Original Article
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Clinical Utility of CT-based Attenuation-correction in Myocardial Perfusion SPECT Imaging

Miyokard Perfüzyon SPECT Görüntülemede, BT Bazlı Atenüasyon Düzeltmenin Klinik Yararı

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Abstract

Objectives: We aimed to investigate and compare the role of computed tomography (CT)-based attenuation-corrected images (AC) with non-attenuation-corrected images (NAC) obtained by single-photon emission computed tomography/computed tomography (SPECT/CT) myocardial perfusion imaging (MPI).

Methods: The data of 124 patients who were applied one-day stress-rest Tc-99m sestamibi SPECT/CT MPI and who had coronary angiography (CAG) results within ±3 months were retrospectively reviewed. AC and NAC images were visually evaluated by two nuclear medicine specialists in a consensus. CAG results were used as the reference standard.

Results: Specificity, sensitivity, and accuracy were calculated as 66%, 61%, 71%, 79% and 69%, 70% for AC and NAC imaging in the whole group, respectively. There was no statistically significant difference between AC and NAC images for specificity, sensitivity, and accuracy in the male and female subgroups. In the diagnosis of right coronary artery (RCA) disease, CT AC significantly increased the specificity from 87% to 96%. However, in the left anterior descending artery (LAD) region, the specificity was significantly reduced from 95% to 77%.

Conclusion: CT-based AC did not significantly contribute to diagnostic performance for increased specificity for the RCA and reduced specificity in the LAD region. Therefore, AC images should always be evaluated side by side with NAC images to benefit from the different advantages of both techniques.

Keywords: Myocardial perfusion, scintigraphy, attenuation correction

Öz

Amaç: Miyokard perfüzyon görüntülemede, atenüasyon artefaktları tetkik spesifitesini etkilemektedir. Çalışmamızda tek foton emisyonlu bilgisayarlı tomografi/bilgisayarlı tomografi (SPECT/BT) sistemi ile elde edilen atenüasyon düzeltmesi yapılmış görüntüler, düzeltme yapılmamış görüntüler ile karşılaştırıldı. Bilgisayarlı tomografi (BT) bazlı atenüasyon düzeltmenin klinik pratiğe katkısı araştırıldı.

Yöntem: Tek gün protokolü ile stres-rest Tc-99m sestamıbı SPECT/BT yapılan ve ±3 ay içinde koroner anjiyografi (CAG) sonuçları mevcut olan 53 kadın, 71 erkek 124 hastanın datası retrospektif olarak incelendi. Atenüasyon düzeltmesi yapılmış ve yapılmamış görüntüler iki nükleer tıp uzmanı tarafından vizüel olarak değerlendirildi. Bulgular referans standart kabul edilen CAG sonuçları ile karşılaştırıldı.

Bulgular: Atenüasyon düzeltmesi yapılmış ve yapılmamış görüntüleme için sırasıyla tüm grupta, spesifite %66, %60; sensitivite %71, %79 ve doğruluk %69, %70 olarak hesaplandı ($p>0,05$). Kadın ve erkek subgruplarında da atenüasyon düzeltmesi yapılmış ve yapılmamış görüntüler arasında, spesifite, sensitivite ve doğruluk için istatistiksel olarak anlamlı fark saptanmadı. Sağ koroner arter (RCA) hastalığının dedekte edilmesinde

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BT ile atenüasyon düzeltmesi, spesifiteyi %87'den %96'ya yükseltti. Ancak sol ön inen arter (LAD) alanında BT bazlı atenüasyon düzeltme ile spesifitenin %95'ten %77 ye gerilediği görüldü (p=<0,0001).

Sonuç: BT bazlı atenüasyon düzeltmesi, RCA alanı için artan spesifite dışında tüm hasta grubunda tanısal performansa anlamlı bir katkı sağlamamış, LAD alanında da spesifiteyi azaltmıştır. Bu nedenle atenüasyon düzeltmesi yapılmış görüntüler, düzeltme yapılmamış görüntüler ile yan yana, klinik veriler eşliğinde değerlendirilmelidir.

