

Can Upstroke Time be a More Significant Predictor for Cardiovascular Disease Than Ankle-Brachial Index?

Yasuyoshi Takei

Department of Cardiology, Tokyo Medical University, Tokyo, Japan

See article vol. 29: 337-344

Ankle-brachial index (ABI) is not only a useful screening method for detecting peripheral artery disease (PAD) but can also be used as a cardiovascular risk marker because ABI is an indicator of systemic atherosclerosis. Low ABI related to severe occlusive arterial disease of the lower extremities and high ABI related to poor arterial compressibility attributable to increased arterial stiffness and calcification of lower limb arteries represent markers of advanced atherosclerosis and vascular diseases in systemic vascular beds. Therefore, patients with low or high ABI are considered to be at high cardiovascular risk, with higher rates of concomitant cardiovascular diseases and higher incidence of cardiovascular events. It has been well known that the prevalence of coronary artery disease (CAD) according to ABI had a reverse “J-shaped” distribution. On the other hand, ABI might be unreliable as a marker of atherosclerosis in patients with calcified and noncompressible lower limb arteries because oscillometric ABI could be pseudonormalized by falsely-elevated ankle blood pressure despite the presence of hemodynamically occlusive arterial disease, possibly leading to misclassifying patients with high cardiovascular risk as being at low risk by ABI measurement alone^{1, 2}. Therefore, an additional vascular parameter should be combined with ABI to improve the accuracy of ABI for detecting subjects with advanced atherosclerosis.

Recently, the waveform of pulse volume recording could be easily obtained in a brief time, and pulse volume-recording parameters, including upstroke time (UT), are automatically calculated by an automated oscillometric device, leading to objective evaluation and clinical application of pulse volume-recording parameters. Using the device, UT or UT

per cardiac cycle (UTCC) has been reported as a significant predictor for cardiovascular disease and all-cause mortality in subjects with normal ABI. Because of dependency on heart rate, UTCC is thought to be a better parameter than UT. In the past years, UT measured in the lower limb was thought to be an additional diagnostic parameter comparing to ABI itself in patients with PAD. In individuals with a normal ABI, who are usually considered not to have advanced atherosclerosis, UT is reported to be a useful vascular marker for detecting CAD³. The phenomenon of the prolonged UTCC with normal ABI is based on various collateral arterial networks with severe PAD, including chronic total occlusion of peripheral arteries. Based on this background, UTCC has been reported to be a significant parameter for mortality prediction in diseased patients such as type 2 diabetes mellitus⁴, chronic kidney disease⁵, or acute myocardial infarction⁶.

In the present study⁷ Su *et al.* investigated the usefulness of UTCC for the prediction of long-term cardiovascular mortality and all-cause mortality in patients with normal ABI after adjusting age, diabetes mellitus, chronic kidney disease, heart failure, left ventricular hypertrophy, brachial-ankle pulse wave velocity (baPWV), and left ventricular ejection fraction (LVEF). In addition, UTCC also has better additive predictive markers of cardiovascular and all-cause mortality than ABI, baPWV, and LVEF. The group with UTCC of > 17.5% has had a high risk for cardiovascular and all-cause mortality since the early phase of the follow-up period (Figure 1 in the present study).

Compared with the ABI recording method, an advantage of the pulse volume-recording method is that the waveform of pulse volume recording that reflects arterial pulsatility might not be significantly affected by the presence of calcified and

