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ORIGINAL ARTICLE

# TwPAD registry: A prospective, multicenter registry of chronic peripheral arterial disease involving lower limbs in Taiwan

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## Abstract

**Background:** Peripheral arterial disease (PAD) is a consequence of systemic atherosclerosis, resulting in arterial narrowing and diminished blood flow, leading to complications like claudication, rest pain, ulcers, gangrene, and functional limitations. Despite its impact on cardiovascular mortality, physical function, and quality of life, PAD has received less attention than other atherosclerotic disorders. This study addresses the paucity of comprehensive clinical data on PAD in Taiwan, aiming to analyze its incidence, risk factors, pharmacological and interventional treatments, and outcomes.

**Methods:** This prospective, multicenter, observational registry includes PAD patients from 10 medical centers or teaching hospitals across Taiwan. Data collected encompass demographic characteristics, medical history, laboratory results, and treatment history. Patients are followed up annually to monitor all-cause mortality, major clinical events (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke), and total cardiovascular events (including hard events, unplanned revascularizations, hospitalizations for endovascular therapy, stroke, transient ischemic attacks, and heart failure).

**Results:** From September 2020 to December 2022, 1005 patients were enrolled. The mean age of the cohort was 70.3 years, with men constituting the majority (59.3%). The prevalence rates of key medical conditions were 68.2% for diabetes, 76.3% for hypertension, 72.6% for hypercholesterolemia, 40.6% for smoking, and 26.2% for end-stage renal disease. Central Taiwan patients were younger and had a higher body mass index (BMI) and prevalence of obesity, but lower rates of comorbidities such as hypertension, diabetes, and smoking history. In contrast, eastern Taiwan patients who were older had a lower BMI and prevalence of obesity, but exhibited higher levels of comorbidity.

**Conclusion:** The TwPAD registry provides comprehensive insights into patient characteristics, treatments, and outcomes. Regional variations in age, BMI, and comorbidity levels were noted between central and eastern Taiwan. Importantly, the registry identified gaps in adherence to guideline-directed medical therapy, particularly in statin use. Continued data collection will support improvements in PAD management nationwide.

**Keywords:** Asian; Epidemiology; Peripheral arterial disease; Registries; Treatment outcome

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## 1. INTRODUCTION

Peripheral artery disease (PAD) is a consequence and manifestation of systemic atherosclerosis, which leads to narrowing of arteries and reduced blood flow. This, in turn, results in complications such as intermittent claudication, ischemic rest pain, ischemic ulcers, gangrene, and functional limitations.[1–3]

PAD often coexists with other atherosclerotic conditions, including coronary artery disease (CAD), carotid artery disease, and cerebrovascular disease. Individuals with both CAD and

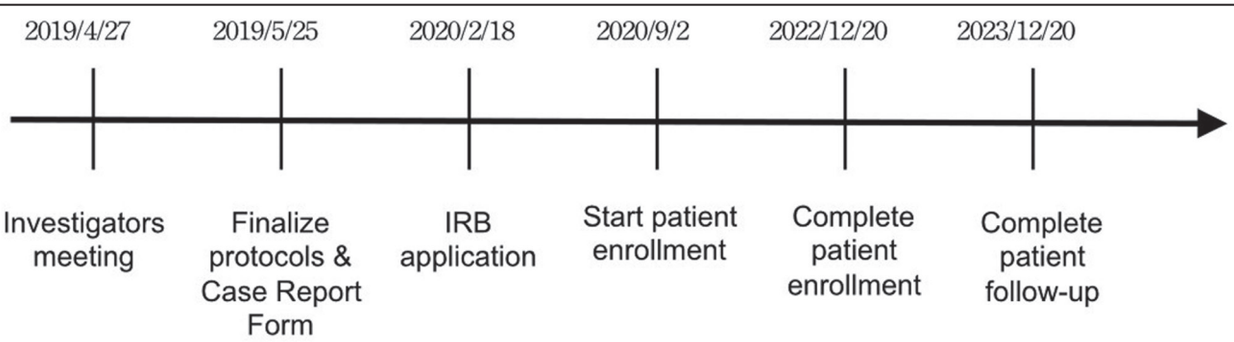


**Fig. 1** Time frame of the registry. IRB = institutional review board.

PAD face a significantly higher risk of cardiovascular mortality compared to those with CAD alone.[4,5] Furthermore, PAD places a substantial burden on patients in terms of their quality of life and financial well-being.[6,7] However, despite its prevalence and significant impact on adverse clinical outcomes, physical function, and overall physical activity, PAD has received less attention compared to other atherosclerotic disorders like myocardial infarction (MI), stroke, and aortic dissection.

The prevalence rates of PAD in the Framingham Offspring Study[8] (a longitudinal study) and Rotterdam Study (a cross-sectional study)[9] were 3.9% and 16.9% in men, and 3.3% and 20.5% in women, respectively. PAD becomes more prevalent with advancing age.[9,10] The occurrence of PAD is relatively rare before the age of 50 but sharply increases, reaching up to 20% or more in individuals over 80 years.[10–12] Traditional risk factors for PAD include smoking, diabetes mellitus (DM), dyslipidemia, and hypertension.[13] In Taiwan, due to the popularity of high-sodium, high-fat, high-sugar, and high-calorie diets, coupled with a high prevalence of smoking, fast-paced lifestyles, and other risk factors like aging, the incidence of PAD has risen substantially.

