Relationships between chronic comorbidities and the atherosclerosis indicators ankle-brachial index and brachial-ankle pulse wave velocity in patients with type 2 diabetes mellitus

Chun-Chuan Lee,[1,2] Ming-Chieh Tsai,[1] Sung-Chen Liu,[1,2] Chi-Feng Pan[2,3,4]

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[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan
[2]Department of Medicine, Mackay Medical Collage, New Taipei City, Taiwan
[3]Division of Nephrology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan
[4]Mackay Medicine, Nursing and Management College, Taipei, Taiwan

Correspondence to
Dr. Chi-Feng Pan;
chifeng@yeahmca.cn

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ABSTRACT

This study aimed to determine associations between ankle-brachial index (ABI) and brachial-ankle pulse wave velocity (baPWV) with different comorbidities in patients with type 2 diabetes mellitus (DM). Records of patients with type 2 DM who received an ABI and baPWV examination between August 2013 and February 2015 were retrospectively reviewed. Associations of ABI and baPWV with chronic kidney disease (CKD), chronic liver disease (CLD), coronary artery disease (CAD) and diabetic nephropathy (DN) were examined by regression analysis. A total of 1232 patients (average age, 65.1±10.0 years) were included in the analysis. CKD and DN were associated with low ABI and increased baPWV (all, P<0.001). No associations were found between CAD and CLD and ABI or baPWV. Thus, regression analysis was performed for CKD and DN. Low ABI was associated with risk of CKD in the crude model (OR 0.724, 95% CI 0.648 to 0.808, P<0.001) and adjusted model (OR 0.872, 95% CI 0.762 to 0.999, P=0.048), whereas baPWV was only significant in the crude model (OR 1.199, 95% CI 1.112 to 1.294, P<0.001). Low ABI was associated with risk of DN in the crude model (OR 0.873, 95% CI 0.780 to 0.977, P=0.018) and adjusted model (OR 0.884, 95% CI 0.782 to 0.999, P=0.048). No association was found for baPWV. In conclusion, low ABI was associated with risk of CKD and DN in patients with type 2 diabetes.

Significance of this study

What is already known about this subject?

- There are many studies on the utility of ankle-brachial index (ABI) and brachial-ankle pulse wave velocity (baPWV) for predicting outcomes in patients with diabetes mellitus (DM), and studies of the associations between ABI and baPWV and comorbidities in patients without diabetes.
- ABI is a powerful prognostic predictor in various clinical settings. The currently considered normal value of 0.9, however, may not rule out arterial disease. Factors such as the presence of DM, diabetic nephropathy (DN), food wounds and kidney diseases may affect the validity of ABI.
- One study demonstrated that the combination of ABI and baPWV is prognostic in patients with diabetes with kidney disease. Another study reported that only baPWV, not ABI, was predictive of mortality in patients with DM.

What are the new findings?

- This study is novel because it examined the relations of ABI and baPWV with chronic comorbidities in patients with DM.
- Our results show that in patients with type 2 DM, a low ABI was associated with chronic kidney disease and DN, but not with coronary artery disease and chronic liver disease. In addition, baPWV was not associated with any of the chronic diseases studied.
- The mean ABI in this study of 1.050±0.128 is within the 'normal range'.

INTRODUCTION

Type 2 diabetes mellitus (DM) is considered to be an independent risk factor for coronary artery disease (CAD) and its equivalents, including peripheral artery disease (PAD), the risk of which is doubled in patients with DM.[1–3] Patients with DM are also at increased risk for a number of other comorbidities including chronic kidney disease (CKD), chronic liver disease (CLD) and diabetic neuropathy (DN).[3] The most common cause of PAD is atherosclerosis, and as such PAD is a significant risk factor for all-cause death and cardiovascular death.[4–6] Patients with DM are also at increased risk of all-cause mortality, and PAD is more frequent in patients with DM than in individuals without diabetes.[7–9] Other independent risk factors for PAD include advanced age, smoking, higher triglyceride (TG) level, higher systolic blood pressure (SBP), elevated high-sensitive C reactive protein, CKD, albuminuria and low glomerular filtration rate (GFR).[10–12]

The two most common ways of diagnosing PAD are measurement of the brachial-ankle pulse wave velocity (baPWV) and ankle-brachial

Significance of this study

How might these results change the focus of research or clinical practice?

