Physica Medica 68 (2019) 69–74

Contents lists available at ScienceDirect

Physica Medica

journal homepage: www.elsevier.com/locate/ejmp

Technical note

A study on the optimization of the administered activity in myocardial perfusion SPECT imaging with Tc-99m according to body measurements

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ARTICLE INFO

Keywords:
MPI SPECT
Administered activity
Body weight
Image count density

ABSTRACT

Purpose: Nuclear medicine myocardial perfusion imaging (MPI) in obese patients requires the administration of higher amounts of radioactivity, to compensate for the loss of photons due to the increased attenuation and scatter. The aim of the present study was to investigate whether an administered activity escalation protocol, proposed to yield the same effective dose irrespective of patient's weight, can also lead to images of comparable count density for all patients.

Materials and methods: 184 pharmacologically induced stress 99m-Tc MIBI and 99m-Tc tetrofosmin SPECT MPI examinations (123 males, 61 females) were included in this study. Body weight, BMI and chest circumference were collected for each patient. The administered activity was adjusted to body weight according to the IAEA protocol. Detector count rate (DCR) from the projection images and normal myocardial count rate (MCR) from the appropriately segmented reconstructed images, with and without attenuation correction, were recorded.

Results: No statistically significant correlation was found between DCR and any anthropometric parameter. A weak correlation was observed between MCR and BMI and between MCR and chest circumference for male patients only, but even these correlations were eliminated after the application of attenuation correction. The anthropometric parameter that generally correlates more strongly with DCR/MBq and MCR/MBq was body weight for men and chest circumference for women.

Conclusion: The IAEA activity escalation protocol used in this study leads to comparable image count densities, irrespective of body weight, for both men and women.

1. Introduction

Radionuclide myocardial perfusion imaging (MPI) with SPECT using Tc-99m tracers is a well-established imaging technique for the diagnosis of ischemic heart disease and one of the most frequently performed diagnostic nuclear medicine procedures. According to the European Association of Nuclear Medicine (EANM) guidelines, the recommended amount of activity to be injected to a normal weight adult patient for a one-day protocol is 250–400 MBq for the first injection and three times more for the second [1]. The amount of administered activity is always a compromise between lowering patient absorbed dose and achieving an acceptable image quality. It is well known that patients with larger body sizes require higher amounts of administered activity in order to compensate for the increased photon attenuation and scatter which result in a reduced number of photons reaching the detector. The opposite is true for lean patients, who could therefore benefit from a lower administered activity, leading to a reduced absorbed dose [2]. However, to our knowledge, there is no universally acceptable protocol for the calculation of the optimal administered activity according to patient's body weight or any other anthropometric parameter.

The currently available methods and formulas to calculate the optimal administered activity with body weight are based on the requirement that all patients, regardless of body weight, should receive approximately the same effective dose during nuclear medicine examinations. The same approach was also adopted for pediatric patients, with the introduction of the EANM pediatric dosage card [3], which has been widely accepted and used throughout Europe. The International Atomic Energy Association (IAEA) in a recent publication [4] has proposed a formula for the calculation of the activity to be administered to

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https://doi.org/10.1016/j.ejmp.2019.11.011
Received 31 July 2019; Received in revised form 20 October 2019; Accepted 13 November 2019
Available online 20 November 2019

overweight and obese patients that should lead to weight independent effective doses.

The image quality of a diagnostic nuclear medicine study depends on many factors, a very important one being an adequate count density in the acquired images. The purpose of this study is to determine whether the administered activity escalation proposed for MPI with Tc-99m tracers by IAEA, leads to comparable count densities (and presumably comparable image quality) regardless of patient weight.

2. Materials and methods

A total of 184 patients, 123 males (66.8%) and 61 females (33.2%) were included in the study. Patients were instructed to refrain from caffeine, tea and chocolate for 24 h before the study. The use of beta blockers was discontinued for 2–3 days. The weight, W (kg), the height, H (m) and the chest circumference at the level of the myocardium, CC (cm) of all patients were measured prior to the examination and the body mass index (BMI) was calculated using the following formula:

$$BMI = \frac{W}{H^2} \quad (1)$$

All patients underwent a one-day stress-first myocardial perfusion SPECT protocol, followed by a rest scan only if the stress study was not normal. Data from the stress study only were used in this work.

