Original Article

Incremental Determinants of The Combined Supine-Prone Protocol for Myocardial Perfusion Scintigraphy

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Abstract

Background: **Myocardial perfusion scintigraphy is an important non-invasive method for diagnosing coronary artery disease, but it is not free from artifacts. Performing the combined supine-prone protocol can bring benefits to images with artifacts from the standard protocol in the supine position. The lack of unanimity in the implementation of the combined protocol may be related to the lack of objective data for the prior selection of patients.**

Objective: **To evaluate which anthropometric profiles may be associated with a greater benefit in excluding artifacts for the optimized performance of the combined protocol.**

Methods: **A cross-sectional and analytical study was carried out with 370 patients at the Nuclear Medicine Group Clinic between April and August 2022. The estimated level of statistical significance was 5%. Statistical analysis using binary logistic regression was used to evaluate the association between anthropometric data and the change in the initial test result after carrying out the combined protocol.**

Results: **The combined protocol promoted a 19.7% increase in the normality ratio of the standard protocol. The variables weight, for both genders [OR = 1.02 (95% CI, 1.0002 – 1.04; p = 0.047)], and bust in women [OR = 1.06 (95% CI, 1. 01 – 1.11; p = 0.014)] represented incremental determinants with statistical significance. Weight greater than 76.5kg for both genders (S: 58.5%; E: 61.5%) and bust greater than 100.0 cm in women (S: 73.9%; E: 53.4%) were the best cutoff points in the receiver operating characteristic (ROC) curve.**

Conclusion: **The optimized implementation of the combined protocol using the described weight and bust measurement criteria can promote greater efficiency in image acquisition.**

Keywords: **Radionuclide Imaging; Myocardial Perfusion Imaging; Prone Position; Anthropometry; Coronary disease.**

Introduction

Myocardial perfusion scintigraphy represents an important non-invasive method in the diagnosis of coronary artery disease (CAD), with sensitivity and specificity of 88 and 74%, respectively.[1] The standard protocol of the exam comprises the acquisition of images with the patient in dorsal decubitus (supine position) after intravenous injection of the radiotracer, obtaining scintigraphic images at rest and post-stress.

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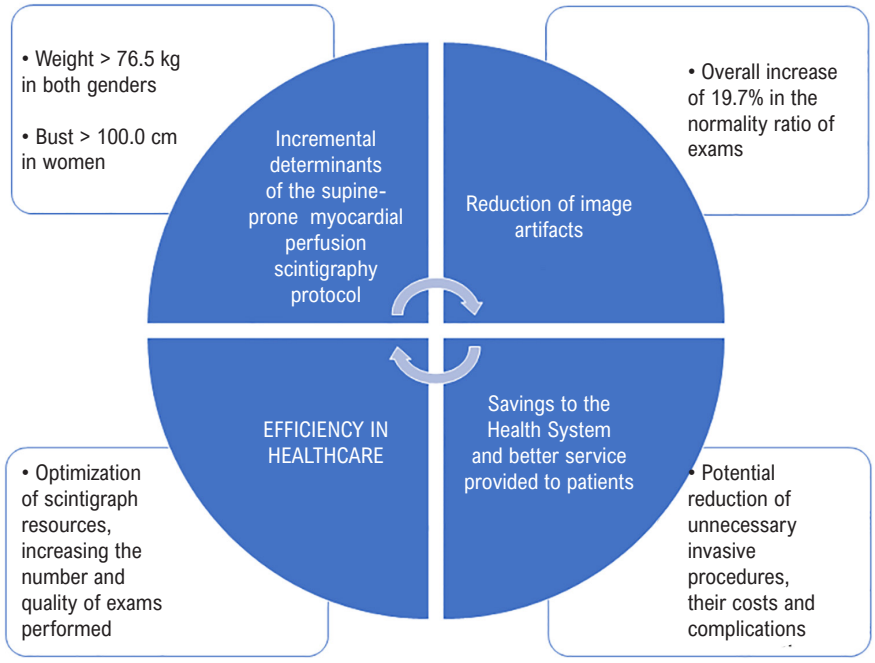
However, myocardial perfusion scintigraphy is a diagnostic tool subject to interference by artifacts, which can be caused by the attenuation of gamma radiation photons by soft tissues interposed between the myocyte and the gamma-camera detector, as well as artifacts resulting from the movement of the patient, among others that degrade the image quality, decreasing the specificity and the percentage of normality (normalcy rate) of the test. Results of exams with artifacts can greatly influence clinical decision-making, sometimes with continuation of the investigation of CAD through unnecessary invasive diagnostic methods, costly to the health system and not free of complications for the patient.[2]

