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Outcome evaluation of percutaneous coronary intervention vs medical therapy alone in patients with chronic coronary syndrome

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Abstract

This study provides real-world evidence by comparing the long-term clinical outcomes of percutaneous coronary intervention (PCI) versus medical therapy alone in patients with chronic coronary syndrome (CCS) diagnosed non-invasively, given the lack of evidence in this population. This retrospective cohort study (2013−2018) utilized data from a medical center's Cardiovascular Disease Databank, which was linked to national mortality records in Taiwan. Propensity score matching (PSM) and stabilized inverse probability of treatment weighting (IPTW) were applied to adjust for baseline differences between the PCI and medication-only groups. Major adverse cardiovascular events (MACE), including all-cause mortality, non-fatal myocardial infarction (MI), and revascularization, were compared between groups. After 1:4 propensity score matching, a total of 4369 patients were included (PCI, N = 1058; medication only, N = 3311). Adjusted Cox proportional hazards models showed that the PCI group had a higher hazard of MACE (aHR, 1.38 [95% CI, 1.22−1.56]), primarily driven by increased revascularization (aHR, 1.65 [95% CI, 1.39−1.95]), compared to the medication-only groups. No significant differences were observed in all-cause mortality (aHR, 1.13 [95% CI, 0.96−1.34]) or MI (aHR, 1.08 [95% CI, 0.77−1.52]). Furthermore, the mean total healthcare cost during the index year was US$3232 (SD = 9896) for the medication-only group, compared with US$10,931 (SD = 8781) for the PCI group. Among CCS patients diagnosed non-invasively, the medication-only group demonstrated comparable all-cause mortality and MI rates, but a significantly lower risk of revascularization compared with the PCI group, while incurring only one-third of the healthcare costs. Clinicians should carefully evaluate the benefits and risks of stent placement in CCS patients.

Keywords: Coronary artery disease, Drug therapy, Percutaneous coronary intervention

1. Introduction

Coronary artery disease is the leading cause of premature and avoidable death worldwide [1]. It is classified into acute or chronic coronary syndrome (CCS) based on clinical presentation. CCS includes obstructive and non-obstructive coronary artery disease, ischemic heart disease diagnosed solely by non-invasive testing, and chronic angina syndromes with varying etiologies

Received 12 November 2025; accepted 24 June 2026.
Available online 28 August 2026

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https://doi.org/10.38212/2224-6614.3604
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[2,3]. Current guideline-directed management emphasizes lifestyle modification and pharmacologic therapy. Percutaneous coronary intervention (PCI) is recommended only for specific cases, such as patients with an ejection fraction (EF) below 35% or high-risk anatomical features [3,4].

This recommendation is based on large randomized controlled trials (RCT), including COURAGE and ISCHEMIA [5,6], which found no significant difference in major adverse cardiovascular events (MACE) between patients undergoing PCI or medical therapy only, with benefits observed only in angina symptom relief in the ORBITA 2 trail [7]. However, these trials included only patients with >70% coronary artery stenosis diagnosed via invasive angiography, which may not reflect real-world CCS scenarios, where diagnosis is often based on non-invasive tests such as treadmill exercise tests (TET), thallium scans, or coronary computed tomography angiography (CCTA). Given the high false-positive rates of these tests, RCT often select more precise assessments such as invasive angiography. Nevertheless, comparing the effectiveness of PCI versus medical therapy alone in patients diagnosed solely through non-invasive testing remains a clinically important question.

Advancements in catheter technology and drug-eluting stent design have significantly reduced the rate of in-stent restenosis to approximately 2% per year [8], thereby minimizing the risks associated with PCI in CCS patients. Additionally, the increasing use of CCTA has enhanced the accuracy of CCS diagnosis. Given these technological improvements, reassessing the role of PCI in contemporary CCS management is both relevant and necessary.

Conversely, the reduction in PCI-related complications may have led to its overuse in CCS patients. Some physicians have coined the term “oculo-stenotic reflex” to illustrate concerns regarding frequent repeat revascularization [9]. In addition to prognostic implications, cost considerations must also be considered. Therefore, evaluating the long-term clinical and economic outcomes of PCI compared with medical therapy alone in CCS patients remains a critical area of research.

This study included patients with positive non-invasive test results and classified them into two groups based on whether they received PCI or medical therapy alone. Differences in outcomes were analyzed, including MACE, all-cause mortality, MI, and the need for repeat revascularization. Since Taiwan's National Health Insurance database does not provide non-invasive test results, a retrospective study was conducted using hospital-based data.