Stress was induced pharmacologically, by intravenous injection of either adenosine (128 patients − 69.6%) or dipyridamole (56 patients − 30.4%). Adenosine was infused intravenously at a rate of 140 μg/kg/min for 4 min. Dipyridamole was injected at a dose of 0.56 mg/kg/min diluted in saline. Aminophylline was administered 3 min after the radiopharmaceutical in order to stop side effects. Both during the adenosine of dipyridamole – induced stress, blood pressure and heart rate were monitored. Supplemental low workload physical exercise (leg movements) was used to relieve the symptoms of discomfort and lower the concentration of the radiopharmaceutical to the bowel.

^{99m}Tc-MIBI (150 patients − 81.5%) or ^{99m}Tc-tetrofosmin (34 patients − 18.5%) was injected 2 min after the beginning of the adenosine infusion, or 4 min after dipyridamole injection. The administered activity, AA (MBq), was adjusted to body weight, W, using the formula proposed by the IAEA [4]:

$$AA = \frac{A}{\left(\frac{W}{70}\right)^{a}} \quad (2)$$

where A = 259 MBq, the typical activity administered to a 70 kg patient for the first injection in an one-day stress-rest protocol, and α equals to −0.871 for ^{99m}Tc-MIBI or −0.834 for ^{99m}Tc-tetrofosmin, respectively.

For each patient, detailed records were kept of the activity of the full syringe before administration (A_{full}), the residual syringe activity after the administration (A_{empty}), and the corresponding measurement and administration times (t_{full}, t_{empty} and t_{admin}). The exact administered activity (A_{admin}) to each patient at the corresponding t_{admin} was then calculated, by subtracting A_{full} from A_{empty}, after applying the appropriate decay corrections.

All activities were measured at a Biodex Atomlab 100 dose calibrator (Biodex Medical Systems, Inc., Shirley, NY), the constancy of which was confirmed daily with a Cs-137 test source.

Tomographic acquisition started approximately 30 min after the administration of the radiopharmaceutical. During that time all patients were given a light meal, in order to reduce the activity uptake to the organs close to the heart.

All acquisitions were performed on a dual-head large field of view tomographic gamma camera (Discovery NM630, General Electric Healthcare, Chicago, IL) equipped with a Low Energy High Resolution collimator. The following acquisition parameters were used for all studies: 180° rotation (from 45° RAO to 45° LPO), 60 projections, matrix size: 64 × 64 pixels, zoom 1.5, pixel size 6.3 mm. The exact acquisition time (t_{acq}) and the detector count rate (total detected counts divided by total acquisition duration) were also recorded for each patient.

All images were reconstructed at the Xeleris 3 processing & review workstation, with standard reconstruction software (Volumetrix, General Electric Healthcare, Chicago, IL) using iterative reconstruction (OSEM, 2 iterations, 10 subsets, Butterworth post-filtering with 0.32 Nyquist cut-off, order 5). Two reconstructions were performed for each patient, one with attenuation correction – AC (Chang, $\mu = 0.12\ cm^{-1}$) and one without AC (which is the clinical practice). Automatic correction for patient motion was applied when it was necessary. The resulting reconstructed myocardial volume was fed into a segmentation algorithm, in order to extract the portion of the myocardium with at least 70% of the maximum counts (in order to exclude ischemic myocardium from the subsequent analysis [5–7]) and the mean count rate (mean segment counts divided by total acquisition time) inside the normal myocardial volume was recorded.