Some techniques were then developed to minimize the impact of potential attenuation artifacts on myocardial perfusion scintigraphy. Among them, there is the combined protocol of supine-prone images, with benefits reported by previous scientific studies in different scenarios.[3-7] The technique consists of positioning patients in prone position on the examination table and performing the acquisition of additional images after the standard image acquisition in supine position in post-stress images. This positioning promotes caudal displacement of the diaphragm and subphrenic organs, potential interference factors

Central Illustration: Incremental Determinants Of The Combined Supine-Prone Protocol For Myocardial Perfusion Scintigraphy



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Health efficiency through the incremental determinants of the combined supine-prone imaging protocol of myocardial perfusion scintigraphy.

by attenuating photons emitted by the inferior wall of the left ventricle, thus enabling better detection of them by the gamma camera (Figure 1).

Changing the patients' position and compressing the soft parts of the chest (breasts, adipose tissue) in the prone position can also, sometimes, promote a better assessment of the anterior wall of the left ventricle (Figure 2), especially in cases of breast attenuation in women.

However, performing additional images in the prone position can affect the logistics of the exams due to the additional time spent. In services with a high volume of exams, it may be difficult to perform the combined protocol in all patients. Furthermore, its implementation in some patients would be unnecessary when there are no attenuation artifacts on images in the supine position. To our knowledge, there are no studies that evaluate anthropometric variables as criteria for the selective identification of patients with greater benefit in obtaining the image in the prone position, representing, therefore, a gap in the Literature that we intend to fill.

Methods

Study design

A cross-sectional and analytical study was carried out. Data were collected prospectively from spontaneous demand patients who sought the Service of the Nuclear Medicine Group (*Grupo de Medicina Nuclear* – GMN), Grupo CAM/Oncoclínicas, Salvador–Bahia, Brazil, in order to investigate CAD through myocardial perfusion scintigraphy, in the period between April and August 2022.

Patients of both genders were selected for the study, complying with the following inclusion criteria: absence of known previous coronary disease; minimum age of 18 years, with no upper age limit; prior indication of a myocardial perfusion scintigraphy exam to check for CAD by the attending physician. Exclusion criteria were: previous myocardial infarction or myocardial revascularization; non-ischemic cardiomyopathy or significant heart valve disease; pacemaker wearers; patients with left bundle branch block; inability to remain in prone position due to orthopedic or other limitations; poor technical quality of the exam performed (e.g. low image statistics, significant patient movement during the exam, significant interposition of extracardiac radioactive activity); non-signing of the Informed Consent.

Eligible patients who agreed to participate in the research protocol were previously assessed before the exam by trained nursing professionals to measure weight (kg), height (m), and waist circumference (cm) for both genders, in addition to measurements of the bust at nipple height (cm), chest circumference (cm), and delta between the bust and chest circumference (cm) for women, and then subjected to a combined supine-prone imaging protocol.

To acquire radionuclide images, a GE Medical Systems dual head gamma camera, model Ventri, was used, with all necessary calibrations and equipment quality controls performed. The technique used to acquire the images was single photon emission computed tomography (SPECT), with low energy high-resolution (LEHR) collimators and an energy window of 15% at 140 Kev, 64x64 matrix, using he radiotracer ^{99m}Tc-sestamibi. Male patients weighing more than 100 kg and female patients weighing more than 90 kg, who underwent the protocol for acquiring the rest and stress stages on different days (2-day protocol), while the others performed the stages of rest and stress on the same day (1-day protocol). The radiotracer dose used was 10 to 14 mCi at rest and 30 to 42 mCi in the stress stage in the 1-day protocol, with image acquisition lasting approximately 10 to 15 minutes in the rest stage and 7 to 9 minutes in the stress stage. In the 2-day protocol, the radiotracer dose injected was 15 to 20 mCi in each step, with a corresponding image acquisition time of 10 to 20 minutes. The images in the prone position were taken immediately after the acquisition of the stress images in the supine position, without the need for a new injection of the radiotracer, with an approximate duration of 7 minutes.

The images acquired were then analyzed by a specialist physician, without knowledge of the anthropometric data and identification of the patients, initially only with the analysis of the images of the standard protocol in the supine position and description of the scintigraphic findings of the exam and, later, a new evaluation with the addition of post-stress images in the prone position. Statistical analysis using binary logistic regression was used to assess the association between anthropometric data and the change in the initial result of the test after performing the combined protocol. This study was approved by the Research Ethics Committee of the School of Medicine and Public Health of Bahia (*Escola Bahiana de Medicina e Saúde Pública*) on March 19th, 2022, under registration CAAE 55279921.6.0000.5544, with all participants signing the Informed Consent, in accordance with resolution 466/2012.

