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Does perfusion CT enable differentiating Alzheimer's disease from vascular dementia and mixed dementia? A preliminary report

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Abstract

The purpose of the study was to evaluate the usefulness of perfusion CT (pCT) in differentiating Alzheimer's disease (AD) from vascular dementia (VaD) and mixed dementia (MixD). pCT was performed in 41 patients (mean age, 68.3 years): 24 with AD, 8 with VaD, and 9 with MixD. Regional perfusion parameters (rCBF, rCBV, and rMTT) were calculated from 31 ROIs in the grey and white matter of the frontal and temporal lobes, basal ganglia, and internal capsules bilaterally. The obtained data for the subgroups of AD, VaD, and MixD patients were compared statistically.

Conclusions: On the basis of rCBF and rCBV values, pCT may be a valuable method of distinguishing between AD and VaD but it seems to be of little significance in differentiating MixD from VaD and of no usefulness in distinguishing between AD and MixD.

Keywords: Alzheimer's disease; Vascular dementia; Mixed dementia; Differential diagnosis; Neuroimaging; Perfusion CT

1. Introduction

In recent years, neuroimaging has become an important tool in the process of diagnosing and distinguishing between different forms of dementia. Computed tomography (CT) and magnetic resonance (MR) enable an evaluation of the degree of cerebral atrophy and the detection of organic causes of dementia. New imaging techniques such as single photon emission computed tomography (SPECT), positron emission tomography (PET), MR spectroscopy (MRS), functional MRI (fMRI), perfusion MRI (pMRI), and perfusion CT (pCT) allow the investigation of brain function, metabolism, activation, molecular composition, and blood perfusion [1,2]. Functional neuroimaging is believed to enable early and accurate diagnosis of dementia, which is very important now that new medications for the treatment of mild and moderate dementia are available. Distinguishing accurately between different types of dementia, for example AD and VaD, is not always possible on purely clinical grounds, but such differentiation is necessary for choosing the best therapeutic approach.

Dynamic CT techniques using inhaled non-radioactive xenon gas (xenon CT) have been performed for the quantitative or semi-quantitative evaluation of cerebral blood flow (CBF) in dementia for years [3,4]. The pCT method, using intravenous iodinated contrast medium, was recently developed. This technique is easier to perform and allows the assessment of more perfusion parameters, e.g. CBF, cerebral blood volume (CBV), mean transit time (MTT), time to peak (TTP), and the permeability surface (PS) [5–7]. pCT is currently widely used in the detection of ischaemic brain diseases [8,9] and also, though less often, in diagnosing brain tumours [10]. To our knowledge, no studies concerning pCT in dementia have been reported so far.

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Table 1
Age, gender, neuropsychological test results and CT findings of the evaluated subject groups

Diagnosis	Number of patients	Gender	Age (mean)	MMSE (mean)	Clock test	CT findings (no. of patients)			
						Cortical atrophy	Subcortical atrophy	Focal vascular lesions	Leukoaraiosis
AD	24	M13 F11	45–79 (68.4)	0–23 (16.3)	I—2 II—14 III—8	24	19	6	6
MixD	9	M2 F7	51–84 (68.4)	10–24 (16.0)	I—0 II—3 III—6	9	5	1	1
VaD	8	M2 F6	58–80 (68.0)	12–22 (17.2)	I—1 II—5 III—2	8	4	1	2

AD — Alzheimer's disease, MixD — mixed dementia, VaD — vascular dementia, M — male, F — female, MMSE — Mini Mental State Examination. Clock test (I–II — mild dementia, III–IV — moderate dementia, V — severe dementia).

The purpose of this study was to assess the value of pCT in three groups of patients: those with AD, VaD and MixD.

2. Materials and methods

Forty-one subjects (24 females, 17 males) with dementia were selected from a larger group of 50 patients who had undergone pCT in order to obtain three age-matched subgroups (mean ages: AD 68.4, MixD 68.4, and VaD 68.0 years). The mean age of all patients was 68.3 years and ranged from 45 to 84 years. The youngest, a 45-year-old patient, was in the AD group.

