

脉搏波速度与2型糖尿病血管并发症的相关性研究进展

李炜祯^{1,2}, 王倩², 董哲毅², 张伟光², 陈香美^{1,2*}

¹广东药科大学临床医学院, 广州 510006; ²解放军总医院第一医学中心肾脏病医学部/解放军肾脏病研究所/肾脏疾病国家重点实验室/国家慢性肾病临床医学研究中心/肾脏疾病研究北京市重点实验室, 北京 100853

[摘要] 2型糖尿病(T2DM)常伴发微血管及大血管病变,但在疾病早期未受到足够重视。因此,需要更多的辅助检测方法对T2DM及高危患者进行早期筛查、辅助诊断。近年来,动脉硬化检测特别是脉搏波速度(PWV)作为一种无创的测量动脉硬度的有效方法,其应用越来越广泛。现有研究表明,动脉硬化增加是T2DM患者血管病变发生发展的重要预测因素。为了更好地在疾病发生前进行预判,以便及早启动健康管理,应用PWV预测动脉硬化显得尤为重要。该文对PWV与T2DM微血管、大血管并发症的相关性进行综述,旨在为早期预判和管理具有血管病变风险的T2DM患者提供参考。

[关键词] 脉搏波速度; 糖尿病, 2型; 动脉硬化; 血管并发症

[中图分类号] R589

[文献标志码] A

[文章编号] 0577-7402(2021)05-0492-06

[DOI] 10.11855/j.issn.0577-7402.2021.05.11

Research progress on the relationship between pulse wave velocity and vascular complications in type 2 diabetes mellitus

Li Wei-Zhen^{1,2}, Wang Qian², Dong Zhe-Yi², Zhang Wei-Guang², Chen Xiang-Mei^{1,2*}

¹School of Clinical Medicine, Guangdong Pharmaceutical University, Guangzhou 510006, China

²Department of Nephrology, the First Medical Center of Chinese PLA General Hospital/Chinese PLA Institute for Nephrology/State Key Laboratory of Kidney Disease/National Clinical Research Center for Chronic Kidney Disease/Beijing Key Laboratory of Kidney Disease Research, Beijing 100853, China

*Corresponding author, E-mail: xmchen301@126.com

This work was supported by the National Natural Science Foundation of China (81700629), the National Key Research and Development Program (2018YFC1704203), the National Science and Technology Major Projects (2019ZX09201-005), the Science and Technology Project of Beijing (D171100002817002), and the Big Data Project of Chinese PLA General Hospital (2019MBD-053)

[Abstract] Type 2 diabetes mellitus (T2DM) is often clinically associated with mi- and macrovascular diseases, but is often ignored in the early stage of the disease. Therefore, more auxiliary detection methods are needed clinically for early screening and auxiliary diagnosis of T2DM and high-risk patients. Arteriosclerosis detection--especially pulse wave velocity (PWV), as a non-invasive and effective method for measuring arterial stiffness, has been applied more and more widely in clinic recent years. Existing studies have shown that increased arterial stiffness is an important predictor of the occurrence and development of vascular diseases in T2DM. The value of PWV in the prediction of atherosclerosis is particularly important in order to better predict the occurrence of disease and start health management as soon as possible. Therefore, the relationship between PWV and mi- and macrovascular complications in T2DM is reviewed in present paper to provide early warning for patients with T2DM who have early vascular risk.

[Key words] pulse wave velocity; diabetes mellitus, type 2; arteriosclerosis; vascular complications

随着我国人口老龄化的加剧及生活方式的改变, 2型糖尿病(type 2 diabetes mellitus, T2DM)

[基金项目] 国家自然科学基金(81700629); 国家重点研发计划(2018YFC1704203); 国家科技重大专项(2019ZX09201-005); 北京市科技计划(D171100002817002); 解放军总医院大数据项目(2019MBD-053)

[作者简介] 李炜祯, 硕士研究生, 主要从事糖尿病合并肾脏疾病方面的研究

[通信作者] 陈香美, E-mail: xmchen301@126.com

的发病率逐年上升^[1]。国际糖尿病联盟发布的数据显示, 2019年全球糖尿病患病率约为9.3%(4.63亿), 预计到2030年及2045年将分别增至10.2%(5.78亿)、10.9%(7.00亿), 其导致的血管并发症也随之增多^[2]。多项研究表明, 脉搏波速度(pulse wave velocity, PWV)对T2DM血管并发症具有较好的预测价值^[3-5]。本文就PWV与T2DM微血管及大血管并发症的相关性研究进行综述, 旨在为早期预判和管

