Impact of ^{18}FDG PET and ^{11}C-PIB PET brain imaging on the diagnosis of Alzheimer's disease and other dementias in a regional memory clinic in Hong Kong

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ABSTRACT

Objective: This study investigated the improvement in the accuracy of diagnosis of dementia subtypes among Chinese dementia patients who underwent [^{18}F]-2-fluoro-2-deoxy-D-glucose positron emission tomography (^{18}FDG PET) with or without carbon 11–labelled Pittsburgh compound B (^{11}C-PIB).

Methods: This case series was performed in the Memory Clinic at Queen Mary Hospital, Hong Kong. We reviewed 109 subjects (56.9% were female) who received PET with or without ^{11}C-PIB between January 2007 and December 2014. Data including age, sex, education level, Mini-Mental State Examination score, Clinical Dementia Rating scale score, neuroimaging report, and pre-/post-imaging clinical diagnoses were collected from medical records. The agreement between the initial and post-PET with or without ^{11}C-PIB dementia diagnosis was analysed by the Cohen's kappa statistics.

Results: The overall accuracy of initial clinical diagnosis of dementia subtype was 63.7%, and diagnosis was subsequently changed in 36.3% of subjects following PET with or without ^{11}C-PIB. The rate of accurate initial clinical diagnosis (compared with the final post-imaging diagnosis) was 81.5%, 44.4%, 14.3%, 28.6%, 55.6% and 0% for Alzheimer's disease, dementia with Lewy bodies, frontotemporal dementia, vascular dementia, other dementia, and mixed dementia, respectively. The agreement between the initial and final post-imaging dementia subtype diagnosis was only fair, with a Cohen's kappa of 0.25 (95% confidence interval, 0.05-0.45). For the 21 subjects who underwent ^{11}C-PIB PET imaging, 19% (n=4) of those with Alzheimer's disease (PIB positive) were initially diagnosed with non–Alzheimer's disease dementia.

Conclusions: In this study, PET with or without ^{11}C-PIB brain imaging helped improve the accuracy of diagnosis of dementia subtype in 36% of our patients with underlying Alzheimer's disease, dementia with Lewy bodies, vascular dementia, and frontotemporal dementia.

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New knowledge added by this study

- Positron emission tomography (PET) with or without Pittsburgh compound B (PIB) brain imaging helps improve the accuracy of dementia subtype diagnosis in Chinese patients.

Implications for clinical practice or policy

- PET with or without PIB brain imaging should be considered in patients with dementia who attend the memory clinic, especially if there is diagnostic difficulty.

Introduction

With ageing of the world's population, the prevalence of dementia increases: 46.8 million people worldwide were living with dementia in 2015. This is projected to reach 74.7 million in 2030 and 131.5 million in 2050, with 60% suffering from Alzheimer's disease (AD).[1] In Hong Kong, the prevalence of mild dementia has been reported to be 8.9% for adults aged 70 years or over, with 64.6% suffering from AD.[2] Appropriate management of demented patients begins with correct diagnosis of dementia subtype that allows earlier implementation of disease-specific treatment. In particular, cholinesterase inhibitors (ChEIs) or N-methyl-D-aspartate receptor antagonists are mostly suitable for the treatment of AD. The current clinical diagnostic guidelines for various types of dementia have limited sensitivities and specificities, however. The sensitivity and specificity of clinical diagnostic

香港一所分區記憶診所內研究^{18}FDG PET和^{11}C-PIB PET腦成像對於診斷阿爾茨海默病和其他認知障礙症患者的影響

佘日峯、夏卓彤、李瑞貞、朱亮榮

目的：本研究探討認知障礙症華籍患者接受氟-18葡萄糖正電子電腦斷層掃描（^{18}FDG PET）並是否有碳11標記匹茲堡化合物B（^{11}C-PIB）的情況下，能否改善對認知障礙症亞型的診斷。