Detector count rate (DCR) and normal myocardial mean count rate with and without AC (MCR and MCR-AC) had to be appropriately corrected to account for two facts: that the actual administered activity was not exactly equal to the nominal and that all acquisitions were not performed at exactly 30 min after pharmaceutical administration. Therefore DCR, MCR and MCR-AC were first multiplied by the factor AA/A_{admin} and then multiplied by an appropriate decay factor in order to correspond to the counts that would have been acquired if the acquisition had started exactly 30 min post administration.

DCR/MBq, MCR/MBq and MCR-AC/MBq were also calculated by dividing DCR, MCR and MCR-AC by A_{admin} and their correlations with all three anthropometric parameters were examined, in order to establish which one is more appropriate to be used in administered activity escalation formulas.

SPSS ver. 24 (IBM Corp. Armonk, NY) was used for data analysis. All variables were tested for normality using the Shapiro-Wilks normality test. Mean values and standard deviations (SD) were calculated for normally distributed variables. Median values and interquartile ranges were calculated for non-normally distributed variables. Correlations between variables were explored using Spearman or Pearson's correlation coefficients, as appropriate. Parametric t-tests and non-parametric Mann-Whitney tests were used to explore significant differences between variables. Statistical significance was considered for $p < 0.05$.

3. Results

Table 1 presents patient demographic and anthropometric data. Patient weight and BMI covered a wide range of values, from underweight to obese class V. There was no statistically significant difference in age between male (M) and female (F) patients; however differences in the anthropometric data were statistically significant, as expected: women were lighter (mean weight M: 89.4 kg, F: 81.5 kg, $p < 0.001$) and shorter (mean height M: 1.71 m, F: 1.55 m, $p < 0.001$). However, there was no statistically significant difference in chest circumference (mean chest circumference M: 105.2 cm, F: 103.5 cm, $p = 0.110$).

The nominal administered activities, based on patient weight and Eq. (2), ranged from 200 to 532 MBq (mean: 311 MBq, standard deviation: 52 MBq), but the actual administered activities, after taking

Table 1
Patients' demographic and anthropometric data.

	Age (yrs)	Weight (kg)	Height (m)	BMI (kg/m^2)	CC (cm)
Range	31–85	52–160	1.40–1.94	18.3–58.3	85–130
Mean	67	87	1.66	31.6	105
Median	68	86	1.67	31.0	104
Interquartile Range	17	21	0.14	6.1	11

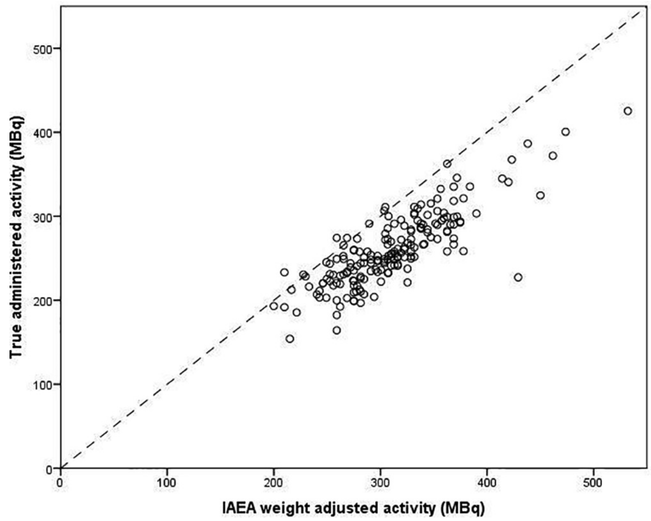

Fig. 1. Actual administered activity as a function of nominal protocol activity.

into account the time delay from radiopharmaceutical preparation to injection and the amount of radiopharmaceutical that remained into the syringe ranged from 154 to 425 MBq (median: 254 MBq, interquartile range: 58 MBq). Fig. 1 shows the actual administered activity as a function of nominal protocol activity (the dotted diagonal shows the line of identity). On average (median), actual administered activities were 54 MBq lower than the nominal ones. The difference between nominal and actual administered activity was not significantly different between patients injected with ^{99m}Tc-sestamibi and those injected with ^{99m}Tc-tetrofosmin ($p = 0.898$).

