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Review

Diagnostic performance of iodine-123-metaiodobenzylguanidine scintigraphy in differential diagnosis between Parkinson's disease and multiple-system atrophy: A systematic review and a meta-analysis

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ABSTRACT

Background and purpose: This study was designed to review the diagnostic performance of iodine-123-metaiodobenzylguanidine (MIBG) scintigraphy in differential diagnosis between Parkinson's disease (PD) and multiple-system atrophy (MSA).
Methods: A comprehensive computer literature search of studies published through March 2011 regarding MIBG scintigraphy in patients with PD and MSA was performed in PubMed/MEDLINE and Embase databases. Only studies in which MIBG scintigraphy was performed for differential diagnosis between PD and MSA were selected. Pooled sensitivity and specificity of MIBG scintigraphy were presented with a 95% confidence interval (CI). The area under the ROC curve was calculated to measure the accuracy of MIBG scintigraphy in differential diagnosis between PD and MSA.
Results: Ultimately, we identified 12 studies comprising a total of 1226 patients (593 patients with PD, 117 patients with other Lewy body disease, 129 patients with MSA, and 387 patients with other diseases). The pooled sensitivity of MIBG scintigraphy to detect PD was 89% (95% CI: 86–91%); the pooled specificity of MIBG scintigraphy to discriminate between PD and MSA was 77% (95% CI: 68–84%). The area under the ROC curve was 0.93.
Conclusions: MIBG scintigraphy is an accurate test for PD detection and differential diagnosis between PD and MSA; this method shows high sensitivity and adequate specificity in this field. Nevertheless, possible causes of false negative and false positive findings should be considered when interpreting the scintigraphic results.

Contents

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1. Introduction

Early diagnosis of Parkinson's disease (PD) and differential diagnosis between PD and multiple-system atrophy (MSA) using clinical criteria or imaging methods are often difficult. Myocardial innervation imaging using ^{123}I-metaiodobenzylguanidine (MIBG) has emerged as a useful method to support the clinical diagnosis of PD [1].

Radiolabeled MIBG is considered an established sympathetic neuron imaging agent useful to study the organs richly innervated by the sympathetic nervous system. MIBG is an analog of guanethidine and is taken up by the postganglionic presynaptic nerve endings of the adrenergic nervous system. After depolarization, MIBG is released into the synaptic cleft like norepinephrine but is not metabolized. Labeling MIBG with iodine-123 allows the visualization of adrenergic innervation in vivo; MIBG scintigraphy not only displays the presence of noradrenergic innervation but also its functional capability [1–5].

About the scintigraphic method of myocardial innervation imaging, ^{123}I-MIBG is intravenously administered at rest and early (from 10 to 30 min after injection) and delayed (from 3 to 4 h after injection) images are obtained. Planar images with anterior view are adequate for the evaluation of cardiac sympathetic function. Tomographic images (SPECT) are often acquired to evaluate the three-dimensional myocardial uptake pattern [1–5].

The most common semi-quantitative indices used for interpretation of myocardial innervation images are the heart to mediastinum ratio (H/M) and the washout rate (WR) obtained from the anterior planar images. Regions of interest (ROIs) are set in the heart (H; target region) and the mediastinum (M; background region) in early and delayed images to obtain the mean count in each ROI, after which the H/M ratio is calculated. Based on the resulting ratio, the degree of accumulation in the heart is evaluated. The WR is an index that indicates the rate at which MIBG is washed out between the early image and the delayed image, via comparison of cardiac counts in the early image. Normal values of these indices have been calculated performing MIBG scintigraphy in control patients and are different between various institutions depending on acquisition conditions [1–5]; the normal limit is based on the computation of the 95th percentile of results in the control group.

Myocardial MIBG scintigraphy was originally used to assess myocardial sympathetic denervation in heart diseases [3]. In recent years, it has been revealed that PD, dementia with Lewy bodies (DLB), pure autonomic failure (PAF) and idiopathic REM sleep behavior disorder (RBD) share one clinicopathological entity: Lewy body diseases (LBD) has thus become a general term for these diseases [4–6]. LBD presents an impairment of adrenergic function and consequently an abnormal myocardial MIBG innervation imaging: the involvement of myocardial postganglionic sympathetic nerves may account for the reduction of myocardial MIBG uptake in patients with PD, as well as in patients with other LBD [1–6].

In contrast with PD, MSA usually presents a preganglionic rather than a postganglionic sympathetic denervation; therefore, myocardial MIBG uptake is usually expected as normal in MSA [5].

The purpose of this study is to systematically review and meta-analyze published data on the diagnostic performance of myocardial MIBG scintigraphy in differential diagnosis between PD and MSA.

2. Methods

2.1. Search strategy

A comprehensive computer literature search of the PubMed/MEDLINE and Embase databases was conducted to find relevant published articles on the diagnostic performance of MIBG scintigraphy in differential diagnosis between PD and MSA. We used a search algorithm that was based on a combination of the terms: (a) "MIBG" OR "metaiodobenzylguanidine" AND (b) "Parkinson" OR "parkinsonism". No beginning date limit was used; the search was updated until March 2011. Only articles in English language were selected. To expand our search, references of the retrieved articles were also screened for additional studies.

2.2. Study selection

Studies or subsets in studies investigating the diagnostic performance of MIBG scintigraphy in patients with PD and MSA were eligible for inclusion.

Only those studies or subsets in studies that satisfied all of the following criteria were included: (a) MIBG scintigraphy performed for differential diagnosis between PD and MSA; (b) sample size of more than 10 patients with PD or MSA included; (c) articles in English language.

The exclusion criteria were: (a) articles not within the field of interest of this review; (b) review articles, editorials, comments, conference proceedings; (c) case reports or small case series (sample size of less than eleven patients with PD or MSA included); (d) articles not including both PD and MSA subjects; (e) retracted articles; (f) articles not in English language; (g) insufficient data to reassess sensitivity (number of true positives and false negatives) and specificity (number of true negative and false positive) from individual studies; (h) studies including patients with heart diseases or taking drugs that influence the myocardial MIBG uptake; (i) overlap in patient data (duplicate publication: in such cases the most complete article was included).

Three researchers (GT, AS and EC) independently reviewed the titles and abstracts of the retrieved articles, applying the inclusion and exclusion criteria mentioned above. Articles were rejected if they were clearly ineligible. The same three researchers then independently reviewed the full-text version of the remaining articles to determine their eligibility for inclusion. Disagreements were resolved in a consensus meeting. Questionnaires to assess the quality of manuscripts were not used.

2.3. Data abstraction

For each included study, information was collected concerning basic study (author names, journal, year of publication, country of origin), patient characteristics (mean age, sex, number of patients which performed MIBG scintigraphy, number and types of parkinsonism investigated), technical parameters (radiopharmaceutical injected dose, time interval between radiopharmaceutical administration and data acquisition, acquisition details, additional SPECT acquisition, presence of a normalcy database), MIBG scintigraphy evaluation (semiquantitative measures as early H/M, delayed H/M or WR, applied reference standard). For each study the number of true positive, false positive, true negative and false negative findings for MIBG scintigraphy in differential diagnosis between PD and MSA were recorded; a true positive result was considered when MIBG myocardial uptake was reduced in patients with clinical criteria of PD; a false positive result was considered when MIBG myocardial uptake was reduced in patients with clinical criteria of MSA. A true negative result was considered when MIBG myocardial uptake was normal in patients with clinical criteria of MSA. A false negative result was considered if MIBG scintigraphy was normal in patients with clinical criteria of PD.

Patients with other LBD such as DLB, PAF and RBD, were excluded from the evaluation, because a differential diagnosis