Notably, the number of studies focusing on PAD is relatively limited compared with other vascular conditions. To our knowledge, few PAD registries[14] have been published in the past decade, underscoring the scarcity of comprehensive data in this domain.

Recent advances in the pharmacological therapy of PAD have significantly improved the prognosis of the disease,[15,16] necessitating a new PAD registry to understand real-world management. In addition, clinical data on PAD in Taiwan are lacking. The purpose of the present study is to analyze the incidence, risks factors, pharmacological treatments, interventional therapies, and outcomes of patients with PAD in Taiwan.

## 2. METHODS

### 2.1. Study design and population

The TwPAD registry was a prospective, multicenter, observational survey of patients presenting to 10 medical centers or teaching hospitals in Taiwan. The protocol was approved by the institutional review board of each hospital, and informed consent was obtained from all participating individuals.

The participants consisted of individuals who had been diagnosed with PAD, regardless of hospital admission status, from September 2020 to December 2022. All patients at entry were over 18 years of age. The criteria for PAD included previous aorto-femoral or limb bypass surgery, percutaneous transluminal angioplasty revascularization of the iliac or infra-inguinal arteries, limb or foot amputation due to arterial disease, or a history of intermittent claudication, and at least one of the following conditions: (a) an ankle/arm blood pressure ratio of <0.90; and (b) presence of significant peripheral artery stenosis (≥50%) as determined by angiography or documented through duplex ultrasound.

Exclusion criteria were as follows: history of atherothrombotic events (acute coronary syndrome, stroke, or transient ischemic attack) within one month; lack of consent from patients or family members based on their own reasons, dementia, or mental illness; life expectancy of <6 months (e.g., malignant metastatic tumor); congenital heart disease with significant hemodynamic abnormalities; pregnancy; and any other condition or circumstance that the researchers deemed inappropriate to enroll.

No specific protocols or recommendations for evaluation and management of PAD were used during this study. The timeframe of registration is shown in Fig. 1.

### 2.2. Baseline data collection

Personal and clinical profiles were captured at enrollment, with specially trained study nurses and qualified cardiologists prospectively collecting data whenever feasible. The data were recorded using a standard case report form and entered into Microsoft Excel (Microsoft, Redmond, WA) by the investigators or research coordinators after patients had read the study information and signed the informed consent. The participating hospitals and names of the principal investigators are listed in Supplementary Table 1, http://links.lww.com/JCMA/A318.

Baseline characteristics, including risk factors, such as hypertension, diabetes, smoking habits, and medication history, were meticulously collected. Medication information, including drug dosages, was obtained through chart review. Biochemical profiles, encompassing blood glucose, lipid profile, and kidney function, were documented.

Body mass index (BMI) was defined as the weight in kilograms divided by the square of the height in meters. Subjects with a BMI of 25 to <30 were considered overweight and subjects with a BMI ≥30 were considered obese, according to World Health Organization (WHO) 2019 definitions. Obese subjects were further classified into class I (BMI, 30 to <35) and class II obesity (BMI, ≥35). Another measure of obesity was a waist circumference of ≥102 cm (40 in) in men or ≥88 cm (35 in) in women. Current smoking was defined as use of at least five cigarette sticks per day on average within the last month before entry into the registry.

### 2.3. Clinical follow-up for adverse cardiovascular events

Following the study protocol, each patient initially stabilized with medical treatment was prospectively and regularly followed up in the individual hospital clinics. Follow-up data collection occurred during outpatient clinic visits, if applicable, and

approximately every 3 months for the first year post-enrollment. Medications were prescribed based on the physician's discretion for each patient. Throughout the follow-up period, adverse cardiovascular events were diligently recorded, encompassing all-cause and cardiovascular deaths, nonfatal MI, nonfatal stroke, unplanned coronary revascularization procedures, unplanned hospitalizations for endovascular therapy (EVT), and other cardiovascular events such as stroke, transient ischemic attack, and heart failure.

### 2.4. Comparison of PAD registry studies

To compare with other PAD registries, we conducted a PubMed search of articles published from January 2010 to December 2023 using the terms "peripheral artery disease" and "registry." We excluded intervention trials, such as the EUCLID trial,[17] EMPA-REG OUTCOME PAD subgroup trial,[18] and VOYAGER PAD trial.[19] Registries not exclusive to PAD patients were also excluded. Finally, our comparisons involved the PORTRAIT registry,[14] K-VIS ELLA registry,[20] and XLPAD registry.[21] The PORTRAIT registry[14] enrolled patients exhibiting an abnormal ankle-brachial index and experiencing new or worsened claudication symptoms. This registry was conducted across 16 PAD specialty clinics in the United States, the Netherlands, and Australia. The K-VIS ELLA registry[20] was a retrospective cohort study focusing on EVT and involved 31 Korean hospitals. The XLPAD registry[21] was dedicated to PAD, specifically comparing stent and non-stent treatment outcomes and associated costs in femoropopliteal interventions across multiple hospitals in the United States.

### 2.5. Statistical analysis

All enrolled patients were included in the analysis, and descriptive summaries were provided for the entire cohort, as well as subgroup analyses. Quantitative data were expressed as mean ± SD, while categorical variables were presented as percentages. Continuous data were compared using either Student's *t* test or Mann-Whitney *U* test, and categorical data comparisons were conducted using the Chi-square test. All statistical analyses were two-tailed, and a significance level of $p < 0.05$ was applied, using IBM Statistics (version 26.0; SPSS Inc., Armonk, NY).