2. Methods

2.1. Study design

This retrospective study selected eligible patients with positive non-invasive test results from the Cardiovascular Disease Databank at National Cheng Kung University Hospital (NCKUH) between January 1, 2013, and December 31, 2018 [10]. NCKUH is a 1198-bed medical center in southern Taiwan. To mitigate immortal time bias, the study employed a landmark design [11], establishing a one-year landmark period after the first positive non-invasive stress test. The requirement for informed consent was waived for this study due to its retrospective design and was approved by the Institutional Review Board of National Cheng Kung University Hospital (IRB number: B-ER-110-416).

2.2. Study population

Adult patients who underwent a non-invasive stress test for the first time and had positive results were included. Positive test results were defined as one of the following: a positive TET report, a medium or large area of perfusion defect on a thallium scan, or more than 50% stenosis of a coronary artery on CCTA.

Patients were excluded if CCTA showed left main coronary artery (LM)stenosis $\geq$50% or if echocardiography found Left Ventricular EF <35%, as these conditions generally require invasive management [3], Other key exclusion criteria were applied to better isolate the impact of non-invasive assessment on subsequent clinical decision-making and outcomes in patients with CCS: 1) Undergoing PCI or coronary artery bypass grafting (CABG) within six months prior to the non-invasive stress test; 2)Being lost to follow-up, deceased, receiving neither antiplatelet nor statin therapy, hospitalized for MI, or undergoing CABG during the landmark period; 3) Since undergoing two or more PCI procedures within three months could indicate staged PCI [12], only patients who underwent a second PCI between four and twelve months after the non-invasive stress test were excluded. These exclusion criteria were to ensure a more homogeneous study population and to reduce confounding from clinical scenarios that mandate invasive intervention regardless of non-invasive test results.

Patients who underwent PCI within the landmark period were classified into the PCI group, while

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those who did not undergo PCI were assigned to the medication group. Clinical information, including age, sex, body mass index, comorbidities, angiographic findings, and medication use during the landmark period, was recorded. Each variable for comorbidity was identified based on physician documentation, laboratory findings, prescribed treatments, and International Classification of Diseases codes. Medication adherence was assessed based on the proportion of days covered (PDC) for antiplatelet or statin therapy. Patients with PDC exceeding 80% during the landmark period were classified as having good medication adherence [13], while those below this threshold were considered to have poor adherence.

2.3. Outcomes

Clinical outcomes were obtained for the study population from electronic medical records at NCKUH until December 31, 2022. The primary endpoint was the incidence of MACE, defined as a composite of all-cause mortality, MI, and coronary revascularization. Secondary endpoints included the individual components of MACE: all-cause mortality, MI, and coronary revascularization. All-cause mortality data were obtained from Taiwan's nationwide all-cause mortality records, while MI and coronary revascularization data were sourced from the Cardiovascular Disease Databank at NCKUH. Healthcare utilization and cost data were retrieved from the NCKUH hospital billing system, including costs covered by Taiwan's National Health Insurance (NHI) and out-of-pocket expenses paid by patients. Healthcare costs converted to US dollars at the average exchange rate of US$1 = TW$30.

2.4. Statistical analysis

Missing data were imputed using the fully conditional specification method for multiple imputation, applied to the Body Mass Index (BMI) variable, which was categorized into four groups: BMI <18.5, 18.5 ≤ BMI <24, 24 ≤ BMI <27, with BMI ≥27 used as the reference group. Propensity scores for receiving PCI were estimated using logistic regression: Baseline covariates were selected a priori based on clinical relevance and prior literature, and were measured before (or at the time of) treatment assignment within the landmark period. Covariates included demographic characteristics (age, sex, and body mass index), comorbidities (diabetes mellitus, hyperlipidemia, hypertension, chronic kidney disease, cancer, heart failure, and atrial fibrillation), medical history (prior myocardial infarction and prior stroke), procedural history (previous percutaneous coronary intervention and coronary artery bypass grafting), and the number of stenotic coronary vessels. The standardized mean differences (SMDs) were used to assess balance between matched or weighted sample, with SMDs >0.1 indicating imbalance results [14]. Two propensity score methods were employed. PSM was chosen as the primary analysis to estimate the average treatment effect among the treated (ATT) for PCI [15], while inverse probability of treatment weighting was conducted as a sensitivity analysis to estimate the average treatment effect (ATE) in the overall study population [16]. PSM was performed using a 1:4 nearest-neighbor matching algorithm without replacement, with a caliper width of 0.2 [17]. We used stabilized inverse probability of treatment weighting in all weighting analyses. For consistency, we refer to this approach as "IPTW" throughout the manuscript. Stabilization multiplies the weights by the marginal probability of treatment, thereby reducing the influence of extreme weights [15].