理具有血管病变风险的T2DM患者提供参考。

1 PWV的基本原理及临床应用

PWV是一种操作简单、非侵入性、可重复进行的测量动脉硬度的新方法^[6]。目前评价动脉硬度的指标较多,常用指标包括颈动脉增强指数、颈-股动脉PWV(cfPWV)^[7]、臂踝PWV(baPWV)、股骨踝关节PWV(faPWV)^[8]、心脏-颈动脉PWV(hcPWV)、心脏-股动脉PWV(hfPWV)、袖带动态PWV(ambulatory brachial cuff-based oscillometric PWV, oPWV)^[9]、心踝血管指数(CAVI)^[10]、踝肱指数(ankle-brachial index, ABI)^[11]、趾肱指数(toe brachial index, TBI)^[12]等。而cfPWV被公认为测量动脉硬度的金标准^[6]。有研究显示,cfPWV与baPWV均为中心动脉硬度的指标,两者呈明显正相关($r=0.73$),且baPWV值平均较cfPWV高约20%^[13]。但测量cfPWV需暴露腹股沟隐私部位,而测量baPWV只需暴露肱动脉和踝动脉,且研究表明baPWV的测量值与cfPWV有较好的一致性,因此,baPWV在临床上的应用更为广泛^[7,14-16]。baPWV的测量方法为:baPWV=[踝-主动脉瓣距离(La)-肱-主动脉瓣距离(Lb)]/踝-肱动脉的压力波波足时间差(ΔT)^[17]。文献报道可用胸骨上切迹代替主动脉瓣的测量位点^[14]。cfPWV的检测方法也类似^[6]。一项针对7656例高血压患者的研究结果显示,baPWV预测心血管疾病的最佳阈值为18.3 m/s^[18]。而无论是哪种检测方法,PWV的数值越大,表明动脉硬化程度越重,患心血管疾病的风险越高。ABI、TBI常用于可疑外周动脉疾病(peripheral arterial disease, PAD)患者的诊断^[19-20]。ABI计算方法为:ABI=踝部动脉收缩压/肱动脉收缩压^[21];TBI的计算方法为:TBI=趾部动脉收缩压/肱动脉收缩压^[12]。欧洲心脏病学会(ESC)最新指南推荐:ABI 1.00~1.40为正常范围, ≤ 0.90 可诊断为下肢动脉疾病(LEAD), >1.40 诊断为动脉硬化(中膜动脉钙化)^[22]。

2 PWV与T2DM微血管并发症的相关性研究

2.1 PWV与糖尿病肾病的相关性

2.1.1 PWV对T2DM进展为糖尿病肾病风险的预测

一项包含43个队列、上百万人的大规模荟萃分析结果显示,蛋白尿在正常范围内的T2DM患者,排除肾脏滤过功能的影响后,白蛋白/肌酐比值(albumin-to-creatinine ratio, ACR)在10~29 mg/g的患者较ACR<10 mg/g的患者PWV高,其全因死亡及心血管死亡风险高1.35~1.42倍^[23]。此外,一项纳入614例蛋白尿正常(ACR<30 mg/g)的T2DM患者的研究发现,随着ACR的增高,PWV明显加快;将

ACR水平按照四分位分为四组,与ACR水平最低的第1组相比,第2、3、4组动脉硬化比例分别增加11.0%、10.4%及13.6%,且第4组患者的动脉硬化发生率较第1组高4.34倍,提示动脉硬化程度与正常尿蛋白范围内较高值的相关性可能是糖尿病进展为终末期肾病的致病因素,即使糖尿病患者的ACR<30 mg/g,仍需加强心血管风险的监测^[24]。另一项关于T2DM微量蛋白尿与PWV关系的研究发现,有微量白蛋白尿组的PWV明显高于无微量白蛋白尿组^[25]。这些研究均表明,即使T2DM并未发展成糖尿病肾病,蛋白尿在正常范围内,PWV仍可预测糖尿病发展为糖尿病肾病的风险。

