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João Miguel Portugal Antas de Barros Barbosa

Myocardial Perfusion Scintigraphy in Myocardial Infarction:
Impact of ST segment elevation and of Diabetes *mellitus*

Cintigrafia de Perfusão Miocárdica no Enfarte do Miocárdio:
Impacto da elevação do segmento ST e da Diabetes *mellitus*

MARÇO, 2021

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Mestrado Integrado em Medicina

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Prof. Doutor José Pedro Lopes Nunes

Trabalho organizado de acordo com as normas da revista:

Journal Of Investigative Medicine

MARÇO, 2021

DECLARAÇÃO DE INTEGRIDADE



UC Dissertação/Projeto (6º Ano) - DECLARAÇÃO DE INTEGRIDADE

Eu, João Miguel Portugal Antas de Barros Barbosa, abaixo assinado, nº mecanográfico 200900021, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro ter atuado com absoluta integridade na elaboração deste projeto de opção.

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Faculdade de Medicina da Universidade do Porto, 9 / 03 / 2021

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UC Dissertação/Projeto (6º Ano) – DECLARAÇÃO DE REPRODUÇÃO

NOME

João Miguel Portugal Antas de Barros Barbosa

NÚMERO DE ESTUDANTE

200900021

E-MAIL

joaoportugalbarbosa@gmail.com

DESIGNAÇÃO DA ÁREA DO PROJECTO

Medicina Nuclear

TÍTULO DISSERTAÇÃO/MONOGRAFIA (riscar o que não interessa)

Myocardial perfusion scintigraphy in myocardial infarction - impact of ST segment elevation and of Diabetes mellitus

ORIENTADOR

Prof. Doutor José Pedro Lopes Nunes

COORDENADOR (se aplicável)

ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTA OBRA APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☒
É AUTORIZADA A REPRODUÇÃO PARCIAL DESTA OBRA (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
DE ACORDO COM A LEGISLAÇÃO EM VIGOR, (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) NÃO É PERMITIDA A REPRODUÇÃO DE QUALQUER PARTE DESTA OBRA.	☐

Faculdade de Medicina da Universidade do Porto, 9 / 3 / 2021

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João Miguel Portugal Antas de Barros Barbosa

DEDICATÓRIA

Há poucos anos atrás, decidi mudar de rumo, pessoal e profissionalmente. Naquilo que foi o ano mais difícil da minha vida até então, a morte do meu Avô materializou a enorme lacuna que existia no meu conhecimento da saúde humana. Até aí, tinha explorado o mundo laboral, munido do meu curso anterior – Ciências Farmacêuticas – chegando, então, à conclusão de que a minha influência na saúde do paciente teria que ser mais interventiva e mais capaz. Esta escolha levou-me à Faculdade de Medicina da Universidade do Porto.

Os últimos 5 anos constituíram uma trajetória para a qual, isolado, seria sempre insuficiente. Consegui completá-la precisamente por não estar sozinho, devendo por isso agradecer e dedicar o presente trabalho:

Ao Professor Doutor José Pedro Nunes, pela assídua, sábia e amável orientação durante o curso no geral, e durante a elaboração deste trabalho em particular;

À minha família – em especial aos meus Pais e irmãos – por todo o apoio incondicional que me deram ao longo da minha vida;

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Aos meus amigos, em especial aos LCR e ao Almirante, pela inabalável amizade com que me brindam todos os dias;

Por fim, à Teresinha, pelo tempo, pelas palavras, pelos atos, pela (imérita) fé em mim e por tudo o que me deu, que qualquer texto será insuficiente para enumerar;

Nas palavras do meu antepassado Manoel de Portugal Marreca, formado pela Escola Médico-cirúrgica do Porto em 1902, *“este trabalho, [...] um thesoiro que fosse, a vós pertenceria”*.

**MYOCARDIAL PERFUSION SCINTIGRAPHY IN MYOCARDIAL INFARCTION -
IMPACT OF ST SEGMENT ELEVATION AND OF DIABETES MELLITUS.**

João Miguel Portugal Antas de Barros Barbosa
Rua do Padrão, 32, 2º Direito
4150-557 Porto
Portugal

joaoportugalbarbosa@gmail.com

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ABSTRACT

Myocardial perfusion scintigraphy (MPS) is frequently used in the evaluation of patients with myocardial infarction (MI). The goal of the present work was to evaluate changes in MPS according to the nature of the infarction (ST elevation versus non-ST elevation status) as well as according to the presence or absence of Diabetes mellitus.

