Use of the Combination of Ankle-brachial Index and Percentage of Mean Arterial Pressure at Ankle for Improving Prediction of All-cause Mortality in type 2 Diabetes Mellitus

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Original investigation

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Abstract

Background: Peripheral artery disease (PAD) in lower extremities is a common complication in type 2 diabetes and has shown to be associated with mortality. The ankle-brachial index (ABI) is a simple noninvasive method to screen PAD, but has limited sensitivity. We hypothesized that using the percentage of mean arterial pressure (%MAP) and ABI in combination would improve prediction of mortality.

Methods: We retrospectively collected the data of patients with type 2 diabetes who had undergone measurement of ABI and %MAP at our hospital. We separated the cohort into four groups according to the ABI and %MAP values, and examined these indices were associated with mortality.

Results: A total of 5101 patients (mean age, 65 ± 11 years) were enrolled. During the follow-up period (median, 22.9 months), 266 (4.8%) of enrolled patients died. The combination of ABI and %MAP was significantly better at predicting mortality than ABI alone. (C index: 0.62 [95% CI: 0.57, 0.65] vs. 0.57 [95% CI: 0.53, 0.62], P = 0.038). In multivariate analysis (with ABI > 0.90 and %MAP ≤ 45% as the reference group), the highest risk of mortality was seen in patients with ABI ≤ 0.90 and %MAP > 45% (hazard ratio = 1.983 [95% CI: 1.380, 2.848], P < 0.001).

Conclusions: Adding %MAP to ABI appears to significantly improve the predictive ability for all-cause mortality in patients with type 2 diabetes.

Background

Diabetes mellitus (DM) is a complex metabolic disorder associated with several chronic complications [1]. One common complication is peripheral artery disease (PAD) of the lower extremities, which is associated with high mortality risk in type 2 DM [2]. The use of ankle-brachial index (ABI) to screen for PAD in diabetic patients with cardiovascular risk is recommended by the American heart association / American college of cardiology (AHA/ACC) guideline on the management of patients with lower extremity peripheral artery disease [3]. However, the commonly used ABI value of < 0.90 has been reported only 75% sensitivity, and the sensitivity is even lower in patients with DM than in those without DM [4, 5]. Since borderline low ABI value between 0.91 and 0.99 is associated with higher risk of PAD and mortality than ABI ≥ 1.00 [6, 7], it is suggested that sensitivity could be increased by raising the cutoff value of normal ABI to 1.00 [4, 8]. Further increase in diagnostic accuracy could be achieved by using other tests in combination with ABI [4]. It has been reported that combination of percentage of ABI and mean arterial pressure (%MAP) at ankle has shown better diagnostic accuracy than increase in ABI cutoff to 1.00 [9].

The %MAP calculated from the pulse volume recording at ankle can be automatically reported by the ABI-measuring machine, and so it is a convenient index for use along with the ABI when screening for PAD [9–11]. A previous study has shown that %MAP > 45% predicts a high mortality risk in patients with ABI > 0.90 [12]. However, the predictive value of the combination of ABI and %MAP for long-term mortality has not yet been investigated in patients with type 2 DM. We hypothesized that the combination of low ABI and high %MAP would be a better predictor of all-cause mortality than low ABI alone. Therefore, this study aimed to determine whether the combination of the two indices, ABI ≤ 0.90 and %MAP > 45%, could be used to improve the predictive power for mortality in patients with type 2 DM.

Materials And Methods

Study design and population

This retrospective cohort study was conducted at Taichung Veterans General Hospital in Taiwan. According to our computer interpretable guideline since August 2016, ABI was suggested via annual diabetes review program of the hospital information system if ABI data had not been available in patients who were older than 50 years and had participated diabetes pay-for performance (P4P) program [13].