There were statistically significant differences between males and females in median DCR (M: 256342, F: 236044, $p < 0,001$) and median MCR-AC (M: 526.1, F: 412.0, $p < 0,001$). However, no statistically significant differences were found in mean MCR (M: 143.2 CPS, F: 133.0 CPS, $p = 0.343$). Furthermore, statistically significant differences were not found between different technetium agents used (sestamibi or tetrofosmin).

The dependence of DCR on (a) patient weight, (b) BMI and (c) chest circumference is presented in Fig. 2, separately for male and female patients. No statistically significant correlation was observed with either anthropometric parameter (Table 2).

Fig. 3 shows the dependence of MCR on (a) patient weight, (b) BMI and (c) chest circumference, separately for male and female patients. MCR for males shows a statistically significant negative correlation with BMI and chest circumference. For females no statistically significant correlation is observed with either anthropometric parameter (Table 2).

Table 2
Spearman correlations and the corresponding p values between image count density parameters and anthropometric data.

		Weight (kg)		BMI (kg/m^2)		CC (cm)	
		Male	Female	Male	Female	Male	Female
DCR (CPS)	ρ	0.120	0.228	0.034	0.181	0.080	−0.002
	p	0.187	0.077	0.712	0.162	0.379	0.990
MCR (CPS)	ρ	−0.175	0.106	−0.189*	0.099	−0.203*	−0.033
	p	0.053	0.415	0.036	0.449	0.024	0.801
MCR-AC (CPS)	ρ	−0.019	0.015	−0.038	−0.074	−0.051	−0.245
	p	0.835	0.909	0.675	0.569	0.572	0.057

*Statistically significant correlations.

After the application of attenuation correction (Fig. 4), the correlations of MCR-AC with all anthropometric parameters weaken and turn statistically non-significant (Table 2).

To address the issue of which anthropometric parameter is more appropriate to be used in activity escalation formulas, the dependence of DCR/MBq, MCR/MBq and MCR-AC/MBq was examined as a function of weight, BMI and chest circumference. Fig. 5 shows all relevant graphs and Table 3 lists all correlation coefficients and the corresponding p values. The strongest correlation of DCR/MBq is observed with body weight, for both men and women. The strongest correlation of MCR-AC/MBq is observed with chest circumference, for both men and women. On the other hand, MCR/MBq for men correlates more strongly with body weight, whereas for women it correlates more strongly with chest circumference.

4. Discussion

The deterioration of image quality in SPECT myocardial perfusion studies of patients with increased body weight is well known in the nuclear cardiology community and is mainly due to the increased photon attenuation and scatter [5–9]. Injecting the same activity in all patients, regardless of weight and, at the same time, increasing acquisition times to compensate for the decrease in count rate, leads to unacceptably long scan durations, especially taking into consideration the uncomfortable position the patients have to maintain during scanning. The only realistic option is to increase administered activity and to do that in a way that would not unnecessarily increase patient dose.

A number of activity escalation formulas have been proposed in the literature [6–9] aiming at a more or less constant myocardial count