A prospective study of 124 consecutive patients with MI was carried out, using MPS.

Patients with ST segment elevation MI (STEMI) had significantly larger values both for percentage and absolute areas of perfusion defects, both at rest and in stress situation, when compared to patients without ST segment elevation (NSTEMI). These patients had significantly lower values for left ventricular ejection fractions (EF), in a similar comparison. The values for perfusion defects at rest for STEMI patients were more than double the values for NSTEMI patients ($17.1 \pm 14.6\%$ versus $6.5 \pm 7.8\%$, $p < 0.001$). Concerning resting left ventricular EF, STEMI patients had a mean value of $47.6 \pm 13.6\%$ and NSTEMI patients had a mean value of $53.2 \pm 12.4\%$ ($p = 0.026$).

Regarding the comparison between patients with and without Diabetes mellitus, none of the parameters under study showed significant differences.

Linear regression analysis, taking percentage of perfusion defect, as dependent variable, yielded an overall significant result, however only ST segment elevation was shown to have an individually significant result.

We conclude that the presence of ST segment elevation but not the presence of Diabetes mellitus is associated to different patterns of MPS in patients with MI.

What is already known about this subject?

Acute myocardial infarction (MI) poses as a significant cause of death and morbidity. Myocardial perfusion scintigraphy (MPS) is frequently used in the evaluation of patients with MI. Specific electrocardiographic findings and risk factors lack correlation with MPS results.

What are the new findings?

The goal of the present work was to evaluate specific changes in MPS according to the nature of the infarction (ST elevation versus non-ST elevation status) as well as according to the presence or absence of Diabetes mellitus. The presence of ST segment elevation was associated to different patterns of MPS in patients with MI. The presence of DM was not associated either to differences in importance of perfusion defects or in the values of left ventricular ejection fraction.

How might these results change the focus of research or clinical practice?

The presence of ST segment elevation in the electrocardiogram was shown to be associated to a decreased cardiac contractility and to an increased perfusion defect, when compared to the absence of this electrocardiographic feature. Therefore, the present paper translates an important and innovative correlation of the presence of ST segment elevation and the myocardial damage extent.

Key words: myocardial perfusion scintigraphy, myocardial infarction, Diabetes mellitus

INTRODUCTION

Acute myocardial infarction (MI) poses as a significant cause of death and morbidity^{1,2}, and is defined as the loss of functional cardiac tissue, due to a cardiac ischemic event¹. Although the incidence of this type of event has declined steadily over the last decades, it still affects about 7 million individuals around the world annually, of which many occur in Europe, with the economic issues it entails³. Risk factors for MI include male gender, smoking, arterial hypertension, dyslipidaemia, Diabetes mellitus and obesity, among others^{1,4,5}.

MI can have different causes and be characterized in very different ways. One of the most used classifications is based on the presence of an elevation of the ST-segment in the electrocardiogram (ECG), thus allowing us to categorize the event as acute myocardial infarction with ST-segment elevation (STEMI) or without ST-segment elevation (NSTEMI)^{1,3}. Furthermore, the fourth universal classification of MI takes into account aetiology and clinical differences, and is divided into 6 types: type 1 (due to atherosclerotic plaque rupture), type 2 (due to a mismatch between supply and demand), type 3 (causing sudden death), type 4 (a - if related with percutaneous coronary intervention, PCI - and b - if related with thrombosis of a coronary stent), and type 5 (related with coronary artery bypass grafting, CABG)¹. Regarding MI presentation and diagnosis, although up to 40% of all MI are unrecognized in assessment through ECG upon admission⁶, first line MI diagnosis relies primarily on ECG findings, such as the already mentioned ST-segment elevation, together with symptoms and physical exam^{3,4}. Second line diagnosis concerns biochemical findings, namely cardiac troponin elevation (CT), a biomarker that is elevated in this context, allowing an early confirmation, as it presents high sensitivity for myocardial necrosis^{3,4}.

