks after reconstruction [27]. Another study showed that higher BMI was an independent risk factor for early anastomotic leakage after colorectal surgery [28]. While geriatric obesity is a growing concern worldwide, Turkey has one of the highest obesity risks in Europe, and sarcopenic obesity was seen in 11% of one geriatric patient cohort; however, in our geriatric patients, the mean BMI of the two groups does not support any association between sarcopenia and obesity [29].

Additionally, our study results show that the mean muscle area assessed by CT between groups was statistically significant. The mean value for the uncomplicated appendicitis group was 125.52 cm², while for the complicated appendicitis group, it was 116.87 cm². This significance might be co-related to the significant difference between groups of the sarcopenia index.

Furthermore, there is a statistically significant difference with a 0.10 margin of error between uncomplicated and complicated cases in terms of subcutaneous fatty tissue area values. This significance is correlated with the significant

difference of the mean BMI values of geriatric patients with different appendicitis statuses.

In our study, our patient cohort did not differ significantly regarding gender for the prediction of complicated appendicitis, so we did not use previously used cut-off values for the CT-assessed sarcopenia index. The cut-off value of sarcopenia which was assessed by ROC analysis was $41.62 \text{ cm}^2/\text{m}^2$, which has shown 71% sensitivity and 52% specificity.

Moreover, the cut-off value of muscle area assessed by ROC analysis was 115.66 cm^2 , which has shown 72% sensitivity and 54% specificity.

Finally, when a ROC analysis was performed with the data yielded by BMI results, the cut-off point for BMI was determined as $24.97 \text{ kg}/\text{m}^2$, with 69% sensitivity and 52% selectivity. The AUC value was also calculated as 0.62 ($p=0.010$). The three cut-off values have similar sensitivity and specificity.

There are several scoring systems for diagnosing acute appendicitis. One of the most used methods, the Alvarado score, has high sensitivity and specificity values, especially to exclude acute appendicitis when the score is less than 5. However, few studies have analysed the scoring systems in geriatric patients. Hence, there is no specific scoring system to discriminate complicated from uncomplicated appendicitis in such patients. So, in that case; among elderly patients, it is not recommended to diagnose or exclude acute appendicitis solely on the basis of the diagnostic scoring system [1,2]. Recently, a CT-based acute appendicitis severity index has been found a reliable parameter predicting complicated appendicitis [30]. Furthermore, using imaging analysis together with the clinical scoring systems may enable better differentiation of cases of complicated and uncomplicated appendicitis [31].

According to our study results, CT-assessed sarcopenia might predict complicated appendicitis in geriatric patients with a moderate degree of sensitivity and specificity and be used separately or in combination with diagnostic scoring systems. Nevertheless, prospective studies with large patient cohorts could better evaluate the predictive value of sarcopenia.

Limitations Of The Study

The present study was carried out retrospectively from a single referral centre with an average number of geriatric patients. There is no consensus on best method for sarcopenia measurement so we used SMI, one of the most frequently chosen sarcopenia indexes assessed by CT. However, radiologist subjectivity might have affected the interpretation of the CT to some degree. The cut-off values of various methods for sarcopenia might be different between countries.

Value of the study

This is the first study analysing the predictive value of CT-assessed sarcopenia for complicated appendicitis in geriatric patients. BMI, as well as the CT-assessed parameters SMI, muscle area, mesenteric fatty tissue area and single slice total area, were analysed.

Conclusion

Geriatric patients who have lower BMI, decreased muscle area and CT-detected sarcopenia have an increased risk of complicated appendicitis. Surgeons should be aware of the factors that can lead to complicated appendicitis, which may result in higher morbidity and mortality rates among the elderly.

Declarations

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Availability of data and materials The datasets used and/or analysed during the current study

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Competing interests The authors declare no competing interests

Author contributions: A.C.Y wrote the main manuscript, Ş.H, M.A.G analyses the Computerized Tomographies of the patients to assess sarcopenia, S.Z, M.F.E edited the manuscript. All authors contributed equally to this manuscript, read, and approved the final manuscript.

The manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work

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Criteria for inclusion in the authors'/ contributors' list: Authors of this study were included in the study according their contribution part of the study.

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Tables

Table 1 Appendicitis status according to the gender

		Gender		Total
		Female	Male	
Appendicitis Status	Non-Complicated	27	47	74
		36,5%	63,5%	100,0%
	Complicated	32	48	80
		40,0%	60,0%	100,0%
Total		59	95	154
		38,3%	61,7%	100,0%
Chi-Square(:0,201; p-value:0,654				

Table 2 Descriptive values of the variables of the age, BMI, sarcopenia index, Muscle Area, Subcutaneous fatty tissue area, mesenteric fatty tissue area, single slice total area

Variables (n=154)	Minimum	Maximum	Mean	Std. Deviation
Age	65	93	73,81	7,17
BMI	17,52	37,98	26,25	4,19
SMI (cm ² /m ²)	19,13	80,97	44,68	9,58
Muscle Area(cm ²)	60,61	217,78	121,03	25,55
Subcutaneous Fatty Tissue Area (cm ²)	13,65	706,25	190,81	99,07
Mesenteric Fatty Tissue Area(cm ²)	9,98	489,59	173,04	90,91
Single Slice Total Area (cm ²)	236,19	1432,12	707,45	233,04

Table 3 Descriptive values of the variables according to the appendicitis status

Appendicitis Status	Variables	Minimum	Maximum	Mean	Std. Deviation
Non-Complicated (n=74)	Age	65	93	73,76	7,55
	BMI (kg/m ²)	19,25	37,98	27,29	4,50
	SMI (cm ² /m ²)	19,13	80,97	46,16	9,17
	Muscle Area (cm ²)	60,61	217,78	125,52	25,07
	Subcutaneous Fatty Tissue Area (cm ²)	13,65	387,46	201	92,72
	Mesenteric Fatty Tissue Area(cm ²)	9,98	389,30	176,06	88,41
	Single Slice Total Area (cm ²)	281,21	1432,12	724,15	248,17
Complicated (n=80)	Age	65	90	73,86	6,85
	BMI (kg/m ²)	17,52	35,45	25,28	3,64
	SMI (cm ² /m ²)	27,18	65,16	43,31	9,79
	Muscle Area (cm ²)	74,91	180,76	116,87	25,44
	Subcutaneous Fatty Tissue Area (cm ²)	29,76	706,25	181,39	104,28
	Mesenteric Fatty Tissue Area (cm ²)	21,05	489,59	170,25	93,64
	Single Slice Total Area (cm ²)	236,19	1420,85	692,01	218,54

Table 4 Statistical Relationship between the variables and appendicitis status

Appendicitis Status		Age	BMI	SMI	Muscle Area	Subcutaneous Fatty Tissue Area	Mesenteric Fatty Tissue Area	Single Slice Total Area	
Non-Complicated (n=74)	Mean	73,76	27,29	46,16	125,52	201,01	176,06	724,15	
	Std. Error of Mean	0,879	0,52	1,06	2,91	10,77	10,27	28,85	
	Median	72	26,22	45,14	126,29	217,24	174,60	674,79	
	Std. Deviation	7,558	4,50	9,17	25,07	92,72	88,41	248,17	
	Minimum	65	19,25	19,13	60,61	13,65	9,98	281,21	
	Maximum	93	37,98	80,97	217,78	387,46	389,30	1432,12	
	Percentiles	25	67	23,89	40,66	110,01	125,91	108,36	543,08
		50	72	26,22	45,14	126,29	217,24	174,61	674,79
		75	78,25	30,51	52,69	140,91	266,31	222,89	853,36
Complicated (n=80)	Mean	73,86	25,28	43,31	116,87	181,39	170,25	692,01	
	Std. Error of Mean	0,76	0,41	1,09	2,84	11,65	10,47	24,43	
	Median	73	24,94	41,99	113,48	178,81	165,44	674,14	
	Std. Deviation	6,85	3,64	9,79	25,44	104,28	93,64	218,54	
	Minimum	65	17,52	27,18	74,91	29,76	21,05	236,19	
	Maximum	90	35,45	65,16	180,76	706,25	489,59	1420,85	
	Percentiles	25	68	22,88	35,23	94,57	94,72	87,91	534,91
		50	73	24,94	41,99	113,48	178,81	165,44	674,14
		75	78,75	27,34	51,25	136,57	226,68	220,46	825,74
p-values		0,712	0,003*	0,042*	0,035*	0,068**	0,693	0,394	