方法：本病例系列於香港瑪麗醫院的記憶診所內進行。2007年1月至2014年12月期間曾到上述診所接受PET檢查（不論是否有^{11}C-PIB）共109名病人（56.9%為女性）均被列入研究範圍。從他們的病歷紀錄搜集以下數據：年齡、性別、教育程度、簡易精神狀態檢查評分、臨床癡呆評定量表評分、神經影像學報告和成像前後的臨床診斷。再用柯恩卡帕係數統計，分析進行PET腦成像前後（不論是否有^{11}C-PIB）對診斷認知障礙症結果的一致性。

結果：最初臨床診斷發現認知障礙症亞型的總體準確度為63.7%，但進行PET後（不論是否有^{11}C-PIB）36.3%病人的診斷有所改變。與進行PET後的診斷結果比較，最初臨床診斷對於不同的認知障礙症亞型的準確度如下：阿爾茨海默病81.5%、路易氏體型失智症44.4%、額顳癡呆14.3%、血管性癡呆28.6%、其他種類的癡呆55.6%和混合性癡呆0%。進行PET前後所得到的認知障礙症亞型一致性只屬一般，柯恩卡帕係數為0.25（95%置信區間：0.05-0.45）。21名接受^{11}C-PIB PET成像的病人中，有19%（4例）最初診斷為非阿爾茨海默病癡呆症，最終被確診為阿爾茨海默病（PIB陽性）。

結論：研究顯示PET腦成像（不論是否有^{11}C-PIB）能改善36%認知障礙症亞型患者的診斷，包括潛在的阿爾茨海默病、路易氏體型失智症、血管性癡呆和額顳癡呆。

criteria for AD, dementia with Lewy bodies (DLB), and frontotemporal dementia (FTD) have been reported as 81% and 70%, 50% and 80%, 85% and 95%, respectively.[3-6] In the most recent diagnostic criteria for AD, additional use of biomarkers of AD has been recommended by the National Institute on Aging and Alzheimer's Association to improve the accuracy of AD diagnosis.[3] Biomarkers for the diagnosis of AD include cerebrospinal fluid (CSF), amyloid pathological imaging (eg carbon 11–labelled Pittsburgh compound B [^{11}C-PIB] positron emission tomography [PET]), and functional imaging (eg [^{18}F]-2-fluoro-2-deoxy-D-glucose [^{18}F-FDG] PET) that yield sensitivities and specificities of at least 90% and 85%, respectively in the diagnosis of AD, DLB, and FTD.[3,7-11] Because of the invasive nature of lumbar puncture in the collection of CSF, neuroimaging modalities such as ^{18}F-FDG PET and ^{11}C-PIB PET are more accepted in routine clinical practice to improve the diagnosis of dementia subtype.

The most common functional neuroimaging is with ^{18}F-FDG[12] and the most common pathological neuroimaging is with ^{11}C-PIB.[13] These molecular imaging markers are imaged using PET. The ^{18}F-FDG measures metabolic activity of the brain; ^{18}F-FDG PET distinguishes well between AD and non-AD dementia.[11] In a systematic review, the sensitivity and specificity for ^{18}F-FDG PET in distinguishing between AD and DLB was 83%-99% and 71%-93%, respectively; and the sensitivity and specificity for ^{18}F-FDG PET in distinguishing between AD and FTD was 97.6%-99% and 65%-86%, respectively.[11] In the same systematic review, ^{18}F-FDG PET predicted patients with mild cognitive impairment (MCI) deteriorating into dementia with sensitivity and specificity of 81%-82% and 86%-90%, respectively.[11] Besides, ^{11}C-PIB can detect the presence of fibrillar amyloid plaques that are a neuropathological marker of AD.[13] Correlation studies with neuropathology have shown a sensitivity of 90% and specificity of 100%; ^{11}C-PIB can reasonably distinguish AD from other types of dementia, eg FTD.[13] Using neuropathology as the gold standard, the sensitivity and specificity was 89% and 83%, respectively.[13] The presence of ^{11}C-PIB retention also predicts the progression of patients with MCI: 50% progress to AD in 1 year and 80% progress to AD within 3 years.[14]

