



Research article

Quantification of epicardial adipose tissue by cardiac CT: Influence of acquisition parameters and contrast enhancement



Mohamed Marwan, Susanna Koenig, Kirsten Schreiber, Fabian Ammon, Markus Goeller, Daniel Bittner, Stephan Achenbach, Michaela M. Hell*

Department of Cardiology, Friedrich-Alexander-Universität Erlangen-Nürnberg, Ulmenweg 18, 91054 Erlangen, Germany

ARTICLE INFO

Keywords:

Epicardial adipose tissue
Cardiac computed tomography
Low-dose acquisition
Contrast-enhanced imaging

ABSTRACT

Purpose: While computed tomography (CT) is frequently used to quantify epicardial adipose tissue (EAT), the effect of different acquisition parameters on EAT volume has not been systematically reported. We assessed the influence of low-voltage acquisition and contrast enhancement on EAT quantification.

Method: Two independent cohorts (100 and 127 patients) referred for routine coronary CT were included. One cohort received a low-voltage and a standard voltage non-contrast acquisition (120 and 100 kV), the other cohort underwent non-contrast and contrast-enhanced CT. EAT volume was quantified using a semi-automated analysis software. Whereas the lower EAT threshold was consistently set at -190 Hounsfield Units (HU), different upper thresholds for EAT were analyzed. Bland-Altman analysis was used to analyze the agreement of EAT volume between scans with different acquisition parameters. We referred to a non-enhanced 120 kV acquisition with an upper threshold of -30 HU.

Results: Mean EAT volume was 159 ± 76 ml as measured in 120 kV non-contrast data sets with an upper threshold of -30 HU. For 100 kV data sets, an upper threshold of -40 HU showed the best correlation ($r = 0.961$, $p < 0.05$). Significant overestimation was found for upper thresholds of -20 and -30 HU and significant underestimation for -50 HU. In non-contrast vs. contrast-enhanced acquisitions, there was a significant underestimation of EAT volume for contrast-enhanced scans (mean difference 31 ml, 95% limits of agreement 27 to -89 ml).

Conclusions: CT-based EAT volume quantification in low-voltage and contrast-enhanced images is feasible. However, adjustment of the upper threshold for detection of fat is mandatory.

1. Introduction

Alterations in epicardial adipose tissue (EAT) volume, a visceral fat depot located within the pericardial sac with immediate proximity to the coronary arteries, have been associated with coronary artery plaque development and vulnerability, myocardial ischemia, increased coronary calcium as well as an increased incidence of cardiovascular adverse events [1–7]. A systemic review by Spearman et al. revealed that EAT volume quantification is significantly associated with clinical outcomes and provides incremental prognostic value over coronary artery calcium scoring [8].

Cardiac computed tomography (CT), owing to its high spatial resolution and true volume coverage of the entire heart, is currently the

preferred method to determine EAT over other imaging modalities, including echocardiography or magnetic resonance imaging. On the basis of CT attenuation thresholds, various software solutions offer a simple semi-automated approach for quantification of EAT with high reproducibility [9]. Quantification of EAT depends on the CT attenuation thresholds used to define adipose tissue. Previously used thresholds range from -250 to -190 Hounsfield Units (HU) for the lower limit and -50 to -30 HU for the upper limit of EAT [2,4,10–12]. However, several technical parameters, including contrast-enhancement, time point of image reconstruction within the cardiac cycle and use of iterative reconstruction algorithms, have been shown to influence EAT quantification [13,14]. Systematic studies to assess the influence of technical parameters on EAT quantification are scarce. Non-contrast CT data

Abbreviations: CT, computed tomography; EAT, epicardial adipose tissue; HU, Hounsfield Units

* Corresponding author.

E-mail addresses: mohamed.marwan@uk-erlangen.de (M. Marwan), su_koenig@gmx.de (S. Koenig), kirsten_schreiber@web.de (K. Schreiber), fabian.ammon@uk-erlangen.de (F. Ammon), markus.goeller@uk-erlangen.de (M. Goeller), daniel.bittner@uk-erlangen.de (D. Bittner), stephan.achenbach@uk-erlangen.de (S. Achenbach), michaela.hell@uk-erlangen.de (M.M. Hell).

<https://doi.org/10.1016/j.ejrad.2019.108732>

Received 10 May 2019; Received in revised form 15 October 2019; Accepted 28 October 2019

0720-048X/© 2019 Elsevier B.V. All rights reserved.

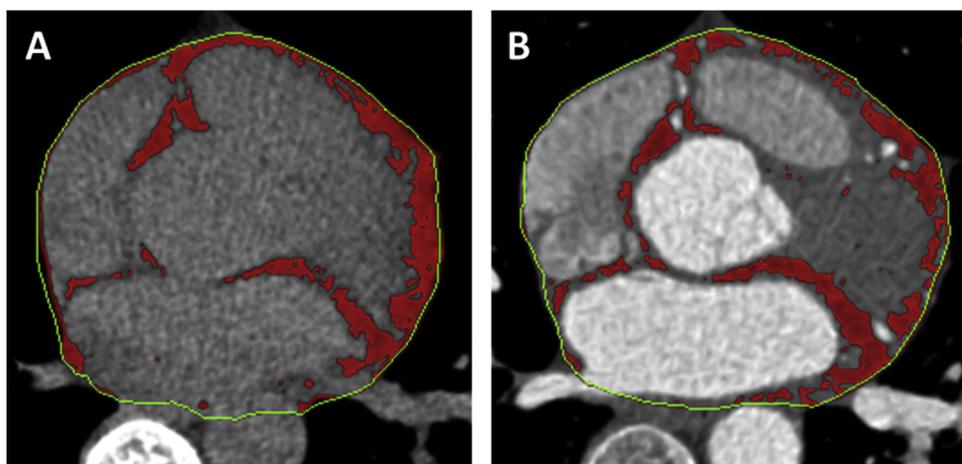


Fig. 1. Semi-automatic quantification of epicardial adipose tissue (EAT) volume in non-contrast (A) and contrast-enhanced CT images (B). The contour of the pericardial sac is automatically traced (green line) and adjusted by the reader, if necessary. The EAT volume (red) is automatically calculated by inclusion of all contiguous 3D voxels with CT attenuations between the specified upper threshold (here -30 HU) and the lower threshold of -190 HU.