Age, SMI, Subcutaneous Fatty Tissue Area: Mann-Whitney U Test

BMI, Muscle Area, Mesenteric Fatty Tissue Area, Single Slice Total Area: Independent Samples T Test

*:p<0,05 ; **:p<0,10

Table 5 Results of ROC Curve Analysis of the variables

	Cut-off Value	Sensitivity	Specificity	AUC-p-value
SMI (cm ² /m ²),	41,62	0,71	0,52	0,60 – 0,042*
Muscle Area (cm ²)	115,66	0,72	0,54	0,60 – 0,032*
BMI (kg/m ²)	24,97	0,69	0,52	0,62 – 0,010*
*:p<0,05				

Figures

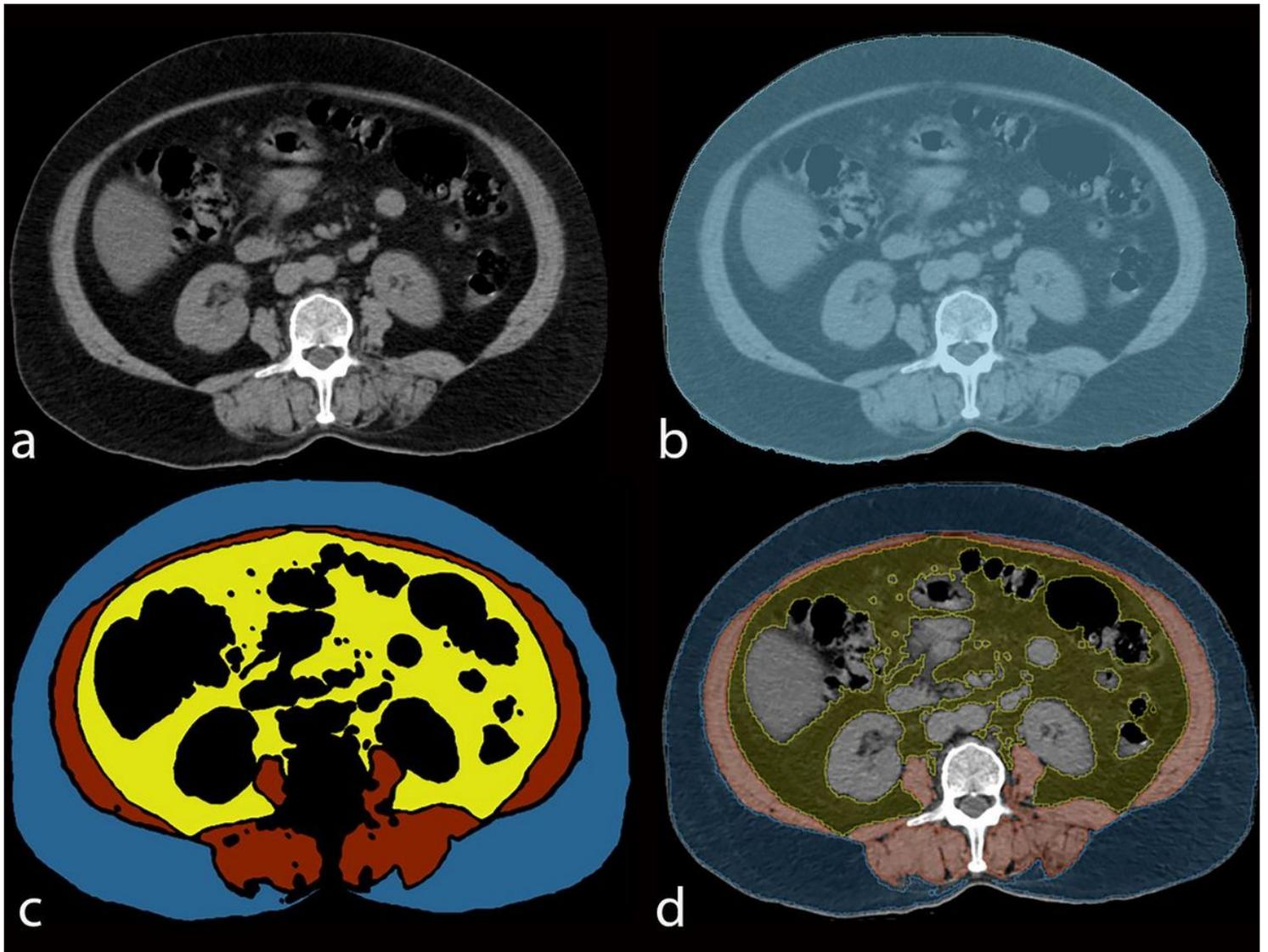


Figure 1

Axial unenhanced CT scan at L3 vertebrae mid-corpus level

a: raw image b: all tissues segmented (single slice) c: Mask images of segmentation, blue represents subcutaneous fatty tissue, red muscle tissue and yellow mesenteric fatty tissue d: Segments on raw CT image

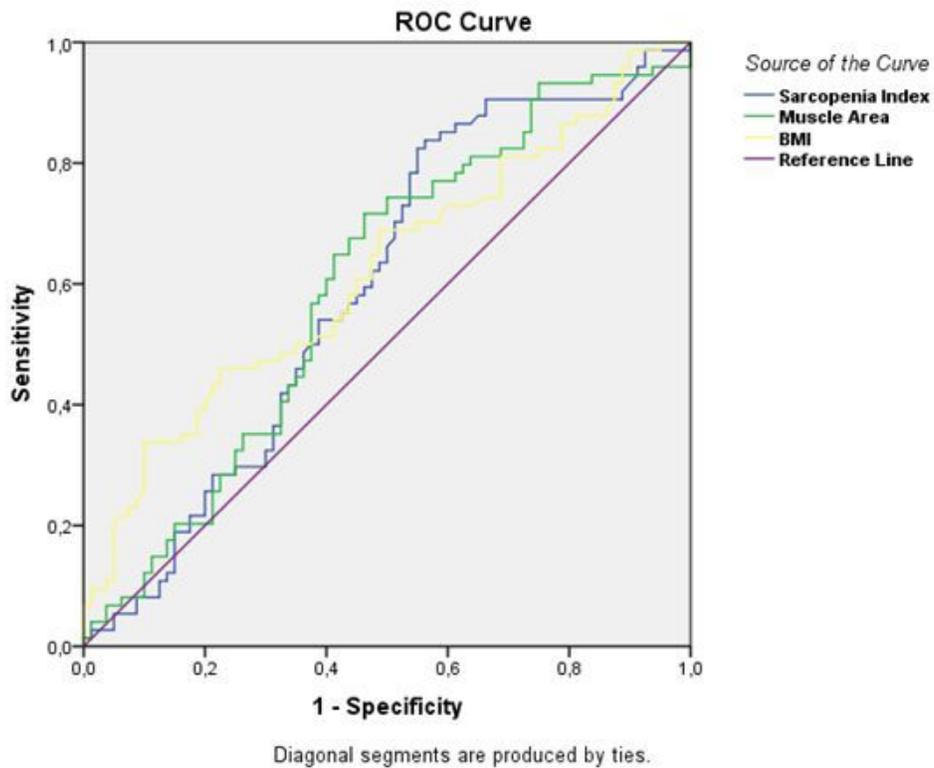


Figure 2

ROC analysis of the sarcopenia index (SMI cm^2/m^2), muscle area and BMI for predicting complicated appendicitis