의학박사 학위논문

관상 동맥의 만성 완전 폐쇄 병변에 대한 관상 동맥 중재 시술과 약물 치료의 장기간 예후 비교

Long-Term Outcomes of Percutaneous Coronary Intervention Versus Optimal Medical Treatment for Chronic Total Occlusions.

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이 논문을 의학박사 학위 논문으로 제출함

2022년　2월

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더불어 어머니(조복남 여사), 아버지 (김학경), 장인 (손철수), 장모님 (이은주) 누나(김라영), 매형 (최종권), 처제 (손고우리), 동서 (김영학), 조카 (최재혁, 최민서)께도 박사 학위 취득에 많은 도움을 주셔서 너무 감사드립니다.

ABSTRACT

BACKGROUND The long-term benefit of recanalization of chronic total occlusion (CTO) remains controversial.

OBJECTIVES To compare the long-term outcomes after percutaneous coronary intervention (PCI) or optimal medical treatment (OMT) for coronary CTO.

METHODS Between January 2003 and December 2018, 3248 patients with coronary CTO were enrolled in the Asan Medical Center-CTO registry. After excluding patients who underwent coronary artery bypass graft (n=502), we classified the patients into the PCI group (n=1837) and the OMT group (n=909). The primary outcome was the composite of death, spontaneous myocardial infarction, stroke, or repeat revascularization. Propensity-score matching was used to assemble a cohort of patients with similar baseline characteristics.

RESULTS In the 653 pairs of propensity score-matched patients, the adjusted risk for the primary composite outcome was significantly lower in the PCI group than in the OMT group during 10-year follow-up (hazard ratio [HR], 0.57; 95% confidence interval [CI], 0.46 to 0.72; $p < 0.001$). These benefits were mainly observed in the reduction of mortality (HR, 0.66; 95% CI, 0.51 to 0.87; $p = 0.003$) and repeat revascularization (HR, 0.67; 95% CI, 0.48 to 0.95; $p = 0.023$). The benefit of PCI was consistently observed in subgroups according to the major risks of cardiovascular disease such as old age, hypertension, diabetes, or advanced coronary artery disease.

CONCLUSIONS As an initial treatment strategy in patients with CTO, PCI was associated with better clinical benefits over OMT in terms of adverse cardiovascular events during long-term follow-up.

Key Words: Atherosclerosis, coronary artery disease, chronic total occlusion, percutaneous coronary intervention, optimal medical treatment

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INTRODUCTION

Coronary chronic total occlusion (CTO) is defined as an atherosclerotic complete vessel occlusion with a Thrombolysis in Myocardial Infarction (TIMI) flow grade of 0 within the occluded segment, and an estimated occlusion duration of ≥3 months [1, 2]. CTOs are relatively common and are found in 18%–30% of all diagnostic coronary angiographies [3, 4]. However, unlike the revascularization of non-obstructive coronary artery disease (CAD), percutaneous coronary intervention (PCI) for CTO carries significant technical complexities and has a low success rate [3, 5]. Although recent advancements in the treatment of coronary CTOs have resulted in improved procedural success with a low risk for procedural complications [6], only one-tenth of patients with CTO subsequently undergo revascularization [3, 5, 7]. The main reason for the low adoption rate of PCI for CTO is the doubt on the effectiveness of recanalization rather than technical difficulties.

In several observational studies, the benefit of successful PCI for CTO was not prominent compared with inevitable optimal medical treatment (OMT) after failing PCI for CTO. However, as patients included in the failed PCI group also reflect the property of the PCI patients, the characteristics of the OMT patients were not properly reflected in the outcomes [8-12]. The DECISION-CTO trial (Drug-Eluting Versus Optimal Medical Treatment Stent Implantation in Patients With Chronic Total Occlusion), the first randomized controlled trial (RCT) between PCI and OMT for CTO, also failed to show a significant benefit of PCI over OMT for CTO [13]. In terms of the patient enrollment in RCTs, patients assigned to OMT are often low-risk patients and do not reflect the characteristics of real-world patients.

Therefore, we analyzed a large-scale observational registry to investigate the comparative outcomes after PCI or OMT on the long-term outcomes in real-world patients with coronary CTO.

MATERIALS AND METHODS

STUDY POPULATION AND DATA SOURCES.

This study was a registry-based analysis on consecutive patients with coronary CTO who underwent either revascularization or OMT between January 1, 2003, and December 30, 2018 at Asan Medical Center (Seoul, Republic of Korea). This registry was designed to investigate the real-world outcomes of CABG, PCI, or medical therapy in patients with CTO (i.e., chronic total occlusion of the three major epicardial vessels having > 2.5 mm of the reference vessel diameter). Patients who underwent prior coronary artery bypass graft and those who had an ST-elevation myocardial infarction (MI) within 24 hours before revascularization or presented with cardiogenic shock were excluded.

After excluding those with initial coronary artery bypass graft (n=502), 2746 patients were finally included in this analysis. Patients with failed PCI were included in the PCI group. The patient flow of the study is shown in **Figure 1**. Patients with multivessel disease in both groups received PCI for obstructive non-CTO lesions. The registry contains information on patient demographics, cardiovascular risk factors, clinical manifestation, hemodynamic status, left ventricular function, disease extent, operative or procedural details, and in-hospital and follow-up outcomes; all data were recorded in the dedicated surgical and PCI databases by independent research personnel.