2.1.2 PWV与蛋白尿的相关性

一项纳入461例日本T2DM患者的研究显示,cfPWV较低的患者其基线ACR及未来出现蛋白尿的概率更低($P=0.002$),且随访5.9年后发现其与cfPWV较高的患者比较更容易出现蛋白尿转阴;PWV与蛋白尿的发生及转阴均明显相关[风险比(HR)=1.23, $P<0.001$; HR=0.72, $P=0.004$],提示PWV为T2DM患者发生蛋白尿的潜在预测因子^[3]。一项中位随访3.1年、纳入1012例亚洲多民族T2DM患者的研究结果表明,蛋白尿进展组的基线PWV较非进展组高,基线PWV增高与蛋白尿进展相关(OR=1.457),提示PWV为蛋白尿进展的独立预测因子^[26]。另一项来自台湾地区的纳入2180例患者的横断面研究将患者按baPWV四分位间距分为四组,与baPWV最低组相比,II、III、IV组的OR值分别为1.12、2.04、2.45,提示baPWV越高,发生蛋白尿的风险越高($P<0.001$)。糖尿病患者蛋白尿与动脉硬化的相关性较无糖尿病患者更强^[27]。

2.1.3 PWV与肾小球滤过率(eGFR)的相关性

有研究报道,不少糖尿病肾病患者的蛋白尿正常,但却出现eGFR下降,采用eGFR来评估疾病进展程度可避免这种情况的发生^[28]。一项纳入577例伴有早期慢性肾脏病(chronic kidney disease, CKD)的T2DM患者的队列研究发现,baPWV为eGFR值快速下降的独立危险因素;基线baPWV值越高,eGFR下降越快,随访1年后,其ACR进展也相对较快^[29]。一项纳入461例T2DM患者的研究发现,与PWV低值组比较,PWV高值组eGFR水平更低,中位随访5.9年发现,PWV与eGFR年变化明显相关(标准化估计值为0.095, $P=0.031$),动脉硬化与T2DM患者eGFR下降速率有关^[3]。另一项纳入13 586例中老年患者的队列研究结果显示,在基线无心血管疾病的患者中,PWV每增高1 m/s,eGFR下降的概率增加10%(OR=1.10, 95%CI 1.04~1.16)^[30]。这些研究结果均提示,baPWV与肾小球滤过率相关,可预测肾脏功能的变化情况,有助于识别肾功

能短期下降的高危患者,改善临床预后。

2.2 PWV与周围神经病变的相关性 一项纳入477例T2DM患者、中位随访6.2年的前瞻性研究结果显示,与无糖尿病周围神经病变的患者比较,有糖尿病周围神经病变的患者主动脉硬度更高,出现蛋白尿、其他糖尿病微血管并发症的概率更高;基线主动脉硬化增加(PWV>10 m/s)时,周围神经病变发生/进展的概率增高1倍;而cfPWV每增加1 m/s,周围神经病变发生/进展的概率增高11%^[4]。另一项纳入381例T2DM患者的横断面研究也验证了这一结论^[31]。

2.3 PWV与糖尿病视网膜病变的相关性 一项纳入846例T2DM视网膜病变患者的研究发现,PWV与糖尿病视网膜病变相关,且其升高与糖尿病视网膜病变的严重程度呈正相关^[32]。有研究表明,下肢外周动脉疾病(peripheral arterial disease, PAD)与增生性糖尿病视网膜病变有关^[33]。另一项研究将双侧肢体ABI<0.9或≥1.3定义为PAD,与0.9≤ABI<1.3比较,ABI<0.9或≥1.3与糖尿病视网膜病变的发生独立相关(HR=2.186)^[21]。

