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Cuban studies on myocardial perfusion imaging technique for detecting ischemic heart disease

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Acronyms
MPI: myocardial perfusion imaging
SPECT: single-photon emission computed tomography

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ABSTRACT

Introduction: Cardiovascular diseases are the leading cause of death in Cuba; 67% of deaths occur due to ischemic heart diseases. In their care process, myocardial perfusion studies are used as functional non-invasive methods for the diagnosis and evaluation of the prognosis of coronary heart disease.
Objective: To define research areas associated with studies of myocardial perfusion in ischemic heart disease in Cuba.
Method: A descriptive research was carried out, based on the documentary analysis of sources obtained by systematized search of primary literature of Cuban authors from the key words myocardial perfusion, ischemic heart disease, and Cuba.
Results: We found that the year of greatest scientific productivity was 2011. Most of the works belonged to the Instituto de Cardiología y Cirugía Cardiovascular in Havana. The last publications were in 2016. No publication was found in 2017.
Conclusions: Studies on myocardial scintigraphy are centralized in the capital. The research works are mainly directed to the use of single-photon emission computed tomography (SPECT) for diagnostic purposes with very little research on as-pects concerning prognostic value in ischemic heart disease. New studies providing fresh viewpoints of myocardial perfusion analysis and demonstrating their benefits in sub-populations at risk must be conducted.
Keywords: Myocardial perfusion imaging, Myocardial ischemia, Single-photon emission computed tomography

Estudios cubanos sobre la técnica de perfusión miocárdica para la detección de cardiopatía isquémica

RESUMEN

Introducción: Las enfermedades cardiovasculares representan la primera causa de muerte en Cuba, el 67% de los fallecimientos ocurre por enfermedades isquémicas. En su proceso de atención son utilizados estudios de perfusión miocárdica como métodos funcionales incruentos para el diagnóstico y evaluación del pronóstico de la enfermedad coronaria.
Objetivo: Definir áreas de investigación asociadas a los estudios de perfusión miocárdica en cardiopatía isquémica en Cuba.
Método: Se realizó una investigación descriptiva, basada en el análisis documen-

tal de fuentes obtenidas por búsqueda sistematizada de literatura primaria de autores cubanos a partir de las palabras claves perfusión miocárdica, cardiopatía isquémica y Cuba.
Resultados: Se identificó que el año de mayor productividad científica fue el 2011. La mayoría de los trabajos pertenecieron al Instituto de Cardiología y Cirugía Cardiovascular de La Habana. Las últimas publicaciones correspondieron al año 2016, no se encontró ninguna en 2017.
Conclusiones: Existe centralización del estudio de perfusión miocárdica en la capital. Las investigaciones se dirigen fundamentalmente a la utilización de la tomografía por emisión monofotónica (SPECT) con fines diagnósticos, con muy poca investigación dedicada a precisiones del valor pronóstico en cardiopatía isquémica. Es necesario la ejecución de nuevos estudios que aporten nuevas perspectivas de análisis de la perfusión miocárdica y demuestren sus beneficios en sub-poblaciones de riesgo.
Palabras clave: Imagen de perfusión miocárdica, Isquemia miocárdica, Tomografía computarizada de emisión de fotón único

INTRODUCTION

In Cuba, the nuclear Cardiology has been developed supported by the National Public Health System. During the last five years, thanks to the support of the International Atomic Energy Agency (IAEA), through the technical cooperation project "Strengthening nuclear cardiology in Cuba for the diagnosis and treatment of patients with coronary heart disease"[1], this has been further strengthened. The use of nuclear cardiology techniques provides a functional perspective to the analysis of myocardial perfusion[2]. The images offered by the myocardiotropic radiotracers reflect the alterations of the myocardial perfusion and therefore, they translate the functional repercussion of the reductions in the arterial diameter. This quality is used in the diagnosis of ischemic heart disease and its monitoring in connection with medical or interventional treatment and also in the risk stratification of patients who have suffered an acute myocardial infarction[1].