Previous studies with ^{18}F-FDG and ^{11}C-PIB PET have focused on highly selected diagnostic groups, and only a few studies have studied their impact in the routine clinical setting of a memory clinic at a tertiary university hospital. The latter are referral centres, and often encounter patients with complicated diagnostic issues. Ossenkoppele et al[15] reported a cohort of 145 patients who underwent ^{18}F-FDG and ^{11}C-PIB PET after clinical assessment. Change in clinical diagnosis was required in 23% with the diagnostic confidence increased from a mean of 71% to 87%. Diagnosis remained unchanged in 96% after PET over the next 2 years.[15] In seven patients with MCI and positive amyloid deposition on ^{11}C-PIB PET, six progressed to AD during follow-up (5 had AD pattern of hypometabolism on ^{18}F-FDG PET).[15] In a retrospective study of 94 patients with MCI or dementia, Laforce et al[16] showed that ^{18}F-FDG PET brain scan led to a change in diagnosis in 29% of patients, and reduced the frequency of atypical or unclear diagnoses from 39.4% to 16%.

To the best of our knowledge, there are no published data on the impact of molecular neuroimaging on accuracy of diagnosis of AD or other dementias in the Chinese population. We hypothesised that brain ^{18}F-FDG with or without ^{11}C-PIB PET imaging can improve the accuracy of diagnosis of common dementia subtypes in a memory clinic. The objective of this study was to investigate the impact of brain ^{18}F-FDG with or without ^{11}C-PIB imaging in improving the accuracy of diagnosis of dementia subtype in a local memory clinic in Hong Kong.

Methods

This was a retrospective study conducted at the Memory Clinic of Queen Mary Hospital, the University of Hong Kong. Patients were referred by general practitioners, neurologists, geriatricians, surgeons, or psychiatrists. All patient records between January 2007 and December 2014 were reviewed. Inclusion criteria were a clinical diagnosis of MCI, dementia of any type, or unclassifiable dementia; and ^{18}F-FDG with or without ^{11}C-PIB PET performed within 3 months after the initial clinical diagnosis. The initial clinical assessment was performed by a geriatrician experienced in dementia care and included detailed history taking from primary carers of the patient, physical examination, cognitive assessment, and laboratory studies (including thyroid function test, vitamin B_{12} level, folate level, and syphilis serology [Venereal Disease Research Laboratory]). Clinical criteria for AD, FTD, DLB, and vascular dementia (VaD) were employed to establish the clinical diagnosis initially, without using any biomarker. The diagnosis of different dementia subtype before neuroimaging was based on the respective diagnostic guidelines. Patients with AD were diagnosed according to the NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association) diagnostic criteria.[17] Patients with DLB were diagnosed by the McKeith criteria.[4] Behavioural variant (bv) of FTD was diagnosed by revised diagnostic criteria reported by the International bvFTD Criteria Consortium[5] and language variant of FTD was diagnosed by latest published criteria.[6] Patients with VaD were diagnosed according to the criteria of the NINDS-AIREN (National Institute of Neurological Disorders and Stroke/Association Internationale pour la Recherche et l'Enseignement en Neurosciences).[18] In this study, we reviewed the medical records of eligible subjects and collected data including age, sex, education level, Mini-Mental State Examination score, Clinical Dementia Rating scale score, molecular imaging report including the standardised uptake value ratio (SUVR) of ^{11}C-PIB PET, and the pre- and post-imaging diagnoses. For patients who were diagnosed with MCI, their progression during subsequent follow-up visits was also reviewed.

The need for ^{18}F-FDG with or without ^{11}C-PIB PET was determined by the geriatrician who performed the initial clinical assessment. The images were evaluated by a radiologist with more than 10 years of experience in reading PET scans. Dementias were classified using the generally accepted criteria. Patients were fasted for at least 4 hours before the PET. The serum glucose level was measured in all patients. For ^{18}F-FDG PET, the patient was rested in a dimly lit room with eyes closed for 30 minutes prior to injection of ^{18}F-FDG via a venous catheter. Another 30 minutes of rest was observed before starting the acquisition. The acquired data were semi-quantitatively compared with age-stratified normal controls using three-dimensional stereotactic surface projections. For PIB imaging, acquisition was performed at 5 minutes and 35 minutes after ^{11}C-PIB injection via a venous catheter, and SUVR images of ^{11}C-PIB between 5 and 35 minutes were generated. Cerebellar grey matter was chosen as reference tissue. In this study, ^{11}C-PIB PET scans were rated as positive (PIB^+; if binding occurred in more than one cortical brain region; ie frontal, parietal, temporal, or occipital) or negative (PIB^-; if predominantly white matter binding).