In the study of patients with suspected or confirmed ischaemic heart disease (e.g. on the aftermath of an MI), patients are frequently required to perform a myocardial perfusion scintigraphy (MPS), to assess ischemic areas of the heart, and potential loss of cardiac function⁷⁻⁹. MPS relies on the differential uptake of a radioisotope by the cardiac tissue, with further quantification/imaging, thus resulting in a myocardial perfusion map^{1,8,9}. Decreased perfusion in certain cardiac areas (shown as one or more perfusion defects) can result from the narrowing of one of

the coronary arteries, or even from a previous infarction that resulted in the replacement of functional tissue with fibrous tissue ^{1,8,9}. Due to its specificity, sensitivity and accuracy ^{7,8}, MPS became an important tool in diagnosis and follow-up of ischemic heart events.

Diabetes mellitus is frequently associated with cardio-vascular disease, and the simultaneous presence of both conditions is associated with a significant mortality risk ¹⁰.

A significant interest exists concerning the different types of connections between Diabetes mellitus and heart disease, making it of interest to study MPS data in relation to the diabetic status of patients.

The goal of the present work was to evaluate specific changes in MPS according to the nature of the infarction (ST elevation versus non-ST elevation status) as well as according to the presence or absence of Diabetes mellitus.

MATERIALS AND METHODS

The present study was a prospective, longitudinal study, and was approved by the Hospital Ethics Committee (Comissão de Ética do Centro Hospitalar Universitário São João). Patients enrolled in the project were given a written version of the protocol for a full evaluation, and later signed an informed consent form, prior to data collection. Inclusion criteria involved: age greater than 18, indication for MPS from September 2019- February 2020 (inpatient or outpatient), and a history of MI. Data collection was carried out prospectively, and included: birth date; gender; MI type; elevation of ST segment in MI event; presence of Diabetes mellitus; presence of arterial hypertension; presence of dyslipidemia; MPS data (both at rest and stress states).

MPS data included left ventricular ejection fraction (EF), percentage of perfusion defect (PPD), area of perfusion defect (APD), end-systolic volume (ESV), end-diastolic volume (EDV), summed motility score (SMS) and summed thickening score (STS).

Diabetes mellitus, arterial hypertension and dyslipidemia were diagnosed according to contemporary European guidelines; in the case of Diabetes mellitus, plasma results and current anti-diabetic medication were taken into account.

A comparison was made between patients with elevated ST-segment MI and patients with non-elevated ST segment MI. A second comparison was carried out, taking patients either with or without Diabetes mellitus.

Myocardial Perfusion Scintigraphy

Patients were requested not to use any caffeine-containing products for twenty-four hours prior to scanning. Some medications had to be suspended before the exam, according to the cardiologist. Pharmacologic stress was induced by intravenous adenosine in a perfusion system (160 µg/kg/min for 6 minutes, with administration of 370 MBq (10 mCi) of 99mTc-tetrafosmin at three minutes if one-day protocol, or 740 MBq (20 mCi) if two-day protocol). After the injection, patients were requested to eat a small quantity of bread with butter and a yoghurt to reduce abdominal activity uptake near the heart and improve image quality of the inferior wall. Stress imaging was performed 40 minutes post-injection. All patients were scanned in

supine position, with their arms placed above their heads and ECG-electrodes on. SPECT images were obtained over a 180° arc with a dual-head gamma-camera (Millennium MG, General Electric, USA or Infinia Hawkeye 4, General Electric, Israel), equipped with parallel-hole, low-energy, high-resolution collimators. Image acquisition was carried out for 15 minutes with 60 views, at 25 cardiac cycles per view, using 64x64 matrix size and a zoom factor of 1.3. A 10% window centered over the 140 keV photo-peak of ^{99m}Tc was used. Images were gated to the ECG using 8 equal intervals per cardiac cycle. CT scans, performed without iodinated contrast, were started immediately after the SPECT was completed in patients with body mass index $\geq 30 \text{ Kg/m}^2$ for attenuation correction. The CT scan parameters used in this study were: slice thickness 4.0 mm, effective mA of 1.0, 140 kV, 2.0 rotations per minute. Rest ^{99m}Tc -tetrofosmin SPECT/CT was performed if the stress study showed perfusion defects, using the same acquisition specifications. Three hours after the stress study, an activity of 740 MBq (20mCi) was administered for rest images, if one-day protocol, otherwise rest images were acquired on another day if two-day protocol, with the same activity. Like the stress study, images were acquired 40 minutes after injection. The images were processed using QGS/QPS in Xeleris Functional Imaging Workstation and were displayed in short, vertical long, and horizontal long axis slices. Gated SPECT imaging allowed the assessment of systolic and diastolic volumes and left ventricular EF.

