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Systemic outcomes of symptomatic peripheral artery disease patients with end-stage renal disease undergoing lower limb endovascular treatment: a propensity score-matched analysis

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Abstract

Background This study investigates the impact of end-stage renal disease (ESRD) on systemic and localized outcomes in peripheral artery disease (PAD) patients following endovascular therapy (EVT), with a focus on major adverse cardiac and cerebrovascular events (MACCEs).

Methods This retrospective cohort study included symptomatic PAD patients, categorized by the Rutherford classification, who underwent EVT at a single tertiary medical center from May 2018 to May 2021. Patients were divided into ESRD and non-ESRD groups. A propensity score-matched (PSM) analysis was performed to minimize confounding factors. The primary outcome was the occurrence of MACCEs, while the secondary outcome was the incidence of major adverse limb events (MALEs).

Results ESRD patients exhibited significantly worse systemic outcomes, with higher MACCE rates compared to non-ESRD patients in both the entire cohort (79.9% vs. 39.9%; HR: 2.69; 95% CI: 1.80–4.02; $p < 0.001$) and the matched cohort (HR: 3.88; 95% CI: 2.30–6.53; $p < 0.001$). They also had higher rates of all-cause mortality and myocardial infarction (MI). For localized outcomes, MALEs were more frequent in the ESRD group in the entire cohort (61.0% vs. 34.9%; HR: 1.84; 95% CI: 1.22–2.76; $p < 0.001$), but no significant difference was observed in the matched cohort (HR: 1.23; 95% CI: 0.76–1.99; $p = 0.40$). ESRD was identified as the sole independent predictor of increased MACCE risk (HR: 2.49; 95% CI: 1.65–3.75; $p < 0.001$).

Conclusions PAD patients with ESRD face significantly worse systemic outcomes, particularly elevated MACCE rates, after EVT. Preventing MACCEs, especially MI, is essential in this high-risk population. Despite more severe limb conditions, ESRD alone did not significantly increase MALE risk after PSM.

Clinical trial number Not applicable.

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Keywords Peripheral artery disease, End-Stage renal disease, Endovascular interventions, MACCEs, MALEs, Systemic outcomes

Background

Chronic kidney disease (CKD) and end-stage renal disease (ESRD) are significant global public health challenges. The Global Burden of Disease analysis (2017) reported a 9.1% prevalence of CKD, with ESRD prevalence rising by a median of 43% between 2003 and 2016 [1, 2]. CKD/ESRD is a strong risk factor for atherosclerotic disease and a key prognostic factor in peripheral artery disease (PAD) [3]. Data from the US National Health and Nutrition Examination Survey indicate that PAD prevalence is 6.5 times higher in patients with an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 compared to those with eGFR ≥ 60 mL/min/1.73 m^2, with nearly one-third of ESRD patients affected by PAD [4, 5].

PAD is a chronic pathological process resulting from atherosclerosis, typically affecting the arteries of the lower extremities [6]. However, the atherosclerotic process associated with PAD shares many common risk factors with other vascular beds, including the cardiovascular and cerebrovascular systems. While traditionally reported outcomes for PAD patients with CKD/ESRD have focused on localized diseases caused by PAD, such as foot wound healing or the amputation rate after lower limb interventions, there has been a lack of emphasis on systemic outcomes, including major adverse cardiac and cerebrovascular events (MACCEs). A meta-analysis reported significantly higher rates of major amputation (OR 1.97; 95% CI, 1.37–2.83; $p < 0.001$) and long-term mortality (OR 2.89; 95% CI, 1.44–5.78; $p = 0.003$) in PAD patients with CKD/ESRD undergoing lower extremity interventions compared to those without CKD/ESRD [7]. However, this analysis did not address the risk of MACCEs, and limited literature exists on this critical issue and its effect size, highlighting the need for further investigation.

Recent randomized controlled trials (RCTs), including BASIL-2 and BEST-CLI, have compared surgical revascularization with endovascular therapy (EVT) in patients with PAD. While BEST-CLI demonstrated superior outcomes with surgical bypass in select patients with adequate vein conduits, BASIL-2 reported higher mortality associated with bypass surgery in high-risk populations [8–10]. However, patients with ESRD were either excluded or underrepresented in these studies, leaving uncertainty regarding the optimal revascularization strategy for this subgroup. Given the elevated comorbidities and surgical risk in PAD patients with ESRD, EVT remains the preferred approach. Notably, one RCT reported improved amputation-free survival (AFS) with EVT compared to surgical bypass in high-risk patients [10]. These findings suggest that EVT may offer more favorable outcomes in this vulnerable population. Therefore, the present study focuses on PAD patients with ESRD undergoing endovascular intervention.

The implementation of Taiwan's National Health Insurance system, which covers over 99% of the population, has contributed to a rapid increase in the number of patients receiving maintenance dialysis. As a result, Taiwan currently has the highest global prevalence of ESRD and the steepest increase in ESRD incidence rates [11–13]. In parallel, the incidence of PAD requiring invasive treatment has also risen significantly. Between 2000 and 2011, the incidence of invasively treated PAD increased from 3.73 to 7.48 per 10,000 individuals. This rise corresponds with a marked increase in lower extremity PAD interventions, particularly EVT, which expanded from fewer than 1,000 procedures annually to over 9,000 [14–16]. Furthermore, a nationwide study of 936 Taiwanese patients with lower extremity PAD undergoing EVT reported 5-year rates of all-cause mortality, major adverse cardiovascular and cerebrovascular events (MACCEs), and non-fatal cardiovascular events of 45.1%, 32.9%, and 43.4%, respectively. Given this growing burden of ESRD and PAD, and the high morbidity associated with both conditions, evaluating the influence of ESRD on MACCE risk following EVT is essential. These trends underscore the need for vigilant management and optimization of cardiovascular care in this vulnerable population.

Methods

Study population

Between May 2018 and May 2021, 296 consecutive patients were retrospectively enrolled from Chang Gung Memorial Hospital. The study adhered to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Board of Chang Gung Medical Foundation (IRB No: 202201849B0), with consent waived.