The pattern of ^{18}F-FDG PET hypometabolism that is suggestive of each subtype of dementia is as follows[6,12,19]:

(1) AD—uni- or bi-lateral parietotemporal hypometabolism with posterior cingulate gyrus involvement or bilateral parietal and precuneal hypometabolism.
(2) DLB—same as AD with added hypometabolism in occipital lobes.
(3) bvFTD—uni- or bi-lateral frontotemporal hypometabolism with or without less-severe parietal hypometabolism.
(4) Semantic dementia—anterior temporal lobe hypometabolism.
(5) Progressive non-fluent aphasia—left posterior frontoinsular hypometabolism.
(6) VaD—well-defined focal defects not fitting the above described patterns.

Statistical analyses

Descriptive statistics were used for data analyses. Continuous variables were expressed as mean ± standard deviation or median (interquartile range) as appropriate. Categorical data were expressed as number and percentages. The agreement between pre- or post-imaging diagnoses of dementia subtype was analysed by the Cohen's kappa (κ) statistic. The Cohen's κ reflected the degree of agreement: <0 = no agreement, 0-0.20 = slight agreement, 0.21-0.40 = fair agreement, 0.41-0.60 = moderate agreement, 0.61-0.80 = substantial agreement, and 0.81-1.00 = almost perfect agreement. All analyses were performed with the Statistical Package for the Social Sciences (Windows version 18.0; SPSS Inc, Chicago [IL], US).

Results

A total of 109 patients (56.9% were female) were recruited of whom 102 had dementia and seven had MCI. Both ^{18}F-FDG and ^{11}C-PIB PET data were available for 45 (41.3%) patients, and 64 patients underwent ^{18}F-FDG only. The final diagnosis of the 102 demented patients after neuroimaging is shown in Table 1.

The accuracy of clinical diagnoses is summarised in Table 2. Overall, PET scans confirmed the clinical impression in 63.7% of patients, and corrected the diagnosis in 36.3%. Using the result of PET scan as the gold standard, the frequency of accurate initial clinical diagnosis was low for FTD, VaD, and mixed dementia (14.3%, 28.6%, and 0%, respectively). The accuracy of clinical diagnosis for AD and DLB was 81.5% and 44.4%, respectively. After excluding subjects with an initial MCI diagnosis, the agreement between the initial and final post-imaging dementia diagnosis was only fair, with a Cohen's κ of 0.25 (95% confidence interval, 0.05-0.45).

Table 3 lists the diagnosis of subjects before and after the availability of ^{18}F-FDG with or without ^{11}C-PIB PET neuroimaging. For subjects with a final diagnosis of AD (n=65), 18.5% (n=12) were initially diagnosed with non-AD dementia (including 3 with DLB, 2 with FTD, 4 with VaD, and 3 with other dementia) and subsequently received symptomatic AD therapy (ie ChEIs and/or memantine). For the 21 subjects who underwent PIB PET imaging, 19% (n=4) of those with AD (PIB$^+$) were initially diagnosed with non-AD dementia. For subjects with an initial diagnosis of AD (n=74), 28.4% (n=21) had a change in diagnosis (including 4 DLB, 6 FTD, 4 VaD, 3 mixed AD plus VaD, and 4 with other dementia). Excluding subjects with DLB and mixed AD plus VaD, 13.7% of all subjects (14 out of 102) had discontinued their previous symptomatic AD therapy. For subjects with a final diagnosis of FTD (n=7), 85.7% (n=6) were initially misdiagnosed as AD. For subjects with a final diagnosis of DLB (n=9), 44.4% (n=4) were misdiagnosed as AD.