From the hospital database, we retrospectively identified all patients with DM who had undergone ABI assessment between August 01, 2016 and July 31, 2019. Moreover, all enrolled patients must have at least one of following inclusion criteria: 1) age ≥ 50 years, 2) diabetic duration ≥ 10 years, 3) current smoker, 4) a history of cardiovascular disease (CVD), 5) hypertension, 6) body mass index ≥ 25 kg/m², 7) hemoglobin A1c (HbA1c) ≥ 7%, 8) total cholesterol ≥ 160 mg/dL (4.1 mmol/L), 9) high-density lipoprotein (HDL) cholesterol < 50 mg/dL (1.29 mmol/L) in women or < 40 mg/dL (1.03 mmol/L) in men, 10) triglycerides ≥ 150 mg/dL (1.69 mmol/L), 11) estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m², and 12) albuminuria. We excluded patients with the following conditions: 1) incomplete laboratory data, 2) not type 2 DM, 3) incomplete ABI, brachial-ankle pulse wave velocity (baPWV), or %MAP data due to uncompleted four-limb assessments, 4) unreliable ABI data due to previous lower-limb surgery, pregnancy, or hemodialysis treatment, or 5) ABI > 1.40.

ABI measurements were made using a validated device (VP-1000 Plus; Omron Healthcare Co. Ltd., Kyoto, Japan). In addition to ABI, this device automatically reports the values of baPWV and %MAP of ankle pulse volume waveform. These data, along with anthropometric data and results of laboratory tests performed within 3 months of the ABI assessment, were extracted from the electronic medical records. For patients who had undergone repeated assessments during this period, only the data of the first assessment were recorded. This research protocol was approved by the Institutional Review Board of Taichung Veterans General Hospital, with a waiver of the need for informed consent.

Assessments

The laboratory data of the following were recorded: total cholesterol, HDL cholesterol, triglycerides, glucose, HbA1c, and creatinine. The eGFR was calculated using the Modification of Diet in Renal Disease equation, i.e., eGFR = 186 × (serum creatinine [mg/dL])⁻¹.154 × (age [years])⁻₀.₂₀₃ (× 0.742, if female) [14]. Urinary albumin-to-creatinine ratio (UACR) was calculated using the formula: UACR = albumin (mg) / creatinine (g); and albuminuria was defined as a UACR ≥ 300 mg/g [14]. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg, or current use of an antihypertensive drug.
The %MAP value was automatically determined based on the ankle pulse volume waveform during ABI measurement. The reproducibilities of the ABI and %MAP have been demonstrated using Bland-Altman plots in our previous study [15]. The lower ABI value, and the higher %MAP and baPWV values between lower limbs in an individual were used for the analyses. ABI ≤ 0.90 and %MAP > 45% were defined as abnormal [12, 15].

### Statistical analysis

Continuous data were summarized as the mean ± standard deviation; differences among four study subgroups were analyzed using the one-way analysis of variance, and the Scheffe post hoc test was conducted to examine the differences between the high %MAP and normal %MAP subgroups in patients with a normal ABI group or a low ABI group. Categorical data were summarized as number with percentage (%) and compared among groups using the chi-square test. The primary endpoint was all-cause mortality. Information on deaths registered up to August 31, 2019 was obtained from the Ministry of Health and Welfare, Executive Yuan, Taiwan.

Improvement in prediction of mortality caused by addition of the %MAP to ABI was assessed by examining the increments in the area under the receiver operating characteristic curve (AUC). The performances of the model containing the combination of ABI and %MAP and the model with ABI alone were evaluated by the C index. Integrated discrimination improvement (IDI) and continuous net reclassification improvement (NRI) were also assessed.

Cumulative risk for the all-cause mortality was assessed using Kaplan-Meier analysis; the log-rank test was used to determine if the differences between groups were significant. Multivariable Cox proportional hazards regression analysis was conducted to identify the independent predictors of mortality; hazard ratio (HR) and 95% confidence interval (CI) were calculated. Two-sided P value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS v22.0 (IBM Corp., Armonk, NY, USA), and R software v3.4.