Anahtar kelimeler: Miyokard perfüzyon, sintigrafi, atenüasyon düzeltme

Introduction

Myocardial perfusion imaging (MPI) is a non-invasive diagnostic test applied in the evaluation of functional severity of known or suspected coronary artery disease (CAD) (1,2). Although the diagnostic currency of MPI is accepted, attenuation developing secondary to the photon absorption caused by soft tissues such as the breast, diaphragm, thoracic wall, and prominent subdiaphragmatic gastrointestinal activity can cause the artifacts. These artifacts can ultimately affect the diagnostic performance of the test (3). Many methods such as electrocardiogram (ECG) gated imaging, prone imaging, and transmission mapping with external radioactive sources have been developed to overcome attenuation artifacts (4,5). Attenuation artifacts are partially eliminated by ECG-gated single-photon emission computed tomography (SPECT) imaging, which is frequently used in clinical practice to assess regional myocardial contractility (6). However, in inhomogeneous attenuation regions, such as thorax, attenuation maps obtained by transmission imaging are thought to be more effective than ECG-gated SPECT in attenuation correction (7). Transmission imaging conducted with external radioactive sources brings several disadvantages, such as cross-talk between emission and transmission energies and suboptimal image quality (8,9). Recently developed combined SPECT and low dose computed tomography (CT) devices can generate the transmission maps with high count and resolution in a short time, and enhance the image quality (10). Many previous studies have shown that SPECT/CT MPI has high diagnostic accuracy in the evaluation of CAD (11). Nevertheless, it increases radiation exposure, can mask some perfusion defects, and reveal false-positive defects with new unexpected artifacts (10,12). Therefore, the discussions continue on the routine usage of SPECT/CT MPI in clinical practice.

Materials and Methods

Patients

A total of 124 patients in the age group of 35-82 (median age 61.8±11.4 years), including 71 males (57.3%) and 53 females (42.7%), who were referred to our clinic for evaluation of myocardial perfusion in 2012 and 2014 with the diagnosis of known or suspected CAD, were enrolled in our retrospective study. One-day stress-rest Tc-99m sestamibi (MIBI) ECG gated SPECT/CT imaging was applied to all subjects. All patients had available CAG data within three months before or after MPI.

Patients who were not able to perform treadmill exercise test due to their clinical condition, who had undergone pharmacological stress, and patients with left bundle branch block or arrhythmia causing insufficient counting statistics/quality in ECG-gated imaging were excluded from the study. The cases were divided into subgroups of females and males. Patients were instructed to read the detailed information form before the procedure and signed the consent form. The study protocol was approved by the Ethics Committee of Clinical Investigations of our hospital with decision number 372/2-97 dated 06.06.2016. The study was performed in accordance with the ethical standards laid down by the Declaration of Helsinki in 1964 and all its subsequent revisions. The medical history and symptoms of the patients are given in Table 1.

Patient Preparation and SPECT/CT Myocardial Perfusion Imaging Protocol

After at least 4 h of fasting, an exercise stress test was performed in patients according to modified Bruce protocol. Calcium channel blockers or beta-blockers were stopped 48 hours before imaging and long-acting nitrates

Table 1. Symptoms and medical history of the patients

Variables	n	Percentile (%)
Hypertension	81	65.3
Hyperlipidemia	62	50
Diabetes	34	27.4
Smoking	60	48.4
Typical angina pectoris	34	27.4
Atypical chest pain	30	24.2
Asymptomatic	60	48.4
Myocardial infarction	12	9.7
Coronary artery bypass grafting	16	12.9
Percutaneous coronary intervention	36	29