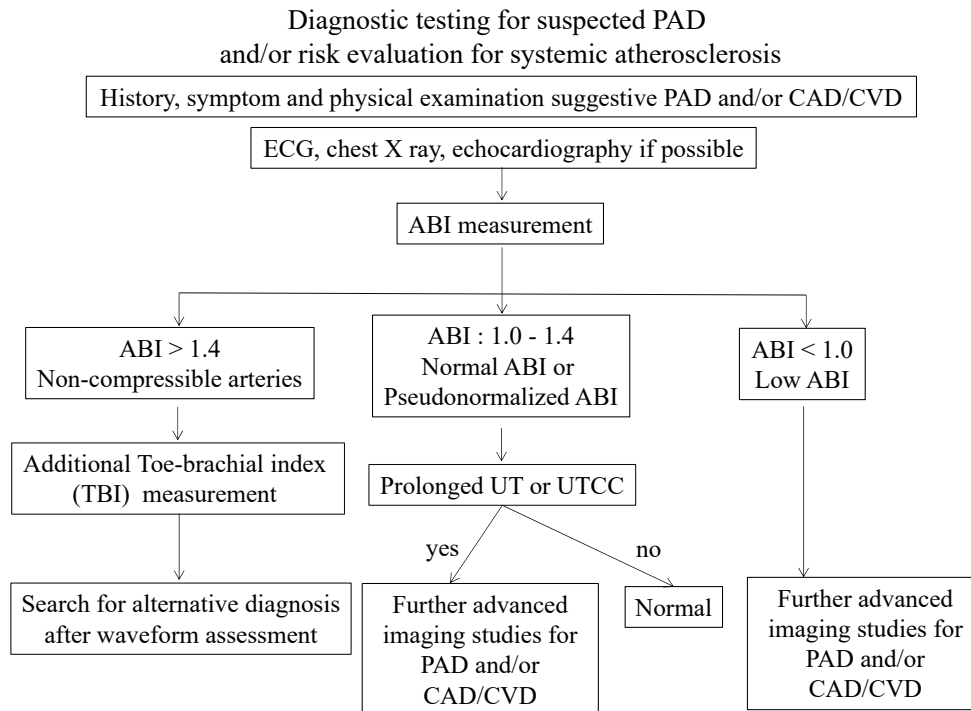


Fig. 1. The diagnostic algorithm for detecting PAD and/or for assessing systemic atherosclerosis

noncompressible arteries⁸⁾, which might contribute to an improvement in the diagnostic accuracy of pulse volume-recorded parameters for PAD in combination with ABI⁹⁾. Patients with PAD with pseudonormalized ABI attributable to noncompressible lower limb arteries may be included among subjects with normal ABI, leading to an underestimation of the prevalence of PAD and incorrect severity assessment of atherosclerosis by ABI measurement alone. One study suggested that those patients with pseudonormalized ABI could be detected by UT calculated from pulse volume recording, which might not be significantly affected by the presence of noncompressible arteries³⁾. Therefore, the recommended procedures for the severity assessment of atherosclerosis by a combination of ABI and UT or UTCC could be as follows. First, patients with low ABI (<1.00) or high ABI (>1.40) should undergo further evaluation to confirm the presence of CAD or cerebrovascular disease (CVD). Second, in subjects with normal ABI ($1.00 \leq \text{ABI} \leq 1.40$), UT or UTCC should be confirmed carefully to detect patients with pseudonormalized ABI who potentially have systemic advanced atherosclerosis. The cut-off values of ABI are in accordance with the latest AHA/ACC guideline on the management for PAD¹⁰⁾. Subjects with normal ABI but with abnormally prolonged UT (≥ 180 msec.) or UTCC should undergo further evaluation to confirm the

presence of CAD or CVD, which may not be significantly affected by the presence of noncompressible arteries (Fig. 1).

There are several limitations regarding UT or UTCC. First, there are not any established cut-off values in UTCC. More evidences about the normal range of UTCC will be needed. Second, UT or UTCC is affected by heart rate, cardiac systolic dysfunction, and aortic valve stenosis. Generally, basic examinations such as electrocardiogram (ECG), chest X ray, and echocardiography for confirming LVEF and valvular heart diseases should be performed before assessing UT or UTCC.