Inclusion criteria included patients aged ≥ 18 years with symptomatic PAD (Rutherford stage 3–6), defined as intermittent claudication or chronic limb-threatening ischemia (CLTI), who underwent lower limb EVT performed by cardiologists or vascular surgeons. Exclusion criteria included acute limb ischemia, trauma, or aneurysms. Intervention sites ranged from the common iliac to the infrapopliteal arteries, identified via Duplex ultrasonography or computed tomography angiography (CTA). EVT procedures involved percutaneous

transluminal angioplasty (PTA) alone or combined with stent placement.

Data collection, definitions and follow-up

Baseline demographics, comorbidities, procedural details, medication history, and follow-up data were collected from medical records. PAD was diagnosed per the 2016 AHA/ACC guidelines using ankle-brachial index and transcutaneous oxygen pressure [17]. Intervention lesions were defined as stenoses ≥ 50% in diameter based on angiography, duplex ultrasonography, or CTA, as determined by the treating investigator.

The choice of endovascular techniques and stenting depended on lesion characteristics (anatomic location, length, calcification) and operator experience. Procedural success was evaluated by performing cardiologists or vascular surgeons using completion imaging (angiography or ultrasound). Multilevel disease was defined as interventions at more than one level in the same limb.

ESRD was classified as dialysis dependency or an eGFR < 15 mL/min/1.73 m^2 (Supplementary Table S1). Mortality causes included cardiac death (e.g., myocardial infarction, heart failure) and sepsis-related deaths (e.g., pneumonia, severe limb infections). Unexplained deaths, such as out-of-hospital cardiac arrests, posed challenges in determining exact causes. Follow-up visits occurred within one-month post-procedure and approximately every three months to monitor clinical outcomes.

CTA and digital subtraction angiography (DSA) images, supplemented by duplex ultrasonography, were independently reviewed by two authors (S.-Y.T. and Y.-S.L.) to evaluate the anatomic complexity of disease. Assessment included the original Bollinger score, which evaluates 10 arterial segments from the infrarenal aorta to below-knee arteries, and the extended Bollinger score, which subdivides the arterial tree from the common iliac artery to the plantar arch into 16 segments [18]. In addition, the Trans-Atlantic Inter-Society Consensus (TASC) II classification was used to grade aorto-iliac and femoral-popliteal lesions [19], and the Global Anatomic Staging System (GLASS) was utilized for infrainguinal disease characterization [20].

Outcomes

The primary outcome was MACCEs, defined as a composite of myocardial infarction (MI), stroke, or all-cause death. Secondary outcomes included: (1) MALEs, defined as major amputation of the index limb (above the ankle) or repeat revascularization (PTA, stenting, or surgical); (2) AFS, defined as survival without major amputation of the index limb [21]; (3) any amputation of the index limb; (4) repeat revascularization of the index limb more than twice; and (5) interventions for the contralateral limb (EVT, surgery, or amputation) post-EVT. Reintervention timing was determined by clinical assessment. Outcome definitions are detailed in Supplementary Table S2.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics, Version 25.0 (IBM Corp., Armonk, NY). Continuous variables were analyzed with Student's *t*-test or Mann-Whitney *U*-test, and categorical variables with the chi-squared or Fisher's exact test. Kaplan-Meier survival analysis with log-rank testing was used for time-to-event outcomes, and Cox regression generated hazard ratios (HRs).

Propensity score matching (PSM) at a 1:1 ratio was applied to reduce confounding between the ESRD and non-ESRD groups, using a caliper width of 0.1 standard deviations. Matching variables included demographics, comorbidities (e.g., diabetes mellitus, coronary artery disease, heart failure), preoperative antiplatelet use, Rutherford classification, intervention history, target lesion level, procedural success, and lesion complexity assessed by the Bollinger score. This approach was used to balance baseline characteristics between groups and minimize selection bias. In addition to PSM, multivariable Cox proportional hazards models were conducted within the matched cohort to adjust for any residual imbalances and further evaluate the independent association between ESRD status and clinical outcomes.

Results

Baseline characteristics for entire population

A total of 296 symptomatic PAD patients who underwent lower limb EVT during the study period were included in the analysis. The mean age was 70.2 ± 11.1 years, with a median follow-up time of 21.1 months (interquartile range: 5.6 to 34.9 months). Comorbidities were common, with 34.1% of patients having CVD, 25.0% with a history of stroke, 75.0% with HTN, and 78.7% with DM. A significant portion (81.4%) presented with CLTI classified as Rutherford grades 4 to 6. Prior interventions at the ipsilateral and contralateral sites were recorded in 15.9% and 19.6% of patients, respectively. Multilevel disease was prevalent, affecting 32.1% of patients, with the femoropopliteal region being the most common target lesion location (61.1%).

Among the cohort, 143 patients (48.3%) had concomitant ESRD. This group tended to be younger and had a higher prevalence of current smoking, CVD, DM, and more advanced Rutherford classification compared to those without ESRD. Additionally, the non-ESRD group received more stent insertions during target lesion treatment. Pre- and post-matching comparisons of anatomic parameters—including TASC classification, GLASS scores, original and extended Bollinger scores, and total lesion length—revealed no significant differences

between the ESRD and non-ESRD groups (Table 1). Propensity score matching was used to achieve balanced baseline characteristics across both groups (Table 2).

Cox proportional hazards analyses in entire population and matched cohorts

The results of the Cox proportional hazards models for primary and secondary outcomes are summarized in Table 3. Although the median follow-up time was 19.2 months (IQR: 5.59–34.07) for the ESRD group and 26.63 months (IQR: 10.08–40.16) for the non-ESRD group, the Kaplan–Meier curves were extended to 48 months to illustrate long-term trends. Approximately 7.8% of patients (23 out of 296) remained at risk at the 4-year mark. As shown in Fig. 1, despite a decreasing number at risk over time, survival differences between the ESRD and non-ESRD groups remained evident, with stable hazard ratios (HRs) and acceptable confidence intervals. However, we acknowledge that estimates at later time points, particularly near 4 years, should be interpreted with caution due to the smaller number of patients at risk.

