

## Clinical usefulness of $^{18}\text{F}$ FP-CIT PET/CT in suspicious early Parkinson disease with comparative effectiveness research

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### Background

Parkinson's disease can be difficult to diagnose, as there are Parkinsonian features of other causes or uncertainty in the early stage of Parkinson's disease (PD). Moreover, it is important to note that missed clinical diagnoses or delayed diagnosis rates were reported in 15-20% of the Parkinson's disease in the early stage.

### Objective

The purposes of this study were: 1) to compare diagnostic accuracy of  $^{18}\text{F}$  FP-CIT PET/CT; 2) to validate of clinical effectiveness of  $^{18}\text{F}$  FP-CIT PET/CT in suspicious early Parkinson disease; and 3) to assess the budgetary impact of FP-CIT PET/CT in early use in the diagnosis of Parkinson's disease.

### Methods

In order to make a comparison between diagnostic accuracy of  $^{18}\text{F}$  FP-CIT PET/CT and clinical diagnoses, systematic reviews were used. Following the search strategy, a total of 172 cases were identified from various databases,

such as Ovid-MEDLINE, Ovid-EMBASE and KoreaMed. among which a final only 1 paper was selected based on the selection and exclusion criteria.

A total of 381 consecutive patients underwent  $^{18}\text{F}$  FP-CIT PET/CT from two centers (Kangnam Severance Hospital, Soonchunhyang Univ. Bucheon Hospital, South Korea) between September 2009 and June 2013. Neurologic specialists in movement disorder referred the patients. Finally, 205 patients were selected as clinically suspicious de novo early PD by the following exclusion criteria: non-confirmative diagnosis within 2 yr of follow-up, anatomical disorders, metabolic illness, repeated stroke, and initial symptom as dementia.

We evaluated inter-observers reliability using the Kappa value between two nuclear medicine physicians to detect PD. The Kappa value was 1.0 for detecting PD using  $^{18}\text{F}$  FP-CIT PET/CT.

In addition, a face-to-face survey was conducted to determine time and money spent in the diagnosis of Parkinson's disease. A total of 104 Parkinson's disease patients participated in the survey, and we performed a budget impact analysis based on the answers from the patient survey.

## □ Results

In systematic reviews, 1 paper was selected(Oh et al., 2012). In this paper, it confirmed the diagnostic accuracy of the  $^{18}\text{F}$  FP-CIT PET/CT for parkinson's disease (PD) patients and compared progressive supranuclear palsy (PSP), multiple-system atrophy (MSA) and healthy controls. The sensitivity and specificity for differentiating PSP from PD were 94% and 92%, respectively and the sensitivity and specificity for differentiating MSA from PD were 90% and 45%, respectively.

In retrospective medical record data, for detecting PD, the mean sensitivity, specificity, and accuracy of  $^{18}\text{F}$  FP-CIT PET/CT was 92.3% (95% CI: 86.2-95.9), 50.8% (95% CI: 38.0-63.5), and 79.5% (95% CI: 74.1-84.9),

respectively. For diagnosis of neurodegenerative Parkinsonian syndrome (NDPS), the mean sensitivity, specificity, and accuracy of  $^{18}\text{F}$  FP-CIT PET/CT for was 93.2% (95% CI: 88.2-90.6), 85.7% (95% CI: 66.4-95.3), and 92.2% (95% CI: 88.3-95.1), respectively. The clinical effectiveness of  $^{18}\text{F}$  FP-CIT PET/CT for diagnosis of PD was evaluated by the change of initial clinical diagnosis in 30.7% (95% CI: 24.4-37.6) of patients and early confirmed diagnosis of PD with an initial Hoehn and Yahr (HY) stage  $\leq 1.5$ , in 50.7% (95% CI: 43.9-57.6) of patients. The clinical effectiveness of  $^{18}\text{F}$  FP-CIT PET/CT for NDPS was evaluated by the change of the initial clinical diagnosis in 33.7% (95% CI: 27.3-40.5) of patients and early confirmed diagnosis of NDPS with a HY stage  $\leq 2.0$ , resulted in 56.6% (95% CI: 49.8-63.4).

In survey, 36.5% of patients answered that it took less than one month to be diagnosed with Parkinson's disease. Most of these patients visited university hospital at the time of appearance of symptoms, of which 89.5% were diagnosed with Parkinson's disease at the first visit. On the other hand, patients who took more than one month to be diagnosed with Parkinson's disease spent more money to be diagnosed, and were more likely to visit more than two types of hospitals. Only 42.4% of these patients were diagnosed with Parkinson's disease at their first visit to a hospital.

As a result of the budget impact analysis, the cost of FP-CIT PET/CT in the diagnosis of Parkinson's disease patients (N=85,888, 2014) is expected to be 88,866 million KRW, whereas 98,671 million KRW was incurred in unnecessary diagnoses to be saved. Consequently, 9,805 million KRW is expected to be saved by reducing the time for diagnosis Parkinson's disease. In consideration of increasing demands in the future, up to 11% of the increase in the current demand will lead to cost savings.

## **□ Conclusions**

$^{18}\text{F}$  FP-CIT PET/CT was useful for the differential diagnosis of suspicious early PD from secondary Parkinsonian syndrome. Furthermore, the clinical

effectiveness of  $^{18}\text{F}$  FP-CIT PET/CT was observed in about 30-50% of the change of the initial diagnosis and early confirmed diagnosis.

**Key words:** Parkinson's disease, Clinical effectiveness, Positron emission tomography, cost effectiveness