TREATMENT STRATEGY AND FOLLOW-UP.

The choice of initial treatment strategy was made at the discretion of the treating physicians and/or patients in consideration of several clinical and anatomic factors after diagnostic coronary angiography. Patients were classified according to the initial treatment strategy (i.e., PCI group vs. OMT group). Study patients were not restricted to those who had isolated CTO disease; thus, revascularizations for obstructive non-CTO lesions were performed in both groups. For patients with multivessel CAD, regardless of the initial treatment strategy, PCI was recommended for all obstructive non-CTO lesions within a vessel diameter ≥2.5 mm (diameter stenosis ≥50% for left main CAD and ≥70% for non-left main CAD). In the PCI group, the treatment sequence of CTO and non-CTO lesions was decided by the operator by considering the safety of the procedure. All PCI procedures were performed according to standard interventional techniques, and the use of specialized

devices or techniques and the use of intravascular ultrasound were made at the operator's discretion. The same type of drug-eluting stent was implanted for all CTO and non-CTO lesions in each patient at the index treatment. Successful PCI was defined as restoration of the TIMI flow grade to 3 with residual stenosis <30%, as determined by the operator.

Pharmacological treatments were optimized in accordance with the accepted guidelines and established standard of care [14, 15]. Patients were prescribed aspirin and statin on a daily basis. β-blockers, calcium channel blockers, or long-acting nitrates were used as anti-ischemic therapy either alone or in combination. An angiotensin-converting enzyme inhibitor or an angiotensin-receptor blocker was considered for secondary prevention. Patients undergoing stent implantation received a P2Y12 receptor inhibitor for at least 12 months in addition to standard medical therapy.

Clinical follow-up was recommended at 1 month, 6 months, 1 year, and annually thereafter via office visits or telephone contact. The follow-up period was extended to June 1, 2020 to ensure that all patients could be followed up for at least 2 years. To ensure the accurate assessment of the clinical endpoints, additional information was obtained from visits or telephone contacts with living patients or family members and from medical records obtained from other hospitals as necessary. For validation of complete follow-up data regarding mortality, information on the vital status and date of death was obtained from electronic healthcare record review and cross-checked through the National Health Insurance Service system of South Korea and the South Korea National Statistics System. The information on vital status was complete in all patients.

OUTCOMES AND DEFINITIONS.

The primary outcome was the composite of death from any cause, spontaneous MI, stroke, or repeat revascularization. Secondary outcomes included the individual components of the primary composite outcome, cardiac death, and CTO-related repeat revascularization. All outcomes were assessed according to the standard endpoint definitions [16-18]. We used all-cause mortality as the survival outcome because it is the most unbiased method for reporting deaths in clinical trials or observational studies. Spontaneous MI was defined as the appearance of newly developed ischemic symptoms or

signs with an increase in cardiac enzyme level to above the upper reference limit requiring re-hospitalization (i.e., emergency admission with a principal diagnosis of MI). We disregarded periprocedural MI due to non-uniform definitions and controversial prognostic impact [19, 20]. Stroke was defined as a sudden onset of a neurologic symptom (e.g., vertigo, numbness, aphasia, dysarthria) resulting from vascular lesions of the brain (e.g., hemorrhage, embolism, thrombosis, rupturing aneurysm) that persisted for >24 hours. Repeat revascularization was defined as any repeat percutaneous intervention or surgical bypass of the treated or non-treated vessel, regardless of whether the procedure was clinical or ischemia-driven. In particular, CTO-related repeat revascularization was defined as performing revascularization on the same lesion according to the clinical course of the patient after establishing an initial treatment strategy for CTO. All clinical events were confirmed by source documentation collected during each event and adjudicated by an independent group of clinicians who were blinded to the type of revascularization treatment [21, 22].

STATISTICAL ANALYSIS.

Analyses for differences in the long-term clinical outcomes after the decision of initial therapeutic strategy for CTOs were performed in the overall cohort and the propensity score-matched cohorts. With regard to baseline characteristics, continuous variables were compared with Student's *t*-test or Wilcoxon rank-sum test for non-normally distributed data, and categorical variables were compared with χ^2 test or Fisher's exact test, as appropriate.

To rigorously control the baseline characteristics of patients according to the treatment strategies, propensity-score matching was used to assemble a cohort of patients with similar baseline characteristics. Propensity score-matched pairs were formed using a greedy algorithm with a caliper of 0.2 standard deviations of the logit of the propensity score (c-statistic = 0.821; Hosmer-Lemeshow statistic = 8.4762; df = 8; p = 0.3884 supported the goodness of fit). The propensity score matching method was determined to be adequate when the overall balance was achieved, indicated by a standardized mean difference of <10%. The details of the propensity score and results are included in the **Supplemental Appendix**.

The cumulative incidence of primary and secondary outcomes was calculated using Kaplan–Meier method, and the log-rank statistic was used to test for differences between groups. In propensity-score matched cohorts, the risks of clinical outcomes were compared using the Cox regression models with robust standard errors that accounted for the clustering of matched pairs.