MACCEs occurred more frequently in the ESRD group compared to the non-ESRD group, both in the entire population (79.9% vs. 39.9%; HR: 2.69; 95% CI: 1.80–4.02; $p < 0.001$) and in the matched cohorts (HR: 3.88; 95% CI: 2.30–6.53; $p < 0.001$) (Fig. 1). In the full cohort, the ESRD group had significantly higher rates of all-cause mortality (53.8% vs. 21.2%; HR: 2.89; 95% CI: 1.66–5.04; $p < 0.001$), cardiac death (21.8% vs. 3.8%; HR: 3.97; 95% CI: 1.32–11.97; $p = 0.008$), non-cardiac death (40.9% vs. 18.0%; HR: 2.56; 95% CI: 1.34–4.88; $p = 0.003$), MI (56.0% vs. 12.6%; HR: 3.68; 95% CI: 1.97–6.88; $p < 0.001$), and poorer AFS (38.4% vs. 75.2%; HR: 2.14; 95% CI: 1.45–3.15; $p < 0.001$). Similar trends were seen in the matched cohorts. However, the incidence of stroke did not significantly differ between the two groups in either the entire population (18.6% vs. 11.3%; HR: 1.68; 95% CI: 0.70–4.06; $p = 0.24$) or matched cohorts (HR: 3.22; 95% CI: 0.85–12.16; $p = 0.069$).

MALEs were more frequent in the ESRD group in the entire population (61.0% vs. 34.9%; HR: 1.84; 95% CI: 1.22–2.76; $p < 0.001$), although no significant difference was observed between the two groups in the matched cohorts (HR: 1.23; 95% CI: 0.76–1.99; $p = 0.40$) (Fig. 2). In the ESRD group, the incidence of major amputation (20.4% vs. 4.5%; HR: 3.80; 95% CI: 1.53–9.42; $p = 0.002$), any amputation (56.8% vs. 34.8%; HR: 1.68; 95% CI: 1.14–2.49; $p = 0.008$), repeat revascularization (54.7% vs. 32.3%; HR: 1.60; 95% CI: 1.03–2.48; $p = 0.035$) was significantly higher in the full population. However, the incidence of two or more repeat revascularizations (21.2% vs. 8.0%; HR: 2.18; 95% CI: 0.93–5.09; $p = 0.066$) was no significantly higher in the full population. After propensity score matching, differences in major amputation (HR: 2.13; 95% CI: 0.73–6.23; $p = 0.16$), any amputation (HR: 1.44; 95% CI: 0.89–2.33; $p = 0.13$), repeat revascularization (HR: 1.09; 95% CI: 0.65–1.83; $p = 0.76$), and two or more repeat revascularizations (HR: 1.15; 95% CI: 0.40–3.28; $p = 0.80$) were not statistically significant, though a trend toward higher rates in the ESRD group remained (Supplement Figure S1).

For contralateral limb intervention, the ESRD group had a higher frequency both in the entire population (62.8% vs. 29.6%; HR: 1.99; 95% CI: 1.24–3.21; $p = 0.004$) and in the matched cohorts (HR: 1.85; 95% CI: 1.06–3.22; $p = 0.029$). Subgroup analysis for the matched population (Supplement Figure S2-3) consistently showed worse MACCE outcomes in the ESRD group across multiple subgroups.

30-day outcomes of MACCEs, males and all-cause mortality

The results of the Cox proportional hazards models for MACCEs, MALEs and mortality within 30 days are summarized in Table 4 and Supplement Figure S4. For MACCEs, the ESRD group showed no significant difference compared to the non-ESRD group in the overall population (6.4% vs. 4.0%; HR: 1.60; 95% CI: 0.57–4.49; $p = 0.37$) and in the matched cohorts (HR: 2.02; 95% CI: 0.61–6.70; $p = 0.24$). Similar findings were observed for MALEs and all-cause mortality.

Predictors of MACCEs.

The results of the univariate and multivariate Cox proportional hazards survival analyses for MACCEs in the entire population are detailed in Table 5. After adjusting for confounding factors, ESRD was confirmed as an independent predictor of elevated risk for MACCEs, with a hazard ratio of 2.49 (95% CI: 1.65–3.75; $p < 0.001$).

Discussion

The study found that ESRD patients had significantly worse outcomes, including higher rates of MACCEs, mortality, MI, and poorer AFS in both the overall and matched cohorts. They also experienced more MALEs and contralateral limb interventions, though MALE differences became non-significant after matching. ESRD was independently associated with increased MACCE risk, with a hazard ratio of 2.49 after adjustment.

Our study provides a detailed analysis of systemic outcomes in PAD patients with ESRD following EVT. Unlike previous studies reporting increased 30-day MACCE rates in hemodialysis patients (5–5.2%) [22, 23], we observed no significant rise (6.4%) in short-term outcomes, even after PSM. However, ESRD was strongly associated with worse long-term outcomes, with significantly higher MACCE rates after EVT (HR: 3.88; 95% CI: 2.30–6.53; $p < 0.001$) and all-cause mortality (HR: 4.54; 95% CI: 2.17–9.48; $p < 0.001$). These findings from the non-matched cohort, which better reflect

Table 1 Baseline clinical characteristics on non-ESRD versus ESRD in entire population