Statistical analysis

Based on the premise of an incremental gain of 15% in the ratio of normality of the exams after the execution of the supine-prone protocol and the percentage of normality of approximately 65% in the exams in the supine position in our Service, a sample size calculation of 370 patients was performed

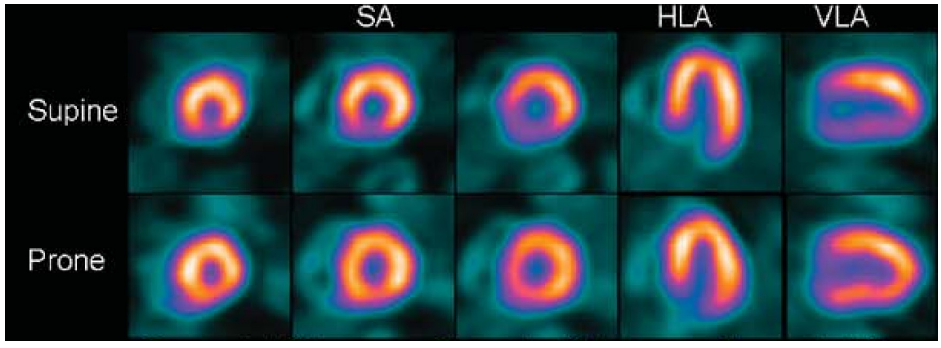


Figure 1 – *Example of diaphragmatic attenuation artifact with reduced uptake on the inferior wall in the post-stress image in the supine position (upper line), corrected in the post-stress image in the prone position (bottom line). Images displayed in 3 axes: short (SA), horizontal long (HLA), and vertical long (VLA). Adapted from Nishina et al, 2006.*[8]

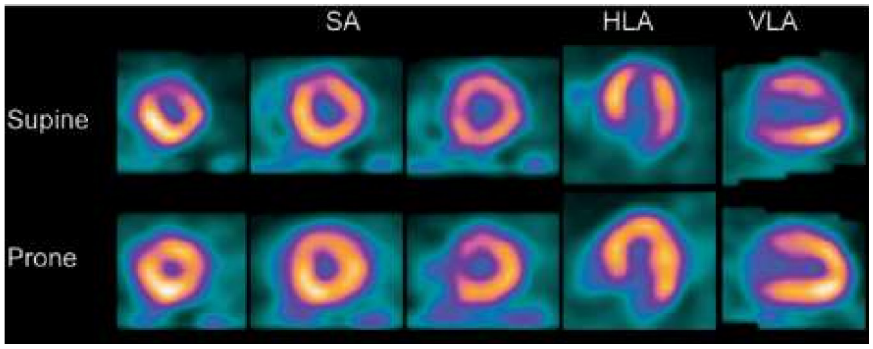


Figure 2 – *Example of artifact due to breast attenuation with reduced uptake in the anterior wall in the post-stress image in the supine position (upper line), corrected in the post-stress image in the prone position (bottom line). Images displayed in 3 axes: short (SA), horizontal long (HLA), and vertical long (VLA). Adapted from Slomka et al, 2007.*[5]

through the WinPepi program, version 11.65. The estimated statistical significance level was 5%.

Initially, descriptive statistics of the collected data were elaborated, in which the categorical variables were expressed in relative frequency and percentages. Numerical variables in our study were evaluated using the Kolmogorov-Smirnov test with Lilliefors correction and showed normal distribution, being expressed as mean and standard deviation.

Then, univariate statistical analyzes were performed using the unpaired Student's *t*-test to identify whether there was a statistically significant difference between the compared groups in relation to each numerical predictor variable with $p < 0.20$ and, thus, be eligible to enter the multiple model with the other numeric predictor variables. Therefore, statistical analysis was performed using binary logistic regression to assess the association between numerical predictor variables and the categorical outcome with or without modification of the result of the examination of the standard protocol of images in supine position after performing the combined supine-prone protocol. The Backward LR procedure was used for binary logistic regression analysis, which included all variables eligible for univariate analysis and, then, step by step, possible combinations of variables were made until arriving at the one(s) that best discriminated as independent predictor(s), with $p < 0.05$, for incremental gain with exclusion of artifacts through the combined supine-prone imaging protocol. 10% of the sample (37 exams) were selected for reanalysis and the Kappa test was used to evaluate interobserver agreement at two moments regarding the outcome variable. ROC curve analysis was used in order to identify the best cutoff point for anthropometric variables to discriminate the group of patients with the highest incremental gain through the combined protocol of supine-prone images.

SPSS software, version 26.0, for Windows was used as an auxiliary tool in the set of analyses previously described.

Results

From April to August/2022, 370 participants were included in the study analysis. Table 1 presents the characteristics of the sample studied in relation to gender, presence and type of comorbidities, as well as the type of stress and protocol performed in the exams.