were discontinued the day before the study if there was no medical contraindication. 8-10 millicuries (mCi) [296-370 megabecquerels (MBq)] Tc-99m MIBI was injected to each patient during exercise when target heart rate was reached or an indication for the exercise termination (physical fatigue, progressive angina, systolic blood pressure lower than 20 mmHg, systolic blood pressure higher than 250 mmHg, ST depression more than 3 mm, etc.) was observed. After the injection, patients were fed with greasy foods that accelerated the hepatobiliary clearance of the radiopharmaceutical. ECG stress images were recorded after about 45 minutes. At least 2 h after the stress test, 24-30 mCi (888-1110 MBq) of Tc-99 m MIBI injected intravenously and resting ECG-gated images were obtained after approximately 45 min following injection. Studies were conducted using a Siemens Symbia T6 (Healthcare, Erlangen, Germany) dual-head SPECT/CT hybrid camera equipped with high-resolution low energy parallel hole collimators. When the patients were in the supine position and the angle between the collimators was 90°, in a 64×64 matrix, a total of 60 projections were acquired using a step & shot technique over a 180° rotation from the 45° right anterior oblique to the 45° left posterior oblique, in 20% energy window centered on the 140 keV energy peak of Tc-99m MIBI and with a zoom factor of 1.33.

For ECG-gated SPECT imaging, all patients were monitored with a 3-lead ECG. Images were gated at 8 frames per cardiac cycle. A low-dose CT study (140 kV, 2.5 mA) of the chest was performed for attenuation mapping during both stress and rest imaging following the emission study. Obtained SPECT and AC images were automatically reconstructed using standard filtered back-projection technique and FLASH 3D iterative reconstruction algorithm, respectively. Emission and transmission data were visually inspected on axial, sagittal, and coronal fusion plans, and misalignments were manually corrected in 50 patients (40.3%).

Evaluation

Analysis of AC and NAC images was performed visually by two nuclear medicine specialists in consensus. Sections on the short, vertical, and horizontal axes obtained by the Cedars Sinai Quantitative Perfusion Gated SPECT (QPS-QGS) software packages (Cedars Sinai Medical Center, Los Angeles, CA) were evaluated.

The left ventricle was evaluated in association with the presence or absence of perfusion defects based on a 17-segment model of three main coronary arterial territories left anterior descending (LAD), left circumflex (LCx), and right coronary arteries (RCA) recommended by the American Heart Association (13).

MPI results were reported as normal in the absence of perfusion defects in both stress and rest images. If the perfusion was normal in resting images in areas where a perfusion defect was detected in stress images, ischemia (reversible defect) was reported. MPI result was reported as infarct (fixed defect) in the presence of a matched perfusion defect in both stress and rest images. However, when NAC images were reported, ECG-gated images were taken into account and areas with a fixed perfusion defect without any wall motion abnormality was interpreted as artifacts.

Coronary Angiography

CAG results of 124 patients obtained within ±3 months were analyzed. CAG findings served as the reference standard for the diagnostic performance of MPI. A reduction in the luminal diameter of ≥50% in at least one of the three coronary arteries was defined as a significant stenosis.

Statistical Analysis

All statistical analysis were performed using the IBM SPSS version 21.0 for Windows program (SPSS, Chicago, Ill.). The mean, standard deviation, minimum, and maximum values of all numerical variables were calculated. NAC and AC images were compared in terms of sensitivity, specificity, and accuracy. The McNemar test was used for statistical difference analysis in assessing the diagnostic accuracy (sensitivity, specificity, accuracy) obtained by NAC and AC imaging. Results with a p value of less than 0.05 were regarded as statistically significant.

Results

Myocardial Perfusion Imaging

In NAC images, perfusion defects were compatible with ischemia and infarction in 48 (38.7%) and 17 (%13.7) cases, respectively. Both ischemia and infarction were detected in 10 cases (8.1%). In 8 cases (6.5%) with a fixed perfusion defect in the inferior myocardial wall, MPI results were evaluated favorably for diaphragmatic attenuation because wall motion was normal in these cases. In 41 patients (33%), MPI findings were reported as normal. When the AC images of all patients were assessed, 39 cases (31.4%) were diagnosed with ischemia, 19 cases (15.3) were diagnosed with infarction, 9 cases (7.3%) were found to have both ischemia and infarction. MPI findings were reported as normal according to AC images in 57 (46%) patients.