The myocardial perfusion scintigraphy data under analysis in the present report corresponds to: 1) percentage of perfusion defect; 2) area of perfusion defect; 3) left ventricular ejection fraction.

Statistical Analysis

The Statistical Package for the Social Sciences software, from IBM (Amonk, NY, USA), version 26, was used to carry out statistical analysis of the collected data. Categorical variables, such as sex and presence of ST-segment elevation, were entered as numbers (male 1, female 2, non-STEMI 0, STEMI 1). Results are presented as arithmetic mean and standard deviation. Differences between group means were assessed using non-parametric Mann-Whitney U test.

Linear regression analysis was carried out, taking percentage of perfusion defect, both at rest and in stress conditions, as dependent variable, and age, sex, ST

segment elevation, presence of left bundle branch block, presence of type 2 myocardial infarction, history of Diabetes mellitus, history of arterial hypertension, and history of dyslipidaemia as independent variables.

A significance level of 0.05 was used.

RESULTS

Of 196 patients under initial evaluation, a total of 72 were excluded, due to incomplete clinical data regarding the patient, or to not fully fulfilling MI diagnosis criteria, thus making the final sample 124 patients (Table 1). In the different sets of data obtained, the sample did not follow a normal distribution, therefore the non-parametric Mann-Whitney U-test was performed to compare groups of patients.

STEMI versus NSTEMI

Regarding the perfusion defect, studied both in percentage and in absolute area, statistical analysis comparing the two groups provided significant differences, in both cases with $p < 0.001$ (Table 2). The values for perfusion defects at rest for STEMI patients was more than double the values for NSTEMI patients ($17.1 \pm 14.6\%$ versus $6.5 \pm 7.8\%$, $p < 0.001$; Table 2). Similar findings were seen with stress images. Concerning left ventricular EF, when patients with STEMI were compared to patients with NSTEMI, there were significant differences between the EF at rest, with a mean value of $47.6 \pm 13.6\%$ for the first group and $53.2 \pm 12.4\%$ for the second group, with a p value of 0.026 (Table 2). Similar findings were seen with stress images.

Further data are presented in Table 2.

Patients with or without Diabetes mellitus

Regarding the comparison between patients with and without Diabetes mellitus, none of the parameters under study showed significant differences, as shown in Table 3.

The mean values for the perfusion defects did not differ when the two groups of patients were compared, for any of the comparisons carried out. The percentage of the perfusion defect at rest was $11.6 \pm 12.6\%$ in patients without Diabetes mellitus, to be compared to $11.1 \pm 12.8\%$ in patients with Diabetes (p value of 0.75).

EF at rest, was not different in the two groups, with a mean result of $50.4 \pm 13.8\%$ for the first group and $50.4 \pm 12.3\%$ for the second group, with a p value of 0.63 (Table 3).

Further data are presented in Table 3.

Linear regression analysis

Linear regression analysis was carried out, taking percentage of perfusion defect, both at rest and in stress conditions, as dependent variable, yielded an overall significant result, however only ST segment elevation was shown to have an individually significant result (as shown in Table 4).

DISCUSSION

In the present report, MPS data obtained in patients with a previous MI were under study. The presence of ST segment elevation in the electrocardiogram was shown to be associated to a decreased cardiac contractility and to an increased perfusion defect, when compared to the absence of this electrocardiographic feature.

The presence of ST segment elevation in patients with MI is frequently associated to the presence of a coronary artery thrombus in the acute setting ^{11,12}. Patients with MI with no elevation of the ST segment are believed usually not to have coronary artery thrombotic acute occlusion ¹³. MI is a known health and economic burden, and is associated with risk factors such as obesity, hypertension and Diabetes mellitus. MI can often lead to tissue and functional changes in the heart, which may be evaluated through MPS. As a functional imaging technique, MPS is widely used, in ischemic heart disease assessment and prognosis.