## 3. RESULTS

### 3.1. Baseline characteristics

A total of 1005 patients were enrolled in the registry. The mean age was 70.5 years and the majority were men, comprising 59.3% of the total. The prevalence rates of various medical conditions within this group were as follows: 68.2% had diabetes, 76.3% had hypertension, 72.6% had hypercholesterolemia, 40.6% were smokers, 31.7% had undergone coronary artery intervention, 59.8% had undergone EVT, 11.2% had atrial fibrillation, and 26.2% had end-stage renal disease (ESRD). The baseline characteristics of the participants are presented in (Fig. 2) and in Table 1.

Patients from Central Taiwan were the youngest, with an average age of 65.8 years. They also had the highest average BMI (25.2 kg/m$^2$) but the smallest waist (81.5 cm) and hip (92.1 cm) circumferences. Furthermore, patients from this region had the lowest rates of smoking history (22%), hypertension (66%), diabetes (49.3%), prior EVT (48.7%), and ESRD (14.7%).

On the other hand, patients from Eastern Taiwan were the oldest, with an average age of 73.1 years. They had the lowest average BMI (23.5 kg/m$^2$) but the largest waist (93.8 cm) and hip (95.6 cm) circumferences. Additionally, patients from Eastern Taiwan had the highest rates of smoking history (56.1%), hypertension (97.6%), diabetes (78%), prior EVT (90.2%), and atrial fibrillation (34.1%).

### 3.2. Baseline laboratory data

Table 2 presents the baseline blood test results and biochemical profiles of enrolled patients. As a whole or in each region, the average fasting glucose levels were more than 126 mg/dL, while the average low-density lipoprotein cholesterol (LDL-C) levels were below 100 mg/dL.

### 3.3. Baseline medication profiles

Table 3 presents an overview of the medications used, including antiplatelet agents (90.8%), renin-angiotensin system blocking agents (angiotensin-converting enzyme [ACE] inhibitors or angiotensin receptor blockers [ARBs], 39.5%), beta-blockers (38.8%), anticoagulants (26.9%), and anti-diabetes

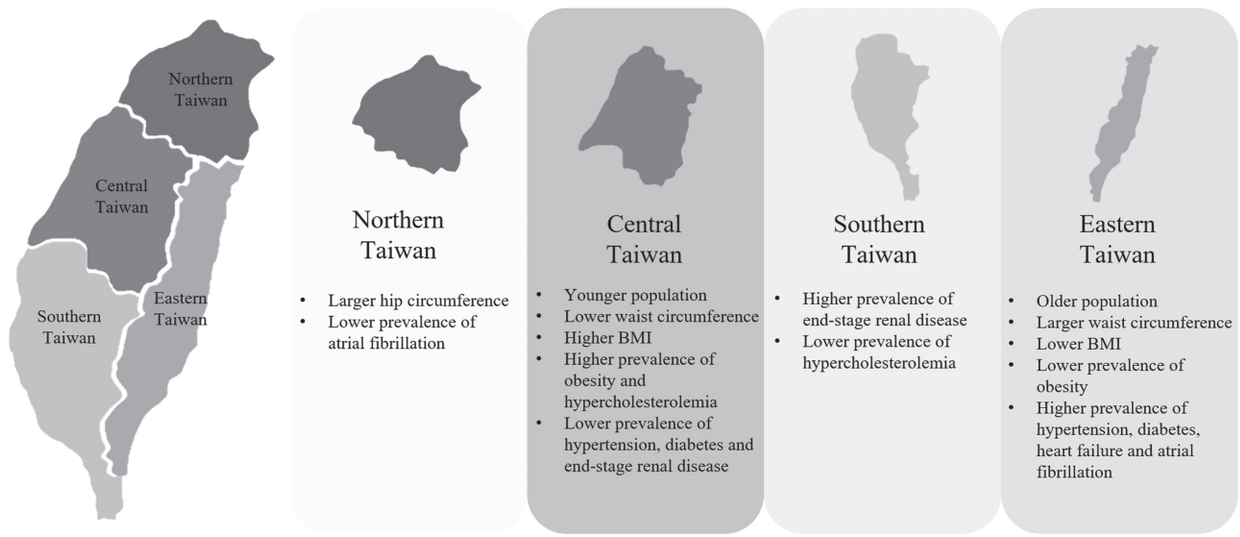


**Fig. 2** Distribution of the population, number of participants, and patient characteristics by region in Taiwan. Dividing Taiwan into four regions, Eastern Taiwan had the oldest average age while Central Taiwan had the youngest. Compared to the other regions, participants from Eastern Taiwan had the lowest average BMI but the largest waist and hip circumferences. BMI = body mass index.

agents (63.6%). Statin therapy was only taken by 54.5% of the enrollees.