Table 1
Patient characteristics.

	Low-voltage vs. standard voltage non-contrast cohort	non-contrast vs. contrast-enhanced cohort
N	127	100
mean age [years; mean \pm SD]	60 \pm 11	62 \pm 9
Male [n (%)]	84 (66)	64 (64)
Body mass index [kg/m ² ; mean \pm SD]	27 \pm 2	27 \pm 4
History [n (%)]		
Hypertension	45 (35)	47 (47)
Diabetes	13 (10)	12 (12)
Dyslipidemia	52 (41)	52 (52)
Smoking	17 (14)	13 (13)
Family history of CAD	25 (20)	28 (28)

CAD, coronary artery disease.

acquired at 120 kV for coronary calcium assessment are commonly used for EAT volume [9,11,15–18]. Technical improvements including optimized imaging protocols at low voltage allow a substantial dose reduction without affecting image quality. In the current study, we systematically assessed quantification of EAT in 120 kV data sets compared to low-voltage data sets at 100 kV using a semi-automatic approach. Furthermore, we systematically addressed EAT quantification of contrast-enhanced data compared to non-contrast data.

2. Materials and methods

2.1. Low-voltage vs. standard voltage non-contrast analysis

For the low-voltage vs. standard voltage non-contrast analysis, we included 137 consecutive patients from a previously published cohort [19]. CT data acquisition was performed using a second generation

Table 2

EAT volume comparison between 120 kV and 100 kV data sets with different upper CT thresholds and correlation of EAT quantification in 100 kV data sets with different upper CT threshold with 120 kV data sets with an upper threshold of -30 HU.

Upper threshold	Mean EAT volume [ml]		<i>p</i> -value	Pearson-correlation coefficient	95% limits of agreement [ml]	EAT volume in 100 kV data sets compared to 120 kV / -30 HU	
	120 kV data sets	100 kV data sets				<i>p</i> -value	Mean difference of EAT volume
-20 HU	180 \pm 85	200 \pm 93	< 0.001	<i>r</i> = 0.955	98;30	< 0.001	35 ml
-30 HU	159 \pm 76	175 \pm 85	< 0.001	<i>r</i> = 0.960	60;33	< 0.001	14 ml
-40 HU	141 \pm 69	154 \pm 77	< 0.001	<i>r</i> = 0.961	35;43	< 0.05	-4 ml
-50 HU	125 \pm 62	137 \pm 69	< 0.001	<i>r</i> = 0.956	26;63	< 0.001	-19 ml

EAT, epicardial adipose tissue; HU, Hounsfield Unit.

dual-source CT scanner (Somatom Definition Flash, 280 ms rotation, $2 \times 128 \times 0.6$ collimation, Siemens Healthineers, Forchheim, Germany). Imaging was first done with tube voltage of 120 kV and subsequently repeated with 100 kV with the use of prospectively ECG-triggered high-pitch spiral acquisition and otherwise unchanged parameters. Tube current for both protocols was set at 80 mAs. For image reconstruction, a B35f convolution kernel was used with a slice thickness of 3.0 mm and an increment of 1.5 mm. Post-processing was performed on a dedicated off-line workstation (Multimodality Workplace, Siemens Healthineers).

2.2. Non-contrast vs. contrast-enhanced analysis

For the non-contrast vs. contrast-enhanced analysis, we retrospectively included 100 patients who underwent clinically indicated CT imaging for coronary calcium detection and coronary CT angiography. Exclusion criteria were an estimated glomerular filtration rate less than 50 mL/min, atrial fibrillation, an implantable pacemaker or cardioverter defibrillator and coronary artery grafts. Covariates, including cardiac history and risk factors, were obtained by a structured interview.

CT data acquisition was performed using a second generation dual-source CT scanner (Somatom Definition Flash). Non-contrast images were acquired by a prospectively ECG-triggered high-pitch spiral acquisition mode protocol with 120 kV tube voltage and 80 mAs tube current. For coronary CT angiography, tube setting was weight adapted with 100 kV and 360 mAs in patients with a body weight < 100 kg and 120 kV and 400 mAs in patients with a body weight \geq 100 kg. Contrast agent transit time was measured using test bolus technique by injecting a bolus of 10 ml contrast agent (350 mg iodine/ml, Imeron, Bracco Imaging, Konstanz, Germany) followed by a saline flush of 50 ml, both at a flow rate of 6 ml/s using a dual-head power injector (CT Stellant, Medrad Inc., Indianola, PA, USA). For coronary CT angiography, 60 ml of contrast agent were injected in an antecubital vein at a flow rate of