	Total	Non-ESRD	ESRD	*p* value
Patients	**296 (100)**	**153 (51.7)**	**143 (48.3)**	
Age - y	70.2 ± 11.1	71.9 ± 11.7	68.4 ± 10.1	0.001
Follow-up intervals - months	21.1 (5.6,34.9)	21.0 (4.0,34.6)	21.8 (6.1,35.3)	0.77
Male sex	179 (60.5)	98 (64.1)	81 (56.6)	0.19
Current smoker	54 (19.6)	40 (26.1)	14 (9.8)	< 0.001
CVD Hx	101 (34.1)	36 (23.5)	65 (45.5)	< 0.001
Stroke Hx	74 (25.0)	41 (26.8)	33 (23.1)	0.46
HTN	222 (75.0)	115 (75.2)	105 (74.8)	0.95
DM	233 (78.7)	107 (69.9)	126 (88.1)	< 0.001
Hyperlipidemia	160 (54.1)	85 (55.6)	75 (52.4)	0.59
Previous statin	140 (47.3)	76 (49.7)	64 (44.8)	0.40
Previous antiplatelet	183 (61.8)	88 (57.5)	95 (66.4)	0.12
Rutherford classification				0.01
3	55 (18.6)	38 (24.8)	17 (11.9)	
4	13 (4.4)	8 (5.2)	5 (3.5)	
5	168 (56.8)	76 (49.7)	92 (64.3)	
6	60 (20.3)	31 (20.3)	29 (20.3)	
Previous ipsilateral intervention	47 (15.9)	19 (12.4)	28 (19.6)	0.09
Previous contralateral intervention	58 (19.6)	28 (18.3)	30 (21.0)	0.56
Intervention left side	151 (51.0)	77 (50.3)	74 (51.7)	0.81
Multilevel disease	95 (32.1)	47 (30.7)	48 (33.6)	0.60
Aortoiliac occlusive disease	68 (23.0)	42 (27.5)	26 (18.2)	0.06
Femoropopliteal lesion	181 (61.1)	92 (60.1)	89 (62.2)	0.71
Infrapopliteal lesion	146 (49.3)	69 (45.1)	77 (53.8)	0.13
Lesion length (mm)	158.9 ± 111.6	158.7 ± 111.8	159.0 ± 111.7	0.98
TASC II classification of aorto-iliac disease ($n = 68$)				0.18
A	30 (44.1)	16 (38.1)	14 (53.8)	
B	20 (29.4)	11 (26.2)	9 (34.6)	
C	6 (8.8)	5 (11.9)	1 (3.8)	
D	12 (17.6)	10 (23.8)	2 (7.7)	
TASC II Classification of femoral popliteal disease ($n = 180$)				0.25
A	20 (11.1)	12 (13.2)	8 (9.0)	
B	88 (48.9)	38 (41.8)	50 (56.2)	
C	23 (12.8)	12 (13.2)	11 (12.4)	
D	49 (27.2)	29 (31.9)	20 (22.5)	
GLASS score ($n = 213$)				0.57
Stage 1	37 (17.4)	17 (17.2)	20 (17.5)	
Stage 2	74 (34.7)	31 (31.3)	43 (37.7)	
Stage 3	102 (47.9)	51 (51.5)	51 (44.7)	
Original Bollinger score	42 (27.25,54)	43 (28,56)	39 (27,51)	0.17
Extended version of the Bollinger score	91 (51.25,119.75)	88 (42.5,119)	95 (56,121)	0.28
Intervention successful rate	282 (95.3)	147 (96.1)	135 (94.4)	0.50
Type of intervention				0.001
PTA only	198 (70.2)	91 (61.9)	107 (79.3)	
Stent	84 (29.8)	56 (38.1)	28 (20.7)	

Values are n (%), mean ± SD or median (interquartile range). CVD, cardiovascular disease; DM, diabetic mellitus; ESRD, end-stage renal disease; GLASS, global limb anatomic staging system; HTN, hypertension; SD, standard deviation; PTA, percutaneous transluminal angioplasty; TASC, Trans-Atlantic Inter-Society Consensus

real-world practice, showed that ESRD was a strong predictor of worse 4-year survival (HR: 2.69; 95% CI: 1.80–4.02; $p < 0.001$). However, the non-matched cohort may not fully represent the broader PAD population, and no prior studies have specifically reported long-term EVT outcomes in patients with both PAD and ESRD. Rising MACCE rates in the ESRD group were largely driven by MI (HR: 4.09; 95% CI: 1.93–8.66; $p < 0.001$), contributing to higher cardiac death rates (HR: 4.76; 95% CI: 1.34–6.92; $p = 0.008$). Despite these risks, adherence to guideline-directed medical therapy (GDMT) [24] was suboptimal, with only 66.4% of ESRD patients

Table 2 Baseline clinical characteristics after the propensity score-matched cohorts

	Non-ESRD	ESRD	*p* value
Patients	**100 (50.0)**	**100 (50.0)**	
Age (years)	70.2 ± 11.8	71.0 ± 9.5	0.58
Follow-up intervals - months	26.6 (10.1,40.2)	19.2 (7.4,35.9)	0.10
Male sex	60 (60.0)	62 (62.0)	0.78
Current smoker	21 (21.0)	13 (13.0)	0.13
CVD history	35 (35.0)	39 (39.0)	0.56
Stroke history	23 (23.0)	27 (27.0)	0.51
HTN	76 (76.0)	70 (70.0)	0.34
DM	78 (78.0)	86 (86.0)	0.14
Hyperlipidemia	55 (55.0)	58 (58.0)	0.67
Previous statin	50 (50.0)	49 (49.0)	0.89
Previous antiplatelet	62 (62.0)	63 (63.0)	0.89
Rutherford classification			0.15
3	23 (23.0)	12 (12.0)	
4	5 (5.0)	5 (5.0)	
5	50 (50.0)	64 (64.0)	
6	22 (22.0)	10 (10.0)	
Previous ipsilateral intervention	15 (15.0)	13 (13.0)	0.68
Previous contralateral intervention	21 (21.0)	22 (22.0)	0.86
Intervention left side	47 (47.0)	54 (54.0)	0.32
Multilevel disease	32 (32.0)	33 (33.0)	0.88
Aortoiliac occlusive disease	25 (25.0)	16 (16.0)	0.12
Femoropopliteal lesion	63 (63.0)	62 (62.0)	0.88
Infrapopliteal lesion	46 (46.0)	56 (56.0)	0.16
Lesion length (mm)	149.8 ± 107.1	157.9 ± 106.5	0.59
TASC II classification of aorto-iliac disease ($n = 41$)			0.72
A	11 (44.0)	7 (43.8)	
B	8 (32.0)	7 (43.8)	
C	1 (4.0)	0 (0)	
D	5 (20.0)	2 (12.5)	
TASC II Classification of femoral popliteal disease ($n = 125$)			0.80
A	10 (15.9)	7 (11.3)	
B	31 (49.2)	33 (53.2)	
C	6 (9.5)	8 (12.9)	
D	16 (25.4)	14 (22.6)	
GLASS score ($n = 148$)			0.70
Stage 1	13 (19.4)	14 (17.3)	
Stage 2	22 (32.8)	32 (39.5)	
Stage 3	32 (47.8)	35 (43.2)	
Original Bollinger score	43 (26.5, 55)	39 (28,51)	0.53
Extended version of the Bollinger score	88 (51.5, 125.75)	93 (54.5, 118.0)	0.91
Intervention successful rate	94 (94.0)	95 (95.0)	0.76
Type of intervention			0.08
PTA only	67 (67.0)	78 (78.0)	
Stent	33 (33.0)	22 (22.0)	