Cumulative incidence functions were used to estimate the incidence of MACE, all-cause mortality, MI, and coronary revascularization. For MI and coronary revascularization, all-cause mortality was treated as a competing risk. The log-rank test and Gray's test were applied to compare the cumulative incidence between the PCI and medication groups. Cox proportional hazards models were used with proportional hazards assumptions tested prior to model execution. To account for competing risks when analyzing MI and revascularization, Fine and Gray's method was used for competing risk survival analysis, and sub-distribution hazard model was applied [18]. Variables with an SMD >0.1 were included as control variables in multivariable survival analyses. Given the known association between medication adherence and clinical outcomes in coronary artery disease patients [19], a stratified analysis was conducted to test the interaction of PCI and medication adherence. A p-value of <0.05 was considered statistically significant. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, U.S.), and forest plots were generated using Tableau Version 2023.1 (Tableau Software, Seattle, Washington, U.S.).

3. Results

3.1. Study population

A total of 14,043 patients who underwent a non-invasive stress test and had positive results were retrospectively screened, and 5736 patients (mean

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age: 65 ± 11 years; 38% female) were included after applying exclusion criteria. Among them, 1069 patients (19%) were classified into the PCI group, while 4667 (81%) were assigned to the medication group (Fig. 1). Table 1 shows the baseline characteristics of the unmatched, matched, and the IPTW adjusted group comparisons. After 1:4 PSM, the matched sample consisted of 4369 patients, with 3311 in the medication group and 1058 in the PCI group. SMDs >0.1 indicated that residual imbalances between the PCI and medication groups, including a lower proportion of female patients, a higher prevalence of previous MI, and a greater proportion of patients with a history of PCI in the PCI group. Following IPTW adjustment, the total sample size was 5724, with 4671 patients in the medication group and 1053 in the PCI group. SMDs for all variables, except for drug use, were <0.1, indicating that the two groups were adequately balanced.

3.2. Clinical outcomes

The mean follow-up duration was 4.3 ± 2.2 years, with a maximum follow-up of approximately nine years. The incidence rate of MACE per 1000 person-years in the propensity score-matched sample was 60.6 (95% CI: 56.7–64.7) in the medication group and 95.9 (95% CI: 86.9–105.5) in the PCI group. Kaplan–Meier analysis on the PSM sample found that the risk of MACE (log-rank test, $p < 0.001$) and all-cause mortality (log-rank test, $p = 0.013$) was significantly higher in the PCI group than in the medication group (Fig. 2). Consistent findings were observed for myocardial infarction (Gray's test, $p = 0.019$) and revascularization (Gray's test, $p < 0.001$) (Fig. 2). Nevertheless, after IPTW adjustment, significant differences were observed only in MACE ($p < 0.001$) and revascularization ($p < 0.001$) (Supplement Fig. 1 (https://doi.org/10.38212/2224-6614.3604)).

Table 2 shows that the PSM and IPTW analyses yielded largely consistent results in Cox regression models adjusted for baseline characteristics and medications. After adjustment, PCI remained associated with a higher risk of MACE in both methods (PSM:aHR, 1.38 [95% CI: 1.22–1.56]; IPTW: aHR,1.41 [95% CI: 1.25–1.59]), while the associations with all-cause mortality (PSM:aHR, 1.13 [95% CI: 0.96–1.34]; IPTW:aHR, 1.05 [95% CI: 0.89–1.24]) and MI (PSM:aHR, 1.08 [95% CI: 0.77–1.52]; IPTW:aHR, 1.10 [95% CI: 0.79–1.53]) were attenuated and no longer statistically significant. Revascularization remained