Subgroup analyses were performed on the basis of clinically relevant variables: age (<75 years vs. ≥75 years), sex, hypertension, diabetes mellitus, congestive heart failure, previous myocardial infarct, chronic kidney disease, site of CTO vessel (left anterior descending vs. left circumflex or right coronary artery), left ventricular ejection fraction, presentation of an acute coronary syndrome, and disease extent. Tests for interaction were performed to assess the heterogeneity of treatment effect among subgroups.

Multivariable Cox regression analyses were performed to identify the independent predictors for the primary and secondary clinical outcomes. Of the previously published baseline clinical and anatomic covariates listed in **Table 1**, those with p values <0.20 on univariate analyses were included in multivariable Cox proportional hazards models. The multivariable models were determined by backward elimination methods (retention threshold: $p < 0.05$). The proportional-hazards assumption considering all variables was confirmed by means of the Schoenfeld residuals test, and no relevant violations of the assumption were found.

All p values were two-sided, and those smaller than 0.05 were considered statistically significant. No adjustment for multiple testing was undertaken. Because of the potential for type I error due to multiple comparisons, all findings of this study should be interpreted as exploratory. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and R version 3.6.1 (http://www.r-project.org).

RESULTS

STUDY POPULATION AND BASELINE CHARACTERISTICS.

Between January 2003 and December 2018, a total of 3453 patients with coronary CTOs were consecutively enrolled in the Asan Medical Center-CTO registry. Among them, we identified 2746

patients who met the inclusion and exclusion criteria, of whom 909 (33.1%) underwent OMT and 1837 (66.9%) underwent PCI. In each group, PCI was performed for non-CTO lesions, including 295 (32.5%) patients in the OMT group and 1223 (66.6%) patients in the PCI group (**Figure 1**).

Baseline clinical and anatomic characteristics according to the initial treatment strategy are summarized in **Table 1.** Before propensity-score adjustment, there were significant differences in several baseline characteristics. Overall, patients in the OMT group were older and had a higher prevalence of comorbidities and more extensive CAD; decreased renal function and low left ventricular ejection fraction were also more commonly observed in the OMT group. In contrast, the proportions of LAD involvement and proximal CTO lesion were higher in the PCI group. The distribution of propensity scores in the OMT group and the PCI group is shown in **Supplementary Figure 1**. The probability of selecting OMT was associated with older age, lower LVEF, history of MI, history of malignancy, CTO in LCx or RCA, and non-CTO complete revascularization (**Supplementary Table 1**). After propensity-score adjustment, 653 pairs of patients were matched and most of the baseline covariates were well-balanced (**Table 1**).

PROCEDURAL OUTCOMES.

Procedural details for both groups are summarized in **Supplementary Table 2**. Of the 1837 patients in the PCI group, the procedure was successful in 1731 (94.2%) patients. Most patients underwent revascularization with stenting, and 2nd DES was used in 60.1%. Two (interquartile range [IQR], 1.0–2.0) stents with a median total length of 51 mm (IQR, 33.0–66.0) and a median diameter of 3.1 mm (IQR, 3.0–3.5) were used for the target CTO lesion. The rate of complete revascularization for CTO lesions was 82.9%.

Although the median stent diameter used for non-CTO lesions were comparable between the PCI group and the OMT group (3.25 mm [IQR, 3.0–3.5] vs. 3.5 mm [IQR, 3.0–3.5]; p = 0.20), the median stent length (32.0 mm [IQR, 23.0–40.0] vs. 38.0 mm [IQR, 24.0–52.0]; p = 0.002) and the total number of stents (1.0 [IQR, 1.0–2.0] vs. 1.0 [IQR, 1.0–2.0]; p = 0.001) were greater in the OMT group. Complete revascularization of non-CTO vessels was achieved in 797 (65.2 %) and 217

(73.6 %) patients in the PCI and OMT groups, respectively ($p < 0.001$). After propensity score matching, differences in the procedure for non-CTO lesions remained except for the non-CTO revascularization rate.

MEDICATION AND TREATMENT TARGETS.

Medical management at discharge was different between the OMT and PCI groups; while the components of OMT for secondary prevention (i.e., anti-platelet agent, beta-blockers, ACE inhibitor/ARB, and statin) were more commonly prescribed in the OMT group, antianginal medications (e.g., calcium channel blockers and nitrate) were more commonly prescribed in the PCI group (**Supplementary Table 3**). After propensity score matching, anti-platelet and calcium channel blockers were more common in the PCI group, and there were no significant differences in the remaining medications between the two groups.

CLINICAL OUTCOMES IN THE UNMATCHED POPULATION.

In the overall population, the follow-up duration ranged from 2 to 18.9 years (mean, 6.5 ± 4.12), which amounts to 17,882 person-years. The information on vital status was complete in all patients. During the entire follow-up period, a total of 564 primary composite events (death, n = 405; spontaneous MI, n = 52; stroke, n = 58; repeat revascularization, n = 115), 297 cardiac death events, and 284 any repeat revascularization events occurred. The unadjusted event rates of primary and secondary outcomes according to initial treatment strategies are described in **Supplementary Table 4**.