Five patients were diagnosed with unclassifiable dementia following neuroimaging, which comprised four females and one male with a mean age of 78 ± 9.4 years. All presented with amnesia. In

TABLE 1. Characteristics of demented patients by final diagnoses after brain ^{18}F-FDG with or without ^{11}C-PIB imaging (n=102)

Diagnostic group	No. of patients	Mean ± standard deviation			Median (interquartile range)	No. (%) of patients
		Age (years)	Education (years)	MMSE	CDR	Sex (female)
AD	65	77.8 ± 8.2	5.4 ± 5.5	18.0 ± 7.1	0.5 (0.5-1.0)	40 (61.5)
DLB	9	75.9 ± 8.1	9.3 ± 5.5	19.1 ± 8.8	0.5 (0.5-1.0)	2 (22.2)
FTD*	7	71.4 ± 10.3	6.6 ± 4.8	21.2 ± 8.4	0.5 (0.5-1.0)	4 (57.1)
VaD	7	80.4 ± 4.7	5.3 ± 7.1	18.6 ± 7.2	0.5 (0.5-1.0)	4 (57.1)
Mixed dementia†	5	78.6 ± 8.1	2.3 ± 2.9	21.2 ± 2.5	1.0 (1.0)	2 (40)
Others‡	9	78.1 ± 6.8	4.9 ± 5.5	23.9 ± 5.0	0.5 (0.5-1.0)	5 (55.6)

Abbreviations: AD = Alzheimer's disease; CDR = Clinical Dementia Rating scale score; ^{11}C-PIB = carbon 11–labelled Pittsburgh compound B; DLB = dementia with Lewy bodies; ^{18}F-FDG = [18F]-2-fluoro-2-deoxy-D-glucose; FTD = frontotemporal dementia; MMSE = Mini-Mental State Examination score; VaD = vascular dementia

* This category consists of 5 semantic dementia, 1 progressive non-fluent aphasia, and 1 unclassified primary progressive aphasia

† This category consists of 1 mixed AD plus Parkinson's disease dementia and 4 AD plus VaD

‡ This category consists of 3 Parkinson's disease dementia, 1 post-radiotherapy dementia, and 5 unclassifiable dementia

TABLE 2. Change in clinical diagnoses of dementia subtypes after ^{18}F-FDG with or without ^{11}C-PIB brain imaging

Final diagnosis (No.)	No. (%) of patients	
	No change in clinical diagnosis after imaging	Change in clinical diagnosis after imaging
AD (65)	53 (81.5)	12 (18.5)
DLB (9)	4 (44.4)	5 (55.6)
FTD (7)*	1 (14.3)	6 (85.7)
VaD (7)	2 (28.6)	5 (71.4)
Mixed dementia (5)†	0	5 (100)
Others (9)‡	5 (55.6)	4 (44.4)
Total (102)	**65 (63.7)**	**37 (36.3)**

Abbreviations: AD = Alzheimer's disease; ^{11}C-PIB = carbon 11–labelled Pittsburgh compound B; DLB = dementia with Lewy bodies; ^{18}F-FDG = [18F]-2-fluoro-2-deoxy-D-glucose; FTD = frontotemporal dementia; VaD = vascular dementia

* This category consists of 5 semantic dementia, 1 progressive non-fluent aphasia, and 1 unclassified primary progressive aphasia

† This category consists of 1 mixed AD plus Parkinson's disease dementia and 4 AD plus VaD

‡ This category consists of 3 Parkinson's disease dementia, 1 post-radiotherapy dementia, and 5 unclassifiable dementia

TABLE 3. Agreement between initial and final diagnoses

Initial clinical diagnosis without PET/PIB brain imaging	Final clinical diagnosis with PET/PIB brain imaging					
	AD (n=65)	DLB (n=9)	FTD (n=7)	VaD (n=7)	Mixed dementia (n=5)	Other dementia (n=9)
AD (n=74)	53	4	6	4	3	4
DLB (n=8)	3	4	0	0	1	0
FTD (n=3)	2	0	1	0	0	0
VaD (n=8)	4	1	0	2	1	0
Mixed dementia (n=1)	0	0	0	1	0	0
Other dementia (n=8)	3	0	0	0	0	5

