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ORIGINAL ARTICLE

Age- and anatomy-related values of blood-brain barrier permeability measured by perfusion-CT in non-stroke patients

Perméabilité de la barrière hémato-encéphalique mesurée par scanner de perfusion : valeurs normales et variations en fonction de l'âge et de l'anatomie

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KEYWORDS
Stroke;
Perfusion-CT;
Permeability imaging;
Normal values;
Hemorrhagic transformation

Summary
Background and purpose. — The goal of this study was to determine blood-brain barrier permeability (BBBP) values extracted from perfusion-CT (PCT) using the Patlak model and possible variations related to age, gender, race, vascular risk factors and their treatment and anatomy in non-stroke patients.
Materials and methods. — We retrospectively identified 96 non-stroke patients who underwent a PCT study using a prolonged acquisition time up to 3 minutes. Patients' charts were reviewed for demographic data, vascular risk factors and their treatment. The Patlak model was applied to calculate BBBP values in regions of interest drawn within the basal ganglia and the gray and white matter of the different cerebral lobes. Differences in BBBP values were analyzed using a multivariate analysis considering clinical variables and anatomy.
Results. — Mean absolute BBBP values were 1.2 ml $100\,g^{-1}\,min^{-1}$ and relative BBBP/CBF values were 3.5%. Statistical differences between gray and white matter were not clinically relevant. BBBP values were influenced by age, history of diabetes and/or hypertension and aspirin intake.

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Conclusion. — This study reports ranges of BBBP values in non-stroke patients calculated from delayed phase PCT data using the Patlak model. These ranges will be useful to detect abnormal BBBP values when assessing patients with cerebral infarction for the risk of hemorrhagic transformation.

Introduction

Hemorrhagic transformation (HT), especially when classified as parenchymal hemorrhage 2 (PH2), is a serious complication of ischemic stroke that can increase mortality up to 11 times [1]. Combined data from six major stroke trials showed that severe hemorrhage with mass effect occurs in 4.8% of stroke patients treated with tPA within 3 hours after symptom onset and up to 6.4% in patients treated between 3 to 6 hours [2]. Damage to the blood-brain barrier (BBB) is considered one of the contributing mechanisms to HT [3]. Early detection of a damaged BBB could potentially be used to identify patients who are more likely to develop HT and might therefore represent a contra-indication to acute reperfusion therapy [4].

Dynamic perfusion-CT (PCT) is a well established tool in the evaluation of acute stroke. With this technique, irreversibly damaged brain tissue and brain tissue at risk can be identified [5—8]. In addition, blood-brain barrier permeability (BBBP) can be derived from PCT data [9—15]. A relatively simple and frequently applied model to calculate BBBP is the Patlak model [16,17]. Applying this model to PCT data [9,10,12—15,18] means using arterial and parenchymal contrast enhancement curves to calculate the rate of contrast transfer from an intravascular to an extravascular compartment, which is a measure of BBBP.

In order to identify abnormal BBBP values and determine whether these abnormal BBBP values predict HT in stroke patients, one must first know the normal range of BBBP values in a control non-stroke population. The goal of this study was to determine BBBP values in non-stroke patients extracted from PCT and possible variations related to age, gender, race, vascular risk factors and their treatment, and anatomy.

Methods

Design

Imaging data obtained as part of standard clinical stroke care at our institution were retrospectively reviewed with the approval of the institutional review board. At our institution, patients with suspicion of acute stroke and no history of significant renal insufficiency or contrast allergy routinely undergo a stroke CT survey including: noncontrast CT (NCT) of the brain, PCT at two cross-sectional positions, CT-angiogram (CTA) of the cervical and intracranial vessels, and post-contrast cerebral CT, obtained in this chronological sequence.

We retrospectively identified a consecutive series of 101 patients admitted to UCSF Medical Center from January 2006 to June 2007 who met the following inclusion criteria:

- admission to the emergency room with signs and symptoms suggesting hemispheric stroke within 12 hours after symptom onset;
- no evidence of hemispheric stroke, intracerebral hemorrhage or other brain abnormalities on the admission NCT;
- no evidence of hemispheric stroke, intracerebral hemorrhage or other brain abnormalities on the admission NCT, on follow-up CT and/or MR imaging or on clinical work-up.

Patient characteristics

Patients' charts were retrospectively reviewed for demographic and clinical data of the day of admission as entered by the clinician. Information was collected on: age, gender, race, history of hypertension, diabetes mellitus, hyperlipidemia or cardiac disease, alcohol use, tobacco use, use of aspirin and other non-steroidal anti-inflammatory drugs (NSAID), anticoagulants anti-hypertensive drugs, diabetes treatment, statins and/or steroids. The final diagnoses for the patients were extracted from the discharge reports.

Imaging protocol

PCT studies were obtained on 16-slice (72 patients) and 64-slice (29 patients) CT scanners. Each PCT study involved successive gantry rotations performed in cine mode during intravenous administration of iodinated contrast material. Images were acquired and reconstructed at a temporal sampling rate of one image per second for the first 45 seconds. Additional gantry rotations were obtained at 60, 90, 120, 150 and 180 seconds. Acquisition parameters were 80 kVp and 100 mAs. Two successive PCT series at two different levels were performed following the non-contrast CT and prior to the CTA. At each PCT level, four 5-mm-thick slices (16-slice CT scanners) or eight 5-mm-thick slices (64-slice CT scanners) were assessed. The first PCT series was obtained at the level of the third ventricle and the basal ganglia and the second PCT series above the lateral ventricles. For each PCT series, a 40 ml bolus of iohexol (Omnipaque, Amersham Health, Princeton, NJ; 300 mg/ml of iodine) was administered into an antecubital vein using a power injector at an injection rate of 5 ml per second for all patients. CT scanning was initiated 7 seconds after start of the injection of the contrast bolus.