Values are n (%), mean ± SD or median (interquartile range). CVD, cardiovascular disease; DM, diabetic mellitus; ESRD, end-stage renal disease; GLASS, global limb anatomic staging system; HTN, hypertension; SD, standard deviation; PTA, percutaneous transluminal angioplasty; TASC, Trans-Atlantic Inter-Society Consensus

on antiplatelet therapy and 44.8% on statins (Table 1). Enhanced efforts are needed to improve GDMT adherence to reduce MACCE risks, particularly MI, in this high-risk population.

For localized outcomes such as MALEs, major amputations, and target lesion repeat revascularization, the study did not find ESRD alone to be a direct influencer after PSM, though the ESRD cohort did show a trend towards worse outcomes. This finding is consistent with a previous study [25] that demonstrated no impact on functional lower limb outcomes in CKD patients undergoing endovascular therapy for CLTI. However, in the full cohort (before PSM), significantly worse localized outcomes were observed in the ESRD group, which was

Table 3 Clinical outcome rates and unadjusted and propensity score–matched hazard ratios on the basis of on-ESRD versus ESRD

	Non-ESRD (*n* = 153, %)	ESRD (*n* = 143, %)	Unadjusted HR (95% CI)	*p* value	Non-ESRD (*n* = 100)	ESRD (*n* = 100)	PSM HR (95% CI)	*p* value
MACCEs	34 (39.9)	80 (79.9)	2.69 (1.80–4.02)	< 0.001	22	57	3.88 (2.30–6.53)	< 0.001
All-cause death	17 (21.2)	46 (53.8)	2.89 (1.66–5.04)	< 0.001	10	35	4.54 (2.17–9.48)	< 0.001
Cardiac death	4 (3.8)	15 (21.8)	3.97 (1.32–11.97)	0.008	4	13	4.76 (1.34–16.92)	0.008
Noncardiac death	13 (18.0)	31 (40.9)	2.56 (1.34–4.88)	0.003	6	22	4.43 (1.79–10.94)	< 0.001
Myocardial infarction	13 (12.6)	41 (56.0)	3.68 (1.97–6.88)	< 0.001	10	29	4.09 (1.93–8.66)	< 0.001
Stroke	8 (11.3)	13 (18.6)	1.68 (0.70–4.06)	00.24	4	9	3.22 (0.85–12.16)	0.069
MALEs	38 (34.9)	60 (61.0)	1.84 (1.22–2.76)	0.003	32	37	1.23 (0.76–1.99)	0.40
Major amputation	6 (4.5)	21 (20.4)	3.80 (1.53–9.42)	0.002	5	10	2.13 (0.73–6.23)	0.16
Repeat revascularization	34 (32.3)	48 (54.7)	1.60 (1.03–2.48)	0.035	29	30	1.09 (0.65–1.83)	0.76
Amputation-free survival	114 (75.2)	71 (38.4)	*2.14 (1.45–3.15)	< 0.001	85	39	*2.13 (1.34–3.39)	< 0.001
Any amputation	43 (34.8)	62 (56.8)	1.68 (1.14–2.49)	0.008	30	39	1.44 (0.89–2.33)	0.13
≧2 repeat revascularization	8 (8.0)	16 (21.2)	2.18 (0.93–5.09)	0.066	7	9	1.15 (0.40–3.28)	0.80
Contralateral limb intervention	27 (29.6)	46 (62.8)	1.99 (1.24–3.21)	0.004	21	32	1.85 (1.06–3.22)	0.029

Values are n (% of the cumulative rates at 4 years according to Kaplan-Meier event rates) or mean ± standard deviation. The p values are from the log-rank test. CI, confidence interval; ESRD, end-stage renal disease; HR, hazard ratio; MACCEs, major adverse cardiac and cerebrovascular events; MALEs, major adverse limb events; PSM, propensity score–matched. *The hazard ratio for the combined endpoint of major amputation or all-cause death