Coronary Angiography

There was significant stenosis in 66 cases according to CAG results. Of the cases, 9 had three vessels, 17 had two vessels, 40 had single-vessel stenosis. 58 (46.8%) patients had no critical stenosis. Table 2 summarizes the MPI results of NAC and AC images according to CAG findings.

In the entire study group, CT increased specificity (60% and 66% for NAC and AC imagings, respectively) and decreased sensitivity and accuracy (79%, 71%, and 70% and 69% for NAC and AC imagings, respectively) (Table 3). However, the results were not statistically significant. Moreover no significant effect of AC imaging was found in the male and female subgroups (Table 3).

Table 2. Compliance with CAG findings of AC and NAC MPI results

			CAG (-)		CAG (+)		Total
			Male	Female	Male	Female	
	NAC	-	20	15	9	5	124
		+	6	17	36	16	
	AC	-	20	18	14	5	124
		+	6	14	31	16	
LCx	NAC	-	46	40	10	3	124
		+	2	6	13	4	
	AC	-	54	36	8	7	124
		+	3	1	6	9	
RCA	NAC	-	38	43	9	6	124
		+	11	1	13	3	
	AC	-	45	44	11	6	124
		+	4	0	11	3	
LAD	NAC	-	45	30	9	8	124
		+	0	4	17	11	
	AC	-	39	25	10	5	124
		+	6	13	16	10	

CAG: Coronary angiography, AC: CT-based attenuation corrected images, NAC: Non-attenuation corrected images, LAD: Left anterior descending artery, RCA: Right coronary artery, LCx: Left circumflex artery, MPI: Myocardial perfusion imaging

In the diagnosis of RCA disease, the sensitivity decreased slightly according to AC imaging. Furthermore, for the RCA region, CT-AC increased specificity and accuracy both in the entire study population and subgroups (there was statistical significance in the study group and the male subgroup regarding specificity). In the LCx territory with AC imaging, sensitivity decreased mildly, while a slight increase was observed in terms of specificity and accuracy. However, CT had no statistically significant effect on the diagnostic performance in the entire group and subgroups of patients in the LCxterritory. In the detection of LAD artery stenosis, with the effect of CT-AC, the sensitivity and accuracy did not significantly change, while specificity significantly decreased. This reduction of specificity, which was determined by attenuation correction in the LAD region, was observed similarly in subgroups as well (Table 4).

Discussion

When evaluating CAD, in addition to morphological information about the location and grade of coronary artery stenosis, functional severity should be determined for the selection of the patient group that will benefit from revascularization (1,14). There are several studies showing the prognostic value of SPECT MPI used for this purpose in evaluating known or suspected CAD (15). However, the diagnostic performance of SPECT MPI is limited by low spatial resolution. The artifacts caused by soft tissue attenuation and subdiaphragmatic activity affect the diagnostic accuracy of SPECT MPI, especially by reducing specificity. Therefore,artifacts reduce the cost-effectiveness of this technique (16). Methods such as ECG-gated imaging, prone imaging, and transmission mapping have been developed for the elimination of attenuation artifacts, but all methods have some limitations. For instance, ECG-gated SPECT, which is very practical for clinical routine use, is problematic in distinguishing artifacts from ischemic tissue.