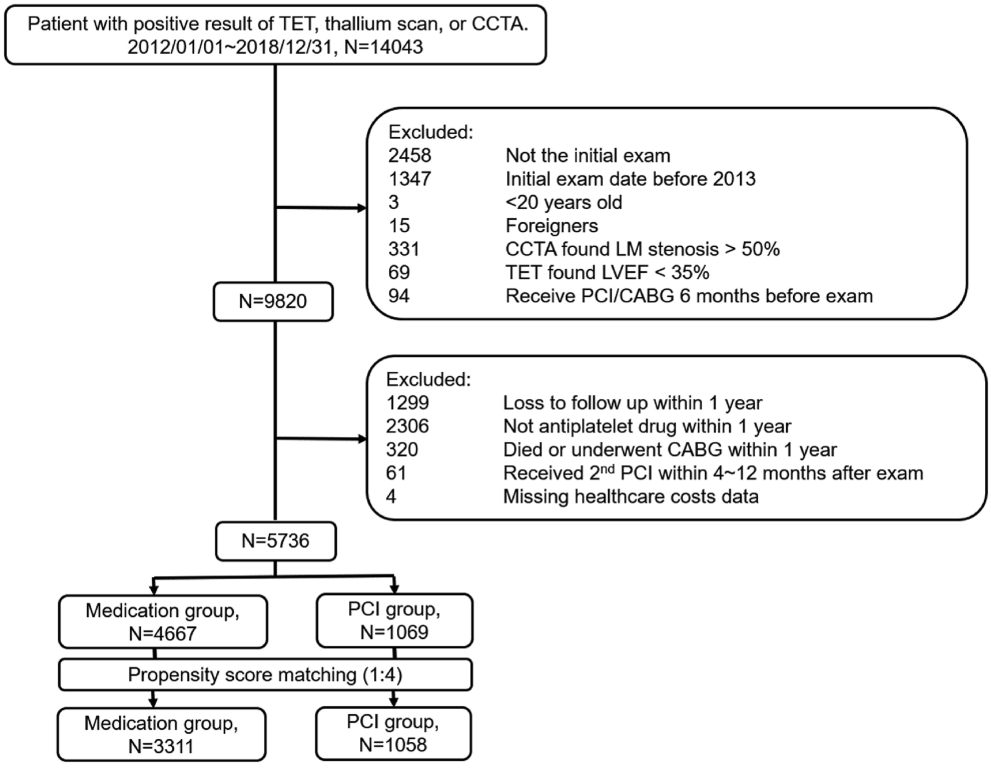


Fig. 1. Flow diagram of the study cohort (CABG: coronary artery bypass grafting; CCTA: coronary computed tomography angiography; LM: left main coronary artery; LVEF: left ventricular ejection fraction; MI: myocardial infarction; N: number of participants; PCI: percutaneous coronary intervention; TET: treadmill exercise tests).

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Table 1. Baseline characteristics.

	Unmatched			PSM			IPTW adjusted		
	Medication group	PCI group	SMD	Medication group	PCI group	SMD	Medication group	PCI group	SMD
	(n = 4667)	(n = 1069)		(n = 3311)	(n = 1058)		(n = 4671)	(n = 1053)	
Age (years old)	64.50 ± 11.45	65.97 ± 10.95	0.13*	65.55 ± 11.19	65.87 ± 10.90	0.03	64.80 ± 11.45	65.30 ± 10.97	0.04
Sex (female)	40.28	27.41	0.27*	31.98	27.50	0.10	37.81	37.22	0.03
Body mass index (kg/m^2)	26.19 ± 4.62	26.06 ± 4.12	0.03	26.25 ± 4.68	26.08 ± 4.12	0.04	26.17 ± 4.62	26.15 ± 4.16	0.00
Hypertension	67.02	77.27	0.23*	74.12	77.03	0.07	68.97	70.21	0.03
Diabetes mellitus	38.29	49.95	0.24*	45.30	49.72	0.09	40.51	41.20	0.01
Dyslipidemia	82.13	93.36	0.35*	93.05	93.29	0.01	84.26	86.19	0.05
Chronic kidney disease	25.09	31.90	0.15*	29.02	31.57	0.06	26.49	28.15	0.04
Heart failure	14.81	20.39	0.15*	17.28	19.75	0.06	15.90	17.32	0.04
Atrial fibrillation	9.81	14.31	0.14*	11.69	13.99	0.07	10.60	10.62	0.00
Cancer	17.61	16.74	0.02	16.76	16.73	0.00	17.45	16.68	0.02
Old myocardial infarction	8.83	19.55	0.31*	11.99	18.81	0.19*	10.89	11.24	0.01
Stroke	7.24	11.41	0.14*	9.15	11.25	0.07	8.07	8.47	0.01
PCI history	9.00	15.72	0.21*	11.48	15.31	0.11*	10.35	10.65	0.01
CABG history	0.26	0.19	0.01	0.30	0.19	0.02	0.25	0.49	0.04
Angiography finding									
Left main disease		5.14			5.01			4.68	
1 vessel disease		28.72			28.83			33.16	
2 vessel disease		27.88			27.98			28.05	
3 vessel disease		43.22			43.01			37.86	
Drug eluting stent		83.91			84.03			84.61	
Medications									
Aspirin	77.82	98.41	0.67*	76.83	98.49	0.70*	77.68	98.74	0.69*
P2Y12 inhibitors	26.81	99.53	2.29*	28.66	99.53	2.19*	27.77	99.66	2.25*
Statin	61.69	77.17	0.34*	69.68	77.13	0.17*	63.46	71.11	0.16*
Nitrate	67.13	99.72	0.97*	69.28	99.72	0.93*	67.78	99.69	0.96*
Calcium channel blocker	39.96	48.27	0.17*	42.25	48.49	0.13*	40.37	46.78	0.13*
Beta blocker	51.32	65.11	0.28*	53.07	65.31	0.25*	51.90	62.92	0.22*
ACEi/ARB	41.61	55.85	0.29*	46.90	55.86	0.18*	42.99	52.31	0.19*
Nicorandil	30.00	34.14	0.09	29.81	34.12	0.09	30.08	33.81	0.08

