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INFLUENCE OF COMPUTED TOMOGRAPHY ATTENUATION CORRECTION IN MYOCARDIAL PERFUSION IMAGING, IN OBESE PATIENTS: CLASSIFICATION BY SEX AND BODY MASS INDEX

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Abstract

Four groups of 71 subjects 47 with body mass index (BMI) between 30 and 35 (27 Male (M1) and 20 Female (F1)) and 24 with BMI above 35 (13 Male (M2) and 11 Female (F2)) who underwent stress-rest , SPECT MPI of a two day protocol, by EANM guideline protocol, with and without the incorporation of the Attenuation correction by computed tomography (CT-AC), for stress and rest separately. For perfusion percentage quantifications, the 5 walls model of left ventricle (LV) was used: anterior (ANT), lateral (LAT), inferior (INF), septal (SEP) and apical (API), using the QGS/QPS™ software. For statistical evaluation it was used the Friedman test. Statistically significant differences were found in comparison of studies with and without attenuation correction (AC) for: F1 in stress and rest studies respectively for LAT ($p=0.006$ and $p=0.034$), INF ($p=0.000$ and $p=0.000$) and in rest study for SEP ($p=0.044$) LV walls; F2 group of stress and rest studies respectively for INF ($p=0.001$ and $p=0.008$) walls; M1 group of stress and rest study respectively for LAT ($p=0.000$ and $p=0.000$), INF ($p=0.000$ and $p=0.000$) SEP ($p=0.003$ and $p=0.001$) walls and just in rest study for API ($p=0.045$) LV walls; M2 group of stress and rest studies respectively for INF ($p=0.000$ and $p=0.000$), LAT ($p=0.020$ and $p=0.014$) and in stress study for SEP ($p=0.003$) LV walls. The influence of CT-AC is bigger within the groups with BMI between 30 and 35.

1. INTRODUCTION

Myocardial perfusion imaging (MPI) acquired by single photon emission computed tomography (SPECT) is a well-established, non-invasive, technique that is used for the evaluation of known or suspected Coronary artery disease (CAD) [1–3]. Nevertheless, due to the attenuation artifacts (AA), the specificity of conventional SPECT MPI has remained suboptimal [1,4]. The presence of abnormal findings caused by breast, diaphragmatic and thoracic wall attenuation results in marked regional variations in myocardial activity that are not related to myocardial perfusion defects [5,4] . These variations are most often found in patients suffering from obesity which tend to have a larger volume of soft tissue and organs that attenuate gamma rays from the heart [6]. In these cases, the number of false positive results can increase, hindering a correct diagnosis.
Some of the AA are different between male and female population as they can be dependent on the quantity of attenuating material adjacent to the heart [7]. In male population it is more common to find attenuation artifacts in the inferior wall of the left ventricle, owing to sub-diaphragmatic attenuation, but in female population the artifacts appear more often in the anterior and sometimes in the lateral walls due to breast attenuation [5].
To overcome this problem, some guidelines recommend the incorporation of attenuation correction (AC) to improve diagnostic accuracy. AC methods measure the tissue interference in the photon (PT) attenuation in order to minimize its impact in the images [8]. They attempt to determinate a real tracer distribution in the tissues and the fraction of the attenuated PT. Physically the attenuation process depends on the thickness and tissue type and the intensity of the incident PT, as shown in the following equation:

$$I = I_0 e \sum_i -x_i \mu_i \quad (1)$$

where I represents the measured ray and I_0 the initial ray intensities, and the index i represents all the different tissue type regions along the trajectory, μ_i are the effective attenuation coefficients for the different tissue regions and x_i are the different thicknesses of the regions included in the study, thus the sum represents the total attenuation through all the regions.
Several AC systems were developed through the years, and the AC by computed tomography (CT-AC) is the one that was used in this study. It has been shown that this system improves the image quality and the diagnostic accuracy and it has several advantages over the others AC methods such as high PT flux, no decay of transmission source and short scans times [9,10]. CT-AC methods require the determination of an attenuation map (AM), which represents the spatial distribution of linear attenuation coefficients (ACo) for patients anatomy regions that are included in the MPI scans [8,11]. These describe the fraction of a beam of energy that is absorbed or scattered per unit of thickness of absorber, of different tissues for each individual patient, therefore the construction of AM is performed in order to correct the attenuated PT, which usually results in an increase of the density photon counts (PC) in areas affected by the attenuation effects (AE).
It is important to acquire a good quality CT AM so as to obtain a high quality myocardial