- The mean ABI value of patients with comorbidities was in the low normal range. This suggests that the current arbitrary normal value may not rule out arterial disease in patients with DM.
- Further studies are necessary to clarify the usefulness of ABI and baPWV in patients with DM.

index (ABI).[13–17] baPWV is a measure of the time it takes the pulse to travel from the brachial artery (considered a central position) to the ankle artery (a peripheral vessel). If the blood vessels are elastic and flexible, the velocity of the wave will be quick with a low time velocity. On the other hand, in the presence of atherosclerosis, which reduces the elasticity of vessels, more time will be required for the wave to travel from the brachial to ankle artery, resulting in a high baPWV. ABI measures the difference in SBP between the upper arm (brachial vein) and the ankle (dorsalis pedis). In general, a high value is good and a low value suggests a low pulse in the ankle and the presence of PAD. Commonly used cut-off values for ABI are: 0.91–1.30: normal; 0.70~0.90: mild occlusion; 0.40~0.69: moderate occlusion; <0.40: severe occlusion and >1.30: poorly compressible vessels.[17] However, ABI is a continuous variable and the normal range (0.91–1.30) is arbitrary. Heald *et al*[6] have suggested that the interval between 0.9 and 1.10, currently considered normal, may not rule out arterial disease.

The effects of diabetes on vascular indicators such as ABI and baPWV are complex, and thus values may be different than in patients without DM.[18] In patients with DM, especially those who have had the disease for a longer duration, and those with renal complications, ABI values are likely to be unreliable because of false elevations, or falsely normal values, caused by medial arterial calcification.[19–21] Clairotte *et al*[17] reported that when ABI is used to screen for PAD, the highest sensitivity and specificity ABI values were between 1.0 and 1.1. Using these results, a currently normal low ABI value might indicate early or moderate atherosclerosis. Nam *et al*[22] reported that DM was the most important factor that affected the validity of ABI, with an OR of approximately 4 for a false-negative result. Other studies have indicated that DN and foot wounds decrease the accuracy of ABI.[23–25]

Studies have shown that both baPWV and ABI are useful for the diagnosis of vascular disease, and can predict mortality in patients with DM.[15 26] Chang *et al*[27] reported that the combination of ABI and baPWV can predict prognosis in patients with diabetes with kidney disease, while a recent study reported that only baPWV, not ABI, was predictive of mortality in patients with DM.[28] While there many studies on the utility of ABI and baPWV for predicting outcomes in patients with DM, and studies of the associations between ABI and baPWV and comorbidities in patients without diabetes,[11 13 14 29–32] few studies have examined the relations of ABI and baPWV with chronic comorbidities such as CKD in patients with DM.[13 27 28] Thus, the purpose of this study was to determine the associations between ABI and baPWV with different chronic comorbidities in patients with type 2 DM.

PATIENTS AND METHODS

We retrospectively reviewed the Mackay Memorial Hospital Data Registry for patients with a diagnosis of type 2 DM (ICD-9: 250.0), who received an ABI examination (examination code: 60007) between August 2013 and February 2015.

Patients were included in the analysis if they were 18 years of age or older, and their medical records indicated a diagnosis of DM (ICD-9: 250.0), or they satisfied one of the following criteria: 1) glycated hemoglobin (HbA1c) ≥6.5%; 2) receiving insulin or an oral hypoglycemic drug. For inclusion in the analysis, patients had to have received both an ABI and baPWV examination.