Heart diseases are the main cause of morbidity and mortality in Cuba[3] and among these, ischemic heart diseases, with a constant increase in deaths to 16.774 in 2015[3-8]. To diminish this trend, it is necessary to promote an early diagnosis culture that includes the dissemination of the myocardial perfusion imaging (MPI) studies' benefits for an effective treatment and reduction of short-term and long-term complications[9-11].

As a general objective of this work, the authors propose: to define non addressed areas of research associated with MPI studies for the detection of ischemic heart disease.

METHOD

A descriptive research, based on the analysis of bibliographical sources, was performed, with a search strategy that included clinical trials, original articles, clinical cases and literature reviews, all made by Cuban authors. Materials were searched in both, Spanish and English languages, in the bibliographic databases SciELO, ScienceDirect, Medline and Elsevier. The systematic searches were carried out using the keywords: myocardial perfusion, ischemic heart disease and Cuba. They were carried out without restriction with respect to the years. The last search was made on June 18, 2017.

For the selection of the works, the following inclusion and exclusion criteria were taken into account:

- There were included scientific articles from Cuban authors, who used the MPI as a diagnostic tool for ischemic heart disease.
- There were excluded those where the full text and the abstract were not available.

From 61 articles initially obtained, 27 met the selection criteria and were the ones used for the present work. The obtained publications were imported directly from the databases into the library of the system of bibliographical references EndNote, what contributed with organization, agility of the research process and possibility of obtaining measurement indicators about the bibliography in a fast way and with integrity.

Each of the articles was analyzed according to the type of content, classifying them as: original, bibliographic review or case presentation (case report).

RESULTS

From the review in the above mentioned databases, a total of 27 items were identified, those shown in **table 1**. The majority of the works are original articles (77.8%), followed –by a wide margin– of the review articles (18.5%), and only one case report was found (**Figure**).

A more detailed description of the original articles where the variables analyzed, the abstract and conclusions are exposed, is shown in **table 2 - supplementary material**.

More than half (14 [51.8%]) were published in Cuban journals: 5 in *Revista Cubana de Medicina*, 4 in *CorSalud*, 2 in *Nucleus*, 2 in *Revista Cubana de Cardiología y Cirugía Cardiovascular*, 1 in *Revista Cuba-*

Table 1. List of scientific papers included in the review[12-35].

1st author, year	Title	Type of article	Source
1. Peix, 1999[12]	*Direcciones actuales en la detección de viabilidad miocárdica en cardiología nuclear.*	Review	*Revista Cubana de Cardiología y Cirugía Cardiovascular*
2. Álvarez, 2000[13]	*Presencia de precondicionamiento isquémico inducido por el ejercicio, en pacientes con enfermedad coronaria.*	Original	*Revista Cubana de Medicina*
3. Peix 2000[14]	*Gammagrafía miocárdica con doble isótopo (201Tl en reposo/ 99mTc-tetrofosmin en esfuerzo) en la detección de hipoperfusión reversible.*	Original	*Revista Española de Medicina Nuclear*
4. Peix, 2002[15]	*Gammagrafía de perfusión miocárdica con Tecnecio 99m-MIBI para predecir al año, la evolución de mujeres referidas para evaluación de dolor precordial.*	Original	*Revista Cubana de Medicina*
5. Ponce, 2002[16]	*Empleo del dipiridamol en la gammagrafía de miocardio con tetrofosmín-Tc99m en pacientes con bloqueo completo de rama izquierda. Resultados preliminares.*	Original	*Revista Cubana de Medicina*
6. Peix, 2006[17]	*Gammagrafía de perfusión miocárdica con tecnecio 99m-MIBI en el diagnóstico de la enfermedad coronaria en mujeres.*	Original	*Revista Cubana de Medicina*
7. Peix, 2007[18]	Ischemia in women with angina and normal coronary angiograms.	Original	Coronary Artery Disease
8. Peña, 2008[19]	*Diagnóstico de isquemia miocárdica silente en diabéticos tipo 2 mediante electrocardiograma, ergometría y Gated-SPECT.*	Original	*Revista Cubana de Investigaciones Biomédicas*
9. Peña, 2009[20]	*Utilidad de la tomografía computarizada de emisión de fotón único sincronizada con el electrocardiograma para la detección de isquemia miocárdica silente en diabéticos tipo 2.*	Original	*Revista Médica de Chile*
10. Peix, 2009[21]	Left ventricular dysfunction secondary to ischemia in women with angina and normal coronary angiograms.	Original	Journal of Women's Health
11. Ramírez, 2010[22]	*Gammagrafía con 99tc-mibi para determinar la efectividad de la heberquinasa en la reperfusión de la arteria relacionada con el infarto.*	Original	*CorSalud*
12. Peña, 2010[9]	*Factores aterogénicos que justifican la tomografía sincronizada de perfusión miocárdica en diabéticos tipo 2 sin clínica cardiovascular.*	Original	Doctoral Theses (Book)
13. Valdés, 2011[23]	*Gammagrafía de perfusión miocárdica en mujeres postmenopáusicas con angina y coronarias epicárdicas angiográficamente normales.*	Original	*CorSalud*

