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

YF Shea *, Joyce Ha, SC Lee, LW Chu

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-imaging 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.

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18FDG PET和
11C-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 (18FDG PET) 並沒有碳-11標記匹茲堡化合物B (11C-PIB) 的情況下，能否改善對認知障礙症亞型的診斷。進行

結果: 對診斷認知障礙症結果的一致性。

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11C-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、神經影像學報告和成像前後的臨床診斷。再用柯恩卡係數統計，分析進行PET腦成像前後（不論是否有11C-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11C-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。柯恩卡係數為0.25 (95%置信間隔0.05-0.45)。21名接受11C-PIB PET成像的病人中，有19名 (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11C-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。

imaging markers are imaged using PET. The 18F-FDG measures metabolic activity of the brain; 18F-FDG PET distinguishes well between AD and non-AD dementia. In a systematic review, the sensitivity and specificity for 18F-FDG PET in distinguishing between AD and DBL was 83%-99% and 71%-93%, respectively; and the sensitivity and specificity for 18F-FDG PET in distinguishing between AD and FTD was 97.6%-99% and 65%-86%, respectively. In the same systematic review, 18F-FDG PET predicted patients with mild cognitive impairment (MCI) deteriorating into dementia with sensitivity and specificity of 81%-82% and 86%-90%, respectively. Besides, 11C-PIB can detect the presence of fibrillar amyloid plaques that are a neuropathological marker of AD. Correlation studies with neuropathology have shown a sensitivity of 90% and specificity of 100%; 11C-PIB can reasonably distinguish AD from other types of dementia, eg FTD. Using neuropathology as the gold standard, the sensitivity and specificity was 89% and 83%, respectively. The presence of 11C-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.

Previous studies with 18F-FDG and 11C-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 reported a cohort of 145 patients who underwent 18F-FDG and 11C-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. In seven patients with MCI and positive amyloid deposition on 11C-PIB PET, six progressed to AD during follow-up (5 had AD pattern of hypometabolism on 18F-FDG PET). In a retrospective study of 94 patients with MCI or dementia, Laforce et al showed that 18F-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 18F-FDG with or without 11C-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 18F-FDG with or without 11C-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 \(^{18}\text{F-FDG}\) with or without \(^{11}\text{C-PIB}\) 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.\(^1\) 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\(^2\) and language variant of FTD was diagnosed by latest published criteria.\(^6\) Patients with VaD were diagnosed by the McKhith criteria.\(^4\) Behavioural variant (bv) of FTD was diagnosed by revised diagnostic criteria reported by the International bvFTD Criteria Consortium\(^2\) and language variant of FTD was diagnosed by latest published criteria.\(^6\) Patients with VaD were diagnosed by the McKhith criteria.\(^4\) Patients with VaD were diagnosed by the McKhith criteria.\(^4\) Patients with VaD were diagnosed by the McKhith criteria.\(^4\) Patients with VaD were diagnosed by the McKhith criteria.\(^4\) The need for \(^{18}\text{F-FDG}\) with or without \(^{11}\text{C-PIB}\) 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 \(^{18}\text{F-FDG}\) PET, the patient was rested in a dimly lit room with eyes closed for 30 minutes prior to injection of \(^{18}\text{F-FDG}\) 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 \(^{11}\text{C-PIB}\) injection via a venous catheter, and SUVR images of \(^{11}\text{C-PIB}\) between 5 and 35 minutes were generated. Cerebellar grey matter was chosen as reference tissue. In this study, \(^{11}\text{C-PIB}\) 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 \(^{18}\text{F-FDG}\) PET hypometabolism that is suggestive of each subtype of dementia is as follows\(^6\)\(^,\)\(^12\)\(^,\)\(^19\):

1. AD—unilateral or b/ilateral 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—unilateral or b/ilateral frontotemporal hypometabolism with or without less-severe parietal 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 (\(\kappa\)) statistic. The Cohen's \(\kappa\) 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 \(^{18}\text{F-FDG}\) and \(^{11}\text{C-PIB}\) PET data were available for 45 (41.3%) patients, and 64 patients underwent \(^{18}\text{F-FDG}\) only. The final diagnosis of the 102 demented patients after neuroimaging is shown in Table 1.
The accuracy of clinical diagnoses is summarized 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 DBL 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 k of 0.25 (95% confidence interval, 0.05-0.45).

Table 3 lists the diagnosis of subjects before and after the availability of 18F-FDG with or without 11C-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 FTD, 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 DBL, 6 FTD, 4 VaD, 3 mixed AD plus VaD, and 4 with other dementia). Excluding subjects with DBL 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 DBL (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 18F-FDG with or without 11C-PIB imaging (n=102)