### 3.4. Characteristics in patients with and without history of EVT

Table 4 presents a comparison of baseline characteristics between patients with a history of EVT and those without. Patients with a history of EVT had a lower average BMI (24.1 vs 25.5 kg/m$^2$) and higher prevalence rates of hypertension (78.7% vs 72.8%) and atrial fibrillation (13.6% vs 7.7%). In addition, women with a history of EVT had a smaller average hip circumference (93.8 ± 10.3 vs 97.0 ± 13.5 cm). Fig. 3A depicts the Rutherford category of patients who underwent previous EVT. Majority of patients (41.4%) were classified as Rutherford category IV, followed by Rutherford category III (32.1%). The data sheds light on the distribution of Rutherford stages among patients who had undergone EVT. Fig. 3B

**Table 1**

**Baseline characteristics**

| | All n = 1005 | Northern Taiwan n = 576 | Central Taiwan n = 150 | Southern Taiwan n = 238 | Eastern Taiwan n = 41 | *p* |
|---|---|---|---|---|---|---|
| Age, y | 70.5 ± 11.5 | 71.5 ± 11.1 | 65.8 ± 12.0 | 70.7 ± 11.4 | 73.1 ± 1.8 | <0.001 |
| Sex, male, n (%) | 596 (59.3) | 352 (61.1) | 88 (58.7) | 129 (54.2) | 27 (65.9) | 0.251 |
| BMI, kg/m$^2$ | 24.7 ± 4.5 | 24.9 ± 4.6 | 25.2 ± 4.4 | 24.1 ± 4.2 | 23.5 ± 5.2 | 0.014 |
| Male | 24.7 ± 4.0 | 24.7 ± 3.9 | 25.7 ± 4.4 | 24.3 ± 3.7 | 23.0 ± 5.3 | 0.011 |
| Female | 24.7 ± 5.2 | 25.2 ± 5.6 | 24.7 ± 4.4 | 23.8 ± 4.7 | 24.4 ± 4.9 | 0.166 |
| <25, n (%) | 567 (57.5) | 318 (56.9) | 73 (49.0) | 148 (62.4) | 28 (68.3) | |
| 25-<30, n (%) | 308 (31.2) | 175 (31.3) | 53 (35.6) | 75 (29.5) | 10 (24.4) | |
| Obesity | | | | | | |
| 30-<35, n (%) | 85 (8.6) | 48 (8.6) | 20 (13.4) | 15 (6.3) | 2 (4.9) | |
| ≥35, n (%) | 26 (2.6) | 18 (3.2) | 3 (2.0) | 4 (1.7) | 1 (2.4) | |
| Waist (cm) | 87.8 ± 12.6 | 89.4 ±12.8 | 81.5 ± 10.8 | 88.1 ± 12.6 | 93.8 ± 11.5 | <0.001 |
| Male | 89.2 ±11.5 | 90.1 ±11.3 | 84.1 ± 10.1 | 90.7 ± 11.9 | 92.2 ± 11.8 | <0.001 |
| Female | 85.6 ± 13.8 | 88.3 ±14.9 | 78.0 ± 8.4 | 84.6 ± 12.8 | 97.0 ± 10.6 | <0.001 |
| Hip (cm) | 95.8 ± 10.7 | 98.0 ±10.8 | 92.1 ± 8.0 | 92.5 ± 10.6 | 95.6 ± 8.4 | <0.001 |
| Male | 96.3 ± 10.0 | 98.2 ± 9.7 | 93.8 ± 8.7 | 93.4 ± 10.5 | 94.4 ± 7.9 | <0.001 |
| Female | 95.1 ±11.7 | 97.6 ± 12.3 | 89.9 ± 6.5 | 91.5 ± 10.7 | 97.9 ± 9.2 | <0.001 |
| Smoking history, n (%) | 408 (40.6) | 251 (43.6) | 33 (22.0) | 101 (42.4) | 23 (56.1) | <0.001 |
| Never | 597 (59.4) | 325 (56.4) | 117 (78.0) | 137 (57.6) | 18 (43.9) | |
| Former | 243 (24.2) | 143 (24.8) | 21 (14.0) | 61 (25.6) | 18 (43.9) | |
| Current | 165 (16.4) | 108 (18.8) | 12 (8.0) | 40 (16.8) | 5 (12.2) | |
| Hypertension, n (%) | 767 (76.3) | 427 (74.1) | 99 (66.0) | 200 (84.0) | 40 (97.6) | <0.001 |
| Diabetes, n (%) | 685 (68.2) | 406 (70.5) | 74 (49.3) | 173 (72.7) | 32 (78.0) | <0.001 |
| Hypercholesterolemia, n (%) | 730 (72.6) | 411 (71.4) | 126 (84.0) | 163 (68.5) | 30 (73.2) | 0.006 |
| Heart failure, n (%) | 180 (17.9) | 110 (19.1) | 20 (13.3) | 37 (15.5) | 13 (31.7) | 0.139 |
| Coronary artery intervention, n (%) | 319 (31.7) | 177 (30.7) | 44 (29.3) | 66 (27.7) | 32 (78.0) | <0.001 |
| LEAD intervention, n (%) | 601 (59.8) | 333 (57.8) | 73 (48.7) | 158 (66.4) | 37 (90.2) | <0.001 |
| Atrial fibrillation, n (%) | 113 (11.2) | 54 (9.4) | 20 (13.3) | 25 (9.5) | 14 (34.1) | <0.001 |
| End-stage renal disease, n (%) | 263 (26.2) | 132 (22.9) | 22 (14.7) | 98 (41.2) | 11 (26.8) | <0.001 |

BMI = body mass index; BNP = B-type natriuretic peptide; Egfr = estimated glomerular filtration rate; Hs-CRP = high-sensitivity C-reactive protein; LDL = low-density cholesterol.

