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Toe brachial index in middle aged patients with diabetes mellitus type 2: Not just a peripheral issue

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ABSTRACT

Aim: To explore risk factors for peripheral arterial disease (PAD) as well as the association between toe blood pressure and subclinical and clinical central vascular disease in patients with type 2 diabetes.

Method: Toe brachial index (TBI) was cross-sectionally analyzed in 742 middle-aged (54–66 years) patients with type 2 diabetes as well as non-diabetic controls and related to other vascular measures (e.g. carotid intima media thickness (IMT), presence of carotid plaque, central arterial stiffness and left ventricular mass index) and previous cardiovascular events.

Results: A TBI ≤ 0.7 was seen in 22% of the patients but only one patient had severe TBI reduction (TBI ≤ 0.3). The corresponding figures in the controls were 13% and 0%, respectively. Mean TBI was significantly lower in patients with type 2 diabetes than in controls (0.81 ± 0.14 vs. 0.87 ± 0.15, $p < 0.001$). In patients with diabetes, a lower TBI was associated with increased central arterial stiffness ($p < 0.001$), IMT ($p < 0.001$) and carotid plaque ($p < 0.001$) as well as with decreasing glomerular filtration rate ($p < 0.001$). Lower TBI was found in patients with previous macrovascular ischemic events. Furthermore, TBI was negatively correlated with age ($p < 0.001$), diabetes duration ($p < 0.001$) and HbA1c ($p = 0.01$).

Conclusion: PAD, assessed with TBI, is common in a Swedish middle-aged diabetes type 2 cohort, affecting about one-fifth. As ankle pressure may be confounded by falsely high values in patients with diabetes due to media calcification we conclude that information about TBI may improve the risk evaluation regarding arteriosclerotic disease in both small and large vessels in type 2 diabetes.

1. Introduction

Diabetes mellitus is of increasing concern as the prevalence continues to increase worldwide and is expected to affect nearly 10% of the adult population in 2030 [1]. A major health issue is the ensuing increased risk of developing cardiovascular (CV) complications in type 2 diabetes with its consequent risk of increased morbidity and mortality. Ankle brachial index (ABI) has previously been shown to correlate to

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Abbreviations: TBI, toe brachial index; BMI, body mass index; LVMI, left ventricular mass index; PWVcf, pulse wave velocity from A.carotis to A.femoralis; PWVcr, pulse wave velocity from A.carotis to A.radialis; IMT, carotid intima media thickness.

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cardiovascular comorbidity and its' benefits has been highlighted, in addition to the Framingham risk score, in clinical practice [2–4]. Indeed ABI has been pointed out as one of the most feasible screening methods for cardiovascular disease (CVD) since it is easy to perform and also inexpensive [5,6]. A drawback is the risk of falsely high values due to stiffened, calcified ankle arteries which is mostly found in subjects with diabetes [3,4,7,8]. This group, with falsely high ABI has shown an equal or even higher mortality risk than low ABI why this group is important to detect [9,10]. As the arteries of the great toe rarely are involved in the calcification process, assessing toe brachial index (TBI) could provide a more accurate risk evaluation [3,4,7,8].

Peripheral arterial disease (PAD) is common in diabetes mellitus, causing suffering and high costs by ulcerations and chronic pain as well as risk for need of limb amputations. Furthermore, PAD is associated with increased mortality [3,11]. Early interventions are important and can decrease the risk of complications [4]. Taken together, measuring TBI seems important for detecting PAD and might also help assessing general vascular status in subjects with type 2 diabetes.

Health care is mostly publicly financed in Sweden, with a small individual contribution of about 300 USD per year. Routine controls for patients with type 2 diabetes are mainly performed in the primary care. All diabetes care, primary as well as hospital based, adhere to the same national guidelines. It is fundamental to gain more insight on how to best assess the risk of different risk factors in subjects with type 2 diabetes since this group of patients have a substantially increased risk for premature cardiovascular morbidity and mortality.

Aortic pulse wave velocity (PWV) measured by tonometry provides a non-invasive estimate of arterial stiffness and is an independent predictive risk factor for all-cause mortality and cardiovascular mortality [12,13]. To the best of our knowledge, the association between PWV and TBI in a larger group of patients with type 2 diabetes has previously not been explored. Intima media thickness (IMT) of the carotid arteries measured by B-mode ultrasound is a well known, non-invasive marker of subclinical atherosclerosis and increased risk of CV morbidity [14,15].

Most studies on PAD and CVD risk are based on ABI. The present study focuses on the association between TBI and vascular organ damage and cardiovascular comorbidities reporting data from a large cohort of 742 middle-aged patients with type 2 diabetes compared to data from non-diabetic controls.

2. Methods

2.1. Settings

The study was conducted as part of CARDIPP (Cardiovascular risk factors in patients with diabetes – a Prospective study in Primary care) analyzing the baseline data from all patients where toe pressure (TP) measurements were conducted. CARDIPP was launched 2005 to evaluate the prevalence and early risk markers for cardiovascular disease and was designed as an observational prospective study [16,17]. The patient enrolment was performed during 2005–2008 and included middle aged (54–66 years) patients with type 2 diabetes, independent of diabetes duration or previous CV burden, consecutively recruited from 22 different primary health care centers in the counties of Östergötland and Jönköping. Patients with severe medical conditions (e.g. terminal cancer) or severe mental disorder were excluded from participation. The catchment area included smaller/middle-sized cities (<150,000 inhabitants) as well as rural areas. As non-diabetic controls, we used age-matched participants from the CAREFUL (Cardiovascular Reference Population) study, i.e. a parallel study to CARDIPP including middle-aged non-diabetic individuals who were subjected to the same study protocol as participants in CARDIPP [18]. The CAREFUL study included randomly selected individuals from a population register aged 50–70 years from the Linköping catchment area. Individuals with known diabetes were excluded, as were those with a family history or own diagnosis of aortic aneurysm.

2.2. Measures

All patients were seen on an extended yearly check up at the primary health care centers. In addition, the patients underwent an extensive physiological investigation at the department of Physiology at Linköping University hospital or at Ryhov Hospital (Jönköping), respectively. At the check-up, history of cardiovascular diseases, current medication and life style was recorded.

2.3. Laboratory measures

Blood samples were obtained in the morning after an overnight fast. The laboratory tests were all analyzed by laboratories at the local primary care centers or hospitals except for apolipoproteins which were analyzed at Linköping University Hospital (Department of Laboratory Medicine). HbA1c was analyzed according to the Swedish Mono-S HPLC standard which is approximately one percent unit lower than the Diabetes Control and Complications Trial (DCCT) standard. Glomerular filtration rate (GFR) was analyzed according to Cockcroft–Gault, MDRD as well as cystatinC estimated. In the regression analyses Cockcroft–Gault estimated GFR was used.

2.4. Physiological examination

Toe pressure (*TP*) was measured after 10 min rest by strain-gauge technique (Medimatic, Hellerup, Danmark) with the patient in supine position and local temperature at foot level at 30 °C. Measurement was done bilaterally. However, in the present study the lowest recorded TP from each patient was used in the analyses. At the same visit, brachial systolic blood pressure (SBP) was measured bilaterally in supine position by an automated oscillometric device (Dinamap PRO 200 Monitor, Critikon, Tampa, Fl, USA) and the arm with the highest pressure was used for further analysis. Simultaneously as TP-measurement a SBP was recorded and used in the subsequent analyses. The *toe brachial index* (*TBI*) was calculated as; systolic toe pressure (mmHg)/systolic brachial pressure (mmHg).