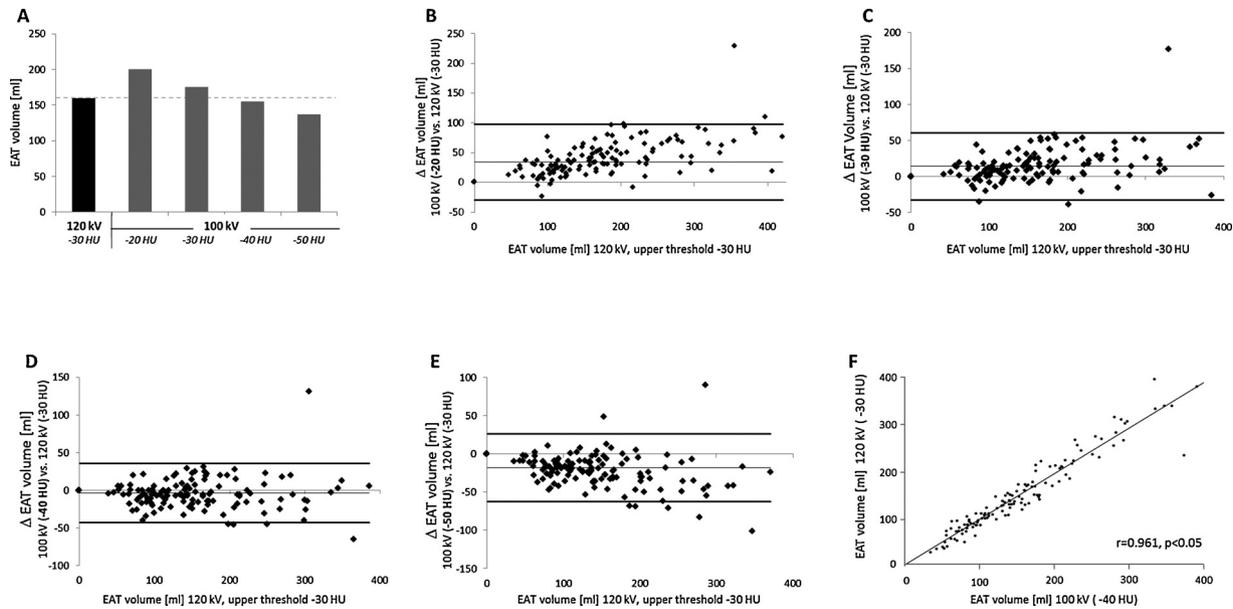


Fig. 2. Quantification of epicardial adipose tissue (EAT) in low-voltage data sets compared to 120 kV CT data sets with different upper CT attenuation thresholds. (A) EAT volume as assessed in 120 kV data sets with an upper threshold of -30 HU compared to low-voltage 100 kV data sets with an upper threshold of -20, -30, -40 and -50 HU. Bland-Altman analysis of EAT volume quantification in 100 kV data sets with upper threshold of -20 HU (B), -30 HU (C), -40 HU (D) and -50 HU (E) compared to 120 kV data sets with upper threshold of -30 HU. (F) Correlation coefficient for EAT quantification in 120 kV data sets with an upper threshold of -30 HU vs. 100 kV data sets with an upper threshold of -40 HU.

Table 3

EAT volumes assessed in non-contrast and contrast-enhanced data sets.

Upper threshold	Mean EAT volume [ml]	EAT volume differences [ml] compared to 120 kV non-contrast data sets, -30 HU	p-value
non-contrast data sets			
-30 HU	166 ± 65		
contrast data sets			
-50 HU	112 ± 43	53.7 ± 33.2	< 0.001
-40 HU	124 ± 47	42.2 ± 30.9	< 0.001
-30 HU	135 ± 50	31.0 ± 29.1	< 0.001
-20 HU	146 ± 53	20.1 ± 27.6	< 0.001
-10 HU	157 ± 56	9.0 ± 26.5	0.001
0 HU	168 ± 59	-2.5 ± 25.9	0.084
+10 HU	181 ± 62	-14.8 ± 25.9	< 0.001
+20 HU	194 ± 66	-28.0 ± 26.6	< 0.001
+30 HU	209 ± 70	-42.8 ± 28.4	< 0.001
+40 HU	225 ± 75	-59.3 ± 31.4	< 0.001
+50 HU	244 ± 80	-77.8 ± 35.9	< 0.001
threshold of visually optimal EAT volume (mean 15 ± 12 HU)	150 ± 52	17.2 ± 29.7	< 0.001
Visually optimized upper threshold			
	non-contrast data sets	contrast-enhanced data sets	p-value
Mean EAT volume [ml]	140 ± 50	150 ± 52	< 0.001
Mean upper threshold [HU]	-43 ± 15	-15 ± 12	< 0.001

EAT, epicardial adipose tissue; HU, Hounsfield Unit.

6 ml/s, followed by a 60 ml flush consisting of 80% saline and 20% contrast agent. A prospectively ECG-triggered acquisition mode was applied when the heart rate was < 65 bpm. In patients with a heart rate ≥ 65 bpm, images were obtained using a spiral acquisition and retrospectively ECG-gated image reconstruction. For image reconstruction, a B35f convolution kernel was used for non-contrast scans with a slice thickness of 3.0 mm and an increment of 1.5 mm. For contrast-

enhanced images, a B26f convolution kernel was applied with a slice thickness of 0.75 mm and an increment of 0.4 mm. Post-processing was performed on a dedicated off-line workstation (Multimodality Workplace, Siemens Healthineers).

2.3. Quantification of epicardial adipose tissue volume

Epicardial adipose tissue volume was measured using a dedicated semi-automatic volume analysis prototype software (Pericardial Fat Prototype, Siemens Healthineers, Forchheim, Germany) [20,21]. All data sets were checked for coverage of the entire epicardial sac. First, upper and lower limits of the pericardial sac were identified by the reader defined as the bifurcation of the pulmonary trunk and, respectively, the slice caudal to the posterior descending artery. Next, the contour of the pericardial sac was automatically traced and adjusted by the reader, if necessary (Fig. 1). For each data set, epicardial fat analysis time took around 3–5 min. If the software was unable to detect the epicardial contour, this data set was excluded. Volume of EAT (in ml) was automatically calculated by inclusion of all contiguous 3D voxels with CT attenuations within a defined threshold. The lower threshold was fixed at -190 HU for all measurements. For the upper threshold, our internal reference was set at -30 HU in 120 kV non-contrast data sets as this is a threshold commonly used for EAT volume analysis in non-contrast scans [9,11,15–18]. As maximum EAT volumes may vary depending on the applied acquisition parameters and non-contrast vs. contrast scans, we used additional upper CT attenuation thresholds: -20, -30, -40 and -50 HU for EAT quantification in 120 kV vs. 100 kV non-contrast data sets and -50 to 50 HU in intervals of 10 HU for EAT quantification in non-contrast vs. contrast-enhanced data sets. Furthermore, a visually selected optimal upper threshold, defined at the threshold accounting for most of the epicardial tissue with as little myocardial tissue as possible, was used for EAT quantification in non-contrast vs. contrast-enhanced data sets.