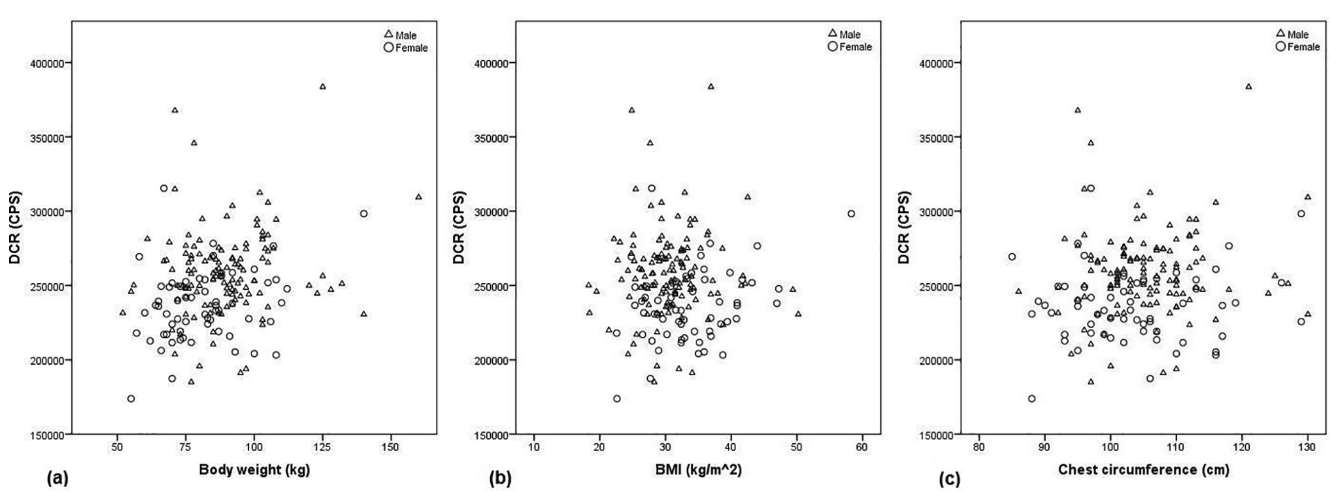

Fig. 2. Detector count rate (DCR), as a function of weight (a), BMI (b) and chest circumference (c), for males and females.

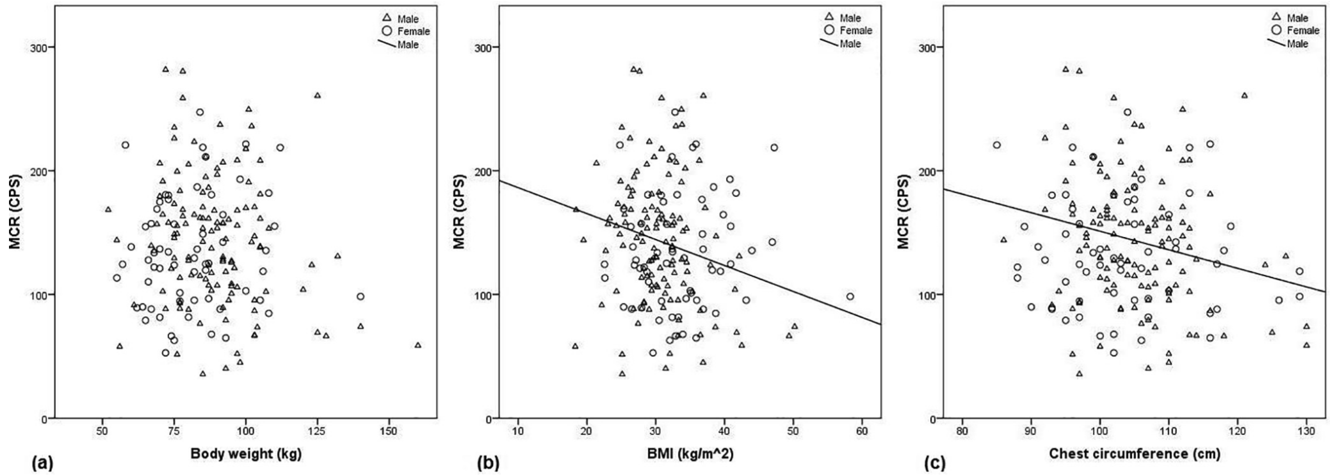

Fig. 3. Mean normal myocardial count rate (MCR), as a function of weight (a), BMI (b) and chest circumference (c), for males and females. Regression lines are shown only for those correlations that are statistically significant.