Table 3. Diagnostic value of NAC versus AC images

	Sensitivity %	p value	Specificity %	p value	Accuracy %	p value
Total (n=124)						
NAC	79 (0.67-0.88)	0.146	60 (0.47-0.73)	0.328	70 (0.61-0.78)	0.864
AC	71 (0.59-0.82)		66 (0.52-0.78)		69 (0.60-0.77)	
Males (n=71)						
NAC	80 (0.65-0.90)	0.134	77 (0.56-0.91)	1.000	79 (0.68-0.88)	0.333
AC	69 (0.53-0.82)		77 (0.56-0.91)		72 (0.60-0.82)	
Females (n=53)						
NAC	76 (0.53-0.92)	1.000	47 (0.29-0.65)	0.356	58 (0.44-0.72)	0.528
AC	76 (0.53-0.92)		56 (0.38-0.74)		64 (0.50-0.77)	

AC: CT-based attenuation corrected images, NAC: Non-attenuation corrected images

While prone imaging, which is used to solve inferior wall artifacts, occasionally causes new artifacts in the anterior wall and prolongs the imaging time. Moreover, transmission maps generated by external radioactive sources, which seem to be more effective in inhomogeneous attenuation regions, also have disadvantages such as suboptimal quality transmission images and additional imaging time (8,9). In the transmission study conducted with the combined SPECT/CT system, the imaging time is not prolonged and the image quality increases due to high counting and resolution. However, new artifacts may arise and additional radiation exposure occurs (9,10).

Some studies evaluating the diagnostic efficiency of AC MPI reported that CT-AC increased specificity and accuracy significantly, while others reported that it decreased sensitivity in CAD detection with the improvement of specificity (17,18,19). In a study conducted with 120 patients, when AC images were compared with NAC imagings, the overall sensitivity decreased significantly from 87% to 70%. Overall specificity increased from 54% to 62%, although it was not statistically significant. In addition, the accuracy did not show any significant difference (12). In our study, there was no statistically significant difference between AC and NAC imaging regarding sensitivity specificity and accuracy. In the entire study group, CT-AC increased specificity from 60% to 66% and decreased sensitivity and accuracy from 79% to 71% and from 70% to 69%, respectively. However, their

Table 4. Diagnostic value of NAC vs AC images according to coronary arterial territories

	Sensitivity (%)	p value	Specificity (%)	p value	Accuracy	p value
RCA						
NAC	52 (0.34-0.69)	NS	87 (0.80-0.94)	0.011	78 (0.70-0.85)	NS
AC	45 (0.28-0.63)		96 (0.92-1.00)		83 (0.75-0.89)	
LCx						
NAC	57 (0.37-0.74)	NS	91 (0.84-0.96)	NS	83 (0.75-0.89)	NS
AC	50 (0.31-0.69)		96 (0.89-0.99)		85 (0.77-0.91)	
LAD						
NAC	62 (0.47-0.76)	NS	95 (0.88-0.99)	<0.0001	83 (0.75-0.89)	NS
AC	63 (0.47-0.78)		77 (0.67-0.86)		73 (0.64-0.80)	
RCA, males						
NAC	59 (0.39-0.80)	NS	78 (0.66-0.89)	0.019	72 (0.60-0.82)	NS
AC	50 (0.29-0.71)		92 (0.84-1.00)		79 (0.68-0.88)	
RCA, females						
NAC	33 (0.03-0.64)	NS	98 (0.93-1.00)	NS	87 (0.75-0.95)	NS
AC	33 (0.03-0.64)		100 (1.00-1.00)		89 (0.77-0.96)	
LCx, males						
NAC	57 (0.34-0.77)	NS	96 (0.86-0.99)	NS	83 (0.72-0.91)	NS
AC	43 (0.18-0.71)		95 (0.85-0.99)		85 (0.74-0.92)	
LCx, females						
NAC	57 (0.20-0.94)	NS	87 (0.77-0.97)	NS	83 (0.70-0.92)	NS
AC	56 (0.30-0.80)		97 (0.86-1.00)		85 (0.72-0.93)	
LAD, males						
NAC	65 (0.44-0.83)	NS	100 (0.92-1.00)	0.0017	87 (0.77-0.94)	NS
AC	62 (0.41-0.80)		87 (0.73-0.95)		77 (0.66-0.87)	
LAD, females						
NAC	58 (0.34-0.80)	NS	88 (0.73-0.97)	0.0074	77 (0.64-0.88)	NS
AC	67 (0.38-0.88)		66 (0.49-0.80)		66 (0.52-0.78)	