Next, in Table 2, the specific age and anthropometric characteristics of the study sample can be verified.

In the initial analysis of the standard protocol with only images in the supine position, it was observed that most of the exams in the sample showed preserved perfusion in the left ventricular walls (63.5%). Among the exams that showed some type of myocardial hypoperfusion (persistent or transient), it was noted that the majority had mild hypoperfusion (125 exams) and only 10 exams in the sample showed moderate hypoperfusion (Graphic 1). No exams with severe hypoperfusion were observed in the studied sample.

After the inclusion of images in the prone position, the analysis of the combined protocol of supine-prone images led to changes in the exam results in 74 patients (20% of the total sample), the majority of individuals represented by the male gender (70.3 %), with pharmacological stress with dipyridamole (52.7%) and the study protocol with rest and stress stages carried out on the same day (85.1%), being the most frequent modalities. There was an overall increase of 19.7% in the proportion of normal exams, a finding that reflects the role of the combined protocol in the exclusion of artifacts. In 0.3% of the total sample, there was no complete normalization of the exam, as in the study that was initially considered as a mixed perfusion disorder on images in the supine position (persistent hypoperfusion with associated ischemia) and, after the combined protocol, was considered only as persistent hypoperfusion – the ischemic component in this case was attributed to attenuation artifact. When analyzing separately the subset of patients who initially had a perfusion deficit on images in the supine position ($n = 135$), this change in the result in 74 patients represents more than half of them after performing the combined protocol of supine-prone images. The kappa test applied after reanalysis of 10% of the total sample showed significant interobserver reliability ($k = 0.983$; $p < 0.001$; agreement = 99.5%).

The inferior wall was the region of the left ventricle that represented the highest absolute number of exams with modified results after analyzing the combined supine-prone imaging protocol. The anterior wall and apex occupied the second position. The other walls were also represented in Graphic 2.

The logistic binary regression analysis between anthropometric data for both genders (weight, height, and abdominal circumference) and the modification of the results of the standard protocol examination, after carrying out the combined supine-prone protocol, highlighted the weight variables at the end of the model [OR = 1.018 (95% CI, 1.0002 – 1.0370; $p = 0.047$)] and male gender [OR = 4.445 (95% CI, 2.4951 – 7.9199; $p < 0.001$)] as potential incremental determinants for the combined protocol. The ROC curve illustrated in Graphic 3 shows the criterion of weight greater than 76.5 kg as the best cutoff point for incremental gain with the supine-prone protocol in both genders – Sensitivity (S): 58,5%; Specificity (E): 61,5%.

Figure 3 shows the radionuclide images of myocardial perfusion of a study participant with significant diaphragmatic attenuation in the inferior wall of the left ventricle, with their respective anthropometric data, and the significant improvement in capture after taking the images in the prone position.

By separately performing the logistic regression analysis between anthropometric data in women (weight, height, abdominal circumference, bust, chest circumference, delta between the bust and chest circumference) and the modification of the initial examination result after the combined supine-prone protocol, the bust variable was at the end of the model that represented a possible incremental determinant for the supine-prone protocol [OR = 1.057 (95% CI, 1.011 – 1.106; $p = 0.014$)]. In Graphic 4, the criterion of a bust greater than 100.0 cm can be seen in the ROC curve as the best cutoff point for incremental gain with the supine-prone protocol (S: 73.9%; E: 53.4%).

Figure 4 below illustrates the radionuclide images of myocardial perfusion of a study participant with breast attenuation in the anterior wall of the left ventricle, with their

Table 1 – Characteristics of the categorical sample

Characteristics	n=370	%
Gender		
Female	226	61.1
Comorbidities		
Yes	292	80.0
High blood pressure	260	70.8
Dyslipidemia	144	41.6
Diabetes mellitus	134	36.5
Stress method		
Pharmacological-dipyridamole	220	59.8
Ergometric	148	40.2
Protocol		
1 day	338	91.4
2 days	32	8.6

Source: the author.

Table 2 – Specific characteristics of the studied sample

Characteristics	Mean	Standard deviation
Age (years)[1]	61.5	11.2
Weight (kg)[1]	74.7	15.2
Height (m)[1]	1.63	0.09
Abdominal circumference (cm)[1]	97.3	0.09
Male	98.7	11.7
Female	96.4	10.9
Bust (cm)[2]	99.8	9.9
Chest circumference (cm)[2]	88.9	9.9
Bust-Chest circumference (cm)[2]	9.9	3.5

[1]Both genders. [2]Only females. Source: the author.

respective anthropometric data, and the improvement in uptake after taking the images in the prone position.