1st author, year	Title	Type of article	Source
14. Peix, 2011[10]	Gated-SPECT imágenes de perfusión miocárdica para la evaluación de pacientes con dolor torácico agudo y un electrocardiograma normal o no de diagnóstico.	Original	*Revista Cubana de Medicina*
15. Peña, 2012[24]	Lipid levels as predictors of silent myocardial ischemia in a type 2 diabetic population in Havana.	Original	MEDICC Review
16. Cabrera, 2012[25]	*Alteración de la perfusión, desplazamiento del ST y arritmias en paciente con espasmo coronario sin lesiones significativas.*	Case Report	Alasbimn Journal
17. Peix, 2012[26]	*Aplicaciones clínicas de las técnicas nucleares en el estudio del sincronismo ventricular.*	Review	*CorSalud*
18. Rochela, 2012[27]	*Asociación de los resultados positivos del SPECT de perfusión miocárdica con 99mTc-MIBI, con la presencia de dislipidemia en pacientes ≥ 40 años de edad.*	Original	*Panorama Nuclear (Nucleus)*
19. Peix, 2012[28]	Gated-SPECT myocardial perfusion imaging and coronary calcium score for evaluation of patients with acute chest pain and a normal or non diagnostic electrocardiogram.	Original	Journal of Nuclear Cardiology
20. Cabrera, 2013[29]	Prognostic value of gated SPECT after reperfusion for acute myocardial infarction.	Original	MEDICC Review
21. Rochela, 2014[30]	*Relación entre la Gammagrafía de Perfusión Miocárdica y el sobrepeso u obesidad, en pacientes mayores de 40 años de edad.*	Original	*Revista Médica Electrónica de Portales Medicos.com*
22. Peix, 2014[1]	*La cardiología nuclear en Cuba.*	Review	*Panorama Nuclear (Nucleus)*
23. Peix, 2014[31]	Gated SPECT myocardial perfusion imaging, intraventricular synchronism, and cardiac events in heart failure.	Original	Journal of Nuclear Cardiology
24. Peix, 2014[32]	Nuclear medicine in the management of patients with heart failure: Guidance from an expert panel of the International Atomic Energy Agency (IAEA).	Review	Nuclear Medicine Communications
25. Peix, 2015[33]	*Experiencia del Instituto de Cardiología en la evaluación del paciente con dolor torácico agudo mediante técnicas de Cardiología Nuclear.*	Review	*CorSalud*
26. Peix, 2015[34]	Stress-rest myocardial perfusion scintigraphy and adverse cardiac events in heart failure patients.	Original	MEDICC Review
27. Padrón, 2016[35]	*Gammagrafía de perfusión miocárdica versus otras técnicas en el diagnóstico de enfermedad arterial coronaria.*	Original	*Revista Cubana de Cardiología y Cirugía Cardiovascular*

na de Investigaciones Biomédicas and 1 in the repository of doctoral theses..