3 PWV与T2DM合并大血管病变的相关性研究

3.1 PWV与T2DM合并心血管疾病的相关性 心血管疾病是糖尿病患者最常见的死因^[34]。一项长达7年、包含5万人的前瞻性研究发现,糖尿病患者的心血管死亡风险是非糖尿病患者的2.13倍^[35]。另一项大型荟萃分析也证实,糖尿病患者的死亡风险是非糖尿病患者的1.2~1.9倍,且有心血管疾病者死亡率更高^[23]。一项纳入618例T2DM患者的横断面研究发现,与无心血管疾病的T2DM患者比较,有心血管疾病的T2DM患者主动脉PWV更高,主动脉PWV与10年心血管疾病风险呈明显正相关,主动脉PWV值每增加1个标准差,发生心血管事件的相对风险增加1.47倍,且大动脉硬化是糖尿病及心血管疾病的共同病理改变^[36]。一项研究纳入627例无心血管事件的T2DM患者随访8年发现,PWV每增加1 m/s,患者发生心血管事件的HR为1.142(95%CI 1.003~1.30, P=0.044)^[37]。上述研究结果表明,T2DM合并心血管疾病的患者较单纯T2DM患者PWV更高,发生心血管疾病及死亡的风险更高。已有研究发现,在糖尿病早期阶段,血管可存在硬化的表现^[38]。通过PWV早期评估血管硬化程度,可对存在心血管疾病风险的患者进行早期预警,并指导临床早期实施干预。多项研究表明,PWV是早期心血管疾病风险的独立危险因素,对心血管事件的预测价值远超过24 h平均动脉压等传统指标^[39-40]。Meta分析也显示,与传统的Framingham危险评分相

比,PWV可提高预测心血管疾病发生风险的有效性^[41]。

3.2 ABI、TBI与T2DM患者合并心血管疾病的相关性 一项纳入1910例T2DM患者的前瞻性队列研究经过7.5年的随访发现,ABI在正常范围内的变化与心血管事件风险(HR=1.13, 95%CI 1.01~1.27)及全因死亡发生率(HR=1.17, 95%CI 1.04~1.31)相关^[42]。另一项纳入741例T2DM患者的队列研究将TBI由低到高分为三组,发现TBI(第1组 vs. 第3组)与不良心血管事件(HR=2.67, 95%CI 1.60~4.50, P<0.001)及全因死亡发生率(HR=1.98, 95%CI 1.16~3.83, P=0.01)明显相关^[12]。这些研究提示动脉硬化检测可为预测糖尿病患者发生心血管疾病提供证据。

3.3 PWV与T2DM患者合并脑卒中的相关性 已有研究显示,PWV对脑卒中的发生、预后具有预测价值,急性卒中患者的PWV越高,则死亡风险越高^[43]。脑卒中急性期测量的PWV可独立预测恢复期的疾病状况,急性期PWV越高,预后越差^[44]。PWV在T2DM人群中对脑卒中同样具有预测价值。有研究对T2DM患者行PWV、MRI检查以评估其动脉硬化及脑梗死的发生情况,结果发现PWV与腔隙性脑梗死明显相关(OR=2.0, P<0.05)^[45]。糖尿病患者的卒中风险是血糖正常者的2~5倍^[46]。一项纳入117例T2DM患者的研究将患者分为糖尿病组、糖尿病合并缺血性卒中组,结果发现糖尿病合并缺血性卒中组的ABI更低,PWV更高^[47],提示ABI及PWV是T2DM患者缺血性卒中的危险因素。

3.4 PWV与T2DM患者合并动脉粥样硬化的相关性 一项纳入T2DM、脑卒中、高血压、冠心病人群的研究发现,T2DM是大动脉粥样硬化(PWV≥12 m/s)的危险因素(OR=2.854)^[5]。此外,一项横断面研究发现,在T2DM人群中PWV与颈动脉斑块评分明显相关($r=0.37$, $P=0.001$)^[48]。在临床研究中,颈动脉内膜中层厚度(intima-media thickness, IMT)常作为颈动脉硬化结构改变的指标^[49]。Taniwaki等^[50]研究发现,与年龄匹配的对照组相比,T2DM患者IMT及PWV明显增高,且IMT与PWV呈明显正相关($r=0.482$, $P<0.0001$)。另一项关于冠状动脉斑块的研究发现,无冠心病症状的T2DM组患者的PWV较健康对照组更高[(9.1±2.2) m/s vs. (7.9±1.4) m/s, $P<0.01$],随访5年后,两组PWV比较差异仍有统计学意义[(9.3±2.3) m/s vs. (8.4±1.8) m/s, $P=0.02$]^[5]。此外,该研究还发现,与健康对照组相比,无冠心病症状的T2DM患者冠状动脉斑块更为常见,且基线PWV与随访时的斑块体积明显相关。