AD was diagnosed in 24 cases according to DSM-IV and NINCDS-ADRDA criteria and VaD in 8 cases according to NINCDS-AIREN criteria. In 9 patients the diagnosis of MixD was established on the basis of clinical history as well as psychiatric and neurological evaluation. The degree of cognitive impairment was assessed by means of the Mini Mental State Examination (MMSE) and the clock drawing test. The majority of the patients presented with mild or moderately severe dementia (Table 1). All patients also underwent neurological examination, EEG, as well as morphological and chemical analyses of the blood and urine. Imaging diagnostics included plain, unenhanced brain CT followed by pCT.

The study was conducted in accordance with the guidelines of the Regional Ethics Committee for conducting research involving humans. Each patient or his/her relative/caregiver provided signed consent to participate in the examination.

2.1. Technique of perfusion CT

All perfusion CT examinations were performed on the same two-detector CT scanner (Dual HiSpeed, GE Medical Systems). In each case, unenhanced CT preceded pCT in order to image the whole brain and choose the best scan at the level of the basal ganglia for perfusion examination. Next, 40 ml of iodinated contrast medium (370 mg of iodine per ml) was injected with an automatic injector at a rate of 4 ml/s. Seven seconds after the start of injection, serial (cine) CT scanning was begun, providing 50 images from the level of the basal ganglia (scanning duration: 50 s, frequency: 1 scan/s, slice thickness: 10 mm). All pCT scans were post-processed on an imaging workstation (GE Medical Systems) with commercial pCT analysis software (Perfusion 2) to create maps of CBF, CBV, and MTT. The software required the placement of small regions of interest (ROIs) on an artery (pericallosal artery) and vein (transverse or superior sagittal sinus), which acted as the reference blood vessels necessary for assessing the perfusion parameters in the brain parenchyma by deconvolution analysis. Next, CBF, CBV, and MTT perfusion maps were created for each patient. On each map, 12 basic ROIs were drawn freehand by the same radiologist (A.Z.), experienced in CT perfusion technique, in the areas of the grey and white matter of the frontal and temporal lobes as well as in the basal ganglia and internal capsules bilaterally (Fig. 1). All symmetric ROIs were similar in size but not in shape. In the grey matter they were irregular in order to delineate cortex accurately and more oval in the regions of the white matter and the basal ganglia. Mean values of CBF, CBV, and MTT were calculated within each of the 12 basic ROIs. Additionally, mean CBF, CBV, and MTT values were calculated for larger regions created by coupling two or more basic ROIs; the frontal lobe, for example, included the mean values from the frontal grey and white matter, and right white matter included the mean values from the frontal and temporal white matter (Tables 2, 3). In total, mathematical quantitative data from 31 ROIs within the brain were obtained. The mean CBF, CBV, and MTT values among the three groups of patients with AD, VaD, and MixD were compared by statistical analysis of variance (ANOVA) followed by the Sheffe's post hoc test (Tables 2, 3).

3. Results

Plain CT revealed cortical atrophy in all subjects and subcortical atrophy in the majority of AD patients and about half of the patients in the remaining groups. Vascular changes (focal lesions or leukoaraiosis) were seen in a minority of patients in all three groups (Table 1).

rCBF and rCBV values in most of the ROIs (21/31 and 27/31, respectively) in the grey and white matter of the bilateral frontal and temporal lobes were significantly lower in the AD patients compared with the VaD subgroup ($p<0.05$). All the decreased rCBF values in the 21 ROIs were associated with significantly lower rCBV parameters. Among AD patients, isolated rCBV reduction was detected in 6 ROIs, mostly in the white matter (bilateral internal capsules, frontal and temporal lobes) and in the right frontal lobe containing both grey and white matter (Tables. 2, 3,