Data were presented as mean ± SD or %. *Standardized mean differences (SMD) between medication group and PCI group >0.1.
Abbreviations: PSM: propensity score matching; IPTW: inverse probability of treatment weighting; SMD: Standard mean difference; ACEi: angiotensin-converting enzyme inhibitors; ARB: angiotensin II receptor blocker; CABG: Coronary artery bypass surgery; PCI: percutaneous coronary intervention.

significantly higher in both methods (PSM:aHR, 1.65 [95% CI: 1.39–1.95]; IPTW:aHR, 1.86 [95% CI: 1.58–2.18]).

Table 3 presents healthcare utilization and costs during the index year, comparing the PCI and medication groups. Total healthcare costs included both National Health Insurance (NHI costs) and out-of-pocket expenses (OOP costs). The mean total healthcare costs during the index year were US$10,931 (SD = 8781) in the PCI group, compared to US$3232 (SD = 9896) in the medication group. PCI group also had a higher mean number of outpatient visits per year (19.7) compared to those in the medication group (17.2).

3.3. Subgroup analyses

The results of the primary analysis on MACE were consistent across prespecified subgroups, including those defined by sex, major comorbidities, and the method of non-invasive stress testing (Fig. 3). Notably, for patients diagnosed using CCTA, the hazard ratio did not differ significantly between PCI and medication groups, whereas significant differences were observed in the treadmill exercise test and thallium scan subgroups. The lack of significance in the CCTA subgroup may be attributable to a small sample size of 14%.

To further explore the observed increase in revascularization following PCI, we conducted additional sensitivity analyses to assess whether poor medication adherence contributed to this outcome. Subgroup Kaplan–Meier analysis stratified by medication adherence demonstrated that the differences in hazards for MACE and revascularization between the PCI and medication groups were notably smaller among patients with good adherence than among those with poor adherence (Supplement Fig. 2 (https://doi.org/10.38212/2224-6614.3604)). In the PSM sample, CCS patients with

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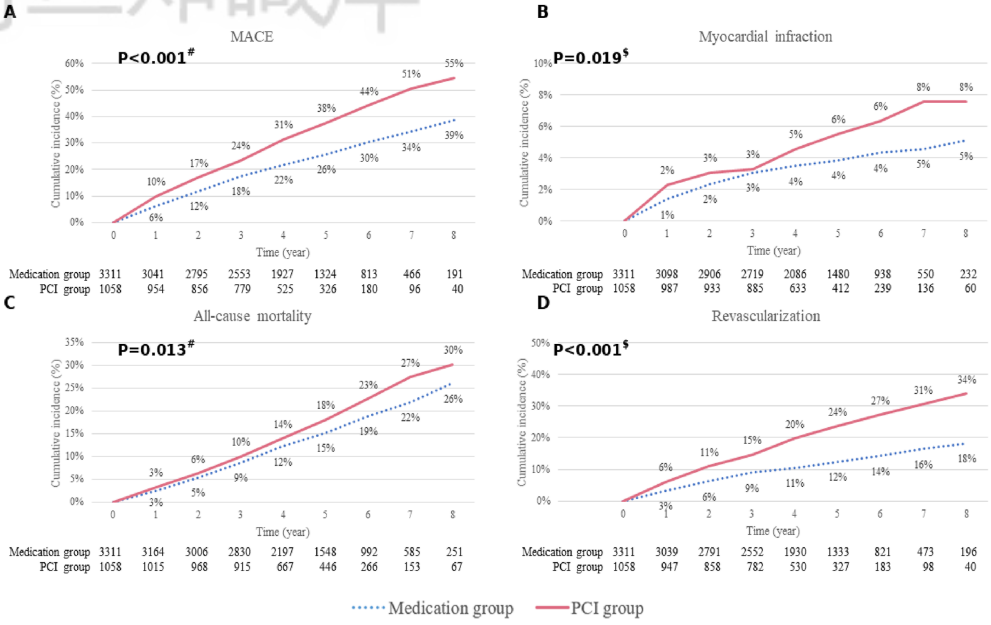


Fig. 2. Cumulative incidence curves of panels: a) MACE (major adverse cardiac events), b) all-cause mortality, c) myocardial infarction, and d) revascularization in patients with PCI or medication groups after propensity score matching (#log-rank test; $Gray's test).

poor adherence exhibited higher hazard ratios for MACE and revascularization compared with patients with good adherence, and the interaction terms were statistically significant (Table 4). This sensitivity analysis underscored that the PCI group had a higher hazard of MACE, primarily driven by revascularization, with an even greater hazard observed among patients with poor medication adherence.