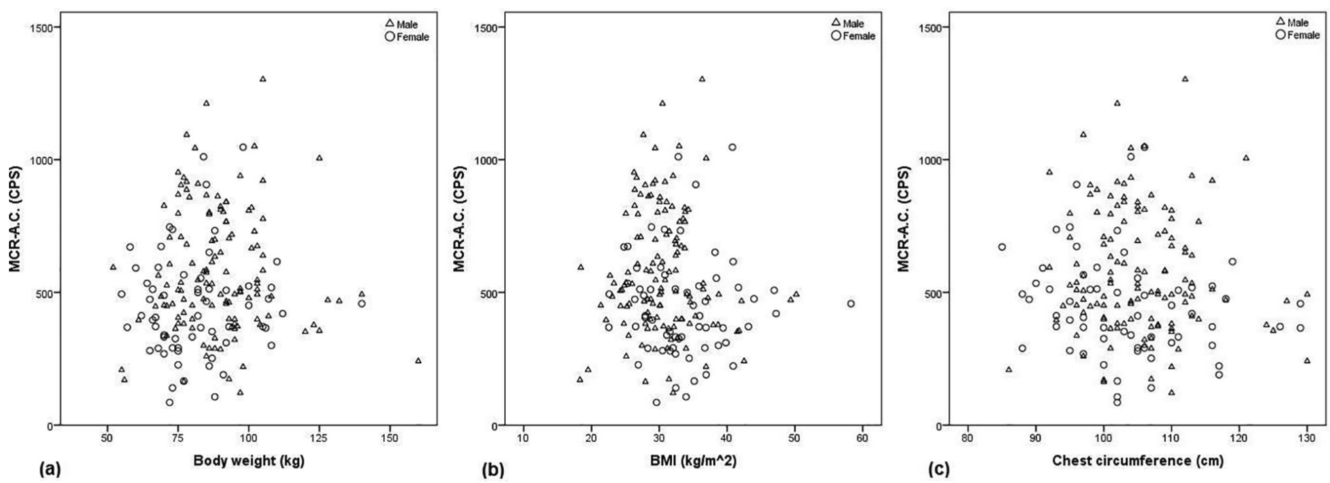

Fig. 4. Mean normal myocardial count rate after attenuation correction (MCR-AC), as a function of weight (a), BMI (b) and chest circumference (c), for males and females. Regression lines are shown only for those correlations that are statistically significant.

density. More recently, formulas that aim at a weight independent patient effective dose were proposed by international regulatory and scientific organizations, an approach that has also guided the administered activity recommendations for pediatric patients [3]. The formula proposed by the IAEA has been used in our department for the last 3–4 years and the goal of this study was to establish whether this formula results also in weight independent myocardial counts.

There was a significant difference between nominal and actual administered activities. The mean residual syringe activity for tetrofosmin, calculated at the time of injection, was 58.5 MBq (20.2% of the nominal activity) and for sestamibi was 51.8 MBq (20%). Flushing the syringes with saline after injection resulted in only a small percent of the residual activity to be re-injected to the patient, as the problem was mainly due to the absorption of the radiopharmaceutical onto the plastic syringe, a known problem [5,8] that is common for many agents and leads to important percentages of residual activity in the cases of tetrofosmin and sestamibi [10–12].

Image quality was considered only in terms of count density, therefore detector and myocardial count rates were chosen as the appropriate variables. Count rates were used instead of total counts because the total counts were affected by the duration of the acquisition, which was not the same for all patients (the technicians in our department tend to increase the acquisition time in obese patients to compensate for the expected reduced count rate). In this study, male and female patients were studied separately, because they presented statistically significant differences in detector and myocardial count rates and different correlations with the anthropometric parameters. A similar behavior was reported by Taylor et al. [6] and O'Connor et al. [7] whereas Notghi et al. [5] found no statistically significant differences in the changes in counts with weight between males and females.

The lack of statistically significant correlations between detector count rate and patients' anthropometric parameters (Fig. 2) is a satisfactory confirmation that the adopted formula for adjusting administered activity to patient's body weight, which was designed to result in weight independent effective doses, also leads to weight (and also BMI and chest circumference) independent image count densities. Moreover, normal myocardial count rate, as calculated from the segmentation of the reconstructed myocardial images, does not correlate significantly with body weight for both male and female patients (Fig. 3a). However, it does correlate with BMI and chest circumference for male patients (Fig. 3b and c). When attenuation correction is applied, all image count parameters become independent on all anthropometric parameters (Fig. 4).