**Table 2**

**Laboratory data**

| | All n = 1005 | Northern Taiwan n = 576 | Central Taiwan n = 150 | Southern Taiwan n = 238 | Eastern Taiwan n = 41 | *p* |
|---|---|---|---|---|---|---|
| AC glucose, mg/dL | 135.5 ± 61.4 | 133.7 ± 61.4 | 129.6 ± 59.2 | 136.3 ± 62.6 | 129.7 ± 59.3 | 0.698 |
| HbA1C, % | 6.9 ± 1.5 | 7.1 ± 1.57 | 6.5 ± 1.1 | 6.8 ± 1.5 | 7.0 ± 1.4 | 0.013 |
| GOT, U/L | 23.8 ± 16.4 | 22.0 ± 13.1 | 23.0 ± 14.6 | 27.7 ± 21.3 | 23.9 ± 1.4 | <0.001 |
| GPT, U/L | 20.2 ± 20.0 | 19.6 ± 16.9 | 21.3 ± 25.2 | 21.3 ± 24.4 | 19.6 ± 15.6 | 0.713 |
| CK, IU/L | 126.7 ± 164.8 | 120.1 ± 156.1 | 110.1 ± 99.7 | 243.2 ± 219.5 | 136.6 ± 200.5 | 0.107 |
| Hb, g/dL | 11.9 ± 2.2 | 12.0 ± 2.2 | 11.8 ± 2.1 | 11.4 ± 2.0 | 12.2 ± 2.0 | 0.004 |
| Hct, % | 35.9 ± 6.2 | 36.7 ± 6.3 | 35.0 ± 5.9 | 34.2 ± 5.8 | 36.9 ± 6.5 | <0.001 |
| RBC, ×10$^6$/μL | 4.0 ± 0.8 | 4.0 ± 0.8 | 4.1 ± 0.7 | 3.9 ± 0.8 | 4.1 ± 0.7 | 0.066 |
| WBC, ×10$^3$/μL | 7.5 ± 2.7 | 7.5 ± 2.6 | 7.0 ± 2.5 | 8.0 ± 3.2 | 6.4 ± 1.8 | <0.001 |
| Platelet, ×10$^3$/μL | 234.2 ± 83.1 | 237.3 ± 81.7 | 214.1 ± 80.4 | 238.7 ± 87.8 | 215.6 ± 76.1 | 0.036 |
| LDL, mg/dL | 84.7 ± 33.2 | 86.3 ± 33.5 | 80.7 ± 23.7 | 80.8 ± 33.5 | 95.0± 41.4 | 0.032 |
| HDL, mg/dL | 45.4 ± 15.2 | 47.0 ± 16.0 | 43.9 ± 13.5 | 42.1 ± 13.0 | 46.6 ± 14.8 | 0.001 |

CK = creatine kinase; GOT = glutamic oxaloacetic transaminase; GPT = glutamic pyruvic transaminase; Hb = hemoglobin, Hct = hematocrit; HDL = high-density lipoprotein; LDL = low-density lipoprotein; RBCs = red blood cell; WBC = white blood cell.

displays the distribution of Rutherford categories across different regions of Taiwan.

### 3.5. Comparison of PAD registry studies

The clinical characteristics of patients in the TwPAD registry were compared with those in three other registries (Table 5). The mean age of patients diagnosed with PAD in previous registries ranged from 66 to 68 years, with approximately 62% to 82% of patients being male.[14,20,21] In contrast, the mean age of patients in the TwPAD registry was older (70 years), with fewer males (59%). Additionally, the Taiwan registry exhibited a higher prevalence of diabetes, hyperlipidemia, heart failure, prior percutaneous coronary intervention, coronary artery bypass grafting, and LEAD intervention. Conversely, fewer patients with a history of smoking and receiving statin treatment were observed in the Taiwan registry.

**Table 3**

**Medication**

| | All n = 1005 | Northern Taiwan n = 576 | Central Taiwan n = 150 | Southern Taiwan n = 238 | Eastern Taiwan n = 41 | *p* |
|---|---|---|---|---|---|---|
| Antiplatelet, n (%) | 913 (90.8) | 517 (89.8) | 137 (91.3) | 220 (92.4) | 39 (95.1) | 0.477 |
| Aspirin, n (%) | 478 (47.6) | 269 (46.7) | 60 (40.0) | 132 (55.5) | 17 (41.5) | 0.017 |
| Clopidogrel, n (%) | 463 (46.1) | 265 (46.0) | 86 (57.3) | 89 (37.4) | 23 (56.1) | 0.001 |
| Ticagrelor, n (%) | 15 (1.5) | 8 (1.4) | 1 (0.7) | 3 (1.3) | 3 (7.3) | <0.001 |
| Prasugrel, n (%) | 1 (0.1) | 0 (0) | 0 (0) | 1 (0.4) | 0 (0) | 0.358 |
| Ticlopidine, n (%) | 13 (1.3) | 13 (2.3) | 0 (0) | 0 (0) | 0 (0) | 0.633 |
| Cilostazol, n (%) | 565 (56.2) | 323 (56.1) | 94 (62.7) | 125 (52.5) | 23 (56.1) | <0.001 |
| ACEi/ARB, n (%) | 397 (39.5) | 284 (49.3) | 24 (16.0) | 82 (34.5) | 7 (17.1) | <0.001 |
| Beta blocker, n (%) | 390 (38.8) | 211 (36.6) | 64 (42.7) | 91 (38.2) | 24 (58.5) | 0.031 |
| Anticoagulant, n (%) | 270 (26.9) | 120 (20.8) | 66 (44.0) | 69 (29.0) | 15 (36.6) | <0.001 |
| Rivaroxaban (2.5 mg) | 131 (13.0) | 55 (9.5) | 30 (20) | 40 (18) | 4 (9.8) | <0.001 |
| Statin, n (%) | 548 (54.5) | 342 (59.4) | 65 (43.3) | 120 (50.4) | 21 (51.2) | <0.002 |
| Antidiabetic agents, n (%) | 639 (63.6) | 397 (68.9) | 60 (40.0) | 150 (63.0) | 32 (78.0) | <0.001 |
| SGLT2-I, n (%) | 102 (10.1) | 81 (14.1) | 2 (1.3) | 13 (5.5) | 6 (14.6) | <0.001 |
| GLP-1 receptor agonist, n (%) | 16 (1.6) | 14 (2.4) | 0 (0.0) | 1 (0.4) | 1 (2.4) | 0.063 |

ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin II receptor blockers; GLP-1 receptor agonist = glucagon-like peptide-1 receptor agonists; SGLT2-I = sodium-glucose transport protein 2 inhibitor.