2.4. Statistics

Statistical analysis was performed using SPSS software (IBM® SPSS® statistics, version 15 for Windows). Continuous variables were assessed

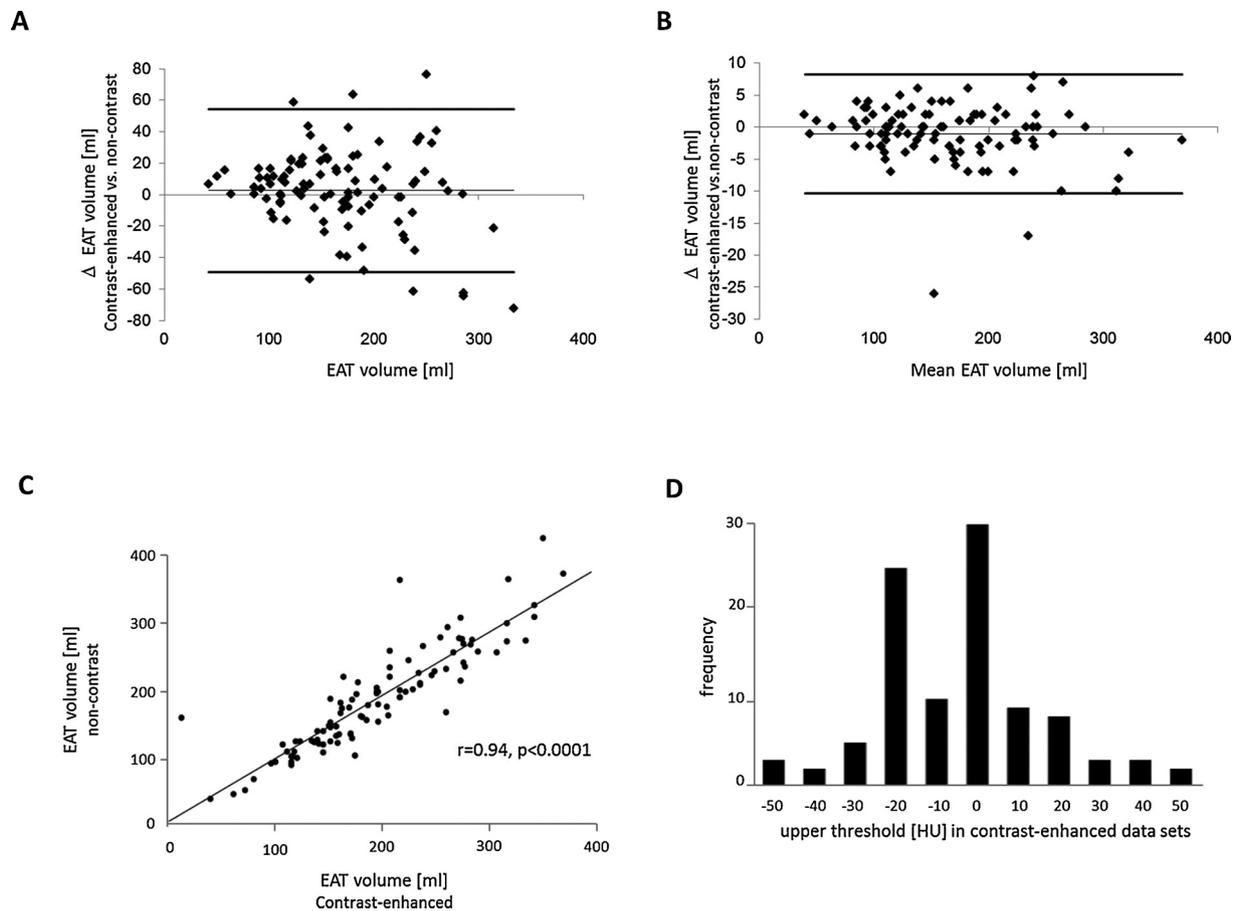


Fig. 3. Quantification of epicardial adipose tissue (EAT) in contrast-enhanced data sets compared to non-contrast data sets. Bland-Altman analysis of EAT volume quantification in contrast-enhanced with an upper CT attenuation threshold of 0 HU (A) and contrast-enhanced with a visually selected optimal upper threshold (B) compared to non-contrast 120 kV data sets with an upper threshold of -30 HU. (C) Correlation coefficient for EAT quantification in contrast-enhanced data sets vs. non-contrast 120 kV data sets with a visually selected optimal upper threshold. (D) Frequency distribution for corresponding volumes assessed in non-contrast data sets at an upper threshold of -30 HU and upper thresholds in contrast-enhanced data sets.

for normality using Shapiro-Wilk Test and expressed as mean \pm SD, if not stated otherwise. Categorical variables were described as frequencies and percentage. Wilcoxon test was applied to assess differences between EAT volumes. Correlation was assessed using Pearson's test. Bland-Altman analysis was used to analyze the agreement of EAT volume between contrast-enhanced and non-contrast scans and 100 and 120 kV scans. All tests were performed two-sided and $p < 0.05$ was considered to be statistically significant.