For the future, patients with polyvascular diseases would increase as society ages. Simple methodology, excellent reproducibility, and validity in the clinical setting are necessary for the evaluation of vascular functions not only in detecting PAD but also for assessing systemic atherosclerosis. Although ABI is an appropriate method, the waveform of pulse volume recording that includes UT or UTCC and % mean artery pressure (%MAP) are also significant. The importance of analysis for the pulse waveform itself has been more emphasized recently. The superiority of the ABI measurement would not have changed; however, further studies are required to establish the diagnostic algorithm including ABI and other pulse waveform recordings such as UT or UTCC for

cardiovascular risk assessment.

Conflict of Interest

Yasuyoshi Takei has declared that no competing interest exists.

References

- 1) Emanuele MA, Buchanan BJ, Abaira C. Elevated leg systolic pressures and arterial calcification in diabetic occlusive vascular disease. *Diabetes Care*, 1981; 4: 289-292
- 2) Potier L, Halbron M, Bouilloud F, Dadon M, Le Doeuff J, Van Ha G, Grimaldi A, Hartemann-Heurtier A. Ankle-to-brachial ratio index underestimates the prevalence of peripheral occlusive disease in diabetic patients at high risk for arterial disease. *Diabetes Care*, 2009; 32: e44
- 3) Maruhashi T, Kajikawa M, Kishimoto S, Hashimoto H, Takaeko Y, Yamaji T, Harada T, Hashimoto Y, Han Y, Aibara Y, Yusoff FM, Hidaka T, Chayama K, Nakashima A, Goto C, Kihara Y, Higashi Y. Upstroke time is a useful vascular marker for detecting patients with coronary artery disease among subjects with normal ankle-brachial index. *J Am Heart Assoc*, 2020; 9: e017139
- 4) Chang LH, Hwu CM, Chu CH, Won JGS, Chen HS, Lin LY. Upstroke time per cardiac cycle is associated with cardiovascular prognosis in type 2 diabetes. *Endocr Pract*, 2019; 25: 1109-1116
- 5) Lee WH, Hsu PC, Chu CY, Chen SC, Chen YC, Lee MK, Lee HH, Lee CS, Yen HW, Lin TH, Voon WC, Lai WT, Sheu SH, Su HM. Upstroke time as a novel predictor of mortality in patients with chronic kidney disease. *Diagnostics (Basel)*, 2020; 10: 422
- 6) Hsu PC, Lee WH, Tsai WC, Chen YC, Chi NY, Chang CT, Chu CY, Lin TH, Lee CS, Lai WT, Sheu SH, Su HM. Upstroke time per cardiac cycle as a novel parameter for mortality prediction in patients with acute myocardial infarction. *J Clin Med*, 2020; 9: 904
- 7) Su HM, Lee WH, Tsai WC, Lin TC, Lu YH, Lee CS, Lin TH, Voon WC, Lai WT, Sheu SH, Hsu PC. Usefulness of upstroke time per cardiac cycle for cardiovascular and all-cause mortality prediction in patients with normal ankle-brachial index. *J Atheroscler Thromb*, 2022; 29: 337-344
- 8) Rutherford RB, Lowenstein DH, Klein MF. Combining segmental systolic pressures and plethysmography to diagnose arterial occlusive disease of the legs. *Am J Surg*, 1979; 138: 211-218
- 9) Hashimoto T, Ichihashi S, Iwakoshi S, Kichikawa K. Combination of pulse volume recording (PVR) parameters and ankle-brachial index (ABI) improves diagnostic accuracy for peripheral arterial disease compared with ABI alone. *Hypertens Res*, 2016; 39: 430-434
- 10) Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, Fleisher LA, Fowkes FG, Hamburg NM, Kinlay S, Lookstein R, Misra S, Mureebe L, Olin JW, Patel RA, Regensteiner JG, Schanzer A, Shishehbor MH, Stewart KJ, Treat-Jacobson D, Walsh ME. 2016 AHA/ACC Guideline on the management of patients with lower extremity peripheral artery disease: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation*, 2017; 135: e686-e725