Is there an incremental value to use myocardial perfusion imaging with or without CT attenuation for the diagnosis of coronary artery disease? A study in Chinese patients

Wen Chong Xin[1] MD,
Xiao Liang Shao[1] MD,
Yue Tao Wang[1] MD,
Jian Feng, Wang[1] MD,
Xiao Song Wang[1] MD,
Ling Yang[2] MD,
Wei Yang[1] MD,
Fei Fei Zhang[1] MD

Wen Chong Xin, Xiao Liang Shao are the first co-authors

1. Department of Nuclear Medicine
2. Department of Cardiology, The Third Affiliated Hospital of Soochow University, Changzhou, 213003, China

Keywords: CT attention correction -Myocardial perfusion imaging -Single photon emission computed tomography -Coronary artery disease

Corresponding author:
Yue Tao Wang MD, Tel.: +86013852040196,
Fax: 86-519-86621235, E-mail: yuetao-w@163.com and
Jian Feng Wang MD, Tel.: +86013775101074,
Fax: 86-519-86621235, E-mail: wjf840623@163.com

Received:
27 December 2017
Accepted revised :
28 February 2018

Abstract

Objective: To evaluate whether computed tomography attention correction (CTAC) has incremental diagnostic value for single photon emission tomography (SPET) myocardial perfusion imaging (MPI) for the detection of coronary artery disease (CAD) in Chinese patients. **Subjects and Methods:** This retrospective study consisted of 181 suspected CAD patients who underwent one-stop SPET examination by MPI combined with a CT scan. Two observers independently evaluated non-attenuation correction (NAC) and CTAC MPI images, and coronary angiography (CAG) results were used as reference standards. The diagnostic efficacies of the two methods were compared. **Results:** a) In the whole group, the sensitivity, specificity and accuracy for the detection of CAD were found to be 75.7%, 55.1% and 63.5% for NAC images and 52.7%, 86.9% and 72.9% for CTAC images, respectively; the areas under the receiver operating characteristic curves (AUC) were 0.654 and 0.698 (P>0.05). b) The accuracy of CTAC and the AUC were significantly higher than those for NAC in Chinese males. c) The accuracy of CTAC was also significantly increased for the right coronary artery (RCA) territory and in overweight patients (BMI≥24), although differences in the AUC were marginally insignificant. **Conclusion:** Compared to NAC MPI, CTAC improved SPET MPI specificity but decreased sensitivity, leading to no obvious improvement in overall accuracy for the diagnosis of CAD in Chinese patients. However, CTAC might be of value in the subgroups of males and overweight patients and for the RCA territory. In routine clinical application, the integration of NAC and CTAC findings combined with CAD pre-test probability could improve MPI diagnostic performance.

Hell J Nucl Med 2018; 21(1): 48-54 *Epub ahead of print: 20 March 2018* *Published online: 25 April 2018*

Introduction

Radionuclide myocardial perfusion imaging (MPI) is a well-established noninvasive method to diagnose coronary artery disease (CAD). According to the Chinese guidelines for stable CAD percutaneous coronary intervention (PCI) therapy, myocardial ischemia determined by MPI is an important basis for the implementation of PCI therapy [1]. However, it was found that obesity and breast tissue in women may cause reduction in radioactivity in the inferior or anterior wall, resulting in false positives in clinical practice. Men are more likely to have diaphragmatic attenuation artifacts, while women mainly have breast-related attenuation, especially those with breast hypertrophy or dense breast tissue. Artifacts caused by tissue absorption result in a significant reduction in radioactivity in the inferior or anterior cardiac wall, mimicking myocardial ischemia and decreasing the specificity in diagnosing CAD.

Researchers have long attempted to use attenuation correction (AC) to improve single photon emission tomography (SPET) specificity. Computed tomography attention correction using CT-derived transmission maps for AC, is one of the most widely used methods. Many studies [2, 3] have shown that CTAC MPI is superior to non-attenuation correction (NAC) in improving the image quality and accuracy in the diagnosis of CAD. However, there was a study showing that CTAC has limited value in this regard [4]. Other researchers [5] even found that CTAC could produce new artifacts while eliminating other artifacts in the apex and anterior wall of the left ventricular regions. Therefore, whether CTAC MPI has additional diagnostic value for CAD is still controversial. Moreover, with the wider availability of hybrid SPET/CT cameras in China, SPET/CT can accomplish both MPI and CTAC simultaneously, but there were few studies that focus on whether CTAC has any incremental value for MPI in Chinese patients with suspected CAD. The purpose of the present study was to evaluate the diagnostic efficacy of CTAC MPI for the detection of

CAD with a SPET/CT one-stop examination in Chinese patients, who have a different somatotype from that of patients in western countries.