Regarding Diabetes mellitus, current literature indicates that this condition is a risk factor for coronary artery disease (CAD), due to its association with greater and more significant vascular disease ¹⁰.

A previous report showed that when STEMI and NSTEMI patients were compared, the former was associated to higher mean values of troponin release, however no differences were seen in the angiographic importance of CAD ¹⁴.

This lack of correlation between the apparent importance of myocardial necrosis and the importance of CAD may be an explanation for the present results concerning patients with Diabetes mellitus. These latter patients are known to often have diffuse coronary artery disease ¹⁵, however the present results show that the presence of this clinical condition is not associated either to differences in importance of perfusion defects or in the values of left ventricular ejection fraction.

Limitations

The number of patients is relatively small, limiting the power of the conclusions reached. All consecutive patients with a diagnosis of MI were under study, regardless of MI type or date of the event. Additionally, post-event revascularization procedure, as well as medication information, were not included in data collection, and could influence MPS data.

CONCLUSIONS

We conclude that the presence of ST segment elevation but not the presence of Diabetes mellitus is associated to different patterns of MPS in patients with MI. The presence of ST segment elevation in the electrocardiogram was shown to be associated to a decreased cardiac contractility and to an increased perfusion defect, when compared to the absence of this electrocardiographic feature.

CONFLICT OF INTEREST

The author certifies that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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TABLES

Table 1.— Descriptive statistics for the variables collected in 124 patients with myocardial infarction. N – number; STD – standard deviation. P- Shown are levels of significance, Mann-Whitney U test, when patients with or without Diabetes mellitus and patients with or without ST segment elevation are compared, respectively.

Total number of patients	124
Male/ female N (%)	94 (75.8%)/ 30 (24.2%)
Age, years (Mean+ STD)	
Overall	68.2±11.4
Patients without Diabetes mellitus (n=78)	67.8±12.1
Patients with Diabetes mellitus (n=46)	68.9±10.0 (p=0.51)
Patients with STEMI (n=58)	66.7±10.0
Patients with NSTEMI (n=66)	69.5±12.4 (p=0.19)
Age, range (years)	36 – 93
Age group, years (n)	
30-49	6
50-69	67
70-89	48
Over 90	3

Table 2.— Data from myocardial perfusion scans in 124 patients with myocardial infarction (MI), according to ST elevation status (Mean + standard deviation). EF – left ventricular ejection fraction. PPD – Percentage of perfusion defect. APD - Area of perfusion defect. P- probability, Mann Whitney U test. N - number.

	ST segment elevation MI N=58	Non-ST segment elevation MI N=66	p
EF/ rest	47.6±13.6	53.2±12.4	0.026
EF/ stress	46.8±13.5	51.7±12.0	0.047
PPD/ rest (%)	17.1±14.6	6.5±7.8	<0.001
PPD/ stress (%)	21.3±14.7	11.3±9.2	<0.001
APD/ rest (cm ²)	26.18±26.68	9.39±12.87	<0.001
APD/ stress (cm ²)	32.90±28.18	15.53±14.58	<0.001

Table 3— Data from myocardial perfusion scans in 124 patients with myocardial infarction (MI), according to presence or absence of Diabetes mellitus (Mean $\pm$ standard deviation). EF – left ventricular ejection fraction. PPD – Percentage of perfusion defect. APD - Area of perfusion defect. P- probability, Mann Whitney U test. N - number.

	No Diabetes mellitus N = 78	Diabetes mellitus N= 46	p
EF/ rest (%)	50.7 $\pm$ 13.8	50.4 $\pm$ 12.3	0.63
EF/ stress (%)	49.7 $\pm$ 13.9	49.9 $\pm$ 11.1	0.38
PPD/ rest (%)	11.6 $\pm$ 12.6	11.1 $\pm$ 12.8	0.75
PPD/ stress (%)	16.1 $\pm$ 12.9	15.8 $\pm$ 13.4	0.75
APD/ rest (cm ²)	18.0 $\pm$ 23.3	15.9 $\pm$ 19.9	0.65
APD/ stress (cm ²)	24.2 $\pm$ 24.4	22.8 $\pm$ 22.3	0.76

Table 4— Linear regression analysis, taking percentage of perfusion defect (at rest) as dependent variable and several independent variables, as measured in 124 patients with myocardial infarction. P- significance level.