During follow-up, the cumulative incidence of the primary composite of death, spontaneous MI, stroke, or repeat revascularization was significantly lower in the PCI group than in the OMT group (**Table 2** and **Figure 2A)**. Similar patterns were observed for the individual component of death (i.e., all-cause death and cardiac death) (**Supplementary Figure 2A, B**) or repeat revascularization (i.e., any repeat revascularization and CTO-related repeat revascularization) (**Supplementary Figure 3A, B**).

CLINICAL OUTCOMES IN THE MATCHED POPULATION.

In the propensity-matched cohort, the difference in the primary outcome between the two groups decreased; however, the adjusted risk was significantly lower in the PCI group. (HR, 0.57; 95% CI, 0.46 to 0.72; $p < 0.001$) (**Table 2 and Figure 2B**). The adjusted risks for death (all-cause death and cardiac death) (**Table 2 and Figure 3A, B**) and repeat revascularization (any repeat revascularization and CTO-related repeat revascularization) (**Table 2 and Figure 4A, B**) were also significantly lower in the PCI group.

In the case of repeat revascularization, there was a difference in the HR according to time. While the difference in the rate of any repeat revascularization between the two treatment groups was prominent in the latter 5 years, the difference in the rate of CTO-related repeat revascularization was evident in the first 5 years.

SUBGROUP ANALYSES IN THE MATCHED POPULATION

Cox regression analysis was performed to assess whether the lower incidence of the primary composite outcome in the PCI group than in the OMT group was consistent among subgroups. The benefit of PCI on the primary composite outcome was consistent across the subgroups according to the major risk factors of cardiovascular diseases such as old age, diabetes, and advanced coronary artery disease. However, there was a significant interaction between the treatment method and the clinical presentation (i.e., acute coronary syndrome vs. chronic coronary syndrome) (**Figure 5**).

INDEPENDENT PREDICTORS FOR CLINICAL OUTCOMES

The independent predictors for the primary composite outcome, its individual components, and repeat revascularization are summarized in **Table 3**. In the overall population, PCI was independently associated with the primary composite outcome (HR, 0.56; 95% CI, 0.47 to 0.68; $p < 0.001$), all-cause death (HR, 0.54; 95% CI, 0.43 to 0.67; $p < 0.001$), and repeat revascularization (HR, 0.72; 95% CI, 0.56 to 0.93; $p = 0.012$). The primary composite outcome was also significantly associated with age, diabetes, previous PCI, previous stroke, chronic renal failure, malignancy, lower ejection fraction, and

more extensive CAD. Despite some differences in the magnitudes of HRs and the corresponding p values, most major correlates of 10-year clinical outcomes in the overall population remained as significant correlates in each treatment group.

DISCUSSION

In this large-sized, real-world cohort of patients with coronary CTO, we evaluated the characteristics of patients and the long-term prognostic impact of initial treatment strategy on major cardiovascular events and mortality. The major findings of this study are that (1) the clinical and angiographic characteristics were significantly different between the PCI group and the OMT group, with the OMT group having more cardiovascular risk factors; (2) after rigorous controlling for baseline characteristics and confounding variables using propensity score matching, PCI showed significant benefits in terms of major adverse cardiovascular events, mainly in terms of the reduction of mortality and repeat revascularization (**Central Illustration**); and (3) these significant benefit of PCI was consistent in subgroup analyses according to the major risk factors of cardiovascular diseases.

In patients with acute coronary syndrome or chronic coronary syndrome, CTO is strongly associated with higher rates of in-hospital and long-term mortality [23, 24]. Theoretically, a successful recanalization of CTO supplying hibernating myocardium carries the functional effect of improving the regional wall motion. Aside from improving angina and quality of life, recanalization of CTO leads to reduced risk of major adverse cardiovascular events and improved survival rates. Nevertheless, RCT studies and meta-analyses showed that PCI did not confer significant benefits in the survival rates.[2, 13, 25] However, the existing studies have a small sample size or short study duration of within 5 years, and mainly include low-risk patients with a higher crossover rate between two treatments strategies, which has the potential to overestimate the effectiveness of OMT. To overcome these issues, the present study evaluated the long-term outcomes in patients with varying risk levels that reflect the real-world setting. A well-organized understanding of the clinical features and prognostic correlates of patients with CTO and the relative treatment effect of PCI or OMT thereof may be helpful for risk-stratification and guiding the revascularization decision-making.

Patients with CTO who are referred to medical treatment have more comorbidities for cardiovascular disease and more complex anatomy. Thus, it is expected that patients in the OMT group would have an increased cardiovascular risk, which was demonstrated in the unadjusted analyses. After rigorous controlling for baseline characteristics and confounding using propensity score matching, the OMT group still showed higher rates of major adverse cardiovascular events and mortality compared with the PCI group. Considering that ischemia was induced in the CTO territory independent of the degree of collateral flow and even in cases of a negative result in the nuclear stress test, these results are reasonable [26]. However, until recently, the role of percutaneous coronary revascularization in CAD has been emphasized in terms of symptom relief and improvement of life rather than hard clinical endpoints [27]. The potential benefits of PCI for CTO are still controversial; however, as can be seen from this study, the benefit of PCI was mainly observed in terms of mortality or cardiac mortality, which could be interpreted as the effect of myocardial ischemia relieved by PCI on long-term prognosis. These benefits of PCI were consistently observed across different subgroups, irrespective of the presence of major cardiovascular risk factors such as old age, hypertension, diabetes, and advanced CAD. PCI itself seems to be an important prognostic determinant and the role of PCI for CTO should be reevaluated.

