The Association between Arterial Stiffness, Initial Stroke Severity, and 3-Week Outcomes in Patients with Ischemic Stroke

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Objectives: Vascular compliance is emerging as a useful cardiovascular risk factor. The aim of this study was to investigate the association between arterial stiffness and stroke severity at presentation and 3 weeks. *Methods:* Forty two patients with acute ischemic stroke (55% male, mean age 71 years) were recruited over 15-months. Stroke subtypes were classified into lacunar circulation infarct (LACI), partial anterior circulation infarct (PACI), and posterior circulation infarct (POCI). Arterial stiffness was measured by QKD (defined as the time interval between the appearance of the Q wave [Q] on the ECG and the arrival of the diastolic Korotkoff [K] sound over the brachial artery in diastole [D]; QKD It is measured in milliseconds) using 24-hour ambulatory blood pressure (BP) and electrocardiogram monitoring. The measured QKD values were then corrected for a heart rate of 60 bpm and a systolic BP of 100 mm Hg ($QKD_{100\text{-}60}$). Stroke severity was assessed on admission and at 3 weeks using the National Institutes of Health Stroke Scale (NIHSS). *Results:* Regression analysis for all patients showed a weak non-significant correlation between arterial stiffness and stroke severity. However, on performing subgroup analysis using Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification, we found that in large-artery atherosclerosis, arterial stiffness predicted stroke severity significantly at baseline (r = .45, b = .093, P = .04), but not significant for cardio embolism or small-artery occlusion subtypes. $QKD_{100\text{-}60}$ and stroke severity were not significantly associated in week 3. There was no difference in NIHSS scores at weeks 0 and 3, or in $QKD_{100\text{-}60}$ between LACI, PACI, and POCI, or dipper versus non-dippers and reverse dippers. *Conclusion:* Further research is needed to explore the association between QKD and stroke severity. **Key Words:** Stroke outcome—arterial stiffness—QKD—$QKD_{100\text{-}60}$—NIHSS.

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Introduction

The concept of arterial compliance as a risk factor in incident ischemic stroke has been discussed in several studies.[1-5] Most of the studies exploring the association between arterial compliance and stroke have measured arterial stiffness using pulse wave velocity (PWV).[5,6] However, PWV measurements might be difficult to perform in the context of an acute stroke. Indirect assessment of arterial compliance based on QKD measurements can offer a less invasive alternative in providing a validated method for assessing arterial stiffness.[7] The use of the QKD interval (which is the time interval between the appearance of the *Q* wave on the electrocardiogram and the disappearance of the Korotkoff sound during diastole on blood pressure [BP] measurements) in acute stroke is appealing as it is relatively easy to measure and does not require observer input, and can be corrected for variations in BP and heart rate (HR).[7]

The Oxfordshire Community Stroke Project Classification, which provides prognostic information about stroke outcomes in the short- and long-term periods,[8-10] is based on epidemiological observational studies, and no pathophysiological measurements were undertaken in its development. Saji et al report that arterial stiffness measured by PWV is independently associated with progressive neurological deficit after acute stroke.[11] However, there are no studies assessing the prognostic value of arterial stiffness measured by QKD and its relation to presenting stroke symptoms and short-term functional outcomes.

The aim of the present study was therefore to explore the association between arterial stiffness (measured by QKD) and the initial and 3-week stroke severity measured by the National Institutes of Health Stroke Scale (NIHSS) in a cohort of patients with acute ischemic stroke. We hypothesized that increased arterial stiffness (shorter QKD intervals) at baseline is associated with more severe strokes at baseline as well as worse outcomes at 3 weeks.

Methods

Seventy-three patients with an initial diagnosis of acute ischemic stroke who were admitted to the Royal Sussex County Hospital, Brighton, United Kingdom, between December 1, 2006, and March 31, 2008, were included. The inclusion criterion was a confirmed World Health Organization diagnosis of acute ischemic stroke.[12] The exclusion criteria were as follows: intracerebral hemorrhage, inability to provide consent, a terminal illness, a previous stroke, a previous direct current cardioversion, myocardial infarction or cardiac arrest within the preceding 6 months, antiarrhythmic medications, or a symptom duration of greater than 48 hours. All patients or their legal representative provided an informed written consent. Ethical approval for the study was obtained from the East Sussex Local Research and Ethics Committee (number 06/Q1905/70).

A thorough history and examination, in combination with a computed tomography or a magnetic resonance imaging head scan, was used to confirm the diagnosis of stroke. We used the Oxford Community Stroke Project Classification (Bamford Classification) to classify stroke subtypes into 4 categories: total anterior circulation infarct (TACI), partial anterior circulation infarct (PACI), posterior circulation infarct (POCI), and lacunar circulation infarct (LACI).[9,13]

Using ambulatory BP measurements, the patients were divided into dippers and nondippers (dippers are individuals whose BP drops by 10%-20% at nighttime compared to daytime; nondippers are those whose BP drops by less than 10% at nighttime compared to daytime readings, and reverse dippers are those whose BP rises at nighttime compared to daytime).[14]

Additional cardiovascular risk factors, including smoking and alcohol consumption, were recorded. Twenty-four-hour ambulatory monitoring (Novacor, Rueil-Malmaison, France) was used to measure the HR, the BP, and the QKD interval. The QKD interval is an indirect measure of arterial stiffness based on the time interval between the onset of the QRS complex on the electrocardiogram and the detection of the last Korotkoff sound from the BP cuff. A longer QKD interval indicates more compliant arteries, as harder (stiffer) arteries propagate the blood flow quicker in a shorter QKD interval.

BP, HR, and QKD interval readings were taken every 30 minutes between 07:00 and 22:00 and every 60 minutes between 22:01 and 06:59, providing a total of 39 measurements. These measurements were used to derive mean QKD values, as well as mean values for 24-hour systolic blood pressure (SBP), diastolic BP, mean arterial pressure (MAP), and pulse pressure (PP). The mean patient QKD was further corrected for an HR of 60 bpm and an SBP of 100 mm Hg to obtain a value of QKD_{100-60}. These measurements were done at baseline only. However, QKD_{100-60} values were used for analysis at baseline and at week 3.

We measured stroke severity at baseline (on admission, day 0) and at week 3 using the NIHSS scoring system.[15] LACI (group 1) was compared with PACI and POCI stroke subtypes (group 2). PACI and POCI (group 2) were grouped together because they are larger strokes affecting more brain tissue. Patients with TACI were excluded as they had either a low GCS and speech impairments or were too unwell to provide informed consent.

The stroke scale variables are described using means and standard deviations. Counts and percentages were given for categorical variables. Baseline characteristics (NIHSS score, QKD_{100-60}, SBP, diastolic BP, PP, and MAP) measured in all patients are presented in Table 1.

Regression analysis (simple linear regression) was undertaken to determine the relationship between NIHSS score and QKD_{100-60} at 0 and 3 weeks. A further subgroup analysis was performed to assess whether there