3.5 PWV与T2DM患者合并高血压的相关性 研究发现, 高血压患者较正常血压者的动脉硬化程度更重、PWV更高, PWV与高血压疾病明显相关^[51]。动脉硬化是原发性高血压患者全因死亡发生率及心血管病死率的独立预测因子^[52]。在T2DM人群中, 合并高血压患者的baPWV较单纯T2DM及单纯高血压患者更高, 差异均有统计学意义($P<0.05$)^[53]。一项关于血压与动脉硬化的Meta分析结果显示, 收缩压每升高20 mmHg, 则PWV每10年增加1.14 m/s^[54]。Karalliedde等^[55]研究发现, 使用缬沙坦、氨氯地平降压药可降低PWV, 这为下一步研究降压药对动脉硬化的作用机制提供了依据。PWV的改变是由血管弹性、血管壁厚度、血管半径、血液密度等因素决定的, 反映了血管的结构和功能的变化^[56], 但现有的研究尚不清楚动脉硬化与高血压的因果关系。

综上所述, PWV无论对T2DM微血管并发症还是大血管并发症均有良好的预测价值。在临床中, 患者常同时患有微血管及大血管疾病。研究发现, 患者存在微血管疾病的数量越多, 未来出现心血管疾病的风险比越高, 提示微血管疾病的发生是心血管风险的预测因素^[57]。这对于早期仅出现微血管疾病(如糖尿病视网膜病变、糖尿病肾病), 尚未发生大血管疾病的患者具有预警作用, 而检测动脉硬化程度为临床判断T2DM患者的血管风险提供了一种新的方法。

4 总结与展望

PWV与T2DM合并微血管疾病、大血管疾病均存在明显相关性。PWV为脉搏波传导距离与传导时间的比值, 反映的是全身血管结构和功能的变化, 不能评估局部血管硬化情况。T2DM发生血管并发症的风险与高血糖、高血压、动脉粥样硬化等危险因素有关。因此, 临床可开展大样本的随机对照试验以排除此类混杂因素的干扰。此外, 下一步研究可观察T2DM患者PWV降低能否降低心血管事件的潜在风险。PWV为非侵入性检查, 对T2DM患者的血管并发症具有良好的预测价值, 未来在临床上的应用必将越来越广泛。