3. Results

Out of 274 data sets of 137 patients in the low-voltage vs. standard voltage non-contrast cohort, 10 data sets were not analyzable by the software in the 100 kV data sets. The final cohort included 127 patients (mean age 60 ± 11 years, 66% males) for assessment of EAT volume in 120 kV and 100 kV non-contrast CT scans. In the non-contrast vs. contrast-enhanced analysis, all data sets of the 100 enrolled patients (mean age 62 ± 9 years, 64% males) were analyzable by the software. For the contrast-enhanced scan, a tube voltage of 100 kV was applied in 59% of the patients and of 120 kV in 41% of the patients. Patient characteristics of both cohorts are listed in [Table 1](#).

3.1. EAT quantification in 120 kV vs. 100 kV non-contrast CT scans

Using the standard upper threshold of -30 HU, EAT volume was significantly overestimated in 100 kV data sets compared to 120 kV data sets (175 ± 85 ml vs. 159 ± 76 ml, $p < 0.001$). [Table 2](#) presents

EAT volumes for different upper thresholds (-20, -30, -40 and -50 HU) in 100 kV and 120 kV data sets.

Compared to the standard setting of 120 kV and an upper threshold of -30 HU, a good correlation for EAT volume quantification in 100 kV data sets and upper CT attenuation thresholds of -20, -30, -40 and -50 HU was observed. The best correlation ($r = 0.961$, $p < 0.05$) and the least mean difference of EAT volume (-4 ml; 95% limits of agreement 35 to -43 ml) compared to 120 kV data sets and an upper threshold of -30 HU was found for 100 kV data sets and an upper threshold of -40 HU. A significant overestimation of EAT volume was found for 100 kV data sets and upper thresholds of -20 and -30 HU as assessed by Bland-Altman analysis ($r = 0.955$, mean difference 35 ml, 95% limits of agreement 98 to -30 ml for -20 HU and $r = 0.955$, mean difference 14 ml, 95% limits of agreement 60 to -33 ml for -30 HU, respectively), whereas 100 kV data sets and an upper threshold of -50 HU underestimated EAT volume significantly ($r = 0.956$, mean difference -19 ml, 95% limits of agreement 26 to -63 ml) ([Table 2](#), [Fig. 2](#)).

3.2. EAT quantification in non-contrast vs. contrast-enhanced data sets

Using a visually optimized upper threshold, the mean EAT volume and the mean upper threshold showed a significant difference (both $p < 0.001$) between non-contrast data sets (mean EAT volume 140 ± 50 ml, mean upper threshold -43 ± 15 HU) compared to contrast-enhanced data sets (150 ± 52 ml, -15 ± 12 HU) ([Table 3](#)). There was a close correlation between EAT volume in non-contrast and contrast-enhanced data sets when using a visually optimized upper

threshold ($r = 0.94$, $p < 0.001$, Fig. 3C). Bland-Altman analysis showed a mean difference of -10 ml (95% limits of agreement 23 to -42 ml) (Fig. 3B). Using a fixed upper threshold of -30 HU, the mean EAT volume was significantly underestimated in contrast-enhanced data sets compared to non-contrast data sets (135 ± 50 ml vs. 166 ± 65 ml for contrast vs. non-contrast enhanced data sets, respectively $p < 0.001$). The smallest difference in EAT volume to non-contrast data sets with an upper threshold of -30 HU (mean volume 166 ± 65 ml) was found for an upper threshold of 4 ± 20 HU (modal value 0 HU, mean volume 168 ± 59 ml, $r = 0.93$, $p < 0.001$) (Fig. 3A). Here, the mean difference in the upper threshold of 4 ± 20 HU was statistically significant ($p < 0.001$). Comparing the mean EAT value measured in non-contrast data sets with an upper threshold of -30 HU with the best corresponding single EAT volume values measured in contrast-enhanced data sets (modal value 0 HU), the mean difference was -1.0 ± 4.6 ml (95% limits of agreement -10 to 8 ml).

4. Discussion

In the present study, we systematically analyzed the effect of low-voltage acquisition and contrast-enhanced images on CT-based quantification of EAT volume compared to frequently used non-contrast 120 kV data sets using a semi-automated approach. We found a systematic overestimation of EAT volume in non-contrast data sets if a low-voltage acquisition protocol was performed and the upper threshold for fat detection was not adjusted. CT images acquired with low-voltage protocols lead to an increased contrast and image noise as a result of the reduced tube voltage source with emission of decreased radiation which causes an overestimation of the EAT contour in a fixed upper threshold setting. Subsequently, adaption of the upper CT attenuation threshold can compensate for this systematic overestimation. In contrast, using identical upper thresholds, quantification of EAT volume in contrast-enhanced data sets underestimates EAT volume compared to non-contrast scans. For the closest possible agreement with EAT volume assessed in 120 kV non-contrast data sets with an upper threshold of -30 HU, an upper threshold of 0 HU for contrast-enhanced data sets would need to be used.

Previous studies have investigated the influence of technical parameters on cardiac CT-based measurement of epicardial fat [13,14]. Of particular interest is the assessment of EAT volume in contrast-enhanced images as they are recommended for detection of coronary artery stenosis in patients with a low- to intermediate risk for coronary artery disease according to current guidelines [22]. In contrast enhanced images, two possible mechanisms may influence the CT attenuation of adipose tissue around the contrasted lumen: partial volume effects and image interpolation (smoothing) as well as the vascular supply of the surrounding adipose tissue by the contrast-enhanced coronary arteries. Partial volume effects and image interpolation are primarily seen in the pericoronary adipose tissue and would manifest itself by decreasing attenuation of the adipose tissue with growing distance from the contrasted coronary artery lumen." So far, only few studies assessed the influence of the upper CT attenuation threshold on EAT volume determination. Variations of the lower threshold have been reported to have a negligible effect on the total EAT volume [23]. Bucher et al. reported significant differences in epicardial fat volume between non-contrast and contrast-enhanced (130.7 ± 49.5 ml vs. 87.2 ± 38.5 ml, $p < 0.001$) data sets at a -30 HU upper threshold. Mean EAT volume for contrast-enhanced data sets at a -15 HU upper threshold (102.4 ± 43.6 ml) could be approximated most closely by non-contrast scans at a -45 HU upper threshold (105.3 ± 40.8 ml) [14]. In our study, we therefore expanded the upper threshold range from -50 to 50 HU and added a visually optimal upper threshold. Close with their results, we found that visually optimal EAT volume is detected at an upper threshold at -43 ± 15 HU in non-contrast data sets and at -15 ± 12 HU in contrast enhanced scans. However, these upper threshold did not result in the closest approximation in EAT volume

