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123I-metaiodobenzylguanidine myocardial scintigraphy with early images alone is useful for the differential diagnosis of dementia with Lewy bodies

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ABSTRACT

123I-metaiodobenzylguanidine cardiac scintigraphy (MIBG) is a useful imaging technique for the diagnosis of dementia with Lewy bodies (DLB). However, MIBG has a serious disadvantage in that it demands a long examination time. The objective of this study was to evaluate statistically the usefulness of the heart/mediastinum ratio (H/M) from the early phase of MIBG for the differential diagnosis of DLB. In total, 113 patients were examined, including 32 non-DLB (19 with Alzheimer's dementia) and 79 DLB patients. The mean early-H/M ratio was 2.83 in the non-DLB group and 1.95 in the DLB group. The mean delayed-H/M ratio was 3.0 in the non-DLB group and 1.76 in the DLB group. With a cutoff point of 2.27 on early images, the sensitivity, specificity, and diagnostic accuracy were 65%, 94%, and 73%, respectively, and the area under the curve was 0.82, indicating moderate accuracy. This analysis indicates that images from the early phase of MIBG alone are sufficient for the differential diagnosis of Alzheimer's disease and DLB.

1. Introduction

123I-meta-iodobenzylguanidine (MIBG) scintigraphy is a useful supplementary tool in the diagnosis of Parkinson's disease (PD) (Braune et al., 1999; Druschky et al., 2000; Orimo et al., 1999). Moreover, Yoshita (1998) and Watanabe et al. (2001) reported that MIBG imaging is useful for differentiating Alzheimer-type dementia (ATD) from dementia with Lewy bodies (DLB, which together with Lewy body disease can be associated with PD, PD with dementia [PDD], and neuropathological continuity). MIBG imaging is described in the supportive feature section of the current revised version of the Consortium on Dementia with Lewy Bodies (CDLB) Guidelines (McKeith et al., 2005). According to this report, a heart/mediastinum ratio (H/M) cutoff point of 1.68 on delayed MIBG images resulted in highly reliable differentiation of DLB from ATD with both the sensitivity and the specificity being 100%, regardless of the presence or absence of parkinsonism (Yoshita et al., 2001). Because of its high diagnostic accuracy, MIBG imaging has become one of the essential imaging methods for diagnosing DLB. However, whereas MIBG imaging is useful, the examination takes approximately four hours, which imposes a significant burden on the patients and their families. In actual clinical settings, many clinicians consider the early images to be sufficiently useful as a differential diagnosis tool. If diagnostically useful, early MIBG imaging alone could reduce the burden imposed by imaging on the patient and improve the accuracy of clinical diagnosis. The aim of the current study was to evaluate the usefulness and validity of early MIBG imaging by statistically testing the hypothesis that early MIBG imaging alone, which we named “simplified MIBG imaging,” is useful in the diagnosis of DLB.

2. Methods

2.1. Subjects

A total of 113 consecutive patients who were requested by our neurology and psychiatry departments to undergo MIBG imaging for suspected DLB between April 1, 2014 and June 30, 2015, and who met the criteria listed below, were included in the analysis. The present

Abbreviations: ATD, Alzheimer's type dementia; CDLB, Consortium on Dementia with Lewy Bodies; DLB, dementia with Lewy bodies; H/M, heart/mediastinum ratio; MIBG, 123I-meta-iodobenzylguanidine; PD, Parkinson's disease; PDD, Parkinson's disease with dementia

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study was conducted following a review by the Ethical Review Board at the authors university, and we certify that there is no conflict of interest with any for-profit organization or corporation. The subjects and their caregivers were notified both verbally and in writing that MIBG imaging test results in all patients would be used for research, and written consent was obtained after receiving verbal acknowledgment of their understanding and agreement.

Patients who had received tricyclic or tetracyclic antidepressants within 6 months prior to examination, patients with serious heart disease such as heart failure with an ejection fraction below 60%, and patients with severe diabetes requiring insulin treatment were excluded. All items on the imaging request form had to be completed for eligible patients' entry, and these included: clinical diagnosis of suspected DLB aiming at its differential diagnosis; age and sex of the patient; presence/absence of complications of diabetes and their severity; presence/absence of complications of heart disease; presence/absence of history of depression and oral administration of antidepressants; mini mental state examination score; presence/absence of parkinsonism; presence/absence of visual hallucinations; and presence/absence of cognitive fluctuations.

In total, 111 patients (53 males and 58 females; mean age, 78.2 years) met these entry criteria for analysis, and 79 of these patients were placed in the group clinically diagnosed with DLB according to the Consensus Criteria for the Clinical Diagnosis of Probable and Possible DLB (Revised CDLB Guidelines). The other 32 patients were placed in the non-DLB group (19 cases diagnosed as having ATD, seven cases diagnosed as having mixed-type dementia, three cases diagnosed as having corticobasal degeneration, two cases diagnosed as having idiopathic normal pressure hydrocephalus, and one case diagnosed as having progressive supranuclear palsy). Table 1 shows the patient characteristics.