### Results

A total of 5569 patients were enrolled in this study, and %MAP was inversely correlated with ABI (Pearson correlation coefficient: -4.70, P < 0.001). Based on the ABI value, all patients were first separated into two groups: a normal ABI group and a low ABI group. Each group was then separated into two subgroups according to the %MAP value. Thus, there were four subgroups: patients with normal ABI and normal %MAP (n = 4601); patients with normal ABI but high %MAP (n = 500); patients with low ABI but normal %MAP (n = 130); and patients with low ABI and high %MAP (n = 338, Fig. 1).

Table 1 showed the baseline characteristics of patients in the different subgroups. Patients with high %MAP were significantly older than patients with normal %MAP in both the normal ABI group (70 ± 12 vs. 64 ± 10 years, P < 0.001) and the low ABI group (73 ± 12 vs. 65 ± 12 years, P < 0.001). The baPWV was significantly higher in the high %MAP subgroup than in the normal %MAP subgroup in both the normal ABI group (P < 0.001) and the low ABI group (P < 0.001). BMI, ABI and eGFR were significantly lower in the high %MAP subgroup than in the normal %MAP subgroup in both the normal ABI group (P = 0.027, P < 0.001, and P < 0.001; respectively) and the low ABI group (all P values < 0.001). Prevalence of CVD, albuminuria and use of antiplatelet drugs were significantly higher in the high %MAP subgroup than in the normal %MAP subgroup in both the normal ABI group (all P values < 0.001) and the low ABI group (P = 0.015, P = 0.004, and P < 0.001; respectively). The proportions of patients using oral antihyperglycemic drugs was significantly lower in the high %MAP subgroup than in the normal %MAP subgroup in both the normal ABI group (P < 0.001) and the low ABI group (P = 0.008). Patients with high %MAP were significantly more likely to be female, to have hypertension and higher systolic blood pressure, to be using antihypertensive drugs and insulin therapy, and to have longer diabetes duration than those with normal %MAP in the normal ABI group (all P < 0.001), but not in the low ABI group.
| Group | Normal ABI (n = 5101) | Low ABI (n = 468) | p‡ | Normal %MAP (n = 4601) | Low %MAP (n = 338) |
|-------|-----------------------|------------------|----|------------------------|------------------|
| Subgroup | | | | | |
| | Normal %MAP | | | | |
| | High %MAP | | | | |
| | mean ± SD | mean ± SD | p† | mean ± SD | mean ± SD | p† |
| Age (year) | 64 ± 10 | 70 ± 12 | <0.001 | 65 ± 12 | 73 ± 12 | <0.001 |
| Male, n (%) | 2559 (55.6%) | 203 (40.6%) | <0.001 | 66 (50.8%) | 196 (58.0%) | 0.192 |
| Diabetic duration (year) | 11 ± 7 | 14 ± 8 | <0.001 | 14 ± 8 | 15 ± 8 | 0.400 |
| Currently smoking, n (%) | 415 (9.0%) | 32 (6.4%) | 0.060 | 11 (8.5%) | 26 (7.7%) | 0.932 |
| CVD, n (%) | 357 (7.8%) | 72 (14.4%) | <0.001 | 22 (16.9%) | 96 (28.4%) | 0.015 |
| BMI (kg/m²) | 25.9 ± 4.1 | 25.3 ± 4.2 | 0.027 | 28.0 ± 5.0 | 25.0 ± 4.0 | <0.001 |
| Systolic BP (mmHg) | 135 ± 19 | 144 ± 24 | <0.001 | 140 ± 20 | 145 ± 25 | 0.139 |
| Diastolic BP (mmHg) | 77 ± 12 | 76 ± 13 | 0.519 | 75 ± 15 | 74 ± 16 | 0.584 |
| Fasting glucose (mmol/L) | 8.2 ± 3.6 | 8.2 ± 3.4 | 0.999 | 8.3 ± 2.9 | 8.7 ± 3.8 | 0.760 |
| HbA1c (%) | 7.5 ± 1.6 | 7.6 ± 1.6 | 0.990 | 7.9 ± 2.0 | 7.8 ± 1.9 | 0.997 |
| Total cholesterol (mmol/L) | 4.1 ± 0.9 | 4.1 ± 1.0 | 0.966 | 4.1 ± 0.9 | 4.0 ± 1.0 | 0.881 |
| HDL cholesterol (mmol/L) | 1.3 ± 0.4 | 1.3 ± 0.4 | 0.999 | 1.2 ± 0.3 | 1.2 ± 0.3 | 0.915 |
| Triglyceride (mmol/L) | 1.6 ± 1.3 | 1.5 ± 1.2 | 0.637 | 2.0 ± 1.9 | 1.7 ± 1.1 | 0.193 |
| eGFR (mL/min/1.73 m²) | 81 ± 28 | 70 ± 34 | <0.001 | 73 ± 34 | 53 ± 32 | <0.001 |
| UACR ≥ 300 mg/g | 498 (10.8%) | 88 (17.6%) | <0.001 | 19 (14.6%) | 94 (27.8%) | 0.004 |
| ABI | 1.11 ± 0.09 | 1.07 ± 0.09 | <0.001 | 0.83 ± 0.08 | 0.68 ± 0.21 | <0.001 |
| baPWV (cm/sec) | 1823 ± 433 | 2087 ± 671 | <0.001 | 1867 ± 690 | 2176 ± 1143 | <0.001 |
| Ankle %MAP (%) | 39.4 ± 3.1 | 47.2 ± 1.8 | <0.001 | 40.9 ± 3.1 | 50.4 ± 3.5 | <0.001 |
| Antiplatelet, n (%) | 1212 (26.3%) | 178 (35.6%) | <0.001 | 64 (49.2%) | 273 (80.8%) | <0.001 |
| Statins, n (%) | 3253 (70.7%) | 351 (70.2%) | 0.855 | 97 (74.6%) | 250 (74.0%) | 0.979 |
| Hypertension, n (%) | 3466 (75.3%) | 414 (82.8%) | <0.001 | 115 (88.5%) | 317 (93.8%) | 0.081 |