between contrast-enhanced and non-contrast data sets which was found for a median upper threshold of 0 HU with an upper threshold of -30 HU (-1.0 ± 4.6 ml). This difference of upper thresholds has to be kept in mind when interpreting previous studies on EAT volume quantification in contrast-enhanced images using a threshold based method. Most studies also applied an upper threshold of -30 HU for contrast-enhanced images [21,24,25]. Based on our current results, it can be assumed that EAT volumes would have been rather underestimated when using an upper threshold of -30 HU.

With the increasing use of coronary CT angiography in clinical routine, strategies to lower radiation exposure have been used and tailored according to patient-specific considerations. Low-voltage acquisition protocols have been constantly evaluated for different indications in cardiac CT including non-contrast scans for coronary calcium scoring and coronary CT angiography for detection of coronary artery stenosis [19,26]. To our knowledge, the present study is the first one to systematically investigate low-voltage CT data sets for quantification of EAT volume compared to traditional 120 kV images. We show that EAT volume can be assessed accurately in 100 kV data sets with insignificant difference to 120 kV data sets if an adaption of the upper threshold is applied. The newest generation of CT systems even allows accurate acquisition with a tube voltage as low as 70 kV. Transferring our results of a 100 kV acquisition to these very low-dose protocols, it may be assumed that EAT volume would be further overestimated and an even stronger adaption of the upper threshold has to be performed with these acquisition parameters. Further studies are needed to investigate a threshold-based approach of EAT volume quantification in very low-dose protocols. Increased EAT volume has been associated with coronary artery disease and several studies suggest a potential of EAT volume as an additional cardiovascular risk predictor for adverse cardiac events [2,27–29]. An association with fatal and nonfatal coronary events during an 8-year follow-up period in more than 4000 patients independently of traditional cardiovascular risk factors has been reported by the Heinz Nixdorf Recall Study [2]. Spearman et al. performed a systemic review on the prognostic value of epicardial fat volume measurements by CT and demonstrated a cut-off value of > 125 ml as most appropriate if binary cutoffs are used [8]. However, further studies will be necessary to investigate the clinical value of epicardial fat quantification for patient management in the context of risk prediction of adverse cardiac events. All the more, for a potential role as a cardiovascular risk factor, there is a dire need for standardized quantification parameters of EAT which would potentially allow for generation of reference values of what would be considered a normal vs. abnormal volume of EAT.

4.1. Limitations

Several limitations in this study need to be acknowledged. First, this study did not include any reference standard, as e.g. histopathology, to confirm absolute EAT volumes. We presented only a relative comparison in EAT volume in data sets applying different technical parameters, though, a good accuracy for CT based assessment of EAT volume has been reported in earlier studies [9,16]. Next, as the approach was semi-automated, few steps were reader-dependent and may have resulted in minor variations in EAT volume assessment. This includes the manual setting of the upper and lower limits of the pericardial sac, the manual correction of the epicardial outline and the manual adaption for the visually optimal lower threshold. Furthermore, different reconstruction kernels and slice thicknesses for non-contrast and contrast-enhanced scans were applied which may makes it more difficult to differentiate between a reconstruction kernel vs. contrast effect. Overall, additional studies will be necessary to confirm the results for a larger patient cohort.

5. Conclusions

In conclusion, CT-based EAT volume quantification in low-voltage and contrast-enhanced images provides comparable results to the most commonly used 120 kV non-contrast images if upper thresholds are adapted correctly. Based on the present cohorts, an upper threshold of -40 HU for 100 kV non-contrast images and 0 HU for contrast-enhanced data sets is recommended.

Declaration of Competing Interest

There is nothing to declare.

Acknowledgements

This study was supported by the German government, Bundesministerium für Bildung und Forschung (01EX1012B, Spitzencluster Medical Valley).

