Eur J Vasc Endovasc Surg (2017) ■, 1–8

Toe Pressure and Toe Brachial Index are Predictive of Cardiovascular Mortality, Overall Mortality, and Amputation Free Survival in Patients with Peripheral Artery Disease

J.-E. Wickström [a], M. Laivuori [b], E. Aro [a], R.T. Sund [c], O. Hautero [a], M. Venermo [b], J. Jalkanen [a], H. Hakovirta [a,*]

[a] Department of Vascular Surgery, Turku University Hospital and University of Turku, Turku, Finland
[b] Department of Vascular Surgery, University Hospital of Helsinki, Helsinki, Finland
[c] Centre for Research Methods, Department of Social Research, University of Helsinki, Helsinki, Finland

WHAT THIS PAPER ADDS

In many vascular units, ankle pressure, ankle brachial pressure, toe pressure (TP), and toe brachial index (TBI) are essential measurements for clinical decision making and are routinely analysed in everyday practice. There are no earlier studies comparing all four variables and patient outcome in a single study setting. Based on the present observations it is suggested that non-invasive measurement of TP and TBI are associated with cardiovascular and overall mortality, as well as amputation free survival of patients with peripheral artery disease.

Objective/Background: Peripheral haemodynamic parameters are used to assess the presence and severity of peripheral artery disease (PAD). The prognostic value of ankle brachial index (ABI) has been thoroughly delineated. Nonetheless, the relative usefulness of ankle pressure (AP), ABI, toe pressure (TP), and toe brachial index (TBI) in assessing patient outcome has not been investigated in a concurrent study setting. This study aimed to resolve the association of all four non-invasive haemodynamic parameters in clinically symptomatic patients with PAD with cardiovascular mortality, overall mortality, and amputation free survival (AFS).

Methods: In total, 732 symptomatic patients with PAD admitted to the Department of Vascular Surgery for conventional angiography at Turku University Hospital, Turku, Finland, between January 2009 and August 2011 were reviewed retrospectively. Demographic factors, cardiovascular mortality, all-cause mortality, and above foot level amputations were obtained and assessed in relation to AP, ABI, TP, and TBI by means of Kaplan–Meier life tables and a multivariate Cox regression model.

Results: The haemodynamic parameter that was associated with poor 36 month general outcome was TP $<$ 30 mmHg. Univariate Cox regression analysis of stratified values showed that TP and TBI associated significantly with mortality. In multivariate analysis both TP and TBI were associated with a significant risk of death. For TP $<$ 30 mmHg and TBI $<$ 0.25 the risk of cardiovascular mortality was hazard ratio [HR] 2.84, 95% confidence interval [CI] 1.75–4.61 [$p < .001$]; HR 3.68, 95% CI 1.48–9.19 [$p = .050$], respectively; all-cause mortality (HR 2.05, 95% CI 1.44–2.92 [$p < .001$]; HR 2.53, 95% CI 1.35–4.74 [$p = .040$], respectively); and amputation or death (HR 2.13, 95% CI 1.52–2.98 [$p < .001$]; HR 2.46, 95% CI 1.38–4.40 [$p = .050$], respectively)...

Conclusion: Among non-invasive haemodynamic measurements and pressure indices both TP and TBI appear to be associated with cardiovascular and overall mortality and AFS for patients with PAD presenting symptoms of the disease.

Article history: Received 21 September 2016, Accepted 9 February 2017, Available online XXX

Keywords: ABI, Amputation free survival, Ankle pressure, Mortality, TBI, Toe pressure

INTRODUCTION

Lower limb peripheral arterial disease (PAD) and, in particular, critical limb ischaemia (CLI) markedly increase the risk of both debilitating limb loss and adverse cardiovascular events. Today, an estimated 200 million people worldwide are affected by PAD, with the number constantly increasing, owing not only to longer life expectancy, but also to manifestation of the disease at a younger age.[1–3] Early detection of PAD and initiation of optimal medical and conservative treatment is thus becoming increasingly important.

Measurements of ankle and toe systolic pressures (AP and TP, respectively) and their relation to that in the arm (ankle brachial index [ABI] and toe brachial index [TBI]) have

* Corresponding author. Turku University Hospital, TE5 Hämeentie 11, 20521 Turku, Finland.
E-mail address: haheha@utu.fi (H. Hakovirta).

1078-5884/

http://dx.doi.org/10.1016/j.ejvs.2017.02.012

Please cite this article in press as: Wickström J-E, et al., Toe Pressure and Toe Brachial Index are Predictive of Cardiovascular Mortality, Overall Mortality, and Amputation Free Survival in Patients with Peripheral Artery Disease, European Journal of Vascular and Endovascular Surgery (2017), http://dx.doi.org/10.1016/j.ejvs.2017.02.012

been widely applied to the initial assessment of peripheral circulation. The diagnostic limitations of ABI have been thoroughly addressed. Decreased ABI (< 0.9) has been shown to be strongly associated with increased risk of myocardial infarction and cardiovascular death.[4,5] However, the usefulness of ABI may be reduced in conditions such as diabetes, chronic kidney disease, and advanced age, owing to arterial stiffening and incompressibility of the leg arteries at ankle level.[6–8] Both low and high ABI among diabetic patients correlate with increased risk of cardiovascular mortality in a U-shaped fashion.[8,9] Thus, arterial stiffening may reduce both the diagnostic and prognostic value of ABI, especially among diabetics.