Discussion

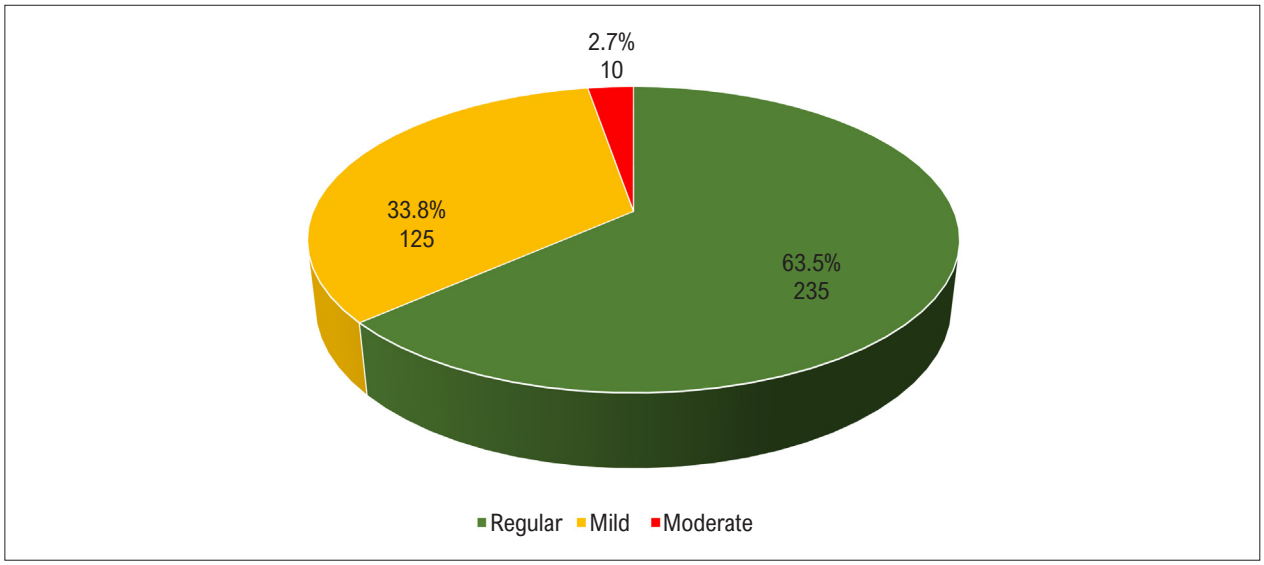
The combined protocol of supine-prone images of myocardial perfusion scintigraphy represents an important method for excluding artifacts and increasing the percentage of normality of the exams. In the present case series, an overall percentage increase of 19.7% in the number of normal exams was observed when compared to images from the standard protocol, only in the supine position. Other studies in the literature had already shown an increase in the percentage of normality through the combined protocol, although with analyses in subgroups (men, women or obese), one of the strengths of this work being the considerable global increase in the percentage of normality when analyzing the entire population studied.

The inferior, anterior, and apex walls were the regions of the left ventricle with the highest frequency of changes after the inclusion of the combined protocol, findings related to the presence of diaphragmatic attenuation artifacts in the inferior wall and attenuation by soft tissues, adipose tissue, and breasts in the anterior and apex walls.