4. Discussions

In this comparative effectiveness study of PCI vs medical therapy alone in lower-risk CCS patients, we found that patients receiving medication-only treatment demonstrated no significant difference in the hazard rate of all-cause mortality or MI compared with those undergoing PCI, while incurring only about one-third of the total healthcare costs. The concordance across PSM (which provides the ATT estimate) and IPTW (which provides the ATE estimate) supports the robustness of the main study findings: the increase in MACE primarily reflects repeated revascularization rather than differences in hard clinical outcomes such as mortality or MI. Moreover, the medication-only group had a lower likelihood of subsequent revascularization. These findings suggest that, for CCS patients diagnosed by non-invasive stress testing, medical therapy achieved comparable clinical outcomes to PCI at substantially lower costs. Furthermore, the risk of revascularization was particularly high among patients with poor medication adherence following PCI.

Unlike previous RCT that primarily used invasive angiography to confirm the diagnosis of coronary

Table 2. Hazard ratios for clinical outcomes among patients comparing the PCI with medication therapy.

	Crude		PSM		IPTW adjusted	
	HR (95% CI)	*p* value	aHR$ (95% CI)	*p* value	aHR& (95% CI)	*p* value
MACE	1.58 (1.41–1.78)	<0.01*	1.38 (1.22–1.56)	<0.01*	1.41 (1.25–1.59)	<0.01*
All-cause mortality	1.23 (1.04–1.44)	0.01*	1.13 (0.96–1.34)	0.12	1.05 (0.89–1.24)	0.57
MI	1.45 (1.06–1.99)	0.02*	1.08 (0.77–1.52)	0.64	1.10 (0.79–1.53)	0.59
Revascularization	1.97 (1.68–2.32)	<0.01*	1.65 (1.39–1.95)	<0.01*	1.86 (1.58–2.18)	<0.01*

Ref: *indicates that the corresponding HR or aHR is statistically significant ($p < 0.05$); bold values indicate statistically significant pvalues ($p < 0.05$); $ adjusted for sex, old myocardial infarction, PCI history, nitrates, calcium channel blocker, beta blocker, ACEi/ARB; & adjusted for nitrates, calcium channel blocker, beta blocker, ACEi/ARB.

Abbreviations: PSM: propensity score matching; IPTW: inverse probability of treatment weighting; ACEi: angiotensin-converting enzyme inhibitors; aHR: adjusted hazard ratio; ARB: angiotensin II receptor blocker; MACE: major adverse cardiovascular events; MI: myocardial infarction.

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Table 3. Healthcare utilization and healthcare costs in the PCI group compared to the medication group in the index year.

	PCI group (N = 1058)	Medication group (N = 3311)
	Mean (SD)	Mean (SD)
Outpatient visits	19.7 (19.2)	17.2 (18.8)
Hospital length of stay	6.8 (11.5)	3.4 (10.2)
NHI costs	7677 (7997)	2756 (9586)
OOP costs	3254 (2303)	476 (1289)
Total healthcare costs[&]	10,931 (8781)	3232 (9896)

Abbreviations: NHI: National health insurance; OOP: out-of-pocket costs; [&] Total healthcare costs equal NHI costs plus OOP costs. All costs are shown in US dollars (US$1 ≈ NT$ 30).

artery disease [5], this study enrolled patients based on non-invasive diagnostic tests. Invasive angiography, the gold standard for diagnosing coronary artery disease, has a complication rate of 0.5–2% and is only necessary for cases of inconclusive non-invasive testing or specific high-risk conditions [20,21]. Compared to invasive angiography, CCTA increases diagnostic yield, has fewer minor procedural complications [22], and therefore serves as an alternative in cases where other non-invasive tests provide inconclusive results [23]. However, CCTA was not the most frequently used method among all non-invasive stress tests; in our study, CCTA accounted for only 14% of cases, which may not fully represent the broader CCS population. Therefore, in addition to CCTA, this study also included patients diagnosed through non-invasive tests, including treadmill exercise testing and thallium scans. The sensitivity and specificity of certain non-invasive stress tests are moderate, particularly TET, which has a specificity of approximately 65% [24]. To mitigate this limitation, our study sample excluded patients who did not receive antiplatelet therapy, as this may suggest that their final clinical diagnosis was not CCS. While some false-positive cases may be present in the study population, this approach better reflects real-world clinical scenarios, enhancing the generalizability of our findings to routine clinical practice.

