

Mgr Paweł Zdanowski

„DIAGNOSING ISCHAEMIC HEART DISEASE USING NUCLEAR MEDICINE TECHNIQUES”

Streszczenie w języku angielskim

Introduction

Diagnosis of cardiovascular diseases is based on both laboratory and imaging methods. Imaging techniques can be divided into two basic categories - tests showing morphological disorders (CT, angiography, MRI, ECHO) and tests allowing the assessment of functional disorders. Nuclear medicine research falls into the latter category. Currently, radioisotope methods allow to assess not only blood flow disorders in the myocardium, but also the nature of metabolic processes, the activity of receptor systems or the activity of the peripheral adrenergic nervous system. At present, nuclear medicine procedures are also used to assess inflammatory processes and cardiac amyloidosis. More and more reports concern also the diagnosis and characterization of atherosclerotic plaque.

Objective

The aim of the doctoral dissertation is to present - based on the literature review and own research - the possibilities of diagnostic radioisotope techniques in clinical practice and to determine their impact on pharmacoeconomic aspects in cardiovascular diseases.

The specific objectives are:

- to demonstrate - based on own research - the effectiveness and diagnostic usefulness of the radioisotope cardiac perfusion examination in the diagnosis of ischemic heart disease,
- to demonstrate - based on the available literature - the usefulness of radioisotope cardiac perfusion examinations in terms of their cost-effectiveness,
- to demonstrate - based on the available literature - the effectiveness of the [18F]FDG-PET examinations in the assessment of myocardial viability,
- to demonstrate - based on the available literature - the usefulness of the study using [123I]mIBG in the assessment of myocardial adrenergic system activity.

Methods

The review part of the dissertation presents the most important issues related to radioisotope research in cardiology based on the literature review. They concern the following issues:

- pharmaco-economic aspects of myocardial perfusion studies in ischemic disease,
- assessment of myocardial viability in the course of ischemic disease using [18F]FDG-PET,
- assessment of the activity of the cardiac adrenergic system using [123I]mIBG.

The section pertaining to own research presents the following:

- results on the risk of using iodinated radiological contrasts and methods of its mitigation. The research is based on the analysis of questionnaires completed by 64 patients,
- results regarding the diagnostic effectiveness of the cardiac perfusion test with the use of [99mTc]Tc-MIBI in ischemic disease depending on the location of ischemia and the degree of arterial stenosis. The article analyzes the results of examinations of patients hospitalized in two hospital wards of the same medical facility. The results of studies conducted in 200 patients with suspected or diagnosed ischemic heart disease (CAD) were initially evaluated. From this group, 83 studies were selected in patients for whom the results of coronary angiography and perfusion scintigraphy (MPS) were available. The following tests were used for statistical analysis: t-Student, Chi2, Fisher-Snedecor, Kruskal-Wallis and Willcoxon.

Results

In article 1 („*Economic premise to medical treatment in myocardial perfusion imaging of coronary artery disease*”) a literature review covering issues in the field of pharmacoeconomics of radioisotope diagnostic imaging of the cardiovascular system was conducted. The scientific database PubMed under the heading „cost-effectiveness, radioisotopic perfusion scan in ischaemic heart disease” showed 11 articles. In total, 6 papers registered in PubMed in 2002-2014 were evaluated and further analyzed. The selection of articles was based on the number of patients examined, the use of an isonitrile derivative ([99mTc]Tc-MIBI) as a radiopharmaceutical, a comparison of the diagnostic effectiveness of a radioisotope method with another imaging method, and the presentation of parameters used in cost-effectiveness analyses. The assessment included coronary angiography, cardiac perfusion scintigraphy (MPS), exercise ECG and magnetic resonance imaging (MRI). The usefulness of these methods was expressed in such indicators as: technique effectiveness, monetary value, or the impact of the study on the length/quality of life (QALY). The procedure of scintigraphy implementation took into account the advancement of the disease and clinical symptoms. Based on the literature review, it was shown that the MPS is a valuable tool in the diagnosis of ischemic heart disease. It allows to: simplify the diagnostic algorithm, obtain significant savings per patient (approx.

\$796), reduce the number of incorrect diagnoses in the emergency room (approx. 29%) and reduce the financial burden caused by incorrect patient qualification (approx. 6%). Own (unpublished) pharmaco-economic data show that obtaining 1 QALY by a patient in Polish conditions, using MPS or coronary angiography as the first examination in the initial diagnosis of ischemic heart disease, is in a cost ratio of 1:6.

Article 2 (*„The role of PET/CT examination in the assessment of myocardial viability”*)

reviewed the literature on the role of PET-CT in the assessment of myocardial viability. The PubMed database was used. Under the heading „[18F]FDG-PET viability of myocardium” 220 articles were found, 8 of which were selected for further analysis. The article determines the usefulness of ECHO after contrast administration, ECHO during a pharmacological test (dobutamine), SPECT after administration of [99mTc]Tc-MIBI, MRI after administration of a contrast agent, or during a pharmacological test with dobutamine/adenosine, PET after administration of [18F]FDG-PET. The last technique based on the assessment of changes in glucose metabolism within deeply ischemic segments of the heart has been described in the most extensive way. The data obtained to date indicate that the sensitivity of [18F]FDG-PET is 89.9-93.0%. The analyzed studies also showed that if 25.8% of the deeply ischemic part of the myocardium shows accumulation of [18F]FDG, then revascularization of this area significantly extends the survival time of patients.