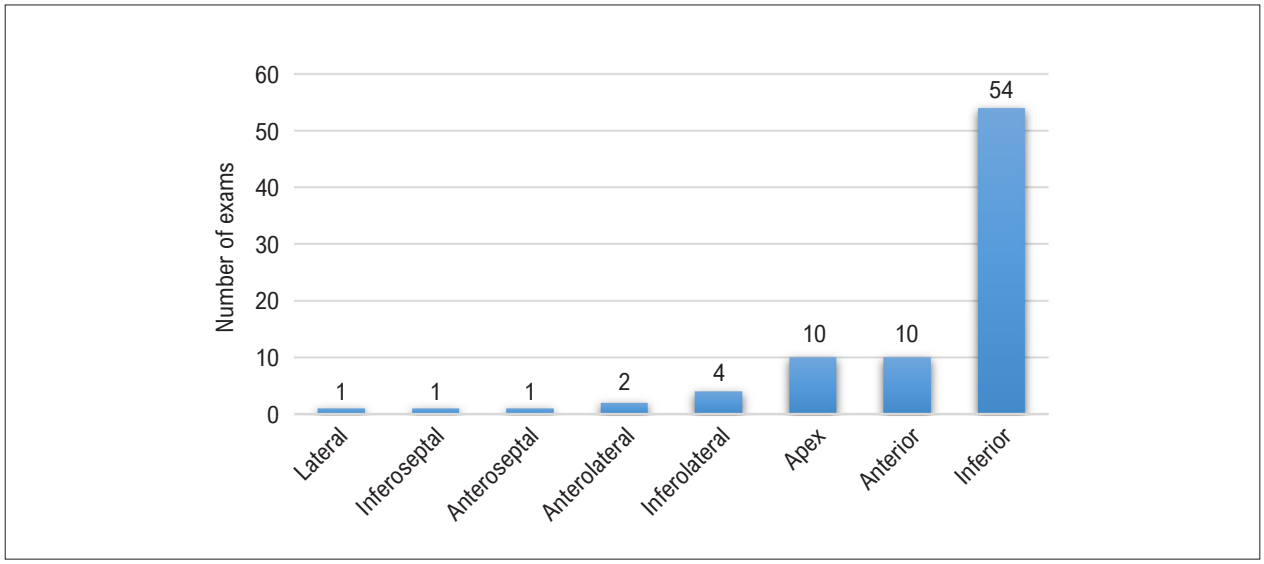
The impact of changing exam results with the combined protocol becomes even more evident when analyzing separately the subset of patients who initially presented perfusion deficits on images only in the supine position (n = 135). In this group of study participants, 74 of them showed a change in the exam results after performing the combined supine-prone imaging protocol. In other words, more than half of the patients (54.8%) had their test results modified by the combined protocol. This number of patients could have been unnecessarily taken to other invasive diagnostic procedures that are not free from complications, such as coronary angiography, if images in the prone position had not been added to the analysis. The combined protocol images do not expose the patient to additional doses of radiation, as they are acquired with the same radiotracer material as the previously performed injection, with only a change in position on the examination table. Furthermore, there is no need for additional costs when purchasing expensive software to correct image attenuation. In addition to the direct benefit to patients, there is also the savings generated for the healthcare system by avoiding expenses related to unnecessary invasive procedures.

Despite the benefits reported in excluding artifacts and increasing the number of normal exams through the combined supine-prone imaging protocol, reported by several authors and corroborated by the present study, there is no universalization of its use in all nuclear medicine services. The additional time spent performing the step in the prone position, in the context of services with a high volume of exams and the associated pressure for high productivity, may explain this heterogeneity in the application of the combined protocol. When considering exams that already present preserved perfusion in the images of the standard protocol in the supine position, the prone position of the combined protocol would not add value and would waste unnecessary additional time in acquiring images of the same patient, while the myocardial perfusion scintigraphy equipment could be used to assist other patients, increasing the total number of exams performed. The lack of objective criteria in the literature that could guide prior screening of patients with a greater chance of benefiting from the combined supine-prone protocol, based on the evaluation of anthropometric data most associated with attenuation artifacts, endorses the importance of this work in the search for its incremental determinants.

The weight variable represented an incremental determinant in a statistically valid way for both genders in the combined supine-prone protocol in the present study. The attenuation promoted by adipose tissue can be considered one of the pillars of this association. The criterion of weight above 76.5 kg was the best cutoff point for the ROC curve in this scenario. In parallel to the data found in the literature, the work of Hidetaka Nishina et al.,[8] showed an increase in the normality ratio of exams by around 17% in the subgroup of obese patients after carrying out the supine-prone protocol. However, it did not identify what would be the anthropometric determinant associated



Graphic 1 – *Standard protocol (supine): percentage of normal and hypoperfused exams.*

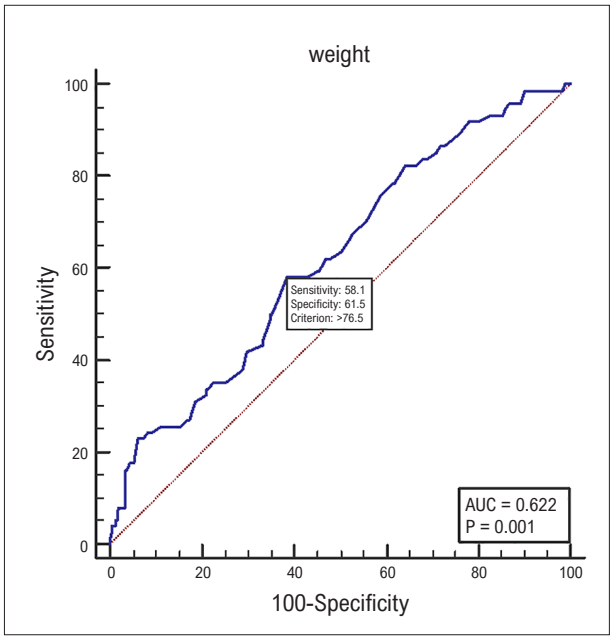


Graphic 2 – *Frequency of myocardial walls that improved uptake with the combined supine-prone protocol.*