Continuous data are presented as the mean ± SD, and categorical data are presented as numbers (percentages).

* low ABI was defined as an ABI value ≤ 0.90 and normal ABI > 0.90; high %MAP was defined as a %MAP > 45% and normal %MAP ≤ 45%.

‡P: denotes a significant difference across the four subgroups.

†P: post hoc analysis between two groups in patients with normal ABI; ‡P: post hoc analysis between two subgroups in patients with normal ABI.

%MAP = percentage of mean arterial pressure, ABI = ankle-brachial index, ACE = angiotensin-converting enzyme, ARB = angiotensin II receptor antagonist, baPWV = brachial-ankle pulse wave velocity, BMI = body mass index, BP = blood pressure, CVD = cardiovascular disease, DPP4 = dipeptidyl peptidase-4, eGFR = estimated glomerular filtration rate, HbA1c = hemoglobin A1c, HDL = high-density lipoprotein, SD = standard deviation, SGLT2 = sodium glucose cotransporter 2, UACR = urine albumin-to-creatinine ratio.
To evaluate how addition of the %MAP result to ABI affected prediction of all-cause mortality, we analyzed the increments in the AUC. We used ABI as the standard risk factor, AUC increased significantly from 0.57 (95% CI: 0.53–0.62) for the ABI alone model to 0.62 (95% CI: 0.57–0.65) for the ABI plus %MAP model (P = 0.038). Furthermore, addition of the %MAP to the ABI yielded a significant IDI of 0.006 (95% CI: 0.002–0.014, P < 0.001) and a significant NRI of 0.119 (95% CI: 0.045–0.183, P < 0.001; Fig. 2).