【参考文献】

- Chinese Diabetes Society. Guidelines for the prevention and control of type 2 diabetes in China (2017 Edition)[J]. Chin J Pract Intern Med, 2018, 38(4): 292-344. [中华医学会糖尿病学分会. 中国2型糖尿病防治指南(2017年版)[J]. 中国实用内科杂志, 2018, 38(4): 292-344.]
- Saeedi P, Petersohn I, Salpea P, *et al.* Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition[J]. Diabetes Res Clin Pract, 2019, 157: 107843.
- Bouchi R, Babazono T, Mugishima M, *et al.* Arterial stiffness is associated with incident albuminuria and decreased glomerular filtration rate in type 2 diabetic patients[J]. Diabetes Care, 2011, 34(12): 2570-2575.
- Cardoso CR, Moran CB, Marinho FS, *et al.* Increased aortic stiffness predicts future development and progression of peripheral neuropathy in patients with type 2 diabetes: the Rio de Janeiro Type 2 Diabetes Cohort Study[J]. Diabetologia, 2015, 58(9): 2161-2168.
- Funck KL, Laugesen E, Øvrehus K, *et al.* Increased high-risk coronary plaque burden is associated with arterial stiffness in patients with type 2 diabetes without clinical signs of coronary artery disease: a computed tomography angiography study[J]. J Hypertens, 2017, 35(6): 1235-1243.
- Laurent S, Cockcroft J, van Bortel L, *et al.* Expert consensus document on arterial stiffness: methodological issues and clinical applications[J]. Eur Heart J, 2006, 27(21): 2588-2605.
- Cortez-Cooper MY, Supak JA, Tanaka H. A new device for automatic measurements of arterial stiffness and ankle-brachial index[J]. Am J Cardiol, 2003, 91(12): 1519-1522, A9.
- Meyer ML, Tanaka H, Palta P, *et al.* Repeatability of central and peripheral pulse wave velocity measures: the Atherosclerosis Risk in Communities (ARIC) study[J]. Am J Hypertens, 2016, 29(4): 470-475.
- Schwartz JE, Feig PU, Izzo JL Jr. Pulse wave velocities derived from cuff ambulatory pulse wave analysis[J]. Hypertension, 2019, 74(1): 111-116.
- Saiki A, Sato Y, Watanabe R, *et al.* The role of a novel arterial stiffness parameter, cardio-ankle vascular index (CAVI), as a surrogate marker for cardiovascular diseases[J]. J Atheroscler Thromb, 2016, 23(2): 155-168.
- Lee CC, Tsai MC, Liu SC, *et al.* Relationships between chronic comorbidities and the atherosclerosis indicators ankle-brachial index and brachial-ankle pulse wave velocity in patients with type 2 diabetes mellitus[J]. J Investig Med, 2018, 66(6): 966-972.
- Chisalita SI, Wijkman M, Davidson LT, *et al.* Toe brachial index predicts major acute cardiovascular events in patients with type 2 diabetes independently of arterial stiffness[J]. Diabetes Res Clin Pract, 2020, 161: 108040.
- Tanaka H, Munakata M, Kawano Y, *et al.* Comparison between carotid-femoral and brachial-ankle pulse wave velocity as measures of arterial stiffness[J]. J Hypertens, 2009, 27(10): 2022-2027.
- Yamashina A, Tomiyama H, Takeda K, *et al.* Validity, reproducibility, and clinical significance of noninvasive brachial-ankle pulse wave velocity measurement[J]. Hypertens Res, 2002, 25(3): 359-364.
- Obeid H, Soulat G, Mousseaux E, *et al.* Numerical assessment and comparison of pulse wave velocity methods aiming at measuring aortic stiffness[J]. Physiol Meas, 2017, 38(11): 1953-1967.
- Teren A, Beutner F, Wirkner K, *et al.* Relationship between determinants of arterial stiffness assessed by diastolic and suprasystolic pulse oscillometry: comparison of vicorder and vascular explorer[J]. Medicine (Baltimore), 2016, 95(10): e2963.