Some differences between men and women were observed in the correlations of the image count parameters expressed per unit administered activity with the three anthropometric parameters examined in this study. Detector count rate per MBq administered activity correlates more strongly with body weight for both males and females:

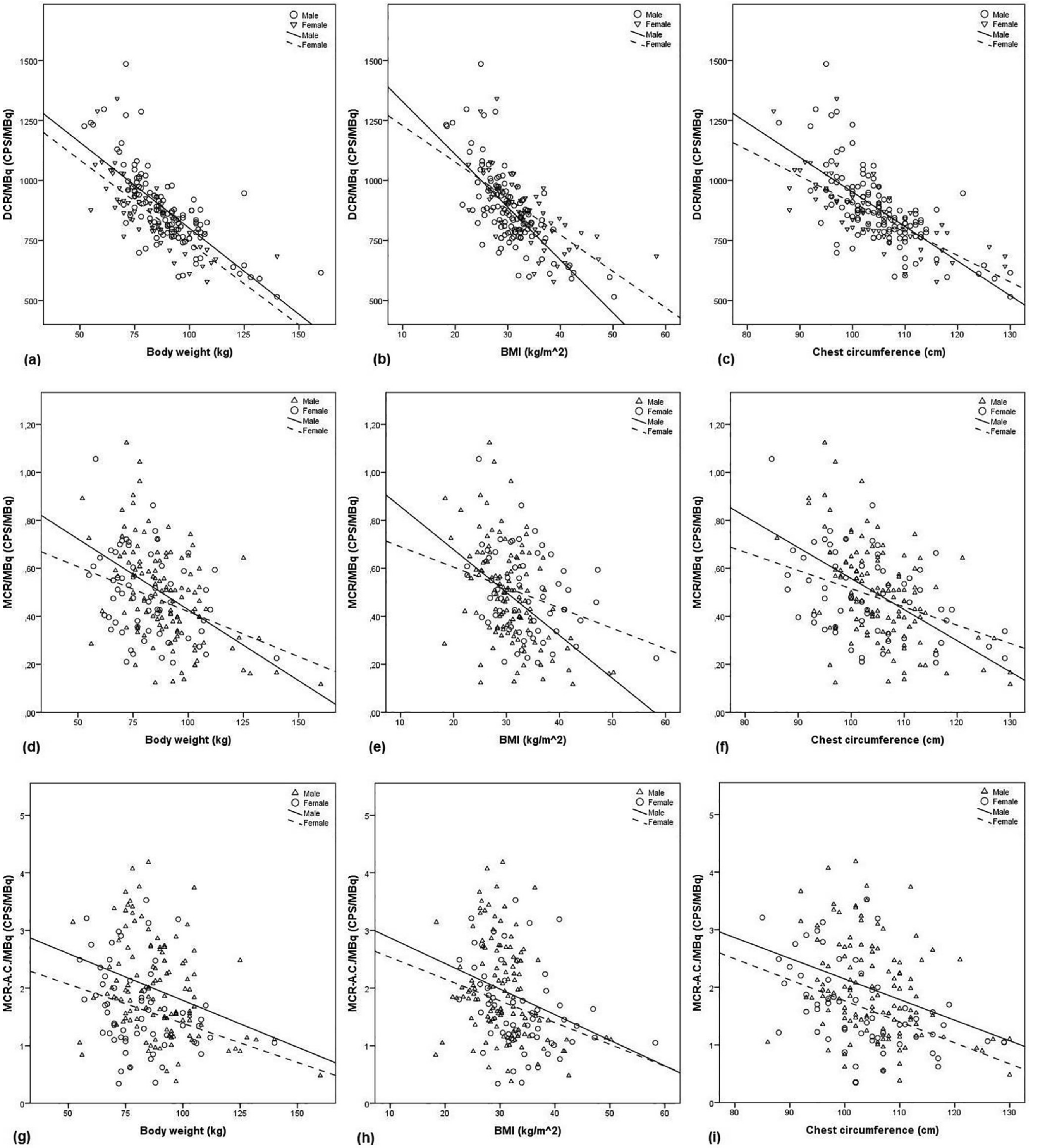

Fig. 5. DCR/MBq, MCR/MBq and MCR-AC/MBq, as a function of weight (a, d and g), BMI (b, e and h) and chest circumference (c, f and i), for males and females.