As digital arteries are generally regarded as less susceptible to vessel stiffness, the use of TP and TBI has been recommended in order to overcome the influence of arterial incompressibility.[6,9] However, among diabetics the diagnostic value of TBI has been questioned.[10,11] The correlation of low TP with increased mortality and decreased amputation free survival (AFS) has been demonstrated in patients with incompressible leg arteries.[12,13]

In addition to AP and ABI, TP is used in the widely accepted TransAtlantic Inter-Society Consensus II (TASC II) classification of limb ischaemia.[14–17] Low TP appears to serve as a prognostic marker for wound healing in PAD.[14] Further risk stratification of patients with CLI based on the severity of tissue loss, ischaemia, and foot infection (WIfI) has recently been created by the Society for Vascular Surgery Lower Extremity Guidelines Committee.[18] Yet, not every patient with haemodynamic criteria for severe ischaemia, even according to WIfI, may require revascularisation.[13]

Even today, data regarding means of identifying which patients with PAD have the greatest risk of major cardiovascular events or amputation is limited. Non-invasive measurement of haemodynamic parameters is feasible and routinely carried out in vascular practice. However, the overall relative prognostic value of AP, ABI, TP, and TBI remains to be further elucidated. We have analysed the relationship between these parameters and mid-term cardiovascular and all-cause mortality, as well as AFS in vascular surgical patients. To the authors' knowledge, there are few previous data comparing all four parameters in a setting that encompasses all symptomatic patients with PAD.

METHODS

Study cohort

This retrospective study consisted of all consecutive symptomatic patients with PAD admitted to the Department of Vascular Surgery, Turku University Hospital, Turku, Finland, for either diagnostic or therapeutic conventional lower limb angiography (digital subtraction angiography [DSA]) from 1 June 2009 to 31 August 2011. The aim was to analyse the influence of peripheral pressures and pressure indices on 36 month survival at the time of clinical presentation with insufficient arterial circulation, before any revascularisation procedures. Although 887 patients were recruited, standardised peripheral pressure measurements were available for only 732 patients. This is a result of poor availability of vascular laboratory measurements outside office hours. Patients were included irrespective of their earlier PAD history. The study protocol was approved by the local ethical committee of the Hospital District of South-West Finland. Owing to the retrospective nature of this study, informed patient consent was not required.

Vascular laboratory

Standardised non-invasive haemodynamic measurements were carried out by experienced vascular technicians at Turku University Hospital Vascular Laboratory. Measurements were obtained with patients in a supine position with feet at heart level, using a Nicolet VasoGuard (Nicolet Vascular Inc. Madison, WI, USA) photoplethysmography (PPG) device in all patients. When stable signals were obtained, brachial, ankle, and digital cuffs were inflated until disappearance of the PPG signal, typically up to 200 mmHg. Brachial pressure, AP, and TP were determined by gradual deflation of the cuffs to the moment of reappearance of a pulsatile signal. Signals were later checked offline. TP was preferentially measured from the great toe or, if it was missing, from the nearest available toe. A mean of 3–5 measurements of TP was used for analysis. Either APs or TPs were available for 732 patients prior to possible revascularisation. AP and ABI were available for 720 patients, and TP and TBI for 717 patients. In 708 patients both measurements were available. Measurements for the clinically relevant limb were registered. When both limbs were symptomatic, measurements for the limb with the lowest TP were registered. Where TP was not available, measurements for the limb with the lowest AP were registered.

TP and TBI were not measurable in 15 patients with previous forefoot amputations or severe tissue loss involving the toes. AP was unavailable for 12 patients, either owing to pain or reduced ability to cooperate. Pressure indices for one patient were not available owing to apparently incompressible arteries in both upper extremities with bilateral non-occluded cuff pressures of > 250 mmHg in the arms.

Data collection

Patient baseline characteristics at admission, which served as the index date for follow-up, were retrospectively collected from the hospital electronic database. Only International Classification of Diseases (ICD) 10 coded diagnoses were registered. The following risk factors were collected for analysis: coronary artery disease (CAD), cerebrovascular disease (CVD), hypertension, active smoking, diabetes, sleep apnea, chronic obstructive pulmonary disease (COPD), end stage renal disease (ESRD), dyslipidemia, AP, ABI, TP, TBI, and serum creatinine level. Baseline medication including statins, clopidogrel, aspirin, warfarin, and

Please cite this article in press as: Wickström J-E, et al., Toe Pressure and Toe Brachial Index are Predictive of Cardiovascular Mortality, Overall Mortality, and Amputation Free Survival in Patients with Peripheral Artery Disease, European Journal of Vascular and Endovascular Surgery (2017), http://dx.doi.org/10.1016/j.ejvs.2017.02.012