Subjects and Methods

Subjects

We retrospectively studied 181 consecutive suspected CAD patients (123 men and 58 women, 61.5±8.7 years old, body mass index (BMI) 25.1±3.0kg/m^2) who underwent SPET/CT scans at the Third Affiliated Hospital of Soochow University from March 2012 to September 2016. The BMI was calculated as follows: BMI=weight (kg)/height (m^2), and patients were considered overweight at a BMI≥24 according to the Chinese guidelines [6]. All patients received invasive coronary angiography (CAG) within three to six months after MPI; single or multi vessels stenosis of more than 50% was defined as CAD [2]. Exclusion criteria were as follows: a) prior myocardial infarction (MI), b) prior PCI or coronary artery bypass graft (CABG), c) cardiac plasma troponin-positive test result, d) age<18 years old and e) pregnancy. The protocol was approved by the ethics committee of the Third Affiliated Hospital of Soochow University, and written informed consent was obtained from each patient.

Imaging acquisition

Each patient underwent a stress-rest technetium-99m methoxy isobutyl isonitrile ^{99m}Tc-sestamibi (^{99m}Tc-MIBI) MPI according to a two day standard clinical protocol. Drugs such as beta-blockers or other drugs that could reduce heart rate or affect adenosine stress test were discontinued before the study. Patients who were able to exercise underwent a treadmill exercise test following the Bruce or modified Bruce protocol, while patients who were unable to exercise were infused intravenously with adenosine, according to standard protocols [7, 8].

Myocardial imaging by SPET was performed 60-90 minutes after injection of ^{99m}Tc-MIBI at a dose of 740-925MBq for both the stress and rest studies. A dual-detector 90° camera (Symbia T16, Siemens Medical Systems, Erlangen, Germany) equipped with a low-energy and high-resolution parallel hole collimator was used for data acquisition, with a 20% window centered on the 140keV peak energy. Sixty-four images covering 180° (from the right anterior oblique at 45° to the left posterior oblique at 45°) were acquired with a 64×64 matrix and 1.45×magnification. Patients were placed in a supine position with their arms over their heads. Tomographic image acquisition for MPI was performed first. A low-dose CT chest scan (voltage, 130kv; tube current, 100mAs; thickness, 3mm; scanning range, approximately 20 cm; and pitch, 1.0) was performed in order to obtain attenuation maps that were automatically applied by the processing software to correct the emission data. If the stress imaging was normal, rest imaging was not performed. According to the interpretation of NAC images by two experienced nuclear physicians, normal stress imaging was defined as an absence of perfusion defects [8].

Image processing and analysis

Image data of SPET were processed using ordered subsets expectation maximization (OSEM) reconstruction software with 16 iterations and 2 subsets. These images were fused with the transmission CT images and then converted into CTAC images. If misregistration of the images was found, we manually co-registered the SPET and CT images. The short axis, horizontal long axis and vertical long axis images from NAC and CTAC MPI were obtained. The operation and processing of the above images was completed by experienced nuclear imaging technologists.

Based on qualitative visual interpretation, images from NAC and CTAC were interpreted independently by two experienced nuclear medicine physicians who were unaware of all clinical data and CAG results. If there were any uncertain perfusion defects or decreases in uptake when interpreting the SPET images, the observers combined the NAC and CTAC results to draw a conclusion. A third expert was called in when there was disagreement between the two experienced nuclear physicians. A perfusion defect on stress images in two or more contiguous segments or slices that were partially or absolutely resolved in the rest images was described as myocardial ischemia. A perfusion defect on stress images in two or more contiguous segments or slices that persisted in the rest images was diagnosed as myocardial infarction. A fixed or reversible perfusion defect was considered as CAD [9]. The assignment of myocardial blood supply was determined according to a reference mentioned in a previous study [10].

Statistical analysis

For all statistical analysis in this study, IBM SPSS (Version 21.0) was used. Continuous data are expressed as the mean ±SD, and categorical data are expressed as frequencies and percentage and were compared using a χ^2 test. Unpaired t tests or Wilcoxon nonparametric tests were performed when appropriate to compare parameters between the two groups. The receiver operating characteristic (ROC) curves were drawn by MedCalc (V.15.2.0) software, and the areas under the ROC curves (AUC) were semi-quantitatively analyzed. A two-sided P value of 0.05 or lower was regarded as statistically significant.

Results

General information of the subjects

The demographic data, clinical characteristics and the CAG results for all patients are listed in Table 1. Among the 181 Chinese patients; their pre-test probability of CAD was 50.2%±23.2%. In this study, the only statistically significant difference between males and females is the prevalence of CAD. Significant differences between overweight and normal-weight participants were observed only for hypertension, diabetes and dyslipidemia.