In this study, the cumulative incidence rate of MI (4–6% at five years) was lower than that reported in the COURAGE trial (approximately 10% at 6–7 years) and the ISCHEMIA trial (approximately 10% at five years) [5,6]. One possible explanation is that the enrollment method included some false-positive cases, as previously discussed. Another contributing factor may be racial differences. Previous studies have shown that South Asian patients have the highest risk of MI, followed by White patients, while patients of Chinese descent exhibit the lowest risk [25,26]. Our results echoed the literature that among Chinese descent with a positive non-invasive test result, the incidence of MI under medical therapy was relatively low, approximately 1–2% at one year and 5–8% at eight years. Given the already low incidence rate, further significant reduction is challenging.

According to our primary and sensitivity analyses, there was no significant difference in the risk

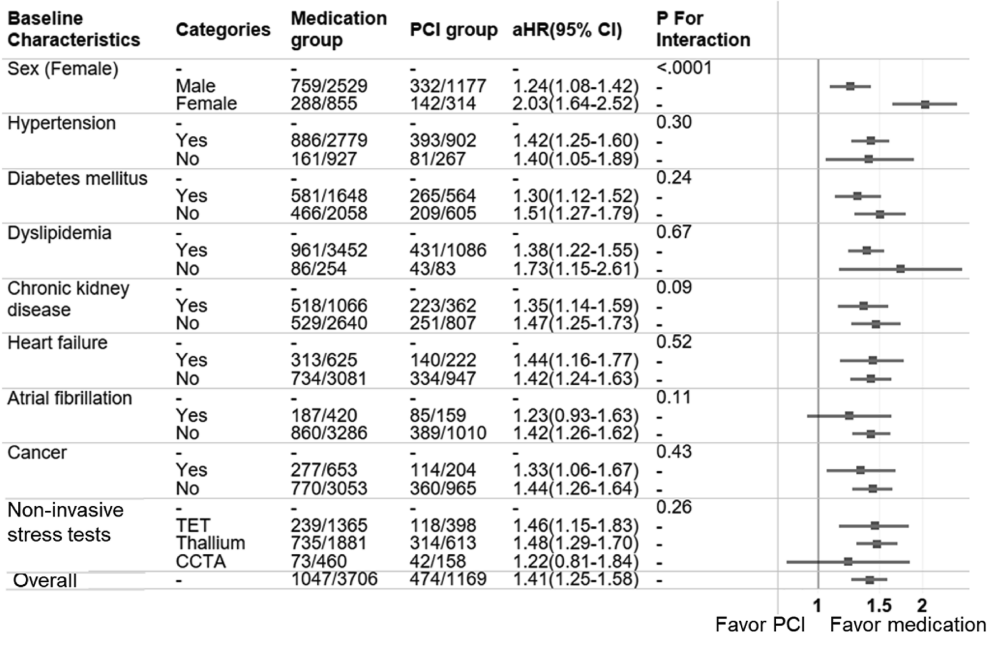


Fig. 3. Subgroup analyses of MACE (major adverse cardiac events) (aHR: adjusted hazard ratio, PCI: percutaneous coronary intervention).

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Table 4. Subgroup analysis of clinical outcomes comparing the PCI with medication therapy by medication adherence.

	Propensity score matched		IPTW adjusted	
	aHR[$] (95% CI)	*p* for interaction	aHR[&] (95% CI)	*p* for interaction
MACE				
Good medication adherence	1.29 (1.12–1.47)*	**<0.01***	1.20 (1.05–1.37)*	**<0.01***
Poor medication adherence	1.99 (1.47–2.68)*		2.51 (1.92–3.29)*	
All-cause mortality				
Good medication adherence	1.10 (0.91–1.33)	0.09	0.93 (0.78–1.13)	**<0.01***
Poor medication adherence	1.59 (1.09–2.34)*		1.79 (1.26–2.54)*	
MI				
Good medication adherence	1.06 (0.73–1.53)	0.60	0.94 (0.66–1.36)	0.49
Poor medication adherence	1.39 (0.58–3.31)		1.59 (0.62–4.09)	
Revascularization				
Good medication adherence	1.45 (1.21–1.74)*	**<0.01***	1.48 (1.24–1.76)*	**<0.01***
Poor medication adherence	2.73 (1.70–4.39)*		4.00 (2.72–5.90)*	