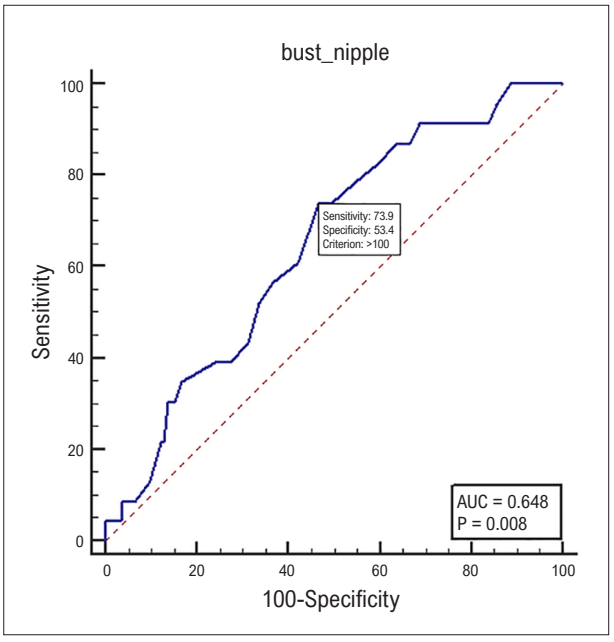
with incremental gain nor its best cutoff point for performing the technique, data found in our series.

The present study showed an association between males and a 4.44 times greater chance of benefit from the combined supine-prone protocol compared to females, most likely due to the greater prevalence of diaphragmatic attenuation artifacts and abdominal fat concentration (android pattern). In the same direction, the article by Vicente Taasan et al.,[4] concluded that the supine-prone protocol promotes increased diagnostic certainty and improves the accuracy of the test in detecting coronary disease in men with related risk factors, especially in obese ones, when compared to the standard protocol in the supine position only. However, as it was an exclusive study on men, it did not show a greater chance of improvement through the combined protocol in men when compared to women, a finding added by this work.

When analyzing females separately, the bust variable was a statistically valid incremental determinant. The measurement of the bust at nipple height with a value greater than 100.0 cm was configured as the criterion for the best cut-off point in the ROC curve. Breast attenuation, added to that of other soft tissues in the thoracic region, may represent a generator of artifacts in myocardial perfusion scintigraphy exams in women. A previous study by Slomka et al.,[5] had demonstrated, after carrying out the supine-prone protocol, an increase of 7 to 12% in the normality ratio of exams in women when compared to the standard protocol in the supine position. However, the objective of this study was not to identify the best cutoff point



Graphic 3 – *ROC curve weight x change with the combined supine-prone protocol.*



Graphic 4 – *ROC curve of bust measurement in women x change with the combined supine-prone protocol.*

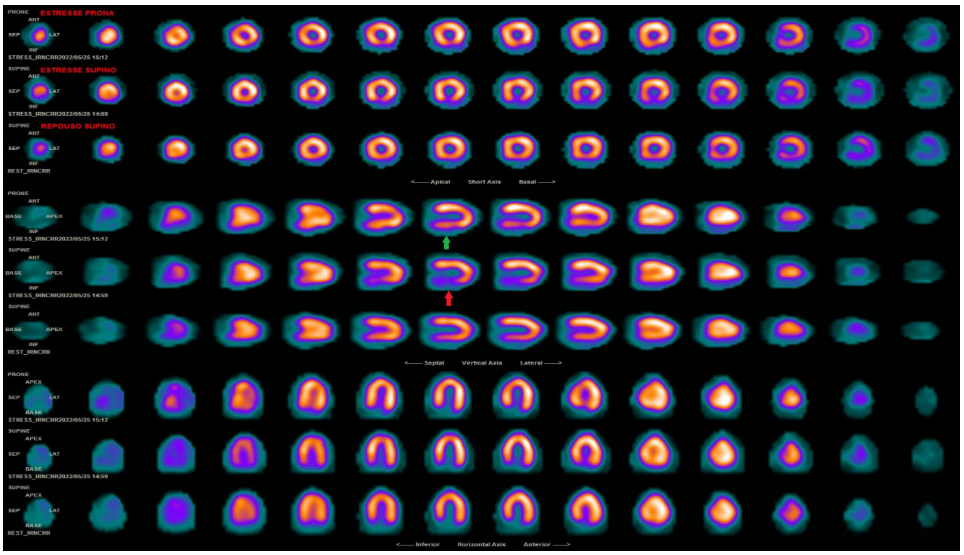


Figure 3 – *Male, 67 years old, 110.0 kg, 1.67 m, abdominal circumference of 122.0 cm, with diaphragmatic attenuation artifact in the lower wall in the post-stress image of the supine position (red arrow), corrected in post-stress image of the prone position (green arrow). Images displayed on 3 axes: short (top lines), vertical long (middle lines), and horizontal long (bottom lines).*

for the incremental determinant for the acquisition of the supine-prone protocol.