Patients with coronary CTO have a high atherosclerotic burden [28]. Therefore, CTO lesions may be considered as surrogate markers of advanced cardiovascular disease rather than mere local lesions of the coronary artery. In addition to local treatments such as PCI, systemic medical treatment to control the risk factors for coronary artery disease should also be emphasized. In our study, while the event rate of CTO-related repeat revascularization during the first 5 years after PCI was lower than that in the PCI group, there was no significant difference between the PCI group and the OMT group after 5 years in terms of disease progression. Considering the gradual progression of atherosclerosis over time, patients with CTO should be treated with OMT in combination with PCI to mediate the natural course of the disease. However, owing to the inherent limitations of observational study, this interpretation should be considered in a provisional and conservative manner. The findings in our

study warrant further investigation and should be confirmed or refuted through large-sized randomized clinical trials with long-term follow-up.

Our study has several limitations that deserve mention. First, as this was a non-randomized, observational study, the present study was subject to potential selection and ascertainment biases. Although we rigorously adjusted for both baseline clinical risk factors and non-CTO lesion characteristics, unmeasured confounders such as frailty or a more detailed atherosclerotic burden could have influenced the observed findings. Second, we did not distinguish whether the CTO was in an infarct-related artery or a non-infarct-related artery. In addition, the viability of the myocardium within the CTO territory was not evaluated. Third, we did not systematically collect detailed information on the long-term status of medication use and compliance with guideline-directed medical management after establishing the initial treatment strategy, which could have varied substantially over time. Finally, quantitative stratification according to how much collateral flow relieves the ischemia burden of CTO territory was not performed. The degree of ischemic burden relief after the initial treatment strategy is not uniform among patients; therefore, further large-sized studies reflecting the accurate ischemic burden of CTO territory are required to determine the prognostic value of recanalization or OMT for CTO.

CONCLUSIONS

In this real-world registry of patients with CTO, we found that PCI was significantly associated with clinical benefits with respect to the primary composite outcome of death, spontaneous MI, stroke, or repeat revascularization after adjusting for clinical covariates. The clinical benefits were mainly observed in terms of the reduction of mortality and repeat revascularization. The benefit of revascularization was consistently observed in subgroup analyses according to the major risk factors for cardiovascular diseases. The role of PCI in patients with CTO should be reevaluated in terms of hard clinical endpoints over time.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Long-term clinical impact of recanalization or

optimal medical treatment in patients with CTO is unclear.

COMPETENCY IN PATIENT CARE: In this large-sized real-world registry of patients with CTO who underwent PCI or OMT, we found a significant clinical benefit of PCI on the long-term primary composite outcome of death, myocardial infarction, stroke, and repeat revascularization. This benefit was mainly observed in mortality and repeat revascularization.

TRANSLATIONAL OUTLOOK: Further research is needed to evaluate the benefits of PCI for CTO in terms of pathophysiology by quantifying the degree of the resolution of ischemic burden. Also, the difference in the treatment effect of PCI should be evaluated according to the degree of risk of cardiovascular disease.

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FIGURE LEGENDS

Figure 1. Study Flowchart

CTO = chronic total occlusion; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft; STEMI = ST-segment elevation myocardial infarction.

Figure 2. Risks of the Primary Composite Outcome According to the Initial Treatment Strategy

Crude (A) and adjusted event curves (B) for the primary composite outcome between optimal medical treatment and percutaneous coronary intervention for patients with chronic total occlusion are shown. The primary composite outcome was defined as the composite of death from any cause, spontaneous myocardial infarction, stroke, or any repeat revascularization. The hazard ratios (HRs) and 95% confidence intervals (CIs) are for the PCI group as compared with the OMT group.

OMT = optimal medical treatment; PCI = percutaneous coronary intervention;

Figure 3. Risks of All-cause or Cardiac Death According to the Initial Treatment Strategy

Adjusted event curves (A) for all-cause death and (B) cardiac death between optimal medical treatment and percutaneous coronary intervention for patients with chronic total occlusion are shown. The hazard ratios (HRs) and 95% confidence intervals (CIs) are for the PCI group as compared with the OMT group.

OMT = optimal medical treatment; PCI = percutaneous coronary intervention

Figure 4. Risks of Repeat Revascularization According to the Initial Treatment Strategy

Adjusted event curves (A) for any repeat revascularization and (B) for CTO-related repeat revascularization between optimal medical treatment and percutaneous coronary intervention for patients with chronic total occlusion are shown. The hazard ratios (HRs) and 95% confidence intervals (CIs) are for the PCI group as compared with the OMT group.

CTO = chronic total occlusion; OMT = optimal medical treatment; PCI = percutaneous coronary intervention

Figure 5. Ten-Year Rates of the Primary Composite Outcome Among Subgroups

Hazard risks for the 10-year rate of primary composite outcome were estimated using the Cox regression analysis in subgroups of patients treated with percutaneous coronary intervention or optimal medical treatment for chronic total occlusion.