(Data in parentheses are 95% confidence intervals). AC: CT-based attenuation-corrected images, NAC: Non-attenuation corrected images, LAD: Left anterior descending artery, RCA: Right coronary artery, LCx: Left circumflex artery, NS: Not statistically significant differences were both non-significant. In the literature, CT-AC improves the specificity in a general manner, while it results in different conclusions in terms of sensitivity and accuracy (20). This difference of outcomes may also be related to group characteristics, subjectivity affecting visual image analysis, and individual differences in interpreters, as well as technical reasons such as software used for reconstruction of the study, the use of scatter correction and resolution recovery (21,22,23). The pattern of the patients in the study group and the effect of the individual trends of the interpreters are also observed in the work of Sharma et al. (19) which used the same method and the same equipment to interpret the image.

Many factors affecting the outcome of clinical trials make it difficult to determine the diagnostic efficacy of CT-AC in CAD detection. However, as AC imaging provides high left ventricular count homogeneity, attenuation correction is thought to facilitate the separation of patients with positive and negative data according to coronary angiography. In a study conducted by Płachcińska et al. (6), specificity and accuracy in CAD detection increased statistically through AC imaging, and the increase in specificity was also observed in the male and female subgroups. According to Huang et al. (24), CT-AC reduced the defect size in the inferior wall in both male and female groups; however, AC imaging was found to be more beneficial in male than in female subgroups as diaphragmatic attenuation artifact in the inferior wall was seen more frequently in men than in women. Moreover, according to this study, attenuation correction increased the specificity for RCA disease from 77.9% to 98.7%; hence, the contribution of attenuation correction was most commonly seen in the RCA territory (24). As the current study demonstrated, the vascular area that most benefited from attenuation correction was RCA. Similar to the literature, attenuation correction yielded a decrease in the sensitivity in the whole group, while the specificity increased in the whole group and male subgroup (6).

In our study, there was no statistically significant difference in sensitivity, specificity, and accuracy between AC and NAC images in the LCx territory, as in the literature, for both whole group and subgroups. Conflicting results are reported for the LAD region (25). There are also papers that have reported that attenuation correction increases the capacitance of the detection of LAD disease (26). In contrast to Wolak et al. (27), AC imaging has also been reported to be useful in female patients (6). Additionally, some publications have argued that apical defects observed in AC images may be secondary to true apical thinning (28). It has been reported that artifacts observed in the anterior wall of NAC images were corrected in AC images (29). In the current study, however, there was no statistically significant change in sensitivity in the whole group between AC and NAC imaging in LAD region, whereas the specificity was observed to decrease in the whole group, besides the subgroups (Figure 1). In accordance with the current study, it has been reported in the literature that CT-AC reduced specificity in LAD territory and it is not sufficient for the elimination of breast artifacts, as well as it has been informed that new defects occasionally arise from the apical, anterior and septal wall with AC imaging (24,30). It is known that the attenuation map (small field of view), which does not contain the entire thoracic wall, can cause these defects in oversized patients. Besides, the underestimation of the attenuation effect on the anterior thoracic wall due tomis registration of the emission and transmission images (caused by patient movement or respiratory motion) can also create new defects (31). Although re-registration seems beneficial, manual correction is based on the visual evaluation, and the correction process can vary depending on the user's experience (32). Furthermore, regardless of misalignment, overestimation of the attenuation correction in the inferior wall, hence, a relative decrease in other segments and false perfusion defects may occur (31). All misalignments in our study were corrected manually. Nonetheless, lower specificity and accuracy values were obtained in AC images in the LAD territory, and there was no statistically significant improvement in the LCx field with attenuation correction. This is thought to be caused by the effect of user-dependent realignment or overcorrection of the inferior wall, as mentioned in the literature.