The body distribution pattern of adipose tissue, not covered by the isolated weight analysis, may represent a limitation to the external validity of this work. The biotypes of patients in other populations, sometimes different from those found in patients in our Nuclear Medicine Service, could impact the results found as criteria for the incremental determinants of the combined supine-prone protocol. Specific studies in other populations may be necessary.

The contribution of the present work to scientific knowledge is based on highlighting the importance of the combined supine-prone protocol, already described in other studies, and adding potential criteria for better selection and management of patients with greater benefit from carrying out this protocol. In this scenario, patients

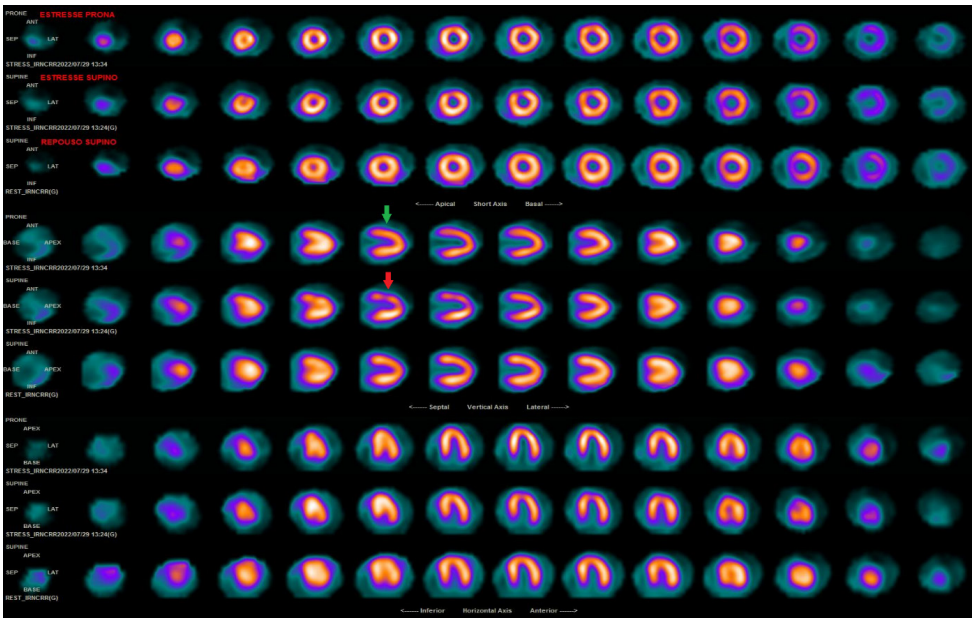


Figure 4 – *Female, 60 years old, 68.0 kg, 1.60 m, abdominal circumference of 97.0 cm, bust measurement of 104.0 cm, with breast attenuation artifact on the anterior wall in the post-stress image of the supine position (red arrow), corrected in post-stress image of the prone position (green arrow). Images displayed on 3 axes: short (upper lines), vertical long (middle lines), and horizontal long (bottom lines).*

of both genders weighing more than 76.5 kg and women with a bust measurement greater than 100.0 cm will have a progressive incremental gain with the combined supine-prone protocol.

Conclusions

It is of utmost importance that Nuclear Medicine Services encourage the use of a combined supine-prone imaging protocol in myocardial perfusion scintigraphy exams. The benefits brought by this technique, notably avoiding unnecessary invasive examinations due to false-positive results of the standard protocol, are extremely valuable.

The identification of specific anthropometric predictors of weight in both genders and bust measurement in women may represent an interesting strategy in better patient management for the combined supine-prone protocol. The selective inclusion of this protocol makes it possible to obtain more efficient images, as it allows the optimization of the gamma camera's resources. In this way, it is possible to select and include patients with the greatest benefit from prone imaging, improving both the quality of the images and enabling the equipment to be used to serve a greater number of patients. Efficiency in the use of resources in the Health Sector, increasingly essential to our population, therefore, constitutes an important paradigm to be constructed by all agents involved.

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Author Contributions

Conception and design of the research, acquisition of data, analysis and interpretation of the data, statistical analysis, writing of the manuscript, critical revision of the manuscript for intellectual content: Costa TO, Rocha MS, Feitosa Filho G, Camargo RA, Macedo C.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

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Study Association

This article is part of the thesis of master submitted by Tiago Oliveira Costa, from Escola Bahiana de Medicina e Saúde Pública.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Escola Bahiana de Medicina e Saúde Pública under the protocol number 55279921.6.0000.5544. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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