| Group | Normal ABI (n = 5101) | Low ABI (n = 468) |
|-------|-----------------------|------------------|
|       | Normal %MAP (n = 4601) | High %MAP (n = 500) | p† | Normal %MAP (n = 130) | High %MAP (n = 338) | p‡ |
|       | mean ± SD | mean ± SD | p† | mean ± SD | mean ± SD | p‡ |
| Antihypertensive drugs, n (%) | 2397 (52.1%) | 307 (61.4%) | < 0.001 | 87 (66.9%) | 257 (76.0%) | 0.060 | < 0.001 |
| ACE inhibitor or ARB, n (%) | 1714 (37.3%) | 213 (42.6%) | 0.022 | 58 (44.6%) | 168 (49.7%) | 0.377 | < 0.001 |
| α-Blocker, n (%) | 255 (5.5%) | 74 (14.8%) | < 0.001 | 11 (8.5%) | 64 (18.9%) | 0.009 | < 0.001 |
| β-Blocker, n (%) | 949 (20.6%) | 138 (27.6%) | < 0.001 | 38 (29.2%) | 135 (39.9%) | 0.041 | < 0.001 |
| Calcium channel blocker, n (%) | 217 (4.7%) | 28 (5.6%) | 0.443 | 12 (9.2%) | 37 (10.9%) | 0.708 | < 0.001 |
| Diuretics, n (%) | 396 (8.6%) | 88 (17.6%) | < 0.001 | 24 (18.5%) | 95 (28.1%) | 0.043 | < 0.001 |
| Insulin therapy, n (%) | 1032 (22.4%) | 159 (31.8%) | < 0.001 | 42 (32.3%) | 132 (39.1%) | 0.213 | < 0.001 |
| Oral antihyperglycemic drugs | 4175 (90.7%) | 424 (84.8%) | < 0.001 | 113 (86.9%) | 254 (75.1%) | 0.008 | < 0.001 |
| Insulin secretagogues, n (%) | 1638 (35.6%) | 190 (38.0%) | 0.311 | 45 (34.6%) | 96 (28.4%) | 0.230 | 0.028 |
| Metformin, n (%) | 1838 (39.9%) | 174 (34.8%) | 0.029 | 54 (41.5%) | 69 (20.4%) | < 0.001 | < 0.001 |
| Thiazolidinediones, n (%) | 2737 (59.5%) | 287 (57.4%) | 0.393 | 72 (55.4%) | 191 (56.5%) | 0.908 | 0.469 |
| α-Glucosidase inhibitors, n (%) | 530 (11.5%) | 40 (8.0%) | 0.022 | 17 (13.1%) | 17 (5.0%) | 0.005 | < 0.001 |
| DPP4 inhibitors, n (%) | 1046 (22.7%) | 95 (19.0%) | 0.065 | 30 (23.1%) | 51 (15.1%) | 0.056 | 0.002 |
| SGLT2 inhibitors, n (%) | 415 (9.0%) | 57 (11.4%) | 0.096 | 8 (6.2%) | 31 (9.2%) | 0.384 | 0.212 |
| Mortality, n (%) | 165 (3.6%) | 45 (9.0%) | < 0.001 | 11 (8.5%) | 45 (13.3%) | 0.197 | < 0.001 |

Incidence of mortality (deaths/100 person-years) | 2.0 | 5.0 | 4.8 | 8.3 |

Continuous data are presented as the mean ± SD, and categorical data are presented as numbers (percentages).

*= low ABI was defined as an ABI value ≤ 0.90 and normal ABI > 0.90; high %MAP was defined as a %MAP > 45% and normal %MAP ≤ 45%.

‡P: denotes a significant difference across the four subgroups.

†P: post hoc analysis between two subgroups in patients with normal ABI; †P: post hoc analysis between two groups in patients with low ABI.