Comparison of sensitivity, specificity, accuracy and AUC for NAC and CTAC for MPI studies in the whole group patients

Table 1. Characteristics of the study populations (n=181).

Clinical characteristics	Value
Age (years old)	61.5±8.7
Sex (male/female)	123/58
BMI (kg/m^2)	25.1±3.0
Pre-test probability of CAD (%)	50.2%±23.2
Chest pain, n (%)	125 (69.1%)
Hypertension, n (%)	129 (71.3%)
Diabetes, n (%)	40 (22.1%)
Dyslipidemia, n (%)	68 (37.6%)
Patients with CAD, n (%)	74 (40.9%)
Single-vessel disease, n (%)	20 (27%)
Double-vessel disease, n (%)	16 (21.6%)
Multi-vessel disease, n (%)	38 (51.4%)
LAD lesions, n (%)	67 (90.5%)
LCX lesions, n (%)	39 (52.7%)
RCA lesions, n (%)	50 (67.6%)

BMI, body mass index; CAD, coronary artery disease; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery.

Compared to NAC MPI, CTAC MPI had a greater specificity (86.9% vs. 55.1%, P<0.001), a reduced sensitivity (52.7% vs. 75.7%, P=0.004) and a slightly higher overall accuracy (72.9% vs. 63.5%, P=0.055) for diagnosing CAD according to the CAG results (Table 2 and Figure 2). The AUC for CTAC MPI was larger than that for NAC MPI (Figure1), but this difference was not statistically significant.

Comparison of sensitivity, specificity, accuracy and AUC for NAC and CTAC for MPI studies in individual coronary arteries (RCA, LAD and LCX)

For the diagnosis of CAD in patients with right coronary artery (RCA) lesions, compared to NAC MPI, CTAC MPI had a significantly increased specificity (93.1% vs. 64.9%, P<0.001), a reduced sensitivity (26.0% vs. 60.0%, P=0.001) and a higher accuracy (74.6% vs. 63.5%, P=0.023). The AUC for CTAC MPI was larger than that for NAC MPI (0.624 vs. 0.596, P=0.463). Of the 107 patients with a normal RCA, there were 48 false-positives with NAC MPI (false-positive rate 44.9%) and 14 false-positives with CTAC MPI (false-positive rate 13.1%), suggesting that 34 cases were corrected by CTAC MPI (an example is illustrated in Figure 5). Additionally, the images of 17 patients with RCA lesions were overcorrected by CTAC MPI (an example is illustrated in Figure 6).

The sensitivity, specificity, accuracy, and AUC for diagnosing CAD patients with left anterior descending coronary artery (LAD) or left circumflex coronary artery (LCX) lesions were not significantly different between NAC and CTAC MPI. The sensitivity, specificity, accuracy and AUC for NAC and CTAC MPI for the detection of clinically relevant CAD (LAD, LCX and RCA) are presented in Table 2 and in Figures 1 and 3.

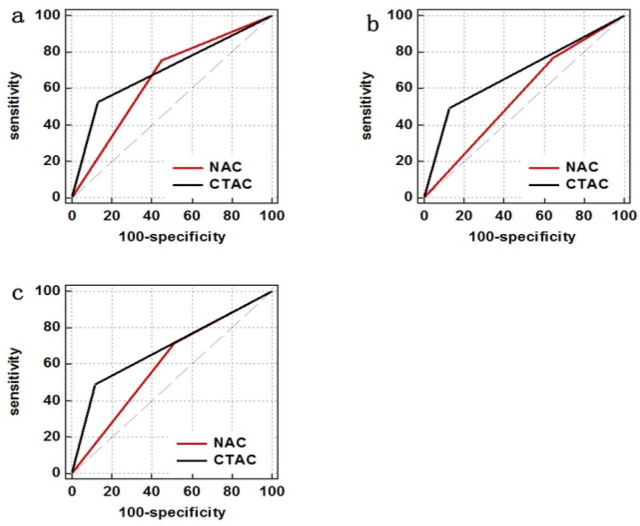

Figure 1. Analysis of the areas under the receiver operating characteristic curves (AUC). a. Overall analysis (AUC for NAC and CTAC studies: 0.654 vs. 0.698, P=0.206). b. Analysis of males (AUC for NAC and CTAC studies: 0.563 vs. 0.681, P=0.0079). c. Analysis of overweight patients (AUC for NAC and CTAC studies: 0.600 vs. 0.686, P=0.054).