**Table 4**

**Baseline characteristics with and without LEAD intervention**

| | No LEAD intervention n = 404 | LEAD intervention n = 601 | *p* |
|---|---|---|---|
| Age, y | 70.1 ± 12.3 | 70.8 ± 11.0 | 0.365 |
| Male, n (%) | 234 (57.9) | 362 (60.2) | 0.464 |
| BMI | 25.50 ± 4.5 | 24.1 ± 4.5 | <0.001 |
| Male | 25.1 ± 3.8 | 24.4 ± 4.0 | 0.025 |
| Female | 26.0 ± 5.3 | 23.8 ± 5.0 | <0.001 |
| <25, n (%) | 199 (50.6) | 368 (62.1) | |
| 25-<30, n (%) | 136 (34.6) | 172 (29.0) | |
| Obesity | | | |
| 30-<35, n (%) | 45 (11.5) | 40 (6.7) | |
| ≥35, n (%) | 13 (3.3) | 13 (2.2) | |
| Waist, cm | 88.2 ± 13.0 | 87.5 ± 12.3 | 0.487 |
| Male | 88.9 ± 11.7 | 89.4 ± 11.7 | 0.676 |
| Female | 87.2 ± 15.0 | 84.4 ± 12.7 | 0.084 |
| Hip, cm | 96.6 ± 1.6 | 95.4 ± 10.1 | 0.172 |
| Male | 96.3 ± 10.9 | 96.4 ± 9.9 | 0.931 |
| Female | 97.0 ± 13.5 | 93.84 ± 10.3 | 0.035 |
| Smoker, n (%) | 150 (37.1) | 258 (42.9) | 0.066 |
| Hypertension, n (%) | 294 (72.8) | 437 (78.7) | 0.030 |
| Diabetes, n (%) | 273 (67.6) | 412 (68.6) | 0.744 |
| Hypercholesterolemia, n (%) | 299 (74) | 431 (71.7) | 0.423 |
| Heart failure, n (%) | 74 (18.3) | 106 (17.7) | 0.792 |
| Coronary artery intervention, n (%) | 110 (27.2) | 217 (34.4) | 0.465 |
| Atrial fibrillation, n (%) | 31 (7.7) | 82 (13.6) | 0.003 |
| End-stage renal disease, n (%) | 91 (22.5) | 172 (18.6) | 0.053 |

LEAD = lower extremity arterial disease.