References

- [1] Y. Otaki, M. Hell, P.J. Slomka, A. Schuhbaeck, H. Gransar, B. Huber, R. Nakazato, G. Germano, S.W. Hayes, L.E. Thomson, J.D. Friedman, S. Achenbach, D.S. Berman, D. Dey, Relationship of epicardial fat volume from noncontrast CT with impaired myocardial flow reserve by positron emission tomography, *J Cardiovasc. Comput. Tomogr.* 9 (4) (2015) 303–309.
- [2] A.A. Mahabadi, J.M. Massaro, G.A. Rosito, D. Levy, J.M. Murabito, P.A. Wolf, C.J. O'Donnell, C.S. Fox, U. Hoffmann, Association of pericardial fat, intrathoracic fat, and visceral abdominal fat with cardiovascular disease burden: the Framingham Heart Study, *Eur Heart J.* 30 (7) (2009) 850–856.
- [3] G.A. Rosito, J.M. Massaro, U. Hoffmann, F.L. Ruberg, A.A. Mahabadi, R.S. Vasan, C.J. O'Donnell, C.S. Fox, Pericardial fat, visceral abdominal fat, cardiovascular disease risk factors, and vascular calcification in a community-based sample: the Framingham Heart Study, *Circulation* 117 (5) (2008) 605–613.
- [4] D. Dey, N.D. Wong, B. Tamarappoo, R. Nakazato, H. Gransar, V.Y. Cheng, A. Ramesh, I. Kakadiaris, G. Germano, P.J. Slomka, D.S. Berman, Computer-aided non-contrast CT-based quantification of pericardial and thoracic fat and their associations with coronary calcium and Metabolic Syndrome, *Atherosclerosis* 209 (1) (2010) 136–141.
- [5] K. Iwasaki, T. Matsumoto, H. Aono, H. Furukawa, M. Samukawa, Relationship between epicardial fat measured by 64-multidetector computed tomography and coronary artery disease, *Clin Cardiol.* 34 (3) (2011) 166–171.
- [6] S. Sarin, C. Wenger, A. Marwaha, A. Qureshi, B.D. Go, C.A. Woomert, K. Clark, L.A. Nassef, J. Shirani, Clinical significance of epicardial fat measured using cardiac multislice computed tomography, *Am J. Cardiol.* 102 (6) (2008) 767–771.
- [7] M.M. Hell, M. Motwani, Y. Otaki, S. Cadet, H. Gransar, R. Miranda-Peats, J. Valk, P.J. Slomka, V.Y. Cheng, A. Rozanski, B.K. Tamarappoo, S. Hayes, S. Achenbach, D.S. Berman, D. Dey, Quantitative global plaque characteristics from coronary computed tomography angiography for the prediction of future cardiac mortality during long-term follow-up, *Eur. Heart J. Cardiovasc. Imaging* 18 (12) (2017) 1331–1339.
- [8] J.V. Spearman, M. Renker, U.J. Schoepf, A.W. Krazinski, T.L. Herbert, C.N. De Cecco, P.J. Nietert, F.G. Meinel, Prognostic value of epicardial fat volume measurements by computed tomography: a systematic review of the literature, *Eur Radiol.* 25 (11) (2015) 3372–3381.
- [9] J.H. Nichols, B. Samy, K. Nasir, C.S. Fox, P.C. Schulze, F. Bamberg, U. Hoffmann, Volumetric measurement of pericardial adipose tissue from contrast-enhanced coronary computed tomography angiography: a reproducibility study, *J Cardiovasc. Comput. Tomogr.* 2 (5) (2008) 288–295.
- [10] G. Thanassoulis, J.M. Massaro, U. Hoffmann, A.A. Mahabadi, R.S. Vasan, C.J. O'Donnell, C.S. Fox, Prevalence, distribution, and risk factor correlates of high pericardial and intrathoracic fat depots in the Framingham heart study, *Circ. Cardiovasc. Imaging* 3 (5) (2010) 559–566.
- [11] N. Alexopoulos, D.S. McLean, M. Janik, C.D. Arepalli, A.E. Stillman, P. Raggi, Epicardial adipose tissue and coronary artery plaque characteristics, *Atherosclerosis* 210 (1) (2010) 150–154.
- [12] K. Ueno, T. Anzai, M. Jinzaki, M. Yamada, Y. Jo, Y. Maekawa, A. Kawamura, T. Yoshikawa, Y. Tanami, K. Sato, S. Kuribayashi, S. Ogawa, Increased epicardial fat volume quantified by 64-multidetector computed tomography is associated with coronary atherosclerosis and totally occlusive lesions, *Circ. J.* 73 (10) (2009) 1927–1933.
- [13] S. Oda, D. Utsunomiya, Y. Funama, H. Yuki, M. Kidoh, T. Nakaura, H. Takaoka, M. Matsumura, K. Katahira, K. Noda, S. Oshima, S. Tokuyasu, Y. Yamashita, Effect of iterative reconstruction on variability and reproducibility of epicardial fat volume quantification by cardiac CT, *J Cardiovasc. Comput. Tomogr.* 10 (2) (2016) 150–155.
- [14] A.M. Bucher, U. Joseph Schoepf, A.W. Krazinski, J. Silverman, J.V. Spearman, C.N. De Cecco, F.G. Meinel, T.J. Vogl, L.L. Geyer, Influence of technical parameters on epicardial fat volume quantification at cardiac CT, *Eur J. Radiol.* 84 (6) (2015) 1062–1067.
- [15] J. Ding, F.C. Hsu, T.B. Harris, Y. Liu, S.B. Kritchevsky, M. Szklo, P. Ouyang, M.A. Espeland, K.K. Lohman, M.H. Criqui, M. Allison, D.A. Bluemke, J.J. Carr, The association of pericardial fat with incident coronary heart disease: the Multi-Ethnic Study of Atherosclerosis (MESA), *Am J. Clin. Nutr.* 90 (3) (2009) 499–504.
- [16] P.M. Gorter, A.S. van Lindert, A.M. de Vos, M.F. Meijis, Y. van der Graaf, P.A. Doevendans, M. Prokop, F.L. Visseren, Quantification of epicardial and pericoronary fat using cardiac computed tomography; reproducibility and relation with obesity and metabolic syndrome in patients suspected of coronary artery disease, *Atherosclerosis* 197 (2) (2008) 896–903.