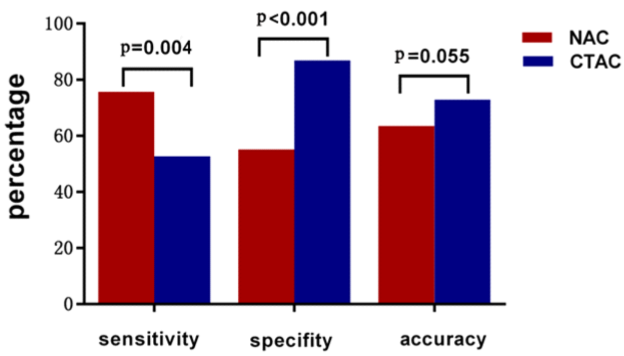

Figure 2. Comparison of sensitivity, specificity and accuracy for NAC and CTAC for MPI studies in the whole group patients.

Comparison of sensitivity, specificity, accuracy and AUC for NAC and CTAC for MPI studies in males and females

For the detection of CAD in Chinese males, compared to NAC MPI, CTAC MPI had a higher specificity (87.1% vs. 35.5%) and accuracy (68.3% vs. 56.1%) and a lower sensitivity (49.2% vs. 77%), and the AUC for CTAC MPI was larger than

__Table 2.__ Comparison of sensitivity, specificity and accuracy for NAC and CTAC for MPI studies in the whole group of patients and for individual coronary arteries.

		Overall	LAD	LCX	RCA
NAC	Sensitivity	75.7%	43.3%	38.5%	60%
	Specificity	55.1%	86.0%	96.5%	64.9%
	Accuracy	63.5%	70.2%	84.0%	63.5%
CTAC	Sensitivity	52.7%	38.8%	25.6%	26.0%
	Specificity	86.9%	90.4%	99.3%	93.1%
	Accuracy	72.9%	71.3%	83.4%	74.6%
	p-value	0.055	0.817	0.887	0.023*

NAC, non-attenuation correction; CTAC, CT attenuation correction; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; P-value refers to test accuracy and P<0.05 is labeled.*

__Table 3.__ Comparison of sensitivity, specificity and accuracy for NAC and CTAC for MPI studies by sex and BMI.

		Males (n=123)	Females (n=58)	Overweight (n=117)	Normal-weight (n=64)
NAC	Sensitivity	77.0%	69.2%	71.4%	84.0%
	Specificity	35.5%	82.2%	48.5%	66.7%
	Accuracy	56.1%	79.3%	58.1%	73.4%
CTAC	Sensitivity	49.2%	69.2%	49.0%	60.0%
	Specificity	87.1%	86.7%	88.2%	84.6%
	Accuracy	68.3%	82.8%	71.8%	75.0%
	P-value	0.049*	0.636	0.028*	0.840

NAC, non-attenuation correction; CTAC, CT attenuation correction; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; P-value refers to test accuracy and P<0.05 is labeled.*

that for NAC MPI (0.681 vs. 0.563). All of these differences were statistically significant (Table 3, Figures 1 and 4).

In diagnosing suspected CAD in females the sensitivity, specificity, accuracy, and AUC showed no significant difference between NAC and CTAC MPI studies.

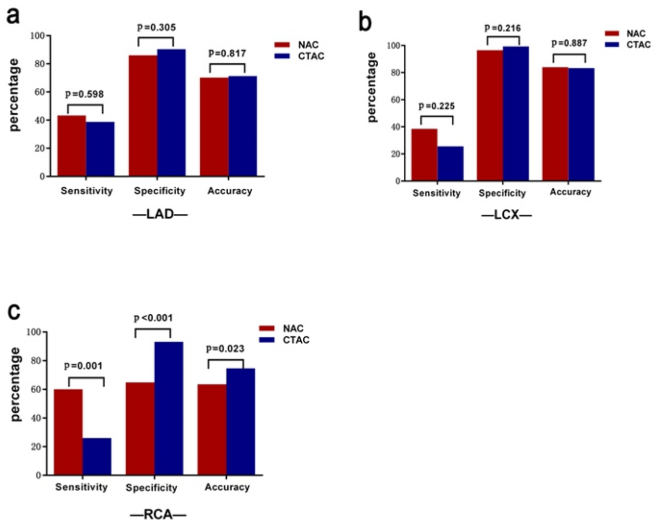

Figure 3. Comparison of sensitivity, specificity and accuracy for NAC and CTAC for MPI studies in individual coronary arteries (LAD (a), LCX (b) and RCA (c)).