Abbreviations: AD = Alzheimer's disease; DLB = dementia with Lewy bodies; FTD = frontotemporal dementia; PET = positron emission tomography; PIB = Pittsburgh compound B; VaD = vascular dementia

TABLE 4. Longitudinal outcome of the seven patients with amnesic mild cognitive impairment

Patient No.	Age (years)	Sex	Years of education	Initial presenting MMSE	Presence of imaging risk factors*	Latest MMSE	Deterioration to dementia	Years of follow-up
1	66	F	11	26	No†	26	No	1
2	84	M	9	27	Yes†	27	No	1
3	69	F	0	23	No	23	No (finally diagnosed with anxiety neurosis)	1
4	76	F	6	21	No	27	No	5
5	74	F	8	26	Yes	22	Yes	5
6	78	M	9	23	Yes	20	Yes	5
7	73	F	4	22	Yes	23	No	3

Abbreviations: ^{11}C-PIB = carbon 11–labelled Pittsburgh compound B; MMSE = Mini-Mental State Examination score; PET = positron emission tomography; PIB = Pittsburgh compound B

* Includes PIB$^+$ or presence of posterior cingulate gyrus hypometabolism with or without temporoparietal hypometabolism

† With ^{11}C-PIB PET scan

addition, one patient presented with apraxia and dysexecutive syndrome and another presented with hyperorality. All of them were PIB$^-$. An AD pattern of hypometabolism was present in four patients (2 with hypometabolism in posterior cingulate gyrus and 2 with hypometabolism in temporoparietal lobes). Isolated hypometabolism in the temporal lobes was present in one patient.

The clinical information of the seven amnesic MCI subjects are summarised in Table 4. None of the three subjects without imaging risk factors for AD deteriorated over a follow-up period of 1 to 5 years. Of the four amnesic MCI subjects with imaging risk factors, two deteriorated into AD over a follow-up period of 5 years.

Discussion

In this study, we showed that ^{18}F-FDG with or without ^{11}C-PIB PET clarified and improved the accuracy of dementia diagnosis in 36.3% of patients, and confirmed the initial diagnosis in 63.7%. Using the results of PET scan as the gold standard, the accuracy of clinical diagnosis was low for FTD, VaD, and mixed dementia collectively. On the one hand, 11.7% of patients (ie 12 out of 102) were started on symptomatic AD therapy after the ^{18}F-FDG with or without ^{11}C-PIB PET neuroimaging investigations. On the other hand, 13.7% of patients (ie 14 out of 102) discontinued symptomatic AD therapy after ^{18}F-FDG with or without ^{11}C-PIB PET because they did not have AD.

We also showed that the accuracy of clinical diagnosis of DLB and FTD was low (44.4% and 14.3%, respectively). This finding was in agreement with a previous study.[20] Both DLB and FTD are commonly misdiagnosed clinically as AD (50% for DLB and 85.7% for FTD).[20] We have previously reported that 100% of our patients with biomarkers that confirmed DLB and FTD presented with memory impairment in our memory clinic.[20] A previous study also reported that 26% of DLB patients were initially misdiagnosed with AD, and 57% of these DLB patients presented with memory impairment.[21] We

understand that an accurate diagnosis of DLB is very important for subsequent management. Patients with DLB are particularly sensitive to neuroleptics.[21] Neuroleptic sensitivity can present as drowsiness, confusion, abrupt worsening of parkinsonism, postural hypotension, or neuroleptic malignant syndrome.[21] Other clinical features of DLB that need to be observed and tackled include well-formed visual hallucinations, rapid eye movement sleep behavioural disorder, and autonomic symptoms (including postural hypotension, sialorrhoea, and urinary and bowel symptoms).[21] By accurately establishing the diagnosis of DLB, careful observation of classic DLB symptoms may reduce unnecessary investigations. Regarding therapeutic implications, DLB is characterised by far greater cholinergic deficits than AD. Hence, most DLB patients will benefit from ChEIs, and the extent of symptomatic improvement should be monitored after such therapy.[22]