%MAP = percentage of mean arterial pressure, ABI = ankle-brachial index, ACE = angiotensin-converting enzyme, ARB = angiotensin II receptor antagonist, baPWV = brachial-ankle pulse wave velocity, BMI = body mass index, BP = blood pressure, CVD = cardiovascular disease, DPP4 = dipeptidyl peptidase-4, eGFR = estimated glomerular filtration rate, HbA1c = hemoglobin A1c, HDL = high-density lipoprotein, SD = standard deviation, SGLT2 = sodium glucose cotransporter 2, UACR = urine albumin-to-creatinine ratio.
Multivariate Cox regression analysis was performed using the patients with normal ABI and normal %MAP as the reference group. The highest risk for mortality was observed in patients with low ABI and high %MAP (HR = 1.983, 95% CI: 1.380, 2.848, P < 0.001), followed by patients with low ABI but normal %MAP (HR = 1.740, 95% CI: 0.939, 3.225) and patients with normal ABI but high %MAP (HR = 1.564, 95% CI: 1.112, 2.199). Furthermore, high %MAP was found to be a significant predictor of all-cause mortality in patients with normal ABI (P = 0.010, Table 2).

**Table 2**

| Crude | Model 1 | Model 2 | Model 3 |
|-------|---------|---------|---------|
|        | HR 95% CI | P     | HR 95% CI | P     | HR 95% CI | P     | HR 95% CI | P     |
| Normal ABI and normal %MAP | 1.000 | 1.000 | 1.000 | 1.000 |
| Normal ABI but high %MAP | 2.510 (1.805, 3.490) | <0.001 | 2.231 (1.597, 3.116) | <0.001 | 2.018 (1.443, 2.823) | <0.001 | 1.564 (1.112, 2.199) | 0.010 |
| Low ABI but normal %MAP | 2.390 (1.298, 4.400) | 0.005 | 2.171 (1.178, 4.000) | 0.013 | 1.965 (1.063, 3.631) | 0.031 | 1.740 (0.939, 3.225) | 0.079 |
| Low ABI and high %MAP | 4.167 (2.997, 5.795) | <0.001 | 3.076 (2.199, 4.305) | <0.001 | 2.539 (1.801, 3.578) | <0.001 | 1.983 (1.380, 2.848) | <0.001 |

Abbreviations: %MAP = percentage of mean arterial pressure, ABI = ankle-brachial index.

Low ABI was defined as an ABI value ≤ 0.90 and normal ABI > 0.90; high %MAP was defined as a %MAP > 45% and normal %MAP ≤ 45%.

**Model 1**: adjusted for age and sex; **Model 2**: adjusted for age, sex, diabetic duration, smoker, cardiovascular disease, and body mass index; **Model 3**: adjusted for age, sex, diabetic duration, smoker, cardiovascular disease, body mass index, hemoglobin A1c, hypercholesterolemia, high-density lipoprotein, triglycerides, estimated glomerular filtration rate, albuminuria, brachial-ankle pulse wave velocity, hypertension, use of insulin, use of statins and use of antiplatelet agents.

### Discussion

The main finding of our study was that high ankle %MAP acted synergistically with low ABI to improve prediction of all-cause mortality in patients with type 2 DM. Using a combination of the two indices, ABI ≤ 0.90 and %MAP > 45%, predicted an approximately two-fold mortality risk than ABI > 0.90 and %MAP ≤ 45%. These results support our previous study which showed that high %MAP was a significant predictor of all-cause mortality in subjects with normal ABI [12]. A recent study has also shown that %MAP was associated with cardiovascular mortality in patients receiving hemodialysis [16]. The strength of the present study is that we demonstrated the synergistic effect of ABI and %MAP for prediction of mortality in a large sample of more than 5000 patients with type 2 DM.

Low ABI indicates a reduced systolic blood pressure at the ankle relative to that in the brachial artery, and this suggests partial occlusion of the ankle arteries [17]. Since the systolic blood pressure will be elevated in a non-compressible artery at the ankle, a false negative PAD diagnosis may occur when ABI alone is used for screening [18, 19]. In the study by Wukich, et al., 42.7% of patients with DM and confirmed PAD had normal ABI value [20].

The %MAP represents the percentage difference between the mean and maximum amplitude of the ankle pulse volume waveform [11]. An occluded artery with a flatted waveform will result in an increased %MAP value [10]. Therefore, the pulse volume recording at the ankle might be a sensitive indicator of an occlusive artery with a non-compressible pattern, which is frequently observed in patients with DM [21].