ACS = acute coronary syndrome; CCS = chronic coronary syndrome; CRF = chronic renal failure; CTO = chronic total occlusion; HF = heart failure; LAD = left anterior descending artery; LCx = left circumflex coronary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarct; OMT = optimal medical treatment; PCI = percutaneous coronary intervention; RCA = right coronary artery; VS = vessel disease

Central Illustration. Impact of Percutaneous Coronary Intervention as Initial Treatment Strategy for Chronic Total Occlusion.

The treatment strategy for chronic total occlusion (CTO) is determined by considering the clinical conditions of the patient and the anatomic suitability of the lesion for intervention. However, the long-term prognostic impact of recanalization for CTO is controversial. After adjusting the baseline characteristics of patients using propensity score according to the initial treatment strategy (PCI vs. optimal medical treatment [OMT]), PCI showed significant clinical benefits over OMT with respect to the primary composite of death, spontaneous MI, stroke, or any repeat revascularization. These benefits were mainly observed in terms of the reduction of mortality and repeat revascularization.

CABG = coronary-artery bypass grafting; CTO = chronic total occlusion; CABG = coronary artery bypass graft; MI = myocardial infarct; OMT = optimal medical treatment; PCI = percutaneous coronary intervention.

Table 1. Baseline Characteristics According to the Initial Treatment Strategies for Chronic Total Occlusion.

Variables	Unadjusted				Propensity score-matched		
	PCI (N=1837)	OMT (N=909)	p Value	Standardized Difference (%)	PCI (N=653)	OMT (N=653)	Standardized Difference
Year of procedure							
2003–2007	487 (26.5%)	31 (3.4%)	<0.001	59.9	68 (10.4%)	30 (4.6%)	3.7
2008–2018	1350 (73.5%)	878 (96.6%)			585 (89.6%)	623 (95.4%)	
Age (years)	61.1±10.6	66.3±10.6	<0.001	49.0%	64.8±9.8	64.8±10.9	0.8%
Men	1508 (82.1%)	733 (80.6%)	0.355	3.7%	525 (80.4%)	538 (82.4%)	5.1%
Body mass index (kg/m^2)	25.5±3.2	24.8±3.4	0.001	21.5%	25.0±3.1	25.1±3.3	3.5%
Diabetes mellitus							
Any	558 (30.4%)	382 (42.0%)	<0.001	24.4%	240 (36.8%)	250 (38.3%)	3.2%
Requiring insulin	88 (4.8%)	64 (7.0%)	0.015	9.5%	45 (6.9%)	42 (6.4%)	1.8%
Hypertension	1091 (59.4%)	630 (69.3%)	<0.001	20.8%	425 (65.1%)	434 (66.5%)	2.9%
Hyperlipidemia	1385 (75.4%)	870 (37.3%)	<0.001	24.1%	556 (85.1%)	542 (83.0%)	5.9%
Current smoker	512 (27.9%)	244 (26.8%)	0.57	2.3%	167 (25.6%)	179 (27.4%)	4.2%
Previous MI	180 (9.8%)	137 (15.1%)	<0.001	16.0%	83 (12.7%)	79 (12.1%)	1.9%
Previous PCI	453 (24.7%)	273 (30.0%)	0.003	12.1%	191 (29.2%)	186 (28.5%)	1.7%
Previous stroke	123 (6.7%)	107 (11.8)	<0.001	17.6%	63 (9.6%)	61 (9.3%)	1.0%
Previous heart failure	52 (2.8%)	55 (6.1%)	<0.001	15.7%	34 (5.2%)	35 (5.4%)	7.0%
Peripheral artery disease	52 (2.8)	51 (5.6)	<0.001	13.9%	34 (5.2%)	29 (4.4%)	3.6%

Chronic kidney disease	62 (3.4%)	57 (6.3%)	<0.001	13.5%	36 (5.5%)	32 (4.9%)	2.8%
Dialysis	40 (2.2%)	39 (4.3)	0.002	12.0%	24 (3.7%)	25 (3.8%)	0.8%
Chronic lung disease	34 (1.9%)	30 (3.3%)	0.018	9.2%	15 (2.3%)	15 (2.3%)	0.0%
Previous malignancy	61 (3.3%)	146 (16.1%)	<0.001	44.1%	52 (8.0)	72 (11.0)	10.5%
Atrial fibrillation	48 (2.6%)	39 (4.3%)	0.018	9.2%	24 (3.7%)	25 (3.8%)	0.8%
Estimated GFR (mL/min)	82.8±20.4	74.4±34.3	<0.001	36.2%	77.4±22.2	77.4±23.5	0.1%
Mean ejection fraction (%)	58.0±8.6	54.4±11.6	<0.001	36.2%	77.4±22.2	77.4±23.5	0.1%
Normal LV function*	1389 (75.6%)	574 (63.1%)			441 (67.5%)	457 (70.0%)	
Mild LV dysfunction*	293 (15.9%)	153 (16.8%)			119 (18.2%)	101 (15.5%)	
Moderate LV dysfunction*	109 (5.9%)	90 (9.9%)			64 (9.8%)	50 (7.7%)	
Severe LV dysfunction*	42 (2.3%)	78 (8.6%)			29 (4.4%)	45 (6.9%)	
Clinical presentation							
Chronic coronary syndrome	1372 (74.7%)	73.4 (80.7%)	<0.001	14.6%	509 (77.9%)	512 (78.4%)	1.1%
Acute coronary syndrome	465 (25.3%)	175(19.3%)			144 (22.1%)	141 (21.6%)	
Extent of the diseased vessel							
1VD	641 (34.9%)	205 (22.6%)	<0.001	36.6%	168 (25.7%)	172 (26.3%)	1.4%
2VD	708 (38.5%)	318 (35.0%)			243 (37.2%)	242 (37.1%)	
3VD	488 (26.6%)	386 (42.5%)			242 (37.1%)	239 (36.6%)	
CTO vessel							
LAD	810 (44.1%)	194 (21.3%)	<0.001	53.8%	168 (25.7%)	180 (27.6%)	4.5%