Dependent variable - percentage of perfusion defect, at rest. Overall ANOVA p - <0.001	p
Age	0.50
Gender	0.11
ST segment elevation	<0.001
Diabetes mellitus	0.21
Arterial hypertension	0.12
Dyslipidemia	0.27
Left bundle branch block	0.42
Type 2 myocardial infarction	0.82

ANEXO 1 – NORMAS DE PUBLICAÇÃO NO JOURNAL OF INVESTIGATIVE MEDICINE

BMJ Journals

Formatting your paper

These are general formatting guidelines across BMJ, please always refer to journal-specific instructions for authors for article type specifications. You can browse the titles on our Journals website.

You can also refer to our formatting checklist to make sure you have covered everything on submission.

Title page

The title page must contain the following information:

Title of the article

Full name, postal address and e-mail of the corresponding author

Full name, department, institution, city and country of all co-authors

Word count, excluding title page, abstract, references, figures and tables

Keywords

Authors can usually opt to (or are required to) choose keywords relevant to the content of the manuscript during the submission process. This assists in the identification of the most suitable reviewers for the manuscript. The selected keywords should also be included in the abstract itself.

Authors and Institutions

On submission of your article through our submission system you will be asked to provide a name, email address and institutional affiliation for all contributing authors. In the final published article author names, institutions and addresses will be taken from these completed fields and not from the submitted Word document. Refer to the BMJ policy on authorship for more information.

Manuscript format

The manuscript must be submitted as a Word document (BMJ Case Reports and Veterinary Record Case Reports request that authors submit using a template which should also be in Word format). PDF is not accepted.

The manuscript should be presented in the following order:

Title page

Abstract, or a summary for case reports (Note: references should not be included in abstracts or summaries)

Main text separated under appropriate headings and subheadings using the following hierarchy: BOLD CAPS, bold lower case, Plain text, Italics

Tables should be in Word format and placed in the main text where the table is first cited. Tables should also be cited in numerical order

Acknowledgments, Competing Interests, Funding and all other required statements

References. All references should be cited in the main text in numerical order

We have added a “submission prefill” tool to all of our journals, which typically reduces time taken to submit a paper by 25 percent. Just upload your manuscript and the system will automatically extract and populate the following submission fields: Title, Abstract, Authors, Institutions, Funders.

Figures must be uploaded as separate files (view further details under the Figures/illustrations section). All figures must be cited within the main text in numerical order and legends should be provided at the end of the manuscript.

Online Supplementary materials should be uploaded using the File Designation “Supplementary File” on the submission site and cited in the main text.

Please remove any hidden text headers or footers from your file before submission.

Style

Acronyms and abbreviations should be used sparingly and fully explained when first used. Abbreviations and symbols must be standard. SI units should be used throughout, except for blood pressure values which should be reported in mm Hg.

Whenever possible, drugs should be given their approved generic name. Where a proprietary (brand) name is used, it should begin with a capital letter.

To ensure a consistent approach, submitted articles should not include Trademark or Registered trademark symbols in the main text, tables or figures.

Figures and illustrations

Images must be uploaded as separate files. All images must be cited within the main text in numerical order and legends must be provided (ideally at the end of the manuscript). Video: [How to improve your graphs and tables](#)

Journal of Investigative Medicine: Submission Guidelines for Original research

Original research should not exceed 5,000 words and six figures or tables (not including supplementary material) — articles must be fully documented reports of original research but should be as concise as possible without compromising the data. Articles should be organized as follows: Title page, Unstructured Abstract (250 words max), Introduction, Materials & Methods, Results, Discussion, Conflict of Interest, Acknowledgments, References, Tables, Figure Legends, Supplementary Material.

The abstract should be followed by three sentences which outline the significance of the study:

What is already known about this subject?

What are the new findings?

How might these results change the focus of research or clinical practice?

Please include a box summarizing in three or four bullet points “what are the new findings?”.