The prevalence of PAD is increasing worldwide, and DM is an important risk factor for PAD [22, 23]. Most patients with PAD are asymptomatic, but they have elevated risk for mortality [22–24]. In Taiwan, annual screening for foot complications is recommended in the clinical guidelines and in the P4P program for patients with DM [13, 25]. In previous studies that have used the cutoff value of ABI ≤ 0.90, the prevalence of PAD in type 2 DM was about 10.0% in patients with a mean age of 63 years in Taiwan, 10.4% in Malay patients (mean age, 63 years) who living in Singapore, and 9.5% in patients (age > 40 years) in the US [26–28]. According to the real-world database, PAD was reported in 18.7% of patients with type 2 DM (mean age, 65 years) in the UK and in 13.6% patients with type 2 DM (mean age, 66 years) in the US [29, 30]. In the present cohort, PAD prevalence was 8.4% when ABI ≤ 0.90 was the only criterion used, but
increased to 17.4% when the combination of ABI ≤ 0.90 and %MAP > 45% were used. In the Taiwan National Health Insurance database, less than 2.2% patients with DM and age ≥ 65 years have a diagnosis of PAD, indicating that the condition is greatly underdiagnosed in clinical practice [31]. Thus, using ABI along with the automatically reported ankle %MAP is an effective and convenient method for PAD screening and for prediction of mortality [9, 12].

The risk factors for abnormal ABI have been well investigated, but the risk factors for high %MAP are still not specified [32, 33]. In the present study, the risk factors significantly associated with %MAP in both the different ABI groups, included age, CVD history, BMI, HbA1c, eGFR, UACR, baPWV, use of antiplatelet agents, type of oral antihyperglycemic drug, and type of hypertensive drug (Table 1). However, we did not include all cardiovascular risk factors in the present study; for example, a higher HbA1c variability has been previously reported to be associated with a higher %MAP [15]. Furthermore, this study has several limitations. First, all participants were from a single teaching hospital, and the results may not be generalizable to all population with type 2 DM. Second, this was a retrospective study and so we could not control the risk factors and treatments received during the follow-up period. Third, the cutoff value of 45% for %MAP is based on the findings of previous studies [12]; we did not assess the normal range of %MAP in the present study.

In conclusion, the use of %MAP along with ABI appears to improve prediction of all-cause mortality in patients with type 2 DM. The %MAP is automatically reported during ABI measurement and so can conveniently be used for improving prognosis prediction in clinical practice.

Abbreviations

%MAP: percentage of the mean arterial pressure; ABI: ankle-brachial index; AUC: area under the receiver-operating characteristic curve; baPWV: brachial-ankle pulse wave velocity; CI: confidence interval; CVD: cardiovascular disease; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; HR: hazard ratio; IDI: integrated discrimination improvement; NRI: net reclassification improvement; P4P: pay-for-performance; PAD: peripheral artery disease; SD: standard deviation; UACR: urinary albumin-to-creatinine ratio.

Declarations

Ethics approval and consent to participate

The study complied with the Declaration of Helsinki, and was approved by the Institutional Review Board of Taichung Veterans General Hospital, with a waiver of the need for informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

YL participated in the data collection and writing of the manuscript. WS contributed to the study design. IL contributed to the study design, the data collection, interpretation of the data, and revision of the manuscript. IL is the guarantor of this work and had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**Figures**

![Study flow diagram](image)

**Figure 1**

Study flow diagram. (Abbreviation: %MAP = percentage of mean arterial pressure, ABI = ankle-brachial index)
Figure 2

Kaplan-Meier curves showing the survival rate across the four groups, categorized based on ankle-brachial index (ABI) of 0.90 and ankle percentage of mean arterial pressure (%MAP) of 45%.

Figure 3

Receiver operating characteristic curves for prediction of all-cause mortality in the ABI alone model and in the ABI + %MAP model. (Abbreviation: %MAP = percentage of mean arterial pressure, ABI = ankle-brachial index, IDI = integrated discrimination improvement, NRI = continuous net reclassification improvement)