- [17] Drafting Group of Expert Consensus, Branch of Refractory Hypertension and Peripheral Arterial Disease, China Association for International Exchange and Promotion of Medical Care. Chinese expert consensus on clinical application of simultaneous measurement of limb blood pressure as well as brachial and ankle pulse wave velocity[J]. *Chin Circ J*, 2020, 35(6): 521-528. [中国医疗保健国际交流促进会, 难治性高血压与周围动脉病分会专家共识起草组. 同步四肢血压和臂踝脉搏波速度测量临床应用中国专家共识[J]. *中国循环杂志*, 2020, 35(6): 521-528.]
- [18] Ohkuma T, Tomiyama H, Ninomiya T, *et al.* Proposed cutoff value of brachial-ankle pulse wave velocity for the management of hypertension[J]. *Circ J*, 2017, 81(10): 1540-1542.
- [19] Wukich DK, Shen W, Raspovic KM, *et al.* Noninvasive arterial testing in patients with diabetes: a guide for foot and ankle surgeons[J]. *Foot Ankle Int*, 2015, 36(12): 1391-1399.
- [20] Williams B, Mancia G, Spiering W, *et al.* 2018 practice guidelines for the management of arterial hypertension of the European society of hypertension and the European society of cardiology: ESH/ESC task force for the management of arterial hypertension[J]. *J Hypertens*, 2018, 36(12): 2284-2309.
- [21] Lee MY, Hsiao PJ, Huang JC, *et al.* Abnormally low or high ankle-brachial index is associated with the development of diabetic retinopathy in type 2 diabetes mellitus[J]. *Sci Rep*, 2018, 8(1): 441.
- [22] Aboyans V, Ricco JB, Bartelink MEL, *et al.* 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS): document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries Endorsed by: the European Stroke Organization (ESO) the task force for the diagnosis and treatment of peripheral arterial diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS)[J]. *Eur Heart J*, 2018, 39(9):763-816.
- [23] Fox CS, Matsushita K, Woodward M, *et al.* Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis[J]. *Lancet*, 2012, 380(9854): 1662-1673.
- [24] Liu JJ, Tavintharan S, Yeoh LY, *et al.* High normal albuminuria is independently associated with aortic stiffness in patients with Type 2 diabetes[J]. *Diabet Med*, 2014, 31(10): 1199-1204.
- [25] Sjöblom P, Nystrom FH, Länne T, *et al.* Microalbuminuria, but not reduced eGFR, is associated with cardiovascular subclinical organ damage in type 2 diabetes[J]. *Diabetes Metab*, 2014, 40(1): 49-55.
- [26] Zhang X, Low S, Sum CF, *et al.* Arterial stiffness is an independent predictor for albuminuria progression among Asians with type 2 diabetes-A prospective cohort study[J]. *J Diabetes Complications*, 2017, 31(6): 933-938.
- [27] Liu CS, Pi-Sunyer FX, Li CI, *et al.* Albuminuria is strongly associated with arterial stiffness, especially in diabetic or hypertensive subjects: a population-based study (Taichung Community Health Study, TCHS)[J]. *Atherosclerosis*, 2010, 211(1): 315-321.
- [28] Chen C, Wang C, Hu C, *et al.* Normoalbuminuric diabetic kidney disease[J]. *Front Med*, 2017, 11(3): 310-318.
- [29] Sheen YJ, Lin JL, Li TC, *et al.* Peripheral arterial stiffness is independently associated with a rapid decline in estimated glomerular filtration rate in patients with type 2 diabetes[J]. *Biomed Res Int*, 2013, 2013: 309294.
- [30] Cândido JSA, Camelo LV, Mill JG, *et al.* Greater aortic stiffness is associated with renal dysfunction in participants of the ELSA-Brasil cohort with and without hypertension and diabetes[J]. *PLoS One*, 2019, 14(2): e0210522.
- [31] Tentolouris A, Eleftheriadou I, Grigoropoulou P, *et al.* The association between pulse wave velocity and peripheral neuropathy in patients with type 2 diabetes mellitus[J]. *J Diabetes Complications*, 2017, 31(11): 1624-1629.
- [32] Liu SC, Chuang SM, Shih HM, *et al.* High pulse wave velocity is associated with the severity of diabetic retinopathy in patients with type 2 diabetes[J]. *J Investig Med*, 2020, 68(6): 1159-1165.
- [33] Chen SC, Hsiao PJ, Huang JC, *et al.* Abnormally low or high ankle-brachial index is associated with proliferative diabetic retinopathy in type 2 diabetic mellitus patients[J]. *PLoS One*, 2015, 10(7): e0134718.
- [34] Gu K, Cowie CC, Harris MI. Mortality in adults with and without diabetes in a national cohort of the U.S. population, 1971-1993[J]. *Diabetes Care*, 1998, 21(7): 1138-1145.
- [35] Bragg F, Holmes MV, Iona A, *et al.* Association between diabetes and cause-specific mortality in rural and urban areas of China[J]. *JAMA*, 2017, 317(3): 280-289.
- [36] Mansour AS, Yannoutsos A, Majahalme N, *et al.* Aortic stiffness and cardiovascular risk in type 2 diabetes[J]. *J Hypertens*, 2013, 31(8): 1584-1592.
- [37] Wijkman M, Länne T, Östgren CJ, *et al.* Aortic pulse wave velocity predicts incident cardiovascular events in patients with type 2 diabetes treated in primary care[J]. *J Diabetes Complications*, 2016, 30(7): 1223-1228.
- [38] Agnoletti D, Mansour AS, Zhang Y, *et al.* Clinical interaction between diabetes duration and aortic stiffness in type 2 diabetes mellitus[J]. *J Hum Hypertens*, 2017, 31(3): 189-194.
- [39] Mattace-Raso FU, van der Cammen TJ, Hofman A, *et al.* Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam Study[J]. *Circulation*, 2006, 113(5): 657-663.
- [40] Willum-Hansen T, Staessen JA, Torp-Pedersen C, *et al.* Prognostic value of aortic pulse wave velocity as index of arterial stiffness in the general population[J]. *Circulation*, 2006, 113(5): 664-670.
- [41] Ohkuma T, Ninomiya T, Tomiyama H, *et al.* Brachial-ankle pulse wave velocity and the risk prediction of cardiovascular disease: an individual participant data meta-analysis[J]. *Hypertension*, 2017, 69(6): 1045-1052.
- [42] Sharif S, Visseren FLJ, Spiering W, *et al.* Arterial stiffness as a risk factor for cardiovascular events and all-cause mortality in people with Type 2 diabetes[J]. *Diabet Med*, 2019, 36(9): 1125-1132.
- [43] Kim J, Song TJ, Song D, *et al.* Brachial-ankle pulse wave velocity is a strong predictor for mortality in patients with acute stroke[J]. *Hypertension*, 2014, 64(2): 240-246.
- [44] Ishizuka K, Hoshino T, Shimizu S, *et al.* Brachial-ankle pulse wave velocity is associated with 3-month functional prognosis after ischemic stroke[J]. *Atherosclerosis*, 2016, 255: 1-5.
- [45] Shan Y, Lin J, Xu P, *et al.* Association of aortic compliance and brachial endothelial function with cerebral small vessel disease in type 2 diabetes mellitus patients: assessment with high-resolution MRI[J]. *Biomed Res Int*, 2016, 2016: 1609317.