Data extracted from the medical records included age, sex and other demographic data, the presence of comorbidities including hypertension (HTN), hyperlipidemia, CAD, cerebrovascular disease and malignancies, body mass index (BMI), current tobacco use, alcohol use, prescribed medications (such as oral antidiabetic agents, insulin, lipid-lowering drugs, antihypertensive drugs, aspirin, clopidogrel, cilostazol and warfarin) and SBP and diastolic BP (DBP). Laboratory data extracted included fasting and postprandial plasma glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), TG, HbA1c, creatinine (Cr), alanine aminotransferase and the presence of microproteinuria. ABI and baPWV results were also recorded.

Hypertension was defined as a history of HTN as indicated in the medical records, or a SBP of ≥140 mm Hg or a DBP of ≥90 mm Hg. Hyperlipidemia was defined as TC >200 mg/dL or LDL-C >130 mg/dL. For analysis, patients were classified based on the presence or absence of chronic diseases that included CKD, CAD, CLD and DN. Chronic diseases were diagnosed based on the medical record data (online supplementary table 1). CKD was defined as proteinuria (urine albumin/urine Cr >30 mg/g or urine protein/urine Cr >150 mg/g), or serum Cr >1.2 mg/dL. CKD risk was classified by estimated GFR (eGFR) and albumin-creatinine ratio (ACR) according to the 2009 Kidney Disease: Improving Global Outcomes recommendations.[33] Patients were considered to have CAD if an echocardiogram or cardiac angiography was positive, or if ICD-9-CM codes 414.00–414.9 were used. Patients were considered to have CLD if they were hepatitis B virus positive, hepatitis C virus positive, had a serum glutamic-pyruvic transaminase (GPT) >40 U/L or if ICD-9-CM codes 571.00–571.9 were applied. DN was defined as patients with impaired nerve conduction velocity based on the diagnostic threshold of DN, or if ICD-9-CM codes 250.60, 250.62 or 357.2 were applied.[34] If a patient had more than one of the chronic diseases studied, they were included in both groups.

MEASUREMENTS

ABI measurement

An ABI <0.9 on either side of the lower extremities was considered diagnostic for PAD.[35 36] In brief, a Colin VP-1000 Doppler ultrasound device (Colin Medical

Technology Company, Komaki, Japan) with an 8 MHz was used to measure the SBP of the bilateral brachial, posterior tibial and dorsal pedal arteries with the patient in a supine position after resting for 20 min. Occluding cuffs that were 26×13 cm were placed just above the malleoli for measurement of ankle pressures. The instrument automatically calculated the right and left ABI by dividing the higher pressure on the dorsal pedal or posterior tibial arteries on right and left side, respectively, by the higher brachial pressure on either side.

baPWV was measured with an automated device (VP-2000; Colin Corporation, Komaki, Japan). Examinations were performed after the patient rested supine for a minimum of 5 min. A pneumatic cuff connected to a plethymographic sensor was used to determine volume pulse waveform. An oscillometric pressure sensor was used to measure BP. Both were placed on both upper arms and ankles. ECG electrodes were placed on both wrists. The average of the left and right side baPWV values was used for analysis. Subjects were divided into the following four quartiles with respect to baPWV values: <1325, 1325–1515, 1515–1765, >1765 cm/s; males were divided into <1379, 1379–1557, 1557–1796, >1796 cm/s and females into <1285, 1285–1489, 1489–1724, >1724 cm/s.[37]