ANEXO 2 – REPORTING GUIDELINES PARA ESTUDOS OBSERVACIONAIS DE COORTE (EQUATOR NETWORK)

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract; (b) Provide in the abstract an informative and balanced summary of what was done and what was found; <i>"A prospective study of 124 consecutive patients with MI was carried out, using MPS".</i> <i>"Patients with ST segment elevation MI (STEMI) had significantly larger values both for percentage and absolute areas of perfusion defects, both at rest and in stress situation, when compared to patients without ST segment elevation (NSTEMI)".</i>	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported <i>"MPS relies on the differential uptake of a radioisotope by the cardiac tissue, with further quantification/imaging,...".</i>	4
Objectives	3	State specific objectives, including any prespecified hypotheses <i>"The goal of the present work was to evaluate specific changes in MPS according to the nature of the infarction (ST elevation versus non-ST elevation status) as well as according to the presence or absence of Diabetes mellitus".</i>	5
Methods			
Study design	4	Present key elements of study design early in the paper <i>"The present study was a prospective, longitudinal study".</i>	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection <i>"Patients enrolled in the project were given a written version of the protocol for a full evaluation, and later signed an informed consent form, prior to data collection. Inclusion criteria involved: age greater than 18, indication for MPS from September 2019- February 2020 (inpatient or outpatient), and a history of MI".</i>	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed <i>"Inclusion criteria involved: age greater than 18, indication for MPS from September 2019- February 2020 (inpatient or outpatient), and a history of MI".</i>	6

Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable <i>"Data collection was carried out prospectively, and included: birth date; gender; MI type; elevation of ST segment in MI event; presence of Diabetes mellitus; presence of arterial hypertension; presence of dyslipidemia; MPS data (both at rest and stress states".</i>	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group <i>"Gated SPECT imaging allowed the assessment of systolic and diastolic volumes and left ventricular EF".</i>	6,7
Bias	9	Describe any efforts to address potential sources of bias <i>The enrollement of consecutive patients.</i>	6
Study size	10	Explain how the study size was arrived at <i>The study used all available and willing consecutive patients during the time available till the date for the presentation of this thesis; the study enrollment was prematurely stopped due to the Covid-19 pandemic.</i>	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why <i>Quantitative data was handled as described in the methods; sub-group analysis used major topics of interest in current cardiovascular research.</i>	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses <i>"Categorical variables,[...] were entered as numbers [...]. Results are presented as arithmetic mean and standard deviation. Differences between group means were assessed using non-parametric Mann-Whitney U test. Linear regression analysis was carried out [...]. A significance level of 0.05 was used".</i>	7, 8

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed; (b) Give reasons for non-participation at each stage; (c) Consider use of a flow diagram; <i>Of 196 patients under initial evaluation, a total of 72 were excluded, due to incomplete clinical data regarding the patient, or to not fully fulfilling MI diagnosis criteria, thus making the final sample 124 patients (Table 1).</i>	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9

		(b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount) <i>Patients were not characterized according to demographic, clinical or social criteria. No patients had missing data. A total of 72 patients were excluded, due to incomplete clinical data regarding the patient.</i>	
Outcome data	15*	Report numbers of outcome events or summary measures over time <i>No outcome data are reported.</i>	N/A
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period <i>Given the relatively small number of patients, linear regression analysis, taking percentage of perfusion defect (at rest) as dependent variable and several independent variables, was chosen to further evaluate major findings.</i>	9
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses <i>Subgroup analysis were reported, as stated above.</i>	9

Discussion

Key results	18	Summarise key results with reference to study objectives <i>"The presence of ST segment elevation in the electrocardiogram was shown to be associated to a decreased cardiac contractility and to an increased perfusion defect, when compared to the absence of this electrocardiographic feature".</i>	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. <i>"The number of patients is relatively small, limiting the power of the conclusions reached".</i>	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence <i>"This lack of correlation between the apparent importance of myocardial necrosis and the importance of CAD may be an explanation for the present results concerning patients with Diabetes mellitus".</i>	11
Generalisability	21	Discuss the generalisability (external validity) of the study results <i>"This lack of correlation between the apparent importance of myocardial necrosis and the importance of CAD may be an explanation for the present results concerning patients with Diabetes mellitus".</i>	11

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based <i>"No funding received for this report".</i>	12
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*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.