2.2. MIBG imaging

The imaging was performed using a Symbia T16 SPECT/CT system (Siemens AG, München, Germany) equipped with an LMEGP collimator. We carried out a 4-min static acquisition (matrix size 128×128, magnification 1.0) 15 min after intravenous injection of 111 MBq MIBG in the right arm, followed by a 20-min SPECT acquisition (matrix size 64×64, magnification 1.45, step-and-shoot 360°) if uptake was observed.

MIBG imaging scans were read and interpreted centrally by a radiologist and a neurologist. In addition, semi-quantitative evaluation of the H/M ratio was performed. The H/M ratio and washout ratio were calculated using the Standardized Method for Automatic Region of Interest (ROI) setting in MIBG (smart MIBG) software (FUJIFILM RI Pharma, Tokyo, Japan; Okuda et al., 2011). This standardized image analysis software for 123I-MIBG imaging was used to determine automatically the mediastinal ROI from information on the cardiac ROI. According to the method reported previously (Nakajima et al., 2012, 2014), each H/M ratio was corrected to that of the standard ME collimator condition.

Table 1
Patient characteristics.

	Non-DLB (n =32)		DLB (n=79)
	ATD (n=19)	Other (n=13)	
Age (years)	74 ± 10.4	79.2 ± 6.0	79.1 ± 6.7
MMSE score	21.7 ± 4.0	21.2 ± 4.1	22.8 ± 3.9
Patients with parkinsonism	6	11	46
Patients with visual hallucinations	6	2	52
Patients with cognitive fluctuations	8	0	11
H/M ratio in early phase (%)	2.72	2.99	1.95
H/M ratio in delayed phase (%)	3.01	2.98	1.76

Means ± SD are shown. ATD, Alzheimer's type dementia; DLB, dementia with Lewy bodies; H/M ratio, heart to mediastinum ratio; MMSE, mini mental state examination; Other, mixed type dementia and corticobasal degeneration, idiopathic normal pressure hydrocephalus, progressive supranuclear palsy.

2.3. Statistical analysis

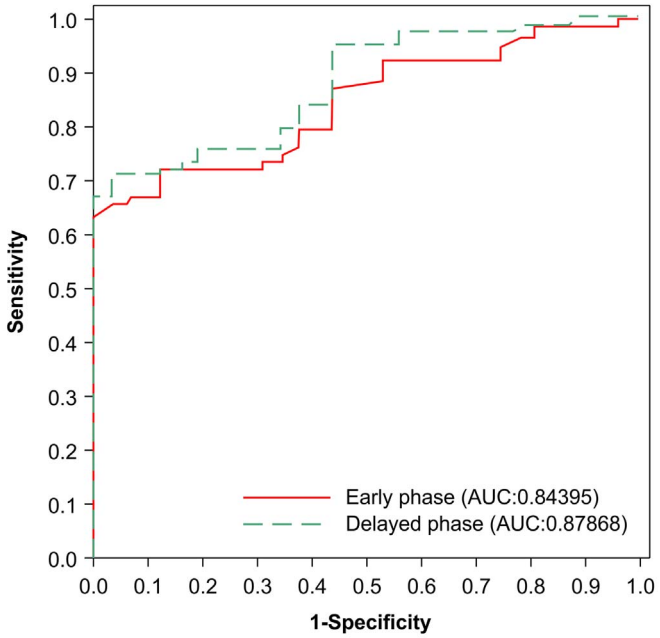
The data obtained from the DLB and non-DLB groups were analyzed by ROC curves to determine the early and delayed image cutoff points for decision-making. In addition, sensitivity, specificity, and accuracy were evaluated, and the difference in these factors in the presence or absence of parkinsonism, visual hallucinations, and cognitive fluctuations (core symptoms according to the revised CDLB Guidelines) were statistically examined.

3. Results

The mean early-H/M ratio was 2.83 in the non-DLB group and 1.95 in the DLB group. The mean delayed-H/M ratio was 3.0 in the non-DLB group and 1.76 in the DLB group.

With a cutoff point of 2.27 on early images, the sensitivity, specificity, and diagnostic accuracy were 67%, 94%, and 75%, respectively, and the area under the curve (AUC) was 0.84, indicating moderate accuracy. In comparison, with a delayed-H/M ratio cutoff point of 2.23, the sensitivity, specificity, and diagnostic accuracy were 71%, 97%, and 78%, respectively, and the AUC was 0.87, indicating moderate accuracy (Fig. 1).

The differences in the differential diagnostic abilities of the early and delayed images relative to the presence or absence of each core feature (parkinsonism, visual hallucinations, cognitive fluctuations), and all core features are described below. Comparing the DLB with parkinsonism group (n=46) with the non-DLB group, the sensitivity, specificity, and diagnostic accuracy were 72%, 100%, 83%, respectively



	Early (cut-off:2.27)		Delay (cut-off:2.23)	
Sensitivity	67%	56-76%	71%	60-80%
Specificity	94%	80-98%	97%	84-99%
Accuracy	75%	66-82%	78%	70-85%

Fig. 1. Statistical analysis of the DLB group versus non-DLB group (DLB: 79 cases, non-DLB: 32 cases).