Statistical analysis

ABI and baPWV values were treated as continuous variables. ABI was defined as the minimal measure of the left side and right side, and the value of baPWV was defined as the maximum measure of the left side and right side. The means and variances of ABI and PWV for each chronic disease were calculated. The parametric t-test and non-parametric Wilcoxon test for the comparison of the presence of disease versus the absence of disease were both reported because the distributions of ABI and baPWV were skewed (online supplementary figures 1,2). Further analysis was performed for the chronic diseases in which there was a significant difference in both ABI and baPWV, and the associations of these diseases with ABI and baPWV were examined with crude and adjusted logistic regression models. The crude model included ABI and baPWV, and the adjusted models were controlled for the following covariates: gender, sex, BMI, hyperlipidemia, HTN, smoking, drinking, CKD risk and insulin use. Results were presented as OR and 95% CI. All statistic assessments were two-sided, and evaluated at a 0.05 level of significance. Statistical analyses were performed using SPSS V.22.0 statistical software (IBM , Armonk, New York, USA).

RESULTS

The records of 2400 consecutive patients were reviewed, and 1232 had a confirmed diagnosis of type 2 DM and/or met the other diagnostic criteria, and received both ABI and baPWV, and thus were included in the analysis. The characteristics of the patients are summarized in table 1. The average age of the patients was 65.1±10.0 years, average BMI was 25.9 kg/m^2 and male:female ratio was 1:1.15. Of the patients, 69.8% had hyperlipidemia, 66.2% had HTN, 24.3% were at least moderate risk for CKD and 21.1% used insulin.

Table 1 Characteristics of patients with type 2 diabetes mellitus (n=1232)

Variable	Mean±SD	Count (%)
Age	65.1±10.0	
BMI	25.9±4.2	
Sex		
Male		572 (46.4)
Female		660 (53.6)
Hyperlipidemia		
Yes		860 (69.8)
No		372 (30.2)
Hypertension		
Yes		814 (66.2)
No		416 (33.8)
Smoking		
Yes		106 (8.6)
No		857 (69.6)
Unknown		269 (21.8)
Drinking		
Yes		50 (4.1)
No		918 (74.5)
Unknown		264 (21.4)
Urine creatinine (mg/dL)	127.6±69.5	
Urine albumin (mg/dL)	23.4±92.4	
Urine ACR	0.2±0.8	
Urine ACR category		
A1 (ACR<3)		1129 (98.0)
A2 (ACR=3–30)		23 (2.0)
Serum creatinine (mg/dL)	1.0±0.69	
eGFR (mL/min/1.73 m^2)	83.4±32.6	
CKD risk		
Low		840 (75.7)
Moderate		144 (13.0)
High		126 (11.3)
Insulin use		
Yes		260 (21.1)
No		972 (78.9)

Data are presented as mean±SD or number (percentage).
ACR, albumin-creatinine ratio; BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

ABI and baPWV results for each chronic disease are shown in table 2. CKD and DN were associated with a low ABI (both, P<0.001), and an increased baPWV (both, P<0.001). No associations were found between CAD and CLD and ABI or baPWV. Thus, regression analysis was performed to examine the associations of ABI and baPWV with CKD and DN.

Crude and adjusted logistic regression analysis results for CKD are presented in table 3. Low ABI was significantly associated with risk of CKD in patients with type 2 DM in the crude model (OR 0.724, 95% CI 0.648 to 0.808, P<0.001) and adjusted model (OR 0.872, 95% CI 0.762 to 0.999, P=0.048). baPWV was only found to be significant in the crude model (OR 1.199, 95% CI 1.112 to 1.294, P<0.001).

Crude and adjusted logistic regression analysis results for DN are presented in table 4.

Table 2 ABI and baPWV values of patients with each chronic disease

Disease	Disease present	Number of patients	ABI				PWV			
			Mean	SD	P value (t-test)	P value (Wilcoxon test)	Mean	SD	P value (t-test)	P value (Wilcoxon test)
CKD	No	1041	1.059	0.119	0.000	0.000	1852.4	387.4	0.000	0.000
	Yes	191	1.003	0.160			1981.5	407.6		
CAD	No	1133	1.053	0.122	0.025	0.069	1868.8	396.0	0.242	0.133
	Yes	97	1.012	0.175			1914.3	362.6		
CLD	No	1127	1.051	0.127	0.856	0.695	1871.4	393.6	0.771	0.552
	Yes	105	1.048	0.133			1883.1	391.1		
DN	No	1004	1.053	0.128	0.037	0.009	1862.7	394.7	0.014	0.011
	Yes	182	1.031	0.130			1940.5	390.6		
Total			1.050	0.128			1872.4	393.2		