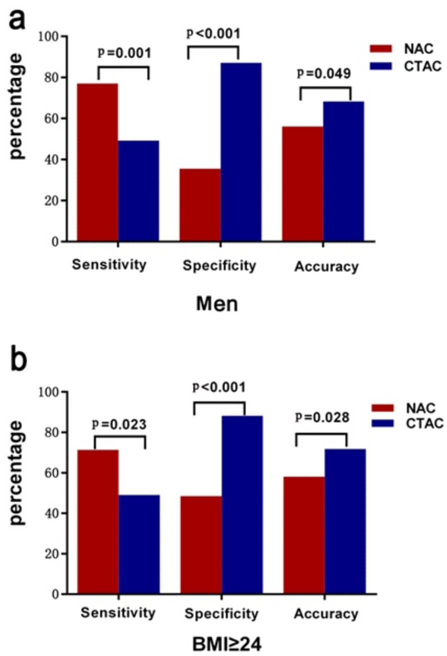

Figure 4. Comparison of sensitivity, specificity and accuracy for NAC and CTAC for MPI studies in men (a) and overweight (b) patients.

Comparison of sensitivity, specificity, accuracy and AUC for NAC and CTAC for MPI studies in overweight and normal-weight patients

Compared to NAC MPI, CTAC MPI showed a higher specificity (88.2% vs. 48.5%, P<0.001) and accuracy (71.8% vs. 58.1%, P=0.028) and a lower sensitivity (49% vs. 71.4%, P=0.023) for the detection of CAD in overweight patients. The AUC for CTAC MPI was slightly larger than that for NAC MPI as well (0.686 vs. 0.600, P=0.054), as shown in Table 3 and

Figures 1 and 4.

In normal-weight Chinese patients the sensitivity, specificity, accuracy and AUC for diagnosing suspected CAD showed no significant difference between NAC and CTAC studies.

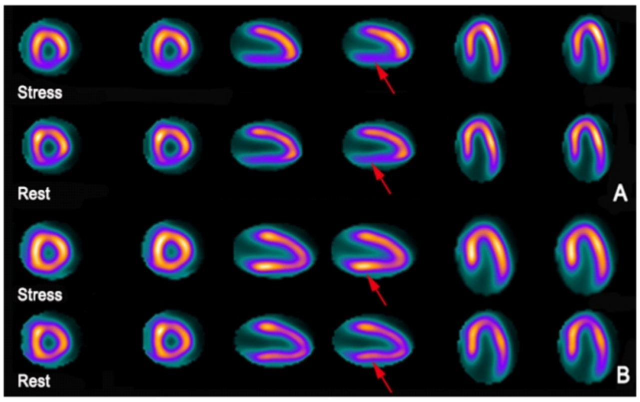

Figure 5. Images from a man (64 years old, BMI=24.5kg/m^2) with atypical chest pain. His angiography revealed no obstruction in the LAD, LCX and RCA territories. CT attenuation corrected images (B-bottom arrow) show a normal tracer distribution for both the stress and rest studies in the inferior wall that was significantly reduced in the NAC images (A-top arrow) due to diaphragmatic attenuation.

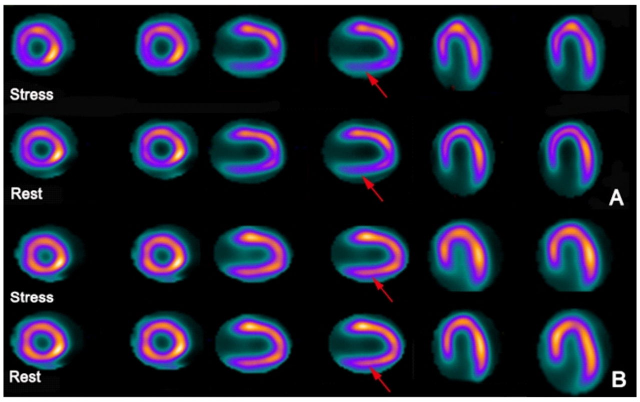

Figure 6. Images from a man (61 years old, BMI=26.2kg/m^2) with chest pain after exertion. His angiography revealed 80% obstruction in the RCA territory. The NAC MPI image (A-top arrow) shows a significant reduction in radioactivity in the inferior wall of the left ventricle under stress and a partly reversible defect at rest, which is considered myocardial ischemic. The CTAC images (B-bottom arrow) show a significant improvement in tracer distribution in both the stress and rest studies in the inferior wall, which is considered normal myocardial perfusion.

Discussion

Myocardial perfusion imaging is widely regarded as a clinically useful, noninvasive imaging test for the diagnosis, risk stratification, and management of CAD [11]. However, the image quality of conventional SPET MPI has remained suboptimal because of non-uniform attenuation artifacts from breast tissue and the diaphragm, resulting in false positives in the anterior or inferior wall and a relatively low specificity, which leads to further increases in the medical test burden [12]. Several methods have been proposed to reduce attenuation artifacts, such as scanning patients in a prone position, integrating gating parameters, such as ventricular wall motion and thickening rate, and using an external source of irradiation, namely, a line source or computed tomography, magnetic resonance (MR) [13], but each method has its limitations [14].