In article 3 (*„Is MIBG really of no use in the diagnosis of heart failure”*) an analysis of the usefulness of the MIBG study was performed on the basis of the literature. Based on the PubMed medical database, 60 articles were found under the heading „123I-MIBG in cardiac examination” , 13 of which were selected for further analysis. The main indication for the examination is to determine the role of the adrenergic nervous system in the course of heart failure (HF). A number of data show that the result of this examination should determine the form of treatment - primarily the use of cardioverters. In the analyzed studies, the degree of radiopharmaceutical accumulation and the severity of functional disorders of the left ventricle were assessed. Total radiopharmaceutical uptake (heart mediastinal ratio (HMR) and radiopharmaceutical wash out (WO or WR) values were based on total radiopharmaceutical uptake.

In article 4 (*„Incidence of acute allergic reactions to contrast medium following CT examination on the basis of analysis of medical record data – preliminary report”*), as part of

own research, the issue of safety of use of contrast agents in radiological examinations of the cardiovascular system was addressed. The study assessed the frequency and severity of allergic reactions to iodine contrast agents used in computed tomography (CT) examinations, focusing on: the method of administration, the use of a medical procedure and patient management. Attention was drawn to the importance of a properly conducted interview before the decision to administer contrast is made, which allows to reduce the frequency of complications, e.g. post-contrast nephropathy, thyroid crisis and even death. This paper emphasizes the higher risk of radiological examinations with the use of contrast agents compared to radioisotope cardiac perfusion examinations during which there is no risk of complications related to the administration of a radiopharmaceutical, and the diagnostic results obtained are similar.

Article 5 („*Evaluation of the SPECT radioisotope perfusion scan in the detection of ischemic heart disease*”) presents the results of our own research. The work is retrospective. The analyzed material allowed to:

- determine predictive factors favoring the occurrence of ischemic heart disease in the study group of patients,
- determine the sensitivity and specificity of MPS, taking coronary angiography as the „gold standard” ,
- assess the usefulness of the MPS examination depending on the location of the stenosis within the main coronary vessels,
- assess the usefulness of MPS in the detection of multivessel disease.

It was shown that in the analyzed group of patients with CAD, the main factor predisposing to the occurrence of the disease is arterial hypertension ($p=0.016$). The highest sensitivity of MPS in the diagnosis of ischemia was found in the group of patients with right coronary artery stenosis ($p=0.029$), circumflex (GO) and marginal (GM) stenosis ($p=0.028$). A comparative analysis was performed between the degree of stenosis of the above vessels and the degree of perfusion disturbance in the MPS study. There was a correlation between the severity of ischemia in the MPS study and the degree of stenosis of both the PTW ($p=0.011$, sensitivity 95% (83.1 - 99.4 C.I.), 83.3% negative predictive value) and the GO/GM complex ($p=0.044$, sensitivity 94.7% (83.1 - 99.4 C.I.), negative predictive value - 83.3%). A correlation has also been noted between the MPS perfusion test result and two- or three-vessel coronary disease. There was a 97% agreement between the presence of permanent or transient defects in MPS

and the presence of stenosis in 2 or 3 coronary vessels exceeding 80% of the vessel lumen. In the group of patients with 50-80% occlusion of the artery diameter, abnormal scintigraphy results were found in 41.7% of patients.

Conclusions

The presented series of publications consists of review articles and author's own works. These articles clearly indicate that techniques in the field of nuclear medicine still play an important role in the diagnosis and prognosis of ischemic disease. They represent various pathophysiological processes of diseases.

- The cardiac perfusion test meets the pharmaco-economic criteria. The introduction of this test in the group of patients with an intermediate risk of disease is associated with measurable benefits for both the patient and the health care system. This test is primarily used in the noninvasive diagnostics of CAD in the group of patients at intermediate risk of ischemic disease.
- Data from the literature indicate that the [18F]FDG-PET examination allows the assessment of the metabolic profile of the myocardium, which is used primarily in the assessment of myocardial viability in areas of deep ischemia. This technique shows very high sensitivity and specificity and should be widely used in clinical practice.
- Data from the literature indicate that the activity of the cardiac adrenergic system assessed using radioisotope methods is very useful in the assessment of the severity of heart failure and in the choice of treatment.
- Own research confirms the significant risk associated with the use of iodine contrast agents in cardiac diagnostics. Thus, in the group of patients requiring diagnostic imaging, the possibility of replacing the radiological procedure with a radioisotope or ECHO examination should always be considered; these methods should be viewed as alternative imaging examinations.

Own (unpublished) pharmacoeconomic data show that obtaining 1 QALY by a patient in Polish conditions, using MPS or coronary angiography as the first test in the initial diagnosis of ischemic heart disease, is in a cost ratio of 1:6.