images (Figure 1), especially when scanning individuals with high BMI which tent to attenuate a significant number of gamma photons coming from the heart. In some cases CT-AC generates differences in quantification perfusion values (Figure 2) of the left ventricle (LV) when compared with non-attenuation corrected (NAC) MPI results [11].

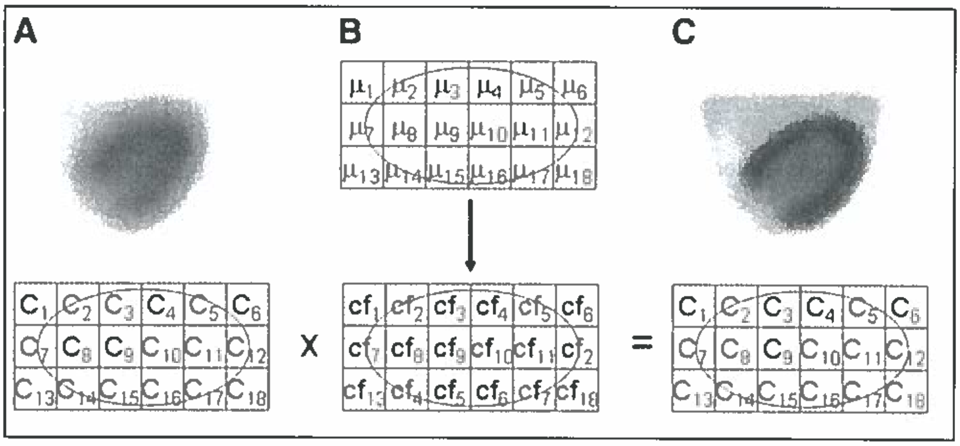

Figure 1: The AC factors (B) are obtained from ACo measurements determined by CT scan and used to correct emission data from uncorrected SPECT MPI scan (A) to generate AC myocardial images (C) with better spatial resolution which results in an improvement of the image quality. *Adapted from [8].*

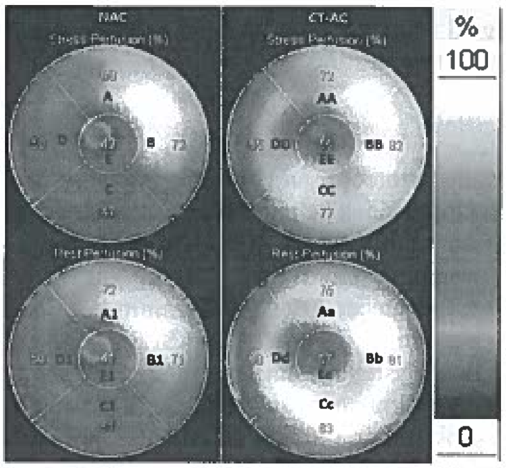

Figure 2: By analysing NAC polar maps is obtained a reduced perfusion rate in the INF (C and C1) and SEP (D and D1) LV walls, both for stress and rest respectively. CT systems correct SPECT data and as a result the perfusion rate increases in the affected areas, INF (CC and Cc) and SEP (DD and Dd) LV walls for stress and rest respectively in the CT-AC polar maps.

The assessment of MPI is performed by either qualitative or quantitative analyses and the quantification of the perfusion rate is a very important tool for the detection of CAD [12]. The most common software used for this process is Quantitative Gated SPECT/Quantitative Perfusion SPECT (QGS/QPS™) which provides automatic segmentation, quantification, analysis and display of static and gated MPI data [13,14].
Genovesi et al. study suggests that the use of AC should be limited to male patients with a BMI higher than 27, but there is no study performed for male and female individuals with the BMI superior than 30, which is considered as obese group by the Centers for Disease Control and Prevention [15].
The aim of this study is to verify the influence in MPI results between CT-AC and NAC data, in patients with BMI between 30 and 35 and higher than 35 for male and female population.