Apostolopoulos et al. (2016) [14] studied 120 patients with suspected CAD and found that CTAC MPI had an increased specificity (62% vs. 54%, P>0.05) and reduced sensitivity (70% vs. 87%, P=0.04) compared to values for conventional NAC studies. However, no statistically significant difference was found in the accuracy of the two methods. Therefore, there was no significant increase in value for the detection of CAD with CTAC studies. The present study also found that CTAC MPI, in the whole group patients, had an increased specificity but a decreased sensitivity for the diagnosis of CAD, and although there was no significant improvement, an increased tendency in the overall accuracy of CTAC MPI was observed, which is consistent with the results above.

Garcia et al. (2007) [15], from 13 different clinical studies (1327 patients), concluded that the specificity of MPI for the detection of CAD increased from 57% to 77% by using AC, and the normalcy rate was enhanced from 72% to 92%, while there were non-significant changes in sensitivity (86% vs. 86%), suggesting that AC in MPI markedly improved the diagnostic accuracy compared to that of NAC MPI.

Hendel et al. (1999) [12] demonstrated that, the normalcy rate of MPI was significantly improved by using AC and scatter correction with resolution compensation without sacrificing the overall sensitivity for the detection of CAD compared to NAC studies. This paper demonstrated the potential value of a new method that incorporates attenuation and scatter correction. Several factors may contribute to the differences between the results of the present study and those of Hendel's study. First, we did not combine scatter correction with resolution compensation when applying CTAC MPI, which may be one of the reasons leading to a marked decrease in sensitivity compared to Hendel's result. Second, a previous study [15] has shown that AC may overcorrect in the inferior wall in some patients with hot areas in the intestine and that an improperly quality-controlled examination may cause confounding imaging artifacts, resulting in false-negative results. We also observed that images for 17 patients with RCA lesions were overcorrected by CTAC MPI in our study. Another study [16] demonstrated that AC MPI not only underestimated the extent of perfusion defects (particularly in the inferior/inferolateral wall) but also resulted in a overestimation of the extent of CAD because of new artifacts (apical and apical-anterior wall count reductions), leading to the misdiagnosis of CAD. The above two factors have been shown to negatively influence the diagnostic performance of AC. It is our opinion that although CTAC MPI could reduce the false-positive rate of CAD and improve specificity, the sensitivity frequently decreases. As a result, CTAC MPI has limited clinical value.

In the present study, when diagnosing CAD with RCA lesions, compared with NAC MPI, CTAC MPI improved specificity but decreased sensitivity, and accuracy was significantly higher despite an insignificant difference in the AUC. However, there were no significant differences for the sensitivity, specificity, accuracy and AUC between NAC and

CTAC MPI in diagnosing CAD with LAD or LCX lesions. Sharma et al. (2012) [4] also found that for the detection of RCA disease with CTAC MPI, sensitivity was reduced, and specificity was significantly improved. Meanwhile, there were also no statistically significant differences for the sensitivity, specificity and accuracy between NAC and CTAC MPI in diagnosing CAD with LAD or LCX lesions, which was similar to the findings of our study. Caobelli et al. (2016) [17] demonstrated that AC MPI had increased diagnostic accuracy for the detection of CAD with RCA lesions and improved the specificity (81% vs. 19%) without a significant loss in sensitivity (83% vs. 96%). No substantial changes were observed in LAD or LCX disease. However, the sensitivity frequently declined in our study. The study by Caobelli use dedicated cadmium-zinc-telluride (CZT) SPET, which provides multiple advantages such as high sensitivity, improved temporal and spatial resolution, and high-energy resolution. This may contribute to the inconsistent results in sensitivity.

In this present study, the specificity of CTAC MPI in diagnosing CAD in males was increased markedly; the resulting incremental value was significant, although the sensitivity was decreased. Malkerneker et al. (2007) [18] reported that, compared to females, the number of doubtful cases in men decreased with additional AC MPI. Others [19] have shown that a reduction in radioactivity and defect size in the inferior wall were observed when considering both males and females but that these were more obvious when considering males alone, in whom CTAC MPI seemed to have potential clinical value for suspected CAD. In this current study, the accuracy of CTAC MPI was higher than that of NAC MPI in males, also indicating the potential clinical value of CTAC MPI in males. A study [11] has shown that the accuracy of CTAC MPI was not improved in a rather small number of females. There were also no substantial changes in sensitivity, specificity and accuracy for the detection of CAD in individual coronary arteries between NAC and CTAC MPI, indicating that CTAC MPI has limited efficacy in females. Moreover, although the doses of ionizing radiation produced by SPET/CT scans for AC were relatively low, the re-exposure to radiation still increased the risk of breast malignancy in females (especially in young females) [20]. Therefore, CTAC MPI is not recommended for females.