LCx	268 (14.6%)	265 (29.2%)			146 (22.4%)	147 (22.5%)	
RCA	759 (44.1%)	450 (49.5%)			339 (51.9%)	326 (49.9%)	
Proximal CTO location	1528 (83.2%)	606 (66.7%)	<0.001	18.5%	517 (79.2%)	451 (69.1%)	10.4%
Collateral flow grade (%)[†]							
0	33 (1.8%)	51 (5.6%)	<0.001	37.0%	15 (2.3%)	41 (6.3%)	16.5%
1	421 (22.9%)	162 (17.8%)			119 (18.2%)	113 (17.3%)	
2	654 (35.6%)	356 (39.2%)			221 (33.8%)	252 (38.6%)	
3	729 (39.7%)	340 (37.4%)			298 (45.6%)	247 (37.8%)	
Non-CTO lesion complete revascularization[‡]	797 (65.2%)[†]	217 (73.6%)[†]	<0.001	40.8%	407 (83.1%)[†]	179 (84.0%)[†]	3.3%

Values are mean ± standard deviation or n (%) unless indicated otherwise. Percentages may not total 100% because of rounding. Glomerular filtration rate was calculated using CKD-EPI equations.

[*]The total does not reach 100% due to a missing value of left ventricular ejection fraction. A total of 4 patients in the PCI group and 14 patients in the OMT group did not show LVEF.

[†]Collateral flow grade was not used as a component of propensity-score analyses due to difficulty in matching according to 4 hierarchical classification.

[‡]The ratio of complete revascularization for non-CTO lesions was calculated as the ratio for patients who underwent PCI for non-CTO lesions. The number of total patients who underwent PCI for non-CTO lesions was 1518 (PCI group: 1223 patients, OMT group: 295 patients) for the overall population and 703 (PCI group: 490 patients, OMT group: 213 patients) for the matched population.

GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; IQR = interquartile range; LDL = low-density lipoprotein; LV = left ventricle; MI = myocardial infarction; PCI = percutaneous coronary intervention; VD = vessel disease

Table 2. HRs for Clinical Outcomes During Follow-Up

Outcomes	Unadjusted		Propensity score-matched		Propensity score-matched+ medication adjusted†	
	HR* (95% CI)	p Value	HR* (95% CI)	p Value	HR* (95% CI)	p Value
Primary composite outcome of all-cause death, spontaneous MI, stroke, or any repeat revascularization						
At 5 years	0.36 (0.30–0.43)	<0.001	0.51 (0.39–0.66)	<0.001	0.52 (0.39–0.70)	<0.001
At 10 years	0.37 (0.32–0.44)	<0.001	0.57 (0.46–0.72)	<0.001	NA†	NA†
All-cause death						
At 5 years	0.33 (0.26–0.41)	<0.001	0.60 (0.44–0.82)	0.001	0.65 (0.45–0.93)	0.02
At 10 years	0.34 (0.28–0.42)	<0.001	0.66 (0.51–0.87)	0.003	NA†	NA†
Any repeat revascularization						
At 5 years	0.75 (0.57–0.99)	0.04	0.77 (0.53–1.12)	0.172	0.68 (0.45–1.03)	0.069
At 10 years	0.67 (0.53–0.86)	0.002	0.67 (0.48–0.95)	0.023	NA†	NA†
Cardiac death						
At 5 years	0.31 (0.23–0.40)	<0.001	0.56 (0.38–0.82)	0.003	0.61 (0.39–0.94)	0.024
At 10 years	0.32 (0.26–0.41)	<0.001	0.63 (0.46–0.88)	0.007	NA†	NA†
CTO-related repeat revascularization						
At 5 years	0.45 (0.30–0.68)	<0.001	0.43 (0.24–0.78)	0.005	0.42 (0.22–0.76)	0.009
At 10 years	0.43 (0.30–0.62)	<0.001	0.44 (0.27–0.74)	0.002	NA†	NA†

*HRs are for the PCI group, as compared with the OMT group.

†HR was calculated up to 5 years under the assumption that discharge medication could have an effect up to 5 years, and values after 5 years were not

estimated.

CI = confidence interval; MI = myocardial infarction; NA = Not available.