<table>
<thead>
<tr>
<th>Diagnostic group</th>
<th>No. of patients</th>
<th>Mean ± standard deviation</th>
<th>Median (interquartile range)</th>
<th>No. (%) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age (years)</td>
<td>Education (years)</td>
<td>MMSE</td>
<td>CDR</td>
</tr>
<tr>
<td>AD 65</td>
<td>77.8 ± 8.2</td>
<td>5.4 ± 5.5</td>
<td>18.0 ± 7.1</td>
<td>0.5 (0.5-1.0)</td>
</tr>
<tr>
<td>DLB 9</td>
<td>75.9 ± 8.1</td>
<td>9.3 ± 5.5</td>
<td>19.1 ± 8.8</td>
<td>0.5 (0.5-1.0)</td>
</tr>
<tr>
<td>FTD* 7</td>
<td>71.4 ± 10.3</td>
<td>6.6 ± 4.8</td>
<td>21.2 ± 8.4</td>
<td>0.5 (0.5-1.0)</td>
</tr>
<tr>
<td>VaD 7</td>
<td>80.4 ± 4.7</td>
<td>5.3 ± 7.1</td>
<td>18.6 ± 7.2</td>
<td>0.5 (0.5-1.0)</td>
</tr>
<tr>
<td>Mixed dementia†</td>
<td>78.6 ± 8.1</td>
<td>2.3 ± 2.9</td>
<td>21.2 ± 2.5</td>
<td>1.0 (1.0)</td>
</tr>
<tr>
<td>Others‡ 9</td>
<td>78.1 ± 6.8</td>
<td>4.9 ± 5.5</td>
<td>23.9 ± 5.0</td>
<td>0.5 (0.5-1.0)</td>
</tr>
</tbody>
</table>

Abbreviations: AD = Alzheimer’s disease; CDR = Clinical Dementia Rating scale score; 11C-PIB = carbon 11–labelled Pittsburgh compound B; DBL = dementia with Lewy bodies; 18F-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 18F-FDG with or without 11C-PIB brain imaging

<table>
<thead>
<tr>
<th>Final diagnosis (No.)</th>
<th>No change in clinical diagnosis after imaging</th>
<th>Change in clinical diagnosis after imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD (65)</td>
<td>53 (81.5)</td>
<td>12 (18.5)</td>
</tr>
<tr>
<td>DLB (9)</td>
<td>4 (44.4)</td>
<td>5 (55.6)</td>
</tr>
<tr>
<td>FTD (7)*</td>
<td>1 (14.3)</td>
<td>6 (85.7)</td>
</tr>
<tr>
<td>VaD (7)</td>
<td>2 (28.6)</td>
<td>5 (71.4)</td>
</tr>
<tr>
<td>Mixed dementia (5)†</td>
<td>0</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Others (9)‡</td>
<td>5 (55.6)</td>
<td>4 (44.4)</td>
</tr>
<tr>
<td>Total (102)</td>
<td>65 (63.7)</td>
<td>37 (36.3)</td>
</tr>
</tbody>
</table>

Abbreviations: AD = Alzheimer’s disease; 11C-PIB = carbon 11–labelled Pittsburgh compound B; DBL = dementia with Lewy bodies; 18F-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
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. Both DLB and FTD are commonly misdiagnosed clinically as AD (50% for DLB and 85.7% for FTD). We have previously reported that 100% of our patients with biomarkers that confirmed DLB and FTD presented with memory impairment in our memory clinic. 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. We

### 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 3: Agreement between initial and final diagnoses

<table>
<thead>
<tr>
<th>Initial clinical diagnosis without PET/PIB brain imaging</th>
<th>Final clinical diagnosis with PET/PIB brain imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD (n=65)</td>
<td>DLB (n=9)</td>
</tr>
<tr>
<td>AD (n=74)</td>
<td>53</td>
</tr>
<tr>
<td>DLB (n=8)</td>
<td>3</td>
</tr>
<tr>
<td>FTD (n=3)</td>
<td>2</td>
</tr>
<tr>
<td>VaD (n=8)</td>
<td>4</td>
</tr>
<tr>
<td>Mixed dementia (n=1)</td>
<td>0</td>
</tr>
<tr>
<td>Other dementia (n=8)</td>
<td>3</td>
</tr>
</tbody>
</table>

### Table 4: Longitudinal outcome of the seven patients with amnesic mild cognitive impairment

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

### 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
understand that an accurate diagnosis of DLB is very important for subsequent management. Patients with DLB are particularly sensitive to neuroleptics. Neuroleptic sensitivity can present as drowsiness, confusion, abrupt worsening of parkinsonism, postural hypotension, or neuroleptic malignant syndrome. 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). 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.

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. In one autopsy study, 64% (n=7) of 11 elderly patients with FTD had anterograde memory loss. 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.

In the past few years, disease-modifying treatments (eg bapineuzumab) have failed to demonstrate their efficacy in clinical trials with AD patients. 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. Thus, including 11C-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. Given the minimally invasive nature of 11C-PIB PET compared with CSF amyloid-beta (A\(\beta\)) 42 measurements, 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, A\(\beta\) aggregation inhibitors, A\(\beta\) and tau immunotherapy. We believe that 11C-PIB PET will play an important role in these clinical trials.

It is considered that 18F-FDG and 11C-PIB PET may detect underlying AD in patients with MCI. In the present study, 50% of MCI patients (ie 2 out of 4) with 18F-FDG and 11C-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. 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 18F-FDG with or without 11C-PIB PET imaging may assist clinical diagnosis.

Conclusions

In this study, 18F-FDG with or without 11C-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.
References