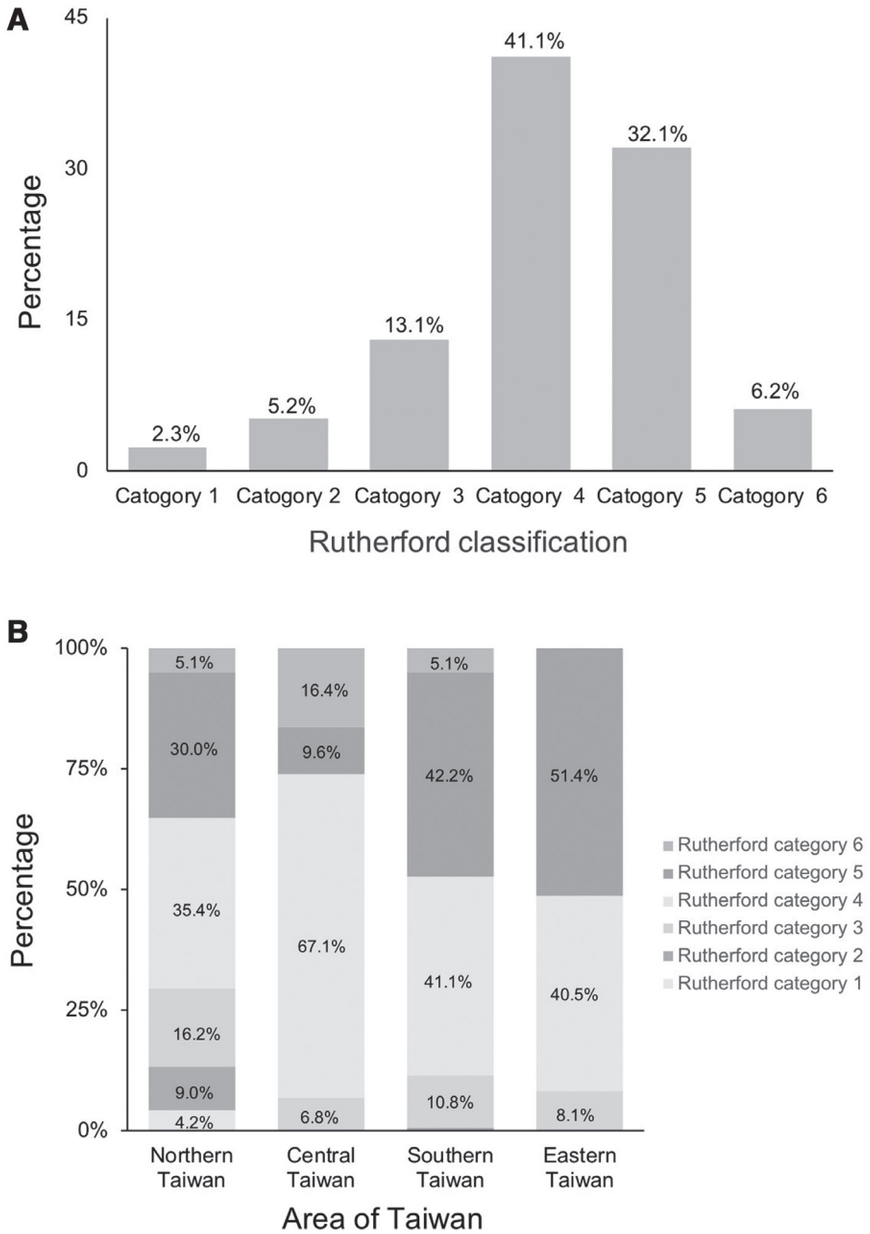


**Fig. 3** Rutherford classification of patients with previous endovascular therapy. A, Rutherford categories for patients with a history of endovascular therapy. B, Bar graphs illustrating the Rutherford categories across four regions of Taiwan.

## 4. DISCUSSION

The TwPAD registry enrolled both symptomatic and asymptomatic PAD patients. In recent decades, PAD has emerged as a significant contributor to morbidity and mortality worldwide, even in high-income European regions.[22] PAD patients, including asymptomatic ones, are still at high risk of cardiovascular mortality. Symptomatic PAD patients, in particular, experience more than a twofold increase in mortality risks compared to reference subjects, and these risks escalate with the severity of the PAD stage.[23] Traditional risk factors for CVD, such as smoking, hypertension, diabetes, and hypercholesterolemia, are prevalent (40.6%-76.3%) in our patients. Despite substantial efforts to mitigate these risks through medical and primary prevention strategies, the persistently high prevalence of risk factors necessitates the exploration of novel therapeutic approaches, both in Western and Asian patient populations. The primary objective of the current study is to provide a comprehensive understanding of long-term outcomes in the context of secondary prevention for patients diagnosed with PAD.

The TwPAD registry will enable future comparative effectiveness studies of various treatment strategies, including medical management, smoking cessation, and EVT. Furthermore, the study sought to delve into the intricate relationship between PAD and risk factors, and to determine if these factors act independently or in conjunction to contribute to the occurrence of adverse cardiovascular events. The findings from this research endeavor are anticipated to yield fresh insights into potential associations between secondary prevention measures and

**Table 5**

**Comparison of baseline clinical characteristics between Taiwan registry and representative PAD registries**

| | TwPAD n = 1005 | PORTRAIT n = 1275 | K-VIS ELLA n = 3073 | XLPAD n = 2162 |
|---|---|---|---|---|
| Age, y | 70.5 ± 11.5 | 67.6 ± 9.4 | 68.4 ± 9.5 | 66.2 ± 10.2 |
| Male, n (%) | 596 (59.3) | 793 (62.2) | 2523 (82.1) | 1630 (75.4) |
| BMI | 24.7 ± 4.5 | 29.0 ± 6.4 | 23.5 ± 3.6 | - |
| Former or current smoker, n (%) | 408 (40.6) | 1134 (89.2) | 1790 (58.2) | - |
| Hypertension, n (%) | 767 (76.3) | 1017 (79.8) | 2257 (73.4) | 1102 (51.0) |
| Diabetes, n (%) | 685 (68.2) | 398 (31.2) | 1378 (58.0) | 112 (23.4) |
| Hyperlipidemia, n (%) | 730 (72.6) | 1015 (79.6) | 1195 (38.9) | 1761 (81.5) |
| Heart failure, n (%) | 180 (17.9) | 127 (10.0) | - | 12 (2.5) |
| Atrial fibrillation, n (%) | 113 (11.2) | 143 (11.2) | - | 35 (7.3) |
| Prior PCI, n (%) | 319 (31.7) | 282 (22.1) | - | 56 (11.7) |
| Prior CABG, n (%) | 33 (32.8) | 243 (19.1) | - | 45 (9.4) |
| Prior LEAD intervention, n (%) | 601 (59.8) | 253 (19.8) | 299 (9.7) | 57 (11.9) |
| Aspirin, n (%) | 478 (47.6) | - | 2592 (84.3) | 1180 (54.6) |
| Clopidogrel, n (%) | 463 (46.1) | - | 2522 (82.1) | 623 (28.9) |
| Cilostazol, n (%) | 565 (56.2) | 141 (11.8) | - | - |
| ACEi/ARB, n (%) | 397 (39.5) | 724 (60.1) | 1366 (44.5) | 862 (39.9) |
| Beta blocker, n (%) | 390 (38.8) | - | 1051 (34.2) | 857 (39.6) |
| Statin, n (%) | 270 (26.9) | 966 (80.6) | 2127 (69.2) | 1090 (50.4) |
| Antidiabetic Agents, n (%) | 548 (54.5) | - | 578 (18.8) | - |

ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin II receptor blockers; GLP-1 receptor agonist = glucagon-like peptide-1 receptor agonists; LEAD = lower extremity arterial disease; SGLT2-I = sodium-glucose transport protein 2 inhibitor.

future adverse events, thereby enhancing our comprehension of effective therapeutic targets and strategies aimed at retarding or preventing the progression of the disease following EVT.

The TwPAD registry has the potential to discern specific subsets of the population, with potential mediation of socioeconomic factors that may place patients at risk for suboptimal processes of care and outcomes. For example, our study revealed some regional differences in baseline characteristics, biochemistries, and interventions, such as that in Central Taiwan, where the patients were the youngest with the highest average BMI, yet demonstrated the smallest average waist circumference, relatively lower average hip circumference, and lower rates of smoking, hypertension, diabetes, prior EVT, and ESRD compared to other regions. Conversely, due to a youth exodus, Eastern Taiwan stands out as one of the regions with a high aging population and holds the highest ratio of elderly individuals living alone. Apart from the oldest average age, patients from Eastern Taiwan had the lowest average BMI but the largest waist and hip circumferences. Additionally, patients from Eastern Taiwan exhibited higher rates of smoking, hypertension, diabetes, prior EVT, and atrial fibrillation. These regional differences and health-related behavior patterns highlight the diverse demographic and health profiles within Taiwan, emphasizing the need for tailored healthcare strategies based on regional characteristics.

In the realm of contemporary pharmacological therapeutic strategies, statins have emerged as potentially life-saving medications widely used in patients with PAD. Previous studies have consistently demonstrated that statins, by lowering LDL-C, are associated with a significant reduction in vascular events.[24,25] This includes a decrease in all-cause mortality, a lower incidence of nonfatal stroke, and a discernible trend toward a reduced risk of MI. LDL-C reduction with lipid-lowering therapy also alleviated clinical symptoms, improved exercise endurance, and slowed down the progression of atherosclerotic plaques in patients with PAD.[26–28]

A real-world nationwide observational study that enrolled patients with DM and PAD using a nationwide DM cohort database in Taiwan from 2000 to 2011 showed that statin therapy was associated with a 25% reduction in lower extremity amputations and 22% risk reduction in cardiovascular mortality, taking into consideration the competing risk of death. These findings suggest that statin therapy not only reduces the risk of adverse cardiovascular events, but also has favorable effects on limb prognosis in DM patients with PAD.[29] Another retrospective cohort study that used data from the Taiwan National Health Insurance Research Database between January 2001 and December 2013 showed that statin therapy was associated with reductions in the risk of all-cause death, cardiovascular death, and the composite adverse limb outcomes of EVT and amputation in patients with kidney failure receiving long-term maintenance dialysis who were diagnosed with PAD and dyslipidemia.[30]

Scientific evidence, as well as recent guidelines, consistently categorize PAD as a high- or very high-risk condition, recommending the achievement of LDL-C levels below specific thresholds (typically <70 or 55 mg/dL).[31–34] This aligns with Taiwan's lipid guidelines for PAD patients, which also advocate for achieving an LDL-C level below 70 mg/dL.[35] However, in this registry, mean LDL-C level was 84.72 mg/dL and only 54% of patients received statin treatment. These findings underscore the importance of raising awareness among physicians about adhering to guideline recommendations. Initiating statin therapy for those not currently receiving it becomes paramount in ensuring comprehensive and guideline-directed care for individuals with PAD.

PAD is often underdiagnosed in Taiwan, largely due to a lack of awareness. To improve recognition and understanding of PAD, targeted healthcare provider training and public awareness campaigns are crucial. Routine PAD screening should be integrated into regular checkups for high-risk groups, particularly diabetes patients, using tests like ABI, and risk stratification tools should prioritize at-risk individuals. In Taiwan, the absence of statin indications in the National Health Insurance may contribute to the low use of statins observed in this registry. Therefore, medications should be made more accessible and affordable, with increased funding to address these gaps.

Few PAD registries have been published in recent years, with a predominant focus on EVT. The PORTRAIT registry,[14] for

instance, enrolled patients with new-onset or recently exacerbated exertional leg symptoms, regardless of whether the symptoms were typical or atypical, excluding those with a lower-limb revascularization procedure in the ipsilateral leg or a current episode of critical limb ischemia. The K-VIS ELLA registry,[20] a retrospective cohort study, specifically enrolled PAD patients who had undergone EVT. The XPAD registry[21] focused on PAD patients undergoing femoropopliteal intervention. In contrast, our registry included both symptomatic and asymptomatic patients at all stages of PAD, with or without intervention, providing a comprehensive real-world dataset.

The following limitations are important when interpreting future results from the registry. Despite encouragement for participating sites to enroll patients consecutively, the current registry design can still lead to selection bias and could not capture the whole PAD population, including asymptomatic patients not recognized by the physicians and patients with acute limb ischemia. Additionally, this study is hospital-based rather than community-based, and not all hospitals throughout the entire country were included. This distinction should be taken into account when interpreting the findings, as the results may not be fully representative of the broader community and may reflect characteristics specific to the hospitals included in the study.

In conclusion, the TwPAD registry is the largest national database involving PAD patients in Taiwan. It has a wealth of information about patient characteristics, treatments, and outcomes. Notably, our registry has unveiled instances of suboptimal adherence to guideline-directed medical care practices in Taiwan. As an ongoing initiative, the registry will continue to collect one-year follow-up data. This prospective approach ensures the continued accumulation of valuable information over time. The TwPAD registry is anticipated to serve as the foundational framework for driving enhancements in the care and management of PAD in Taiwan.

## APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://links.lww.com/JCMA/A318.

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