ABI, ankle-brachial index; baPWV, brachial-ankle pulse wave velocity; CAD, coronary artery disease; CKD, chronic kidney disease, CLD, chronic liver disease, DN, diabetic neuropathy.

Low ABI was significantly associated with risk of DN in patients with type 2 DM in the crude model (OR 0.873, 95% CI 0.780 to 0.977, P=0.018) and adjusted model (OR 0.884, 95% CI 0.782 to 0.999, P=0.048). No association was found for baPWV in the crude or adjusted model.

DISCUSSION

In this study, we examined the association of ABI and baPWV with four chronic diseases in patients with type 2 DM. Regression analysis indicated that a low ABI was associated with CKD and DN, but not with CAD and CLD, and baPWV was not associated with any of the chronic diseases studied. However, the mean ABI value for patients with comorbidities in the present study population seemed to fall in the lower normal range (ABI=1.0–1.09).[16] If there were correlation between PAD and chronic comorbidities, our data support the results of other studies which suggested that the typically used ABI cut-off points (ABI<0.9 for PAD) could not be used in all types of patients with diabetes. Clairotte *et al*[17] reported that when ABI is used to screen for PAD, the highest sensitivity and specificity ABI values were between 1.0 and 1.1, suggesting that a currently normal low ABI value might indicate early or moderate atherosclerosis.

The incidences of DM and PAD have been steadily increasing over the past decades, with the occurrence intimately related to the worldwide obesity epidemic.[38 39] PAD is the result of atherosclerosis, and is thus associated with cardiovascular ischemic events and death, and has similar risk factors as cardiovascular disease including HTN, hypercholesterolemia, smoking and DM.[7–12] Persistently elevated glucose levels (diabetes) results in microvascular damage and subsequent cardiovascular disease, CKD and DN in addition to other comorbidities.[3] While both ABI and PWV

Table 3 Crude and adjusted logistic regression analysis for CKD

	Crude model		Adjusted model	
	OR (95% CI)	P value	OR (95% CI)	P value
ABI (per 0.1*)	0.724 (0.648 to 0.808)	<0.001	0.872 (0.762 to 0.999)	0.048
baPWV (per 200*)	1.199 (1.112 to 1.294)	<0.001	1.055 (0.945 to 1.177)	0.344
Male			1.665 (1.112 to 2.494)	0.013
Age			1.034 (1.011 to 1.059)	0.004
BMI			0.986 (0.940 to 1.034)	0.564
Hyperlipidemia			1.980 (1.265 to 3.101)	0.003
Hypertension			1.315 (0.833 to 2.075)	0.240
Smoking				0.031
Yes vs no			2.305 (1.166 to 4.555)	0.016
Unknown vs no			3.002 (0.570 to 15.793)	0.194
Alcohol				0.383
Yes vs no			1.723 (0.706 to 4.203)	0.232
Unknown vs no			0.557 (0.104 to 2.990)	0.495
CKD risk				<0.001
Moderate vs low			4.772 (2.972 to 7.662)	<0.001
High vs low			15.898 (9.745 to 25.935)	<0.001
Insulin use			1.357 (0.879 to 2.095)	0.169

*Indicates per units of change in logistic regression analysis, because the values of the OR depend on the unit of covariate. Scales of unit are independent to P values.
ABI, ankle-brachial index; baPWV, brachial-ankle pulse wave velocity.; BMI, body mass index; CKD, chronic kidney disease.