Study Limitations

Our study was planned retrospectively with a single centered, relatively small patient sample. Another limitation of our study is that a functional diagnostic test such as SPECT MPI for the diagnosis of CAD is compared with an anatomical method such as invasive angiography as a reference method. Moreover, we did not have a prognostic value of AC MPI in our study because there were no follow-up details of the patients. According to our own clinical experience, AC imaging contributes to the detection of perfusion defects in the inferior wall; however, it reduces specificity in the evaluation of the anterior wall. Therefore, it should be kept in mind that the inferior wall defects, which are only observed in NAC images, and anterior wall defects, which are detected only in AC images, may be artefacts. It is thought that NAC images should be evaluated primarily for the findings of anterior, anteroseptal, anterolateral walls and apex.

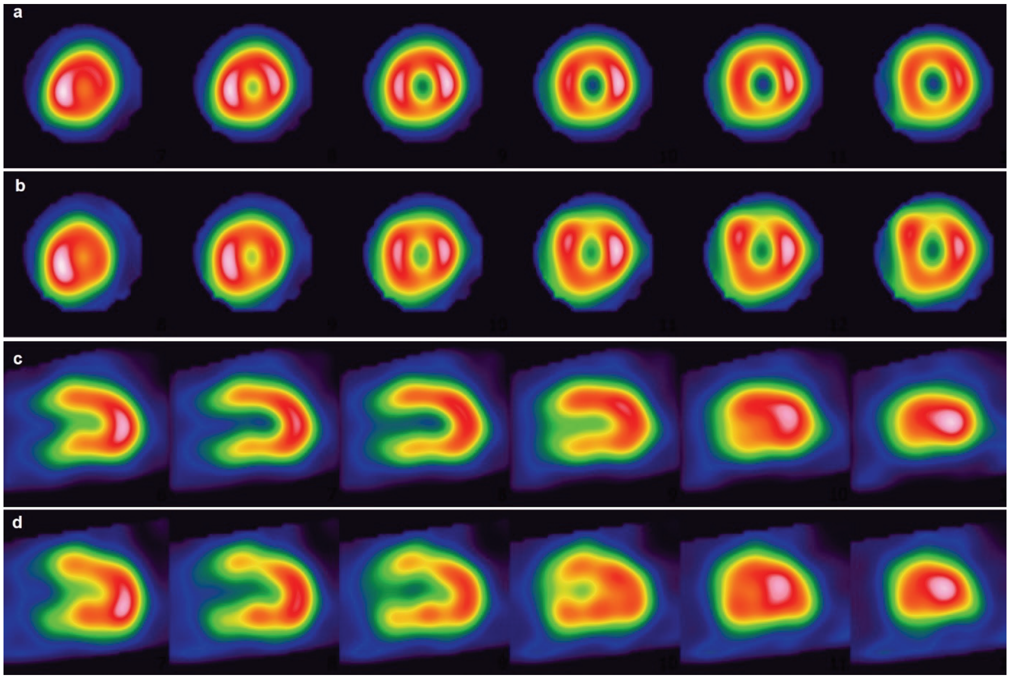

Figure 1. Non-attenuation corrected images (a, c) and CT-based attenuation corrected images (b, d) in short- and vertical long-axis planes. CT-based attenuation correction overcomes the perfusion defect related to diaphragmatic attenuation in the inferior myocardial wall. However, an anterior wall defect occurs as a new artifact
CT: Computed tomography

Conclusion

In conclusion, when using CT-based attenuation correction in MPI, a visual review of raw data along with the reconstructed images is required for the correct registration of the emission and transmission data. Additionally, AC images should always be evaluated side by side with NAC images to benefit from the different advantages of both techniques.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Clinical Investigations of our hospital with decision number 372/2-97 dated 06.06.2016. The study was performed in accordance with the ethical standards laid down by the Declaration of Helsinki in 1964 and all its subsequent revisions.

Informed Consent: Informed consent was obtained.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.H., N.Ç., Concept: F.H., N.Ç., Design: F.H., N.Ç., Data Collection or Processing: F.H., N.Ç., Analysis or Interpretation: F.H., Literature Search: F.H., Writing: F.H.

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