Table 3. Independent Predictors for Clinical Outcomes in Overall Population and Each Treatment Groups

	Overall		OMT		PCI		$p_{interaction}$
	HR (95% CI)	**p Value**	**HR (95% CI)**	**p Value**	**HR (95% CI)**	**p Value**	
Primary composite outcome*							
CTO-PCI	0.56 (0.47–0.68)	<0.001					
Age >75	1.94 (1.59–2.36)	<0.001	1.83 (1.42–2.36)	<0.001	2.93 (2.20–3.91)	<0.001	0.017
Diabetes mellitus	1.34 (1.11–1.60)	0.002	1.82 (1.44–2.30)	<0.001	1.50 (1.18–1.91)	0.001	0.262
Diabetes mellitus requiring insulin	1.53 (1.14–2.06)	0.01	2.19 (1.51–3.17)	<0.001	2.52 (1.72–3.70)	<0.001	0.601
Previous PCI	1.23 (1.03–1.48)	0.02	1.07 (0.84–1.38)	0.584	1.36 (1.06–1.75)	0.017	0.188
Previous stroke	1.48 (1.16–1.89)	0.002	1.57 (1.13–2.17)	0.007	2.19 (1.54–3.11)	<0.001	0.174
Chronic renal failure	2.28 (1.69–3.06)	<0.001	2.45 (1.67–3.57)	<0.001	4.43 (2.97–6.59)	<0.001	0.034
History of cancer	2.12 (1.66–2.71)	<0.001	2.34 (1.79–3.06)	<0.001	1.94 (1.13–3.32)	0.016	0.544
Severe LV dysfunction	2.53 (1.89–3.40)	<0.001	2.06 (1.43–2.96)	<0.001	4.59 (2.86–7.37)	<0.001	0.045
Disease extent (3 vessel disease)	1.29 (1.04–1.59)	0.02	1.33 (0.98–1.79)	0.069	1.53 (1.14–2.04)	0.004	0.787
All-cause death							
CTO-PCI	0.54 (0.43–0.67)	<0.001					
Age >75	2.48 (1.99–3.09)	<0.001	2.28 (1.72–3.02)	<0.001	3.90 (2.83–5.38)	<0.001	0.014
Diabetes mellitus	1.60 (1.31–1.95)	<0.001	1.70 (1.30–2.23)	<0.001	1.89 (1.42–2.51)	<0.001	0.605
Previous stroke	1.62 (1.23–2.14)	0.001	1.84 (1.29–2.62)	0.001	2.35 (1.56–3.55)	<0.001	0.377
Chronic renal failure	2.94 (2.15–4.02)	<0.001	3.03 (2.00–4.57)	<0.001	5.42 (3.50–8.38)	<0.001	0.057

History of cancer	2.38 (1.82–3.13)	<0.001	2.91 (2.17–3.92)	<0.001	2.32 (1.26–4.27)	0.007	0.511
Severe LV dysfunction	3.33 (2.40–4.61)	<0.001	2.85 (1.93–4.21)	<0.001	5.38 (3.14–9.21)	<0.01	0.266
Any repeat revascularization							
CTO-PCI	0.72 (0.56–0.93)	0.012					
Previous PCI	1.58 (1.23–2.02)	<0.001	1.42 (0.96–2.12)	0.082	1.48 (1.09–2.03)	0.013	0.876
Disease extent (3 vessel disease)	2.23 (1.63–3.05)	<0.001	1.35 (0.83–2.22)	0.231	2.58 (1.75–3.82)	<0.001	0.083
CTO site (LCx)	0.65 (0.45–0.94)	0.021					
Cardiac death							
CTO-PCI	0.49 (0.38–0.63)	<0.001					
Age >75	3.16 (2.46–4.05)	<0.001	2.76 (2.01–3.81)	<0.001	4.08 (2.81–5.94)	<0.001	0.121
Diabetes mellitus	1.88 (1.49–2.37)	<0.001	2.38 (1.73–3.29)	<0.001	1.80 (1.29–2.52)	0.001	0.237
Congestive heart failure	1.71 (1.14–2.56)	0.01	2.84 (1.75–4.59)	<0.001	7.22 (4.40–11.9)	<0.001	0.008
Previous stroke	1.90 (1.40–2.58)	<0.001	2.25 (1.53–3.33)	<0.001	2.69 (1.69–4.27)	<0.001	0.569
Chronic renal failure	2.98 (2.10–4.23)	<0.001	3.28 (2.04–5.25)	<0.001	6.91 (4.30–11.1)	<0.001	0.028
Severe LV dysfunction	3.07 (2.08–4.55)	<0.001	3.86 (2.52–5.89)	<0.001	6.89 (3.83–12.4)	<0.001	0.414
Disease extent (3 vessel disease)	1.44 (1.07–1.94)	0.016	1.98 (1.27–3.11)	0.003	1.69 (1.13–2.53)	0.011	0.523
CTO lesion-related revascularization							
CTO-PCI	0.37 (0.25–0.54)	<0.001					
CTO site (LCx)	0.42 (0.24–0.75)	0.003	0.75 (0.42–1.34)	0.328	0.72 (0.44–1.18)	0.196	0.904

*HRs are for the PCI group as compared with the OMT group.

CI = confidence interval; CTO = chronic total occlusion; LCx = left circumflex coronary artery; LV = left ventricle; MI = myocardial infarction; NA = Not

available; PCI = percutaneous coronary intervention

Figure 1. Study Flowchart