Table 3 shows that the absolute values of the correlation coefficients between DCR/MBq and body weight, both for males and females, are larger compared to those between DCR/MBq and BMI and those between DCR/MBq and CC. On the contrary, normal myocardial count rate per MBq administered activity (MCR/MBq) correlates more strongly with body weight for males and with chest circumference for females. This could be due to the significant attenuation of the female breast tissue. A similar behavior was observed by O'Connor et al. [7] for rest 99m-Tc sestamibi studies. Between weight, BMI and body surface area, Notghi et al. [5] found that the strongest relationship was with body weight, but they had not analyzed separately males from females. It is interesting to note that, in males, the application of Chang's attenuation correction weakens the correlations between the myocardial image count parameters and all three anthropometric parameters, whereas in females some correlations become stronger (especially with chest circumference). However, given the fact that (a) attenuation correction is not routinely performed in clinical practice and (b) the differences in correlations are rather small, adopting the same escalation formula based on body weight for both men and women seems a reasonable and practical simplification in everyday practice.

Table 3
Spearman correlations and the corresponding p values between image count density parameters per MBq administered activity and anthropometric data.

		Weight (kg)		BMI (kg/m^2)		CC (cm)	
		Male	Female	Male	Female	Male	Female
DCR/MBq (CPS/MBq)	ρ	−0.747*	−0.832*	−0.680*	−0.761*	−0.681*	−0.816*
	p	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
MCR/MBq (CPS/MBq)	ρ	−0.466*	−0.315*	−0.423*	−0.296*	−0.454*	−0.379*
	p	< 0.001	0.014	< 0.001	0.021	< 0.001	0.003
MCR-AC/MBq (CPS/MBq)	ρ	−0.305*	−0.375*	−0.276*	−0.409*	−0.312*	−0.549*
	p	0.001	0.003	0.002	0.001	< 0.001	< 0.001

*Statistically significant correlations.

5. Limitations

There are a few limitations in this study. First of all, only pharmacologically stressed patients were studied, because exercise stress testing is not performed as frequently in our department. One can expect to obtain higher count rates for exercise stressed patients [7]. A second limitation is that rest acquisitions were not included in the study, because many patients had a normal stress scan and, therefore, did not continue with the resting phase. Nevertheless, according to previous publications [5,7] stress and rest studies are not expected to have statistically significant differences with respect to count rate correlations with body weight. A third limitation is that the chest circumference in all patients was not measured in the exact examination position (right arm at patient's right side and left arm raised above patient's head) and therefore there could be some systematic error in these measurements, especially for female patients. Another limitation is that the overall quality of the myocardial perfusion images was not assessed in this study, only count densities were considered. In radionuclide imaging, however, if image acquisitions are performed under optimal technical conditions, the major contributing factor to the image quality is statistical noise, which is directly related to count densities. A final limitation is that myocardial counts can be also affected by several other factors (coronary flow reserve, presence of CAD, dyslipidemia, diabetes) which were not considered in the analysis.

6. Conclusion

The adopted administered activity escalation formula according to body weight proposed by the IAEA, intended to result in weight independent effective doses to patients performing SPECT myocardial perfusion imaging, also results in weight independent image count densities, leading to presumably comparable image quality. However, it should be always kept in mind that, although the independence of image quality on the patients' anthropomorphic characteristics can be demonstrated in real patients, the independence of the effective dose cannot be guaranteed, since effective dose estimates are based on simulations on anatomical phantoms representing reference patients.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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