2. METHODOLOGY

2.1. Study population

Retrospective evaluation of MPI data since January 2014 until January 2015 of 71 subjects (40 male and 31 female) who underwent stress-rest, SPECT MPI of a two days protocol, with ^{99m}Tc-tetrafosmin, for suspected CAD. The selected subjects had a body mass index (BMI) above 30, and they were divided into four groups: BMI between 30 and 35 (27 male (M1) and 20 female (F1)) and BMI above 35 (13 male (M2) and 11 female (F2)).

2.2. Stress Testing

All subjects underwent pharmacological stress test with the intravenous radiotracer injection 10-20 s after regadenoson administration. During the stress induction the vital signs were monitored with an ECG signal with 12 leafs and the blood pressure was measured at the beginning and at the end of the stress testing.

2.3. SPECT data acquisition

All patients had 2 day imaging protocol, and the images were acquired 45 minutes after ^{99m}Tc-tetrafosmin intravenous injection. The injected activity varied with the patient's weight: 400 MBq were used for patients with < 90 kg, 600 MBq for patients between 90 and 110 kg and 800MBq for patients weighing more than 110 kg, as it is recommended by the Administration of Radioactive Substances Advisory Committee guidance notes.
All image acquisitions were performed using a hybrid SPECT/CT dual-head gamma camera (Infinia Hawkeye 4; GE Medical Systems). Emission data were acquired using parallel-hole, low energy, and high resolution collimator with the patients in supine position. Body contour was used for the acquisition orbits, over 180 degree arcs starting on the right anterior oblique and ending in the left posterior oblique projections, with use of 60 stops each of 3 degree. For each stop, the emission data were acquired for 25 seconds. The matrix used for the image

acquisition was 64x64 pixel. All images were acquired on the 140 keV photopeak with a 20% symmetrical window.

2.4. CT attenuation maps acquisition

The SPECT images were followed by CT examination, with acquisition parameters of 120 kV, 2.5 mA, pitch of 1.9, rotation speed of 3 s per rotation, 512x512 pixel matrix and slice thickness of 5mm.

After the CT acquisition, the obtained images were transformed into SPECT attenuation maps by the following steps: first, the CT images were transformed into a volume with the same voxel and pixel size as SPECT images, in order to perform the SPECT and CT image fusion [8]. In the second step, CT Hounsfield values were transformed into linear attenuation coefficients, with the same energy as the SPECT emission photons (140 keV) [16]. Next, the obtained attenuation maps were smoothed in all directions with a Gaussian filter to adjust the resolution to that of the SPECT images [8]. Finally, the CT-based attenuation coefficients were included to reconstruct AC SPECT data.

2.5. Acquired data processing

All studies were uniformly processed, by the same operator, with commercially available QGS/QPS™ software on a Xeleris 2.0 workstation. Both NAC and CT-AC SPECT emission images data were reconstructed by use of OSEM/MLEM™ software. Thereby, tomographic slices were generated and displayed as vertical long-axis, horizontal long-axis and short-axis slices. SPECT emission data were co-registered and fused with CT data. The co-registration of the images was semi-automatic, therefore the fusion images were visually inspected to ensure the correctness of the image alignment. The predetermined attenuation coefficients were applied to SPECT emission data to perform the CT-AC.

2.6. Quantitative Image Analysis

For further quantitative analysis it was performed the segmentation of the LV into 5 walls: anterior (ANT), lateral (LAT), inferior (INF), septal (SEP) and apical (API), as shown in the Figure 3, in order to quantify the perfusion percentage of all the walls independently. Stress and rest results were registered separately. This process was carried out for each individual subject of the study.