Ref: * indicates that the corresponding subgroup-specific aHR is statistically significant ($p < 0.05$); bold values indicate statistically significant *p* values for interaction ($p < 0.05$); [$] adjusted for sex, old myocardial infarction, PCI history, nitrates, calcium channel blocker, beta blocker, and ACEi/ARB; [&] adjusted for nitrates, calcium channel blocker, beta blocker, and ACEi/ARB.
Abbreviations: aHR, adjusted hazard ratio; PSM, propensity score matching; IPTW, inverse probability of treatment weighting; MACE, major adverse cardiovascular events; MI, myocardial infarction.

of all-cause mortality or MI between PCI and medical therapy alone. These findings suggest that the higher incidence of MACE observed in the PCI group was mainly attributable to repeat revascularization events and are consistent with previous studies [5,6,27], indicating that PCI does not improve outcomes in CCS patients. However, some observational studies have suggested that PCI improves survival and reduces the risk of MI [28]. One possible explanation for these conflicting results is variation in baseline characteristics and the severity of coronary artery disease among study populations. In patients with high-risk coronary anatomy, previous studies have demonstrated that PCI improves outcomes [29]. To ensure comparability, our study excluded high-risk patients, such as those with left main coronary artery disease or an ejection fraction <35% found by the non-invasive stress tests. In addition, the proportion of patients who received CABG or PCI in this study was lower than in previous RCT [6], suggesting that the CCS patients included had less disease severity. Our data indicate that PCI does not improve outcomes in these lower-risk CCS patients.

Furthermore, our results showed that the risk of revascularization was higher in the PCI group than in the medication only group. One possible explanation is that patients who underwent PCI may have overestimated its benefits and were more inclined to undergo repeat PCIs to relieve symptoms [30]. Another plausible explanation could be the increased likelihood of repeat non-invasive stress testing and invasive coronary angiography following PCI [31], leading to a higher rate of repeat revascularization [9]. Additionally, in-stent restenosis may contribute to this risk, although its incidence remains low [8]. Given these findings, clinical assessment of PCI indications should be more rigorous. Patients must be adequately educated on the risks and benefits of PCI to support informed decision-making, optimize treatment planning, minimize unnecessary interventions, and improve overall care quality.

Previous studies have demonstrated a consistent decline in medication adherence over time following PCI, which has been associated with worse clinical outcomes [32]. Our findings corroborated these reports and underscored the critical role of medication adherence in optimizing PCI outcomes. Conversely, for CCS patients with poor medication adherence, PCI may not be a suitable intervention. Ensuring adherence to medical therapy remains essential in achieving better long-term outcomes in this population.

This study has several limitations. First, being a single-center study, there was no information on patients' medication use, interventions, and healthcare costs from other hospitals. Adherence was also assessed solely through prescription records at a single center, which may not fully reflect actual medication-taking behavior. Nevertheless, the primary outcome of all-cause mortality was ascertained from Taiwan's comprehensive nationwide registry. Second, due to its retrospective study design, certain clinical variables, such as angina symptoms and lifestyle habits, were not available from medical records, preventing an assessment of symptom relief following PCI. Third, the severity of coronary artery disease could not be comprehensively assessed, and there was a potential for false-positive and false-negative cases, as patients were enrolled based on

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positive non-invasive test results rather than confirmed by invasive coronary angiography. These factors might have contributed to selection bias. Furthermore, revascularization events are largely influenced by clinical decision-making and the intensity of surveillance. In the absence of differences in mortality or MI, the observed disparity in MACE may therefore reflect the effect of follow-up interventions prompted by the initial procedure, rather than harm inherent to PCI itself. Finally, our study was based on retrospective data that could not infer causation directly. We applied propensity score matching to improve exchangeability, which is one of the key causal assumptions, between the PCI and medication groups. However, this method accounted only for observed confounders. Residual confounding, such as ischemia burden beyond what was captured by non-invasive tests or clinical judgment in decision-making, could not be entirely ruled out.

In conclusion, among CCS patients diagnosed by a positive non-invasive stress test, medical therapy alone, compared with PCI, demonstrated no significant difference in all-cause mortality and MI, and was associated with a significantly lower risk of revascularization. Subgroup analyses of medication adherence further suggested that PCI should be performed with careful monitoring of adherence to optimize patient outcomes. These findings provide valuable insights for physicians and CCS patients in selecting the most appropriate treatment strategy and may help reduce unnecessary stent placement.

Acknowledgments

This work was supported by the Ministry of Science and Technology (MOST), Taiwan (grant number MOST 111-2627-M-006-003), and the National Science and Technology Council (NSTC), Taiwan (grant number NSTC 113-2314-B-006-066-MY2).

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