As it can be observed in **table 1**, the first study that used the MPI for the diagnosis of ischemic heart disease, found in our search, was in the year 1999. The year of greatest scientific productivity was 2011. Most of the works belonged to the *Instituto de Cardiología y Cirugía Cardiovascular* of Havana. The last publications corresponded to the year 2016, none to 2017.

Only 3 (11.1%) of the analyzed works[15,29,31] studied prognostic values of ischemic heart disease based on the results of the MPI study.

DISCUSSION

The single-photon emission computed tomography (SPECT) represents the more used MPI technique in nuclear cardiology. The analysis of the evaluated studies showed interesting results that confirm its usefulness.

The myocardial ischemia causes characteristic metabolic changes that are associated with reduced contractile function. Under normal conditions, cardiac metabolism is exclusively aerobic. The heart responds to the energy requirements, mostly, by the oxidative metabolism of fatty acids and lactate. During the ischemia, the metabolism of fatty acid stops working and the one aerobic and anaerobic of the glucose predominates[12].

The left ventricular ejection fraction is an optimum element for the evaluation of ischemic heart disease. Women with ischemic heart disease showed a worse functional status, as evidenced by the greater involvement of exercise capacity, despite having an anatomical disease less extensive than their male counterpart[15].

The combination of the results of a normal stress test with images of normal MPI and normal ventricular function (ejection fraction> 55%) have an excellent prognosis, with an annual combination of death rate from cardiac causes and nonfatal myocardial infarctions lower than 1% and an annual mortality rate less than 0.2%[29].

Peix *et al.*[28] ensure that patients with acute chest pain and risk of low to intermediate coronary artery disease, with normal resting MPI, have very low probability of cardiac events in the first year.

The MPI is a functional assessment comprising the whole coronary tree[20]. Its studies are based on the property owned by some substances emitting gamma radiation for entering the cytosol of the cardiomyocytes. The cardiac distribution depends on two factors: the coronary blood flow and the integrity of myocardial cells. This determines its growing use in Cardiology, especially in the field of ischemic heart disease[9].

The MPI study is a functional assessment, since the fixation of the radiotracer in the myocardium depends on the regional blood flow and cellular integrity. This allows the detection of perfusion defects caused by the reduction of blood supply in a certain territory corresponding to a stenotic vessel, induced by pharmacological stress or overload. It also allows to observe –in some cases– the perfusion in areas of viable myocardium, although they correspond to a vessel that may be totally occluded, they may have been receiving their perfusion and maintaining their cellular integrity (hibernating myocardium) via collateral circulation developed over time, which is part of the foundation of feasibility studies[9]. The diagnosis of myocardial viability is important for patients to be performed myocardial revascularization, either surgical or through coronary angioplasty[12].

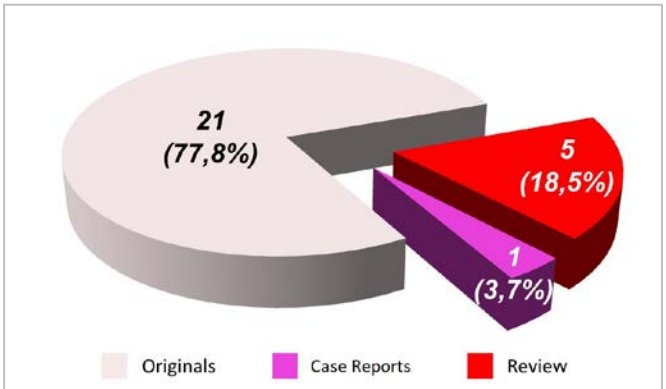

Figure. Classification of articles according to their typology.