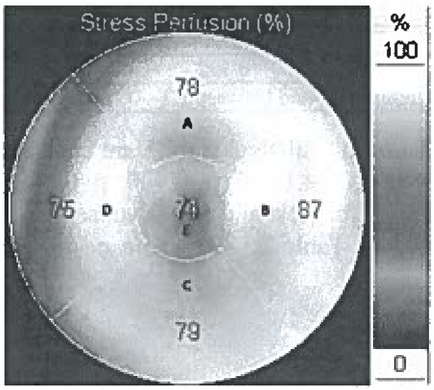

Figure 3: Segmentation of the LV into 5 walls, anterior (A), lateral (B, inferior (C), septal (D) and apical (E), with subsequent quantification of the Stress Perfusion percentage for each LV wall, performed by QGS/QPS™ software.

2.7. Statistical Analysis

All statistical analysis were executed using Statistical Package for the Social Sciences (SPSS) v.22, software. In order to execute the statistical evaluation it was used Friedman test for non-parametrical pared samples (CT-AC and NAC data), as the data did not followed a normal distribution [17]. For all the groups included in the study, a significance level of 5% was used.

3. RESULTS

Quantification of the perfusion rate of LV using CT-AC and NAC data

The findings of AC and NAC quantitative assessment, of the LV perfusion rate, for female and male groups, are shown in Table 1 and 2 respectively. As a result, CT-AC systems introduce some statistical significant differences in the perfusion quantification when applied to the NAC MPI.

For F1 group statistically significant differences between AC and NAC results were found in the LAT and INF walls respectively for the Rest (p=0.034; p=0.000) and Stress (p=0.006; p=0.000) studies and in SEP walls just for Rest (p=0.044) studies as shown in Table 1. For F2 group no significant differences were obtained except in the INF LV walls for Rest (p=0.008) and for Stress (p=0.001) as represented in Table 1.

Table 1: Results of the *p-values* obtained from the perfusion rate comparisons of the LV walls, between AC and NAC SPECT MPI data, on the female study population with BMI between 30 and 35 (F1 group) and above 35 (F2 group).

WOMEN	$30 \leq BMI \leq 35$		$BMI > 35$	
	AC – NAC LV Walls	p - value	AC – NAC LV Walls	p - value
STRESS	ANT	0.240	ANT	0.647
	LAT	0.006*	LAT	0.073
	INF	0.000*	INF	0.001*
	SEP	0.076	SEP	0.944
	API	0.240	API	0.504
REST	ANT	0.159	ANT	0.622
	LAT	0.034*	LAT	0.181
	INF	0.000*	INF	0.008*
	SEP	0.044*	SEP	0.833
	API	0.192	API	0.218
* statistical significant differences found between CT-AC and NAC perfusion percentage results				

For male exams, in the M1 group statistical significant changes in LV perfusion between CT-AC and NAC were observed on the LAT (p=0.000; p=0.000), INF (p=0.000; p=0.000) and SEP (p =0.001; p=0.003) walls, for Rest and Stress subsequently and on the API walls just for Rest (p=0.045) as presented in Table 2. The same occurrence can be detected in the M2 group, on the same anatomical regions, except the API walls areas. Nevertheless, significant variations among AC and NAC data on the SEP walls are only evident in the Stress study (p=0.003). The remaining differences are present on both, Rest (p=0.014, for LAT walls; p=0.000, for INF walls) and Stress (p=0.020, for LAT walls; p=0.000 for INF walls) studies as verified in Table 2.

