Ultrasound Tissue Pulsatility Imaging Suggests Impairment in Global Brain Pulsatility and Small Vessels in Elderly Patients with Orthostatic Hypotension

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Background: Orthostatic hypotension (OH) is highly prevalent in the elderly, and this population can be exposed to serious complications, including falls and cognitive disorders, as well as overall mortality. However, the pathophysiology of OH is still poorly understood, and innovative methods of cerebral blood flow (CBF) assessment have been required to accurately investigate cerebrovascular reactivity in OH. *Objectives:* We want to compare brain tissue pulsatility (BTP) changes during an orthostatic challenge in elderly patients over 80 with and without OH. *Materials and Methods:* Forty-two subjects aged 80 and over were recruited from the geriatric unit of the Hospital of Tours, France, and were divided into two groups according to the result of an orthostatic challenge. The noninclusion criteria were any general unstable medical condition incompatible with orthostatic challenge, having no temporal acoustic window, severe cognitive impairment (Mini Mental Status Examination <15), history of stroke, and legal guardianship. We used the novel and highly sensitive ultrasound technique of tissue pulsatility imaging to measure BTP changes in elderly patients with (n = 22) and without OH (n = 17) during an orthostatic challenge. *Results:* We found that the mean brain tissue pulsatility related to global intracranial pulsatility, but not maximum brain tissue pulsatility related to large arteries pulsatility, decreased significantly in OH patients, with a delay compared with the immediate drop in peripheral blood pressure. *Conclusion:* Global pulsatile CBF changes and small vessels pulsatility, rather than changes in only large arteries, may be key mechanisms in OH to account for the links between OH and cerebrovascular disorders. **Key Words:** Orthostatic hypotension—cerebral autoregulation—ultrasound—neuroimaging.

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Introduction

Orthostatic hypotension (OH), characterized by a significant drop in blood pressure (BP) with orthostasis, is highly prevalent in the elderly. Up to 30% of the general population over 70 suffer from OH[1] and may be exposed to complications including not only syncope and falls but also cognitive[2] and psychiatric disorders,[3] as well as an overall increased mortality.[4]

The pathophysiology of OH is considered a consequence of aging or of some pathologic conditions in which the peripheral nervous system and the peripheral arteries become less efficient to adjust to changes in blood volume, which dramatically increase in the lower body and decrease in the upper body with orthostasis. In normal condition, the cerebrovascular system, via the mechanism of cerebral autoregulation (CA), prevents excessive drop in cerebral blood flow (CBF), which may otherwise result in brain hypoperfusion and syncope.[5]

OH has been associated with impairment of CA, but the role of CA in OH has been reported variously in the literature: some studies found a significant decrease in CBF with orthostasis, suggesting an impaired CA in some OH patients only,[6] whereas other studies found no evidence of CA impairment in OH patients.[7] These inconsistent results may be due to the almost exclusive use of transcranial Doppler (TCD) to measure CA, as TCD informs about large vessels only, although there is a debate on whether CA relies on small or large arteries, with the requirement for innovative methods of CBF assessment.[5,8]

Some recent ultrasound (US) methods, including tissue pulsatility imaging (TPI), could investigate with more accuracy the CBF changes and CA in OH patients. In its principle, TPI is similar to TCD except that, rather than focusing on only large arteries, it relies on the echo B-mode of modern US scanner to measure the natural movements of large brain regions, which allows for a very high spatio-temporal level of detection (micrometers/milliseconds) of brain volume changes related to pulsatile CBF. Indeed, periodic changes in blood volume cause the brain to expand and relax over the cardiac cycle, and TPI measures the pulsatile signals from thousands of sample volumes on a US image plane, consistent with the principle of plethysmography.[9]

TPI has been validated on phantoms[9] and on healthy volunteers to assess brain tissue pulsatility (BTP) in a visual task[10] and in a CO_2 challenge,[11] confirming that BTP is closely related to CBF changes, consistent with the notion that pulsatile CBF is a major determinant of brain pulsatility.[12] More recently, our team found that TPI was informative in clinical setting, especially in elderly depressed patients who exhibited a global decrease in BTP[13] and in patients with small vascular disease who showed a striking correlation between BTP and white matter hyperintensities as seen on magnetic resonance imaging.[14]

In this study, we used TPI to compare BTP changes during an orthostatic challenge in elderly patients over 80 with and without OH. We decided to investigate BTP in very old patients because they are frequently concerned about OH, and yet only few studies have been conducted in this population. Besides, we believe that TPI is suitable for CBF investigation in frail population.

Methods

Subjects

Forty-two subjects aged 80 and over were recruited from the geriatric unit of the Hospital of Tours, France, and were divided into two groups according to the result of an orthostatic challenge. The noninclusion criteria were any general unstable medical condition incompatible with orthostatic challenge, having no temporal acoustic window, severe cognitive impairment (Mini Mental Status Examination <15), history of stroke, and legal guardianship. The exclusion criterion was excessive movements during the OH challenge, and three subjects were excluded for this reason. The study was approved by the local human ethical committee and all subjects gave their nonopposition to the protocol.

Clinical Assessments

Clinical assessments were performed by the physicians of the geriatric unit of the Hospital of Tours, France, and included the recording of demographic data, medical history, BP, treatments, and Mini Mental Status Examination score.

Orthostatic Challenge

Orthostatic challenges were performed according to the recently updated international consensus of experts on OH.[15] An automatic BP monitor (EDAN M3, Thames Medical, UK) was used to measure BP, with the armband positioned on the right arm. After 5 minutes of supine rest, BP was recorded in the supine position, then immediately after standing (T0) and every minute for 3 minutes (T1min – T3min). The orthostatic test was considered positive if the decrease in BP values reached at least 20 mm Hg or 10 mm Hg, for systolic or diastolic BP, respectively, at any time of the orthostatic challenge. Orthostatic tests were performed before the US protocol to assign the subjects either in the OH-positive or OH-negative group, and then the second time during the US procedure.

US Protocol and Data Analysis

A single biophysics engineer (P.A.D.), trained for TCD, performed the US protocol during an orthostatic challenge on an Antares medical scanner with a PX4-1 phased-array transducer (Siemens Healthcare, Erlangen, Germany; 1.82 MHz emission frequency, 70° field of view, 112 × 3 elements [1.5 D]). The probe was positioned perpendicularly to the skull on the right temporal window and maintained by a mechanical holder specifically design to prevent shifts of the region of acquisition during the orthostatic challenge. Color Doppler was used to center the US beam on the middle cerebral artery. The US scanner was then switched on echo B-mode, and to limit US attenuation we adjusted the depth of acquired data between 3 and 9 cm, thus recording BTP in a large area around the Willis circle.

The protocol consisted of five acquisitions of 10 seconds, manually synchronized with each BP measures, at an