Compared to NAC MPI we found that the accuracy of CTAC MPI was significantly higher in overweight patients (BMI ≥24), although the difference in the AUC was marginally insignificant. Researchers [21, 22] found that CTAC MPI provided a more significant improvement in accuracy in obese patients than in normal-weight patients. However, for patients with different BMI, the benefit of CTAC is still questioned. Gruning et al. [23] suggested that easily available parameters, such as body mass and chest circumference, cannot be used to predict which patients will benefit from AC. Shawgi et al. [24] also found that AC could be of value in patients with a normal BMI.

Usually, in Europe and the United States, an overweight person is defined as having a BMI≥27, while in China a BMI≥ 24 is considered overweight because the somatotype of the Chinese population is much smaller. This difference may be the reason for the limited diagnostic efficacy of CTAC MPI in overweight patients with a suspected of CAD in China.

In the clinical setting, CTAC images should be interpreted together with NAC images. For example, if perfusion was normal on NAC images, then it might be assumed that a decrease in uptake or defects in anterior wall perfusion observed on CTAC images are not clinically significant. However, if there was a decrease in uptake or perfusion defects in the inferior wall on the NAC images but these images were corrected by CTAC, then the defects on the NAC image could be considered as attenuation artifacts. The pre-test probability of CAD should also be taken into account for the best diagnostic performance. For patients with low or low-to-intermediate pre-test probability of CAD, perfusion defects or decreases in uptake on NAC images are more likely to be considered as attenuation artifacts; for patients with an intermediate or high pre-test probability of CAD, the possibility of underestimating the presence or the extent of CAD by CTAC should be considered.

Study limitations

An important limitation of this study is that the number of patients recruited was relatively small, and approximately 37.8% of CAD patients had a borderline disease (50%-70%). The ability to auto regulate a borderline disease is not affected under stress, thus coronary flow reserves are normal or near normal. Therefore, this could be one of the reasons for the relatively low sensitivity of this study. Additionally, all patients in this study underwent CAG within a period of three to six months after MPI, which is a rather long period for using GAG as "gold" reference standard. Such a long interval suggests that the decision to perform CAG was not guided by MPI results, but rather by medically uncontrolled symptoms, new symptoms or acute coronary events, which in turn possibly indicates rapid coronary lesion propagation. If a substantial number of patients of this study were subjected to CAG later than 2-3 months post MPI, this may have affected MPI sensitivity.

Additionally, non-uniform tissue attenuation is not the only factor that contributes to the degradation of SPET images. Scatter correction with compensation resolution was not used in our study. The combination of additional scatter correction and AC might further improve diagnostic accuracy. These results still need to be determined through a multicenter prospective study, with a large sample size.

In conclusion, in a sample of Chinese patients suspected to have CAD, CTAC improved SPET MPI specificity but decreased sensitivity, leading to no obvious improvement in overall accuracy for the diagnosis of CAD. However, CTAC might be of value in the subgroups of males and overweight patients and in RCA territory. In routine clinical application, the integration of NAC and CTAC findings combined with the CAD pre-test probability could improve MPI diagnostic perfomance.

Authors' contributions

YT Wang and JF Wang conceived this study, and participated in its design and coordination. WC Xin and XL Shao drafted the manuscript. YT Wang, JF Wang and WC Xin processed and analyzed the images. All authors read and approved the final manuscript.

Acknowledgment

This research was supported by Natural Science Foundation of China (81471690); Key Development Foundation of Jiangsu Province (BE2015635); Major Project of Changzhou City Health Bureau (ZD201409); Basic Research Funds of Changzhou Science and Technology Bureau (CJ20160030); Social Development Foundation of Changzhou Science and Technology Bureau, Jiangsu Province, China (Ce20175029); National Natural Science Foundation for Young Scientists (81701734).

The authors declare that they have no conflicts of interest.