- [17] G.L. Wheeler, R. Shi, S.R. Beck, C.D. Langefeld, L. Lenchik, L.E. Wagenknecht, B.I. Freedman, S.S. Rich, D.W. Bowden, M.Y. Chen, J.J. Carr, Pericardial and visceral adipose tissues measured volumetrically with computed tomography are highly associated in type 2 diabetic families, *Invest Radiol.* 40 (2) (2005) 97–101.
- [18] P.M. Gorter, A.M. de Vos, Y. van der Graaf, P.R. Stella, P.A. Doevendans, M.F. Meijis, M. Prokop, F.L. Visseren, Relation of epicardial and pericoronary fat to coronary atherosclerosis and coronary artery calcium in patients undergoing coronary angiography, *Am J. Cardiol.* 102 (4) (2008) 380–385.
- [19] M. Marwan, C. Mettin, T. Pflederer, M. Seltmann, A. Schuhback, G. Muschiol, D. Ropers, W.G. Daniel, S. Achenbach, Very low-dose coronary artery calcium scanning with high-pitch spiral acquisition mode: comparison between 120-kV and 100-kV tube voltage protocols, *J Cardiovasc. Comput. Tomogr.* 7 (1) (2013) 32–38.
- [20] S. Gaubeta, L. Klinghammer, D. Jahn, A. Schuhback, S. Achenbach, M. Marwan, Epicardial fat and coronary artery calcification in patients on long-term hemodialysis, *J Comput. Assist. Tomogr.* 38 (5) (2014) 768–772.
- [21] M.M. Hell, S. Achenbach, A. Schuhbaeck, L. Klinghammer, M.S. May, M. Marwan, CT-based analysis of pericoronary adipose tissue density: relation to cardiovascular risk factors and epicardial adipose tissue volume, *J Cardiovasc. Comput. Tomogr.* 10 (1) (2016) 52–60.
- [22] M. Task Force, G. Montalescot, U. Sechtem, S. Achenbach, F. Andreotti, C. Arden, A. Budaj, R. Bugiardini, F. Crea, T. Cuisset, C. Di Mario, J.R. Ferreira, B.J. Gersh, A.K. Gitt, J.S. Hulot, N. Marx, L.H. Opie, M. Pfisterer, E. Prescott, F. Ruschitzka, M. Sabate, R. Senior, D.P. Taggart, E.E. van der Wall, C.J. Vrints, E.S.C.C.F.P. Guidelines, J.L. Zamorano, S. Achenbach, H. Baumgartner, J.J. Bax, H. Bueno, V. Dean, C. Deaton, C. Erol, R. Fagard, R. Ferrari, D. Hasdai, A.W. Hoes, P. Kirchhof, J. Knuuti, P. Kolh, P. Lancellotti, A. Linhart, P. Nihoyannopoulos, M.F. Piepoli, P. Ponikowski, P.A. Sirnes, J.L. Tamargo, M. Tendera, A. Torbicki, W. Wijns, S. Windecker, R. Document, J. Knuuti, M. Valgimigli, H. Bueno, M.J. Claeys, N. Donner-Banzhoff, C. Erol, H. Frank, C. Funck-Brentano, O. Gaemperli, J.R. Gonzalez-Juanatey, M. Hamilos, D. Hasdai, S. Husted, S.K. James, K. Kervinen, P. Kolh, S.D. Kristensen, P. Lancellotti, A.P. Maggioni, M.F. Piepoli, A.R. Pries, F. Romeo, L. Ryden, M.L. Simoons, P.A. Sirnes, P.G. Steg, A. Timmis, W. Wijns, S. Windecker, A. Yildirir, J.L. Zamorano, 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology, *Eur Heart J.* 34 (38) (2013) 2949–3003.
- [23] M.B. Elming, J. Lonborg, T. Rasmussen, J.T. Kuhl, T. Engstrom, N. Vejstrup, L. Kober, K.F. Kofoed, Measurements of pericardial adipose tissue using contrast enhanced cardiac multidetector computed tomography-comparison with cardiac magnetic resonance imaging, *Int. J. Cardiovasc. Imaging* 29 (6) (2013) 1401–1407.
- [24] A.A. Mahabadi, N. Reinsch, N. Lehmann, J. Altenbernd, H. Kalsch, R.M. Seibel, R. Erbel, S. Mohlenkamp, Association of pericoronary fat volume with atherosclerotic plaque burden in the underlying coronary artery: a segment analysis, *Atherosclerosis* 211 (1) (2010) 195–199.
- [25] P. Maurovich-Horvat, K. Kallianos, L.C. Engel, J. Szymonifka, C.S. Fox, U. Hoffmann, Q.A. Truong, Influence of pericoronary adipose tissue on local coronary atherosclerosis as assessed by a novel MDCT volumetric method, *Atherosclerosis* 219 (1) (2011) 151–157.
- [26] M.M. Hell, D. Bittner, A. Schuhbaeck, G. Muschiol, M. Brand, M. Lell, M. Uder, S. Achenbach, M. Marwan, Prospectively ECG-triggered high-pitch coronary angiography with third-generation dual-source CT at 70 kVp tube voltage: feasibility, image quality, radiation dose, and effect of iterative reconstruction, *J. Cardiovasc. Comput. Tomogr.* 8 (6) (2014) 418–425.
- [27] V.Y. Cheng, D. Dey, B. Tamarappoo, R. Nakazato, H. Gransar, R. Miranda-Peats, A. Ramesh, N.D. Wong, L.J. Shaw, P.J. Slomka, D.S. Berman, Pericardial fat burden on ECG-gated noncontrast CT in asymptomatic patients who subsequently experience adverse cardiovascular events, *JACC Cardiovasc. Imaging* 3 (4) (2010) 352–360.
- [28] K. Harada, T. Amano, T. Uetani, Y. Tokuda, K. Kitagawa, Y. Shimbo, A. Kunimura, S. Kumagai, T. Yoshida, B. Kato, M. Kato, N. Marui, H. Ishii, T. Matsubara, T. Murohara, Cardiac 64-multislice computed tomography reveals increased epicardial fat volume in patients with acute coronary syndrome, *Am. J. Cardiol.* 108 (8) (2011) 1119–1123.
- [29] S. Partovi, A. Arbab-Zadeh, Epicardial fat volume quantification by noncontrast CT: trimming away the fat from the meat, *J. Cardiovasc. Comput. Tomogr.* 9 (4) (2015) 310–312.