Table 4 Crude and adjusted logistic regression analysis for DN

	Crude model		Adjusted model	
	OR (95% CI)	P value	OR (95% CI)	P value
ABI (per 0.1*)	0.873 (0.780 to 0.977)	0.018	0.884 (0.782 to 0.999)	0.048
baPWV (per 200*)	1.110 (1.028 to 1.199)	0.008	1.052 (0.953 to 1.162)	0.316
Male			0.893 (0.619 to 1.287)	0.543
Age			1.002 (0.982 to 1.022)	0.867
BMI			0.982 (0.940 to 1.025)	0.403
Hyperlipidemia			1.000 (0.688 to 1.454)	0.999
Hypertension			0.982 (0.667 to 1.444)	0.926
Smoking				0.686
Yes vs no			1.258 (0.652 to 2.426)	0.493
Unknown vs no			0.632 (0.075 to 5.317)	0.673
Alcohol				0.801
Yes vs no			1.147 (0.461 to 2.857)	0.768
Unknown vs no			1.939 (0.232 to 16.209)	0.541
CKD risk				0.505
Moderate vs low			1.262 (0.763 to 2.090)	0.365
High vs low			1.286 (0.760 to 2.176)	0.349
Insulin user			1.612 (1.091 to 2.382)	0.016

*Indicates per units of change in logistic regression analysis, because the values of the OR depend on the unit of covariate. Scales of unit are independent to P values.

ABI, ankle-brachial index; baPWV, brachial-ankle pulse wave velocity.; BMI, body mass index; CKD, chronic kidney disease; DN, diabetic neuropathy.

are useful for the diagnosis of PAD in patients without DM, the effects of DM on indices such as ABI and PWV are complex, and thus interpretation of the results may be different than in patients with DM.[18]

The Kyushu Prevention Study of Atherosclerosis followed 3628 outpatients with DM for a mean of 3.2±2.2 years.[26] Excluding patients with an ABI of <0.9, an elevation of baPWV was significantly correlated with the incidence of coronary artery events, cerebrovascular events, and all-cause mortality. Recursive partitioning analysis indicated that a PWV of 14 m/s was a statistically adequate cut point for predicting cardiovascular events and 24 m/s for predicting mortality. A separate analysis of the same cohort of patients found that a borderline ABI value (0.91≤ABI≤0.99) in patients with diabetes was associated with significantly higher risks of mortality and PAD as compared with a normal value (1.00≤ABI≤1.40).[15] Nam *et al*[22] studied 158 legs in 79 consecutive patients with a diagnosis of PAD established by angiography who also had their ABI measured. An ABI <0.9 was considered abnormal, and with that cut point the sensitivity of ABI was 61% and specificity was 87% for a diagnosis of PAD. The ORs of a false-negative ABI were 4.36 in patients with DM, 3.41 in patients with distal lesions, 3.02 in elderly patients and 1.13 in patients with mild stenosis.

Our results indicated an association of ABI and CKD and DN. In a similar study, Chang *et al*[40] followed 362 patients with type 2 DM for a mean of 4.8 months. Patients were groups according to ABI (<0.9 vs ≥0.9), and with or without albuminuria. Patients with an ABI <0.9 and albuminuria had a significantly higher risk of composite events and all-cause mortality than those in the other groups. In a related study, Liu *et al*[41] examined patients at high risk of cardiovascular disease and measured kidney function and ABI. Their analysis showed that high ABI values were associated with increased risk of CKD in patients with DM and high risk of cardiovascular disease. A study of elderly patients with type 2 DM reported that low eGFR with and without albuminuria were both independently associated with PAD as determined by ABI.[31] Hsieh *et al*[32] studied the effects of renal function on PAD diagnosed by ABI in Chinese patients with type 2 DM. Interestingly, after adjustment for age, BMI, BP, HbA1c, TC, HDL-C, LDL-C and TG levels, serum Cr >1.5 mg/dL, eGFR <60 mL/min and urinary ACR >30 mg/g were independent risk factors for PAD in men, and serum Cr >1.4 mg/dL and urinary ACR >30 mg/g were independently associated with PAD in women with diabetes. Mostaza *et al*[10] reported that in patients with HTN and without known vascular disease, a reduced GFR and albuminuria were independently associated with an ABI <0.9.