Perfusion defects are assessed based on the extent, seriousness, reversibility and affectation of one or more territories. They are classified in extensive and not extensive, according to the number of myocardial segments involved. The severeness is determined according to the percentage of uptake compared to the area of greatest uptake in the polar image of the left ventricular. The classifications of seriousness respond to slight defect (uptake between 50-59%), moderate (uptake between 60-69%) and severe (uptake below 50%). The reversibility of the myocardial perfusion defect is cataloged as total, partial or null[9].

In another study[11], aimed at detecting the prevalence of ischemia in diabetic patients with coronary risk factors, the presence of diabetes was shown as only risk factor significantly associated with an abnormal MPI study. It was also demonstrated that reversible perfusion defects and the presence of coronary calcium are more frequent in diabetic patients[11].

The MPI test allows to prove the presence of ischemia, when during the application of physical or pharmacological stress, coronary spasm is triggered. The sudden reduction of blood flow causes a sectorial decrease of the MPI with less radiotracer uptake, originating reversible perfusion defects which indi-

cate ischemia zones[25].

Padrón García *et al.*[35], in 2016, evidenced the superiority of the MP scintigraphy with SPECT-synchronized versus the score of coronary calcium and conventional stress test in the detection of significant coronary artery disease in patients with inconclusive diagnostic phase, prior noninvasive studies. Currently, the SPECT-synchronized scintigraphy is the most widely used within the nuclear techniques, due to the possibility of evaluating perfusion, function and atrioventricular synchronism in the same examination[26].

In the study "*Factores aterogénicos que justifican la tomografía sincronizada de PM en diabéticos tipo 2 sin clínica cardiovascular*"[9], 43.1% of the patients who had glycemia greater than 5.5 mmol/L showed a positive SPECT-synchronized for asymptomatic myocardial ischemia (silent), and type 2 diabetics with fasting blood glucose levels above 5.5 mmol/L had three times more SPECT-synchronized positive for ischemia than patients whose numbers were below these levels, confirming the importance of glycemic control in type 2 diabetic patients for avoiding cardiovascular complications. In addition, 42.9% of type 2 diabetic patients without cardiovascular symptoms, with more than ten years of disease evolution, had a positive SPECT-synchronized[9].

Valdés Martín *et al.*[23], in 2011, showed that stress-induced ischemia is associated with a reduced post-stress ejection fraction and an endothelial dysfunction in women without finding ischeminc alterations in the Holter.

The SPECT is a useful diagnostic tool for coronary heart disease in women, but presents important interpretation problems that can generate false positives because women have smaller hearts, weighing an average of 7 grams less than men, which causes that little defects of radiotracer uptake are at the lower limit of resolution of the detector. Another problem are the attenuation defects in the anterior and inferior segments due to breast attenuation (in women) or diaphragmatic, respectively[15,17,23]. In this way, the 140 keV monoenergetic photopic of technetium-99m is associated with less attenuation than the thallium-201; hence, technetium compounds are more useful in the case of women[17].

Most authors agree that the SPECT-synchronized technique, due to its cost, should not be used as a screening method, although it allows an early diagnosis, with greater accuracy and which has a high sensitivity value. However, they demonstrate the high utility (and sensitivity) of the technique in patients with intermediate risk. Some works suggest to conduct more studies for achieving the identification of the risk factors that must lead to a MPI study, which early, and with greater certainty, determines the presence of asymptomatic ischemia in type 2 diabetic patients[9,19]. It is necessary to determine subpopulations of high risk that may benefit from their employment, and where the cost/effectiveness ratio is adequate[9].

The reviewed works confirm the benefits of MPI studies for the identification of ischemic heart disease; however, no work attempted to analyze the possible prognosis of this disease in diabetic patients, therefore, the authors of the present study suggest to widen this issue in future works.

CONCLUSIONS

There is a centralization of the myocardial perfusion study in the Cuban capital. Research works are aimed primarily at the use of SPECT for diagnosis, very few dedicate studies to specify the prognostic value in coronary heart disease. It is necessary the application of other research studies providing new perspectives of analysis of myocardial perfusion and which demonstrate its benefits in sub-populations at risk.

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