Similarly, FTD may be misdiagnosed as AD. The former can also present initially with memory impairment, as illustrated by our FTD patients. There is increasing evidence that elderly patients with FTD often present with memory impairment.[5,23,24] In one autopsy study, 64% (n=7) of 11 elderly patients with FTD had anterograde memory loss.[23] Current treatment guidelines do not advise giving ChEIs or memantine treatments to FTD patients. Thus, such medications should be stopped to prevent unnecessary adverse effects.[25]

In the past few years, disease-modifying treatments (eg bapineuzumab) have failed to demonstrate their efficacy in clinical trials with AD patients.[26] Detailed post-hoc analyses with AD biomarkers have shown the problem of diagnosing AD in subjects recruited in these studies. Only approximately 80% of these subjects had AD amyloid pathology, according to the presence of amyloid PET scan.[26] Thus, including ^{11}C-PIB PET to confirm brain amyloid in study inclusion criteria can help ensure recruitment of genuine AD patients to future clinical trials of disease-modifying treatments for AD.[27] Given the minimally invasive nature of ^{11}C-PIB PET compared with CSF amyloid-beta (Aβ) 42 measurements,[7] it is likely to be a more acceptable choice for patients in clinical trials. At present, there are ongoing clinical trials of AD treatments including secretase inhibitors, Aβ aggregation inhibitors, Aβ and tau immunotherapy.[27] We believe that ^{11}C-PIB PET will play an important role in these clinical trials.

It is considered that ^{18}F-FDG and ^{11}C-PIB PET may detect underlying AD in patients with MCI.[28] In the present study, 50% of MCI patients (ie 2 out of 4) with ^{18}F-FDG and ^{11}C-PIB PET imaging findings positive for AD showed deterioration over a follow-up period of 5 years. Although recommending PET brain imaging in MCI patients is still debatable, we believe that this investigation can help clinicians to better plan future and long-term treatments. In particular, disease-modifying drugs for AD or MCI due to AD may prove to be effective in the coming decade. Finally, in the present study, five patients were diagnosed with unclassifiable dementia. In the four patients with an AD pattern of hypometabolism, AD may still be present as they may have diffuse plaques or amorphous plaques that do not bind well to PIB. Alternatively they may have another type of dementia that requires pathological confirmation, eg argyrophilic grain disease or neurofibrillary tangle–only dementia.[29] We will follow up the remaining patient with isolated hypometabolism in the temporal lobes to see whether additional FTD features develop.

There were several limitations to the present study. This was a retrospective case series and as such we were unable to collect further information such as the pre-imaging or post-imaging confidence of diagnosis. The diagnosis of dementia relied on the clinical diagnostic criteria without pathological confirmation. Therefore, we were also unable to compare the relative accuracy of clinical diagnosis and PET diagnosis with pathological diagnosis. For patients with MCI, some were not followed up for sufficiently long to ascertain whether or not they had deteriorated and developed dementia. Structural imaging (including computed tomography or magnetic resonance imaging) of the brain was not analysed as a separate variable but integrated into the pre-functional imaging clinical diagnoses of dementia subtypes. Our case series is likely to have selection bias as PET imaging is mostly a self-paid service in Hong Kong. The exception is for patients who are retired civil servants or recipients of Comprehensive Social Security Assistance. Demented patients who could not afford PET may differ to the patients selected. Although the PET images were analysed and read by radiologists experienced in PET, the interpretations depended heavily on individual experience and training; also, radiologists were not blinded to clinical information written on the request form. Despite these limitations, our study should be more reflective of day-to-day practice in a memory clinic and how ^{18}F-FDG with or without ^{11}C-PIB PET imaging may assist clinical diagnosis.

Conclusions

In this study, ^{18}F-FDG with or without ^{11}C-PIB brain imaging improved the accuracy of diagnosis of dementia subtype in 36% of patients with underlying AD, DLB, VaD, and FTD who presented to our memory clinic.

Declaration

All authors have disclosed no conflicts of interest.

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