- [46] Stamler J, Vaccaro O, Neaton JD, *et al.* Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial[J]. *Diabetes Care*, 1993, 16(2): 434-444.
- [47] Li T, Wu XJ, Chen XM, *et al.* Ankle-brachial index and brachial-ankle pulse wave velocity are risk factors for ischemic stroke in patients with Type 2 diabetes[J]. *Neural Regen Res*, 2017, 12(11): 1853-1859.
- [48] Masugata H, Senda S, Yoshikawa K, *et al.* Relationships between echocardiographic findings, pulse wave velocity, and carotid atherosclerosis in type 2 diabetic patients[J]. *Hypertens Res*, 2005, 28(12): 965-971.
- [49] Nezu T, Hosomi N, Aoki S, *et al.* Carotid intima-media thickness for atherosclerosis[J]. *J Atheroscler Thromb*, 2016, 23(1): 18-31.
- [50] Taniwaki H, Kawagishi T, Emoto M, *et al.* Correlation between the intima-media thickness of the carotid artery and aortic pulse-wave velocity in patients with type 2 diabetes. Vessel wall properties in type 2 diabetes[J]. *Diabetes Care*, 1999, 22(11): 1851-1857.
- [51] Kim EJ, Park CG, Park JS, *et al.* Relationship between blood pressure parameters and pulse wave velocity in normotensive and hypertensive subjects: invasive study[J]. *J Hum Hypertens*, 2007, 21(2): 141-148.
- [52] Laurent S, Boutouyrie P, Asmar R, *et al.* Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients[J]. *Hypertension*, 2001, 37(5): 1236-1241.
- [53] Kulkarni NB, Ganu MU, Godbole SG, *et al.* Effect of age and blood pressure on surrogate markers of atherosclerosis in patients with type 2 diabetes mellitus[J]. *J Clin Diagn Res*, 2014, 8(6): BC08-BC11.
- [54] Wilson J, Webb AJS. Systolic blood pressure and longitudinal progression of arterial stiffness: a quantitative Meta-analysis[J]. *J Am Heart Assoc*, 2020, 9(17): e017804.
- [55] Karalliedde J, Smith A, DeAngelis L, *et al.* Valsartan improves arterial stiffness in type 2 diabetes independently of blood pressure lowering[J]. *Hypertension*, 2008, 51(6): 1617-1623.
- [56] Tomiyama H, Shiina K. State of the art review: brachial-ankle PWV[J]. *J Atheroscler Thromb*, 2020, 27(7): 621-636.
- [57] Brownrigg JR, Hughes CO, Burleigh D, *et al.* Microvascular disease and risk of cardiovascular events among individuals with type 2 diabetes: a population-level cohort study[J]. *Lancet Diabetes Endocrinol*, 2016, 4(7): 588-597.

(收稿日期: 2020-10-23; 修回日期: 2021-01-12)

(责任编辑: 张小利)