Table 2: Results of the *p-values*, obtained from the perfusion rate comparisons of the LV walls, between AC and NAC SPECT MPI data, on the male study population with BMI between 30 and 35 (M1 group) and above 35 (M2 group)

Men	30 ≤ BMI ≤ 35		BMI > 35	
	AC – NAC LV Walls	p - value	AC – NAC LV Walls	p - value
STRESS	ANT	0.486	ANT	0.348
	LAT	0.000*	LAT	0.020*
	INF	0.000*	INF	0.000*
	SEP	0.003*	SEP	0.003*
	API	0.529	API	0.771
REST	ANT	0.500	ANT	0.627
	LAT	0.000*	LAT	0.014*
	INF	0.000*	INF	0.000*
	SEP	0.001*	SEP	0.075
	API	0.045*	API	0.698

* statistical significant differences found between CT-AC and NAC perfusion percentage results

4. DISCUSSION

As described in the literature, the sub-diaphragmatic attenuation is the one that generates the most common AA in the INF walls of the LV, resulting in a decrease of the perfusion percentage [18]. This AA do not only affects the male study population (M1 and M2) as was previously described in literature [19], but is also present in female groups F1 and F2, due to the large abdominal area causing the diaphragmatic attenuation reducing PT count density in the INF walls [6]. This AA is corrected by CT-AC system leading to statistical significant differences in the quantification perfusion values in the affected areas.

According to the results LAT walls present statistical significant differences between CT-AC and NAC data excepting the F2. For F1 group the perfusion differences are explained by the breast attenuation since all the studies were performed in the supine position with no brassiere causing the lateral positioning of the breast tissues which attenuate gamma photons prevenient from the heart. Once again, this AA is corrected by the CT-AC system and it can explain the differences between corrected NAC quantitative results [19].

The distance of the gamma camera detectors to the patient can also be a factor that affects the quantitative results of the perfusion. As it is known if the distance between detectors and the source is increased, the scatter effect will be more intense, increasing the noise in the pictures

and degrading its contrast and spatial resolution. In consequence, the areas that are exposed to this effect will appear with perfusion variations in myocardial activity which are not real perfusion defects. AC methods correct the perfusion quantification [20], increasing perfusion percentage quantitative results in areas that are affected by improving the spatial resolution and the image contrast. For this reasons CT-AC and NAC data present differences when this problem arises. It can be observed in M1 and M2 groups where the distance problem may have caused the perfusion differences in the LAT walls. Nevertheless, some man have a large volume of breast tissue and like F1 the soft tissue attenuation is responsible for the variations of corrected and non-corrected results. Unexpectedly no statistical differences were found in the LAT walls for female population with BMI > 35. It can be explained by poor AC provided by CT systems as CT parameters were not modified even when scanning patients with very high weight in order to obtain good quality AM. Still this result need to be investigated.
Variations found in the SEP walls for M1 (Stress and Rest), M2 (Stress) and F1 (Rest) groups and API walls for M1 (Rest) group can be explained by truncation artifacts emerged from CT-AC techniques [21]. Those rise when attenuation maps do not contain the whole thoracic wall of the patient. In consequence AE in anterior direction are underestimated creating false quantitative results which differ from NAC outcome. Otherwise, the differences between CT-AC and conventional MPI results can be caused by overestimation of the AE in the SEP and API left myocardium walls [4,21].
All the groups, except the F2, present quantitative variations in in the SEP walls. M2 group just presents different results on the Stress and F1 groups on the Rest studies.
No statistical differences were found in the ANT walls as it was described by the majority of the literature, for the female population [5] probably due to the lateral positioning of the breast tissues during the scans, which do not results in the ANT LV walls attenuation but in the LAT attenuation.
CT-AC affects the MPI quantification results in several LV walls. It's very important to recognise and try to avoid AC generated artifacts by being alert for body truncation, patient motion, accurate registration of AM and emission data. Many authors suggest that it's important that both non-corrected and corrected image sets should be reviewed to understand which of the results can be accepted as real.

5. CONCLUSIONS

As demonstrated significant differences were found between CT-AC and NAC MPI data for male and female population, in various areas of the LV. Some of the differences were no expected neither described by the literature. Therefore all the members of the staff involved in MPI exams should be aware not only of the AA but also of the pitfalls of the CT-AC.
In the future this study should be continued with a larger study population and adding other parameters such as brassiere size, for females, abdominal perimeter, for males and female, and the quantification of the soft tissues thickness adjacent to the heart in order to correlate the AC and NAC MPI differences with the patients anatomy.

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