Our results did not find associations of the diseases examined and baPWV; other studies, however, have provided different results. Yoshimura *et al*[19] measured baPWV and flow volume and the resistive index of the popliteal artery by cine-mode phase-contrast MRI in patients with type 2 diabetes with an ABI >0.9 and age-matched non-diabetic control subjects. The authors found that impaired lower extremity circulation as determined by MRI was associated with nephropathy in patients with diabetes with a normal baPWV. A recent review of the literature reported that in the general population with chronic diseases such as HTN, DM and end-stage renal disease, a 1 m/s increase in baPWV was associated with a 12% increase in cardiovascular events; however, the reliability of baPWV measurement was reduced in the presence of PAD.[29] Ikura *et al*[28] studied patients with DM who received a lower extremity amputation, and reported that baPWV, but not ABI, predicted mortality. Lee *et al*[30] studied ABI and baPWV in patients with ischemic stroke and healthy individuals with no history

of stroke. They reported that baPWV was a reliable surrogate marker of ischemic stroke, and that baPWV could be used to predict small vessel disease and ABI to predict large arterial disease.

While we studied ABI and baPWV individually, Chang *et al*[27] reported that the combination of ABI and baPWV was more predictive of outcomes (all-cause mortality and composite events) in patients with DM than either measure alone.

Associations between lipid levels and ABI have been rarely studied. In an interesting population-based cross-sectional survey that included 2982 participates 60 years of age or older, Zhan *et al*[42] reported that the TC/HDL–C ratio was significantly associated with low ABI in non-smokers, and the association was independent of TC, TG, HDL–C and LDL-C levels. While we did not find an association between ABI or baPWV and CLD, recent studies have suggested an association of arterial stiffness with non-alcoholic fatty liver disease and liver fibrosis in patients without or with DM.[43–45]

There are a number of limitations to this study that should be considered. All patients were from a single institution, and data were collected from the medical records. We did not independently confirm the diagnosis of DM or comorbidities, or ABI and PWV results. While the overall number of patients was large, the numbers of patients with individual comorbidities were relatively small. Since the study was a cross-sectional study, data regarding the rate of progression of CKD were not available. Patients were not stratified by stage of CKD. However, renal function was quantified by the urine ACR or the serum eGFR. We believe these measures provide similar evidence to explain the relation between the chronic comorbidities and the atherosclerosis.

CONCLUSIONS

In patients with type 2 DM, a low ABI was associated with CKD and DN, but not with CAD and CLD, and baPWV was not associated with any of the chronic diseases studied. In addition, the mean ABI value of patients with comorbidities was in the low normal range. Further studies are necessary to clarify the usefulness of ABI and baPWV in patients with DM.

Contributors C-CL: conception and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript; guarantor of integrity of the entire study; statistical analysis; definition of intellectual content; literature research; clinical studies; experimental studies; obtaining funding; administrative, technical or material support; supervision. M-CT: conception and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript; guarantor of integrity of the entire study; statistical analysis; definition of intellectual content; literature research; clinical studies; experimental studies; obtaining funding; administrative, technical or material support; supervision. S-CL: conception and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript; guarantor of integrity of the entire study; statistical analysis; definition of intellectual content. C-FP: conception and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript; guarantor of integrity of the entire study; statistical analysis; definition of intellectual content. All authors have read and approved the final version of the manuscript submitted.

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Patient consent Detail has been removed from this case description/these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

Ethics approval This study was approved by the Institutional Review Board of our hospital, and because of the retrospective nature the requirement of informed patient consent was waived.

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