Bibliography

1. Section of Interventional Cardiology of Chinese Society of Cardiology of Chinese Medical Association,Specialty Committee on Prevention and Treatment of Thrombosis of Chinese College of Cardiovascular Physicians,Editorial Board of Chinese Journal of Cardiology. Chinese guideline for percutaneous coronary intervention(2016). *Chin J Cardiol* 2016; 44: 382-400.
2. Masood Y, Liu YH, Depuey G et al. Clinical validation of SPECT attenuation correction using x-ray computed tomography-derived attenuation maps: Multicenter clinical trial with angiographic correlation. *J Nucl Cardiol* 2005; 12: 676-86.
3. Huang JY, Huang CK, Yen RF et al. Diagnostic Performance of Attenuation Corrected Myocardial Perfusion Imaging for Coronary Artery Disease: A Systematic Review and Meta-analysis. *J Nucl Med* 2016; 57: 1893-8.
4. Sharma P, Patel CD, Karunanithi S et al. Comparative accuracy of CT attenuation-corrected and non-attenuation-corrected SPECT myocardial perfusion imaging. *Clin Nucl Med* 2012; 37: 332-8.
5. Germano G, Slomka PJ, Berman DS. Attenuation correction in cardiac SPECT: the boy who cried wolf? *J Nucl Cardiol* 2007; 14: 25-35.
6. Chen CM, Kong LZ. Chinese adult overweight and obesity prevention and control guidelines. *Beijing: People's Health Press* 2006: 44-5.
7. Yao ZM, Wang Q, Tian YQ et al. A multi-center trial on the study of ATP stress myocardial perfusion imaging in the detection of coronary artery disease. *Chin J Nucl Med Mol Imaging* 2014; 34: 292-5.
8. Wang JF, Wang YT, Zhou RJ et al. Enhancement with coronary artery calcification score in detection of coronary heart disease by myocardial perfusion SPECT imaging. *Chin J Nucl Med Mol Imaging* 2017; 37: 274-8.
9. Raza H, Jadoon LK, Mushtaq S et al. Comparison of non-attenuation corrected and attenuation corrected myocardial perfusion SPECT. *The Egyptian J Radiol Nucl Med* 2016; 47: 783-92.
10. Cerqueira MD, Weissman NJ, Dilsizian V et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *J Nucl Cardiol* 2002; 9: 240-5.
11. Genovesi D, Giorgetti A, Gimelli A et al. Impact of attenuation correction and gated acquisition in SPECT myocardial perfusion imaging: results of the multicentre SPAG (SPECT Attenuation Correction vs Gated) study. *Eur J Nucl Med Mol Imaging* 2011; 38: 1890-8.
12. Hendel RC, Berman DS, Cullom SJ et al. Multicenter clinical trial to evaluate the efficacy of correction for photon attenuation and scatter in SPECT myocardial perfusion imaging. *Circulation* 1999; 99: 2742-9.
13. Kong E, Cho I. Clinical issues regarding misclassification by Dixon based PET/MR attenuation correction. *Hell J Nucl Med* 2015; 18: 42-7.
14. Apostolopoulos DJ, Savvopoulos C. What is the benefit of CT-based attenuation correction in myocardial perfusion SPET? *Hell J Nucl Med* 2016; 19: 89-92.
15. Garcia EV. Spect attenuation correction: an essential tool to realize nuclear cardiology's manifest destiny. *J Nucl Cardiol* 2007; 14: 16-24.
16. Savvopoulos CA, Spyridonidis T, Papandrianos N et al. CT-based attenuation correction in Tl-201 myocardial perfusion scintigraphy is less effective than non-corrected SPECT for risk stratification. *J Nucl Cardiol* 2014; 21: 519-31.
17. Caobelli F, Akin M, Thackeray JT et al. Diagnostic accuracy of cadmium-zinc-telluride-based myocardial perfusion SPECT: impact of attenuation correction using a co-registered external computed tomography. *Europ Heart J Cardiovasc Imag* 2016; 17: 1036-43.
18. Malkerneker D, Brenner R, Martin WH et al. CT-based attenuation correction versus prone imaging to decrease equivocal interpretations of rest/stress Tc-99m tetrofosmin SPECT MPI. *J Nucl Cardiol* 2007; 14: 314-23.
19. Huang R, Li F, Zhao Z et al. Hybrid SPECT/CT for attenuation correction of stress myocardial perfusion imaging. *Clin Nucl Med* 2011; 36: 344-9.
20. Tootell A, Szczepura K, Hogg P. Comparison of effective dose and lifetime risk of cancer incidence of CT attenuation correction acquisitions and radiopharmaceutical administration for myocardial perfusion imaging. *Br J Radiol* 2014; 87: 756-61.
21. Tamam M, Mulazimoglu M, Edis N et al. The value of attenuation correction in hybrid cardiac SPECT/CT on inferior wall according to body mass index. *World J Nucl Med* 2016; 15: 18-23.
22. Corbett JR, Cahill JM, Kritzman JN et al. 15.33: Diagnostic accuracy of hybrid SPECT/CT for attenuation correction of stress myocardial perfusion imaging in women compared to men. *J Nucl Cardiol* 2008; 15: S19-S20.
23. Grüning T, Brogsitter C, Khonsari M et al. X-ray-based attenuation correction of myocardial perfusion scans: practical feasibility and diagnostic impact. *Nucl Med Commun* 2006; 27: 853-8.
24. Shawgi M, Tonge CM, Lawson RS et al. Attenuation correction of myocardial perfusion SPET in patients of normal body mass index. *Hell J Nucl Med* 2012; 15: 215-9.