attributed to the more severe condition of lower limbs in ESRD patients—88.1% of ESRD patients presented with CLTI compared to 75.2% of non-ESRD patients. This mirrors real-world practices, where more severe disease is associated with higher incidences of MALEs and major amputations. (Supplement Figure S5). After adjusting for confounding factors, ESRD was not independently associated with an increase in localized outcomes. Given the high prevalence of CLTI and worse limb outcomes in ESRD patients, closer surveillance for early signs of CLTI is crucial to enable timely intervention. While preventing PAD progression before CLTI is not well established, current guidelines recommend prompt detection and treatment of CLTI to improve outcomes [26]. Previous studies have reported major amputation rates ranging from 18 to 40% at three years for ESRD patients who underwent prior revascularization for PAD [27–30], with a reintervention rate of about 40% at the three-year mark [27–29]. In the current study, the estimated 3-year major amputation rate in ESRD patients was 17.5%, which is slightly lower than rates reported in previous studies. Cultural values and preferences regarding limb salvage may have contributed to this difference. However, the need for revascularization remained high, with 69.8% of ESRD patients undergoing repeat procedures within three years (Supplementary Figure S1)—a rate that exceeds those reported in other studies. The authors suggest that cultural values in Taiwan may have played a role in patients' decisions regarding amputation, resulting in a lower rate of major amputations and a higher frequency of revascularizations for non-functional limbs, as patients often hold higher expectations for limb salvage. Additionally, in the ESRD group, 7.9% of patients died from sepsis caused by severe CLTI-related infections above the ankle, with 60% of these patients having refused major amputation to control the infection (Supplement Table S3). To address this serious issue, early patient education regarding the risks of infection, multidisciplinary team discussions, and prompt management of localized infections may be critical strategies to prevent progression to systemic sepsis and mortality.

Several studies have explored predictors of MACCEs in patients with PAD after EVT. According to Cho et al. [31], factors such as age, ESRD, and a history of coronary artery bypass graft (CABG) were identified as predictors of MACCEs. However, in the present study, ESRD was the sole independent predictor of increased MACCE risk, underscoring the importance of recognizing and managing ESRD as a major risk factor in PAD patients undergoing EVT. This finding suggests that while other factors like age and prior CABG may contribute to MACCEs in some cohorts, ESRD plays a more dominant role in adverse systemic outcomes in PAD patients treated with EVT.

Given the unique healthcare environment in Taiwan, where the National Health Insurance system provides extensive coverage, the study cohort includes a higher proportion of ESRD patients (48.3%) in the study cohort. These patients typically have more severe disease and more comorbidities, increasing their operative risks. Given these factors, endovascular therapy was favored over surgical revascularization in this study, a preference supported by earlier research [32] showing a nearly threefold increase in the use of endovascular procedures compared to a decline in surgical revascularization rates. Surgical revascularization has been linked to higher complication rates in patients on dialysis. In the recent study, The BEST-CLI trial [8] demonstrated that surgical revascularization with autogenous vein grafting yielded better long-term limb outcomes than EVT in PAD patients with CLTI. However, only about 10.6% of the trial participants had ESRD, limiting the applicability

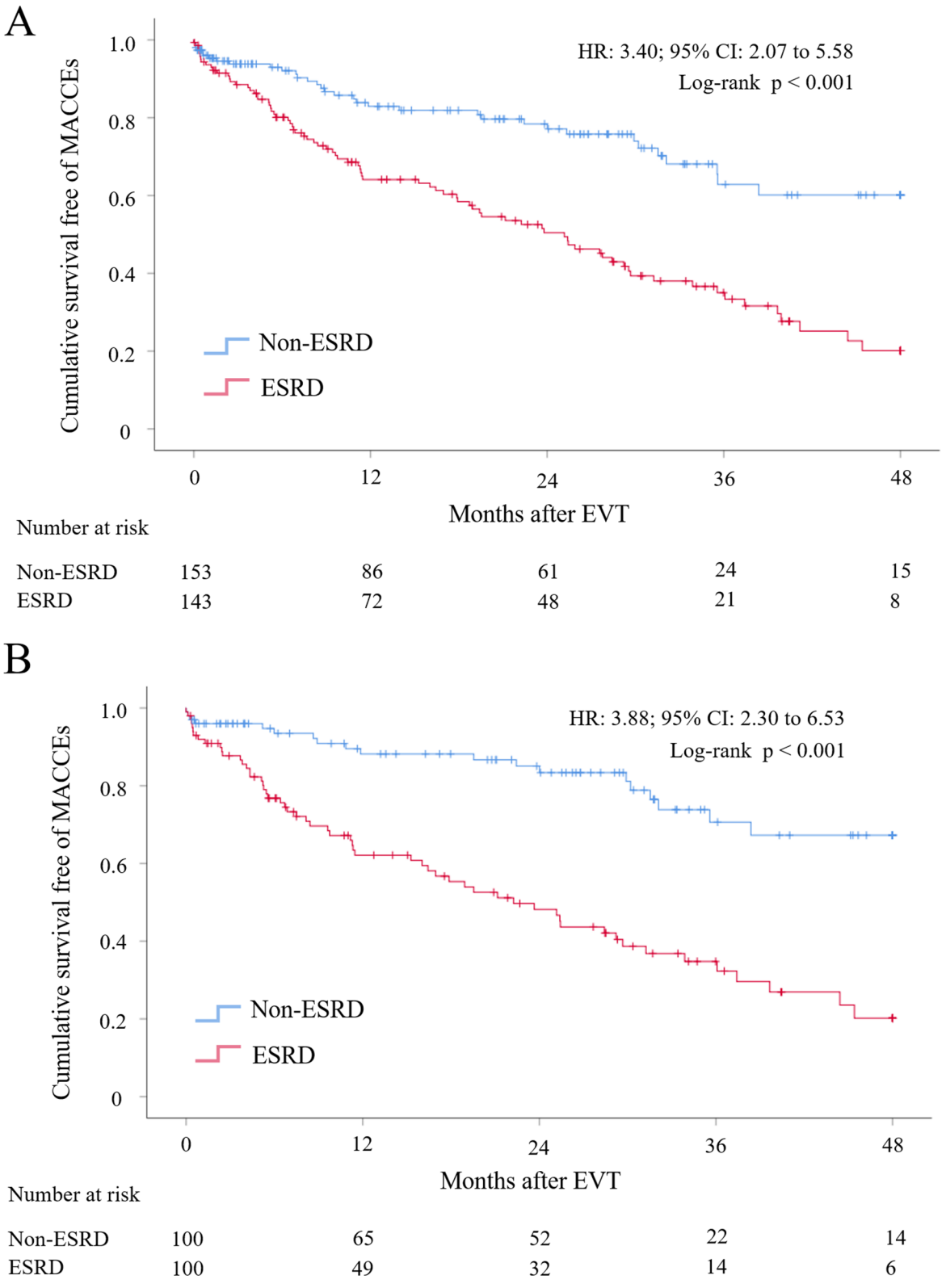

Fig. 1 Kaplan-Meier survival curves for MACCEs: non-ESRD versus ESRD. (A) entire population survival curves (B) propensity score-matched survival curves. CI = confidence interval; ESRD = end-stage renal disease; EVT = endovascular treatment; HR = hazard ratio; MACCEs = major adverse cardiac and cerebrovascular events

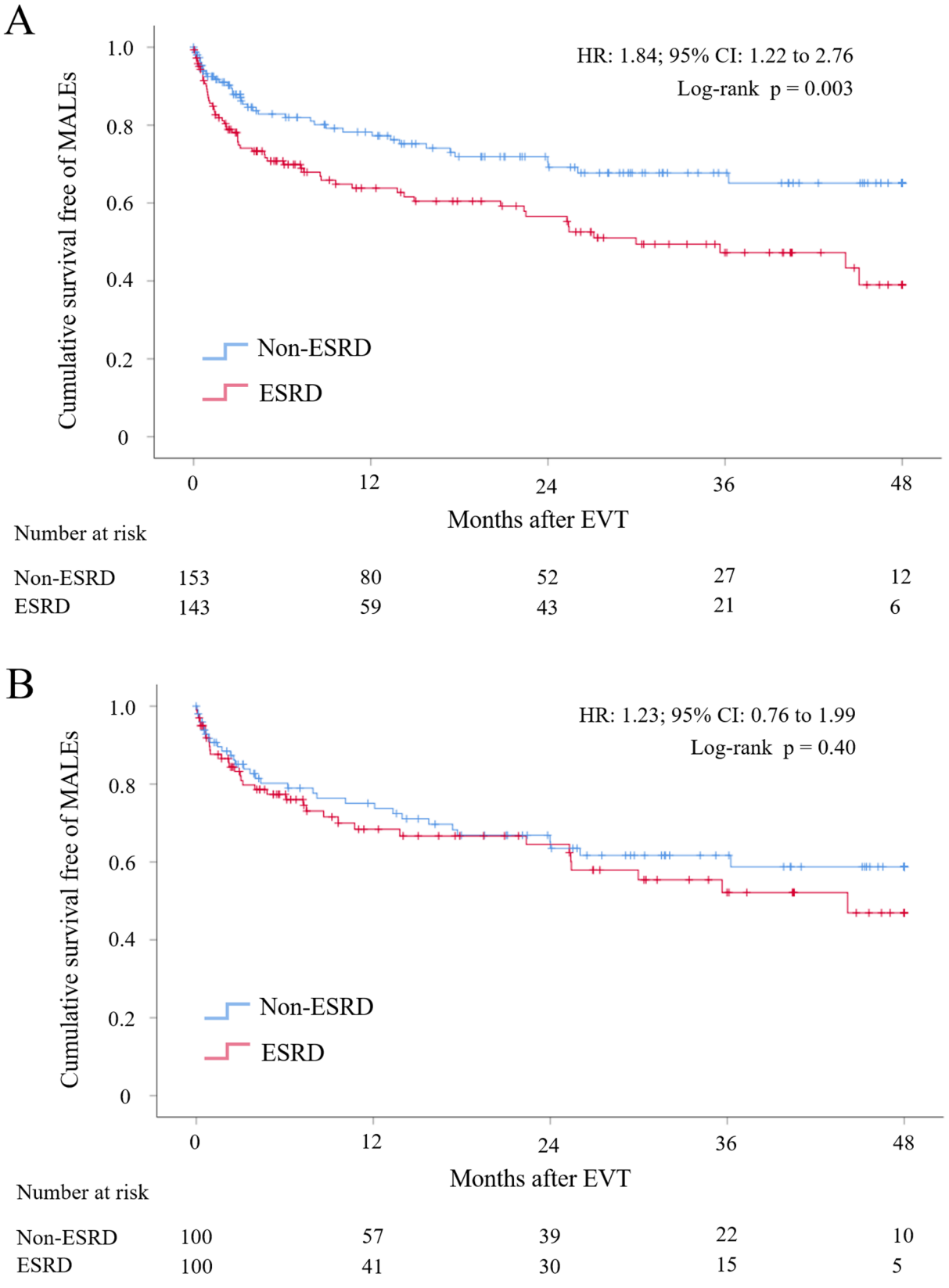

Fig. 2 Kaplan-Meier survival curves for MALEs: non-ESRD versus ESRD. **A**. entire population survival curves **B**. propensity score-matched survival curves. CI = confidence interval; ESRD = end-stage renal disease; EVT = endovascular treatment; HR = hazard ratio; MALEs = major adverse limb events

Table 4 Clinical outcome rates and unadjusted and propensity score–matched hazard ratios on the basis of on-ESRD versus ESRD within 30 days

	Non-ESRD (*n* = 153)	ESRD (*n* = 143)	Unadjusted HR (95% CI)	*p* value	PSM HR (95% CI)	*p* value
MACCEs	6 (4.0)	9 (6.4)	1.60 (0.57–4.49)	0.37	2.02 (0.61–6.70)	0.24
All-cause death	3 (2.0)	5 (3.5)	1.76 (0.42–7.38)	0.43	2.49 (0.48–12.85)	0.26
MALEs	11 (7.5)	18 (13.0)	1.75 (0.83–3.71)	0.14	1.33 (0.56–3.16)	0.52

Values are n (% of the cumulative rates at 30 days according to Kaplan-Meier event rates) or mean ± standard deviation. The p values are from the log-rank test. CI, confidence interval; ESRD, end-stage renal disease; HR, hazard ratio; MACCEs, major adverse cardiac and cerebrovascular events; MALEs, major adverse limb events; PSM, propensity score–matched

Table 5 Predictors of MACCEs after endovascular intervention

MACCEs	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age (per 1-yr increase)	1.01 (0.99–1.03)	0.22		
Male	1.03 (0.71–1.51)	0.87		
Current smoker	0.62 (0.37–1.04)	0.07	0.80 (0.48–1.36)	0.41
CVD Hx	1.34 (0.92–1.95)	0.12		
Stroke Hx	1.09 (0.71–1.65)	0.71		
ESRD	2.69 (1.80–4.02)	< 0.001	2.49 (1.65–3.75)	< 0.001
HTN	1.27 (0.81–1.99)	0.30		
DM	1.32 (0.82–2.12)	0.25		
Hyperlipidemia	0.93 (0.64–1.35)	0.70		
Previous antiplatelet	1.15 (0.78–1.68)	0.49		
CLTI	1.77 (1.06–2.97)	0.03	1.46 (0.87–2.46)	0.16
Previous ipsilateral intervention	1.23 (0.78–1.92)	0.38		
Previous contralateral intervention	0.93 (0.59–1.47)	0.75		
Multilevel disease	1.22 (0.82–1.81)	0.32		
Stent	0.73 (0.48–1.12)	0.15		

CI, confidence interval; CLTI, chronic limb-threatening ischemia; CVD, cardiovascular disease; DM, diabetic mellitus; ESRD, end-stage renal disease; HR, hazard ratio; HTN, hypertension; MACCEs, major adverse cardiac and cerebrovascular events

of the results to the broader ESRD population. Notably, a subgroup analysis of patients with ESRD revealed comparable outcomes between the bypass and EVT groups. Similarly, the BASIL-2 trial [10] included only 4.3% of dialysis patients, further restricting the generalizability of the findings. These limitations indicate a need for more studies focused on ESRD patients to guide optimal treatment strategies A meta-analysis [7] reported no significant increase in repeat revascularization rates with a surgical revascularization strategy for ESRD patients (OR: 1.09; 95% CI, 0.53–2.24; $p = 0.82$), while endovascular therapy was associated with an increase in repeat procedures (OR: 1.84; 95% CI, 1.32–2.56, $p < 0.01$). However, another study [33] found that the choice of revascularization strategy did not affect AFS (HR: 0.92; 95% CI, 0.67–1.27; $p = 0.62$). Interestingly, surgical revascularization was unexpectedly associated with an increased risk of major amputation compared to EVT (HR: 1.59; 95% CI, 0.98–2.58; $p = 0.06$) in dialysis patients, pointing to the ongoing debate about the optimal revascularization approach in this high-risk population.

Limitations

This study has several limitations, including its retrospective, non-randomized design and relatively small sample size, which constrain the strength of the findings. While baseline covariates differed significantly between the control and treatment groups, 1:1 PSM was used to reduce potential confounding bias. Approximately 22.3% of patients had aortoiliac occlusive disease, limiting the generalizability to those with infrainguinal lesions. For the chronic limb-threatening ischemia (CLTI) analysis, unequal case numbers between groups-higher in the ESRD group even after PSM—necessitated a subgroup analysis, which confirmed worse MACCE outcomes in the ESRD group regardless of CLTI or intermittent claudication. Cultural factors may have led to an underestimation of major amputation rates and an overestimation of repeat revascularization rates. In our study, we included only patients who underwent endovascular therapy (EVT), recognizing that the optimal revascularization strategy—EVT versus surgical bypass—for this high-risk population remains controversial. Therefore, our findings may not be generalizable to patients who undergo surgical bypass. Additionally, while the average follow-up period was 34.9 months, we analyzed

outcomes up to 4 years, and results beyond the mean follow-up should be interpreted with caution. Despite these limitations, the findings reflect real-world clinical practice and provide valuable insights into managing PAD in ESRD patients after EVT.

Conclusions

In both the overall cohort and after PSM, PAD patients with ESRD had significantly worse systemic outcomes following EVT compared to those without ESRD, including higher MACCE incidence, all-cause mortality, and myocardial infarction (MI) risk. Preventing MACCEs, particularly MI, is critical in this high-risk group. While the ESRD group exhibited more severe limb conditions and worse localized outcomes in the full cohort, PSM analysis revealed no significant increase in MALE incidence attributable to ESRD alone. These findings highlight the systemic impact of ESRD and underscore the importance of optimizing medical therapy to improve outcomes in PAD patients with ESRD.

Abbreviations

AFS	Amputation-free survival
AHA/ACC	American College of Cardiology/ American Heart Association
CI	Confidence interval
CKD	Chronic kidney disease
CLTI	Chronic limb-threatening ischemia
CVD	Cardiovascular disease
DM	Diabetic mellitus
eGFR	Estimated glomerular filtration rate
ESRD	End-stage renal disease
EVT	Endovascular treatment
GBD	Global burden of diagnosis
GDMT	Guideline-directed medical therapy
GLASS	Global limb anatomic staging system
HR	Hazard ratio
HTN	Hypertension
MACCEs	Major adverse cardiac and cerebrovascular events
MALEs	Major adverse limb events
MI	Myocardial infarction
NHANES	National Health and Nutrition Examination Survey
NHI	National Health Insurance
OR	Odd ratio
PAD	Peripheral artery disease
PSM	Propensity score-matched
PTA	Percutaneous transluminal angioplasty
TASC	Trans-Atlantic Inter-Society Consensus
RCT	Randomized control trial

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Not applicable.

Author contributions

S.-Y. T., C.-H. Y.; Data collection: S.-Y. T., T.-Y. H., H.-Y. L.; Data analysis: S.-Y. T., Y.-C. W., C.-H. Y.; Writing: S.-Y. T., T.-Y. H., H.-Y. L., Y.-C. W., C.-H. Y.

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Data availability

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

Declarations

Ethics approval and consent to participate

The study adhered to the ethical guidelines of the 1975 Declaration of Helsinki. It was reviewed and approved by the Institutional Review Board of Chang Gung Medical Foundation (Institutional Review Board of Chang Gung Medical Foundation, IRB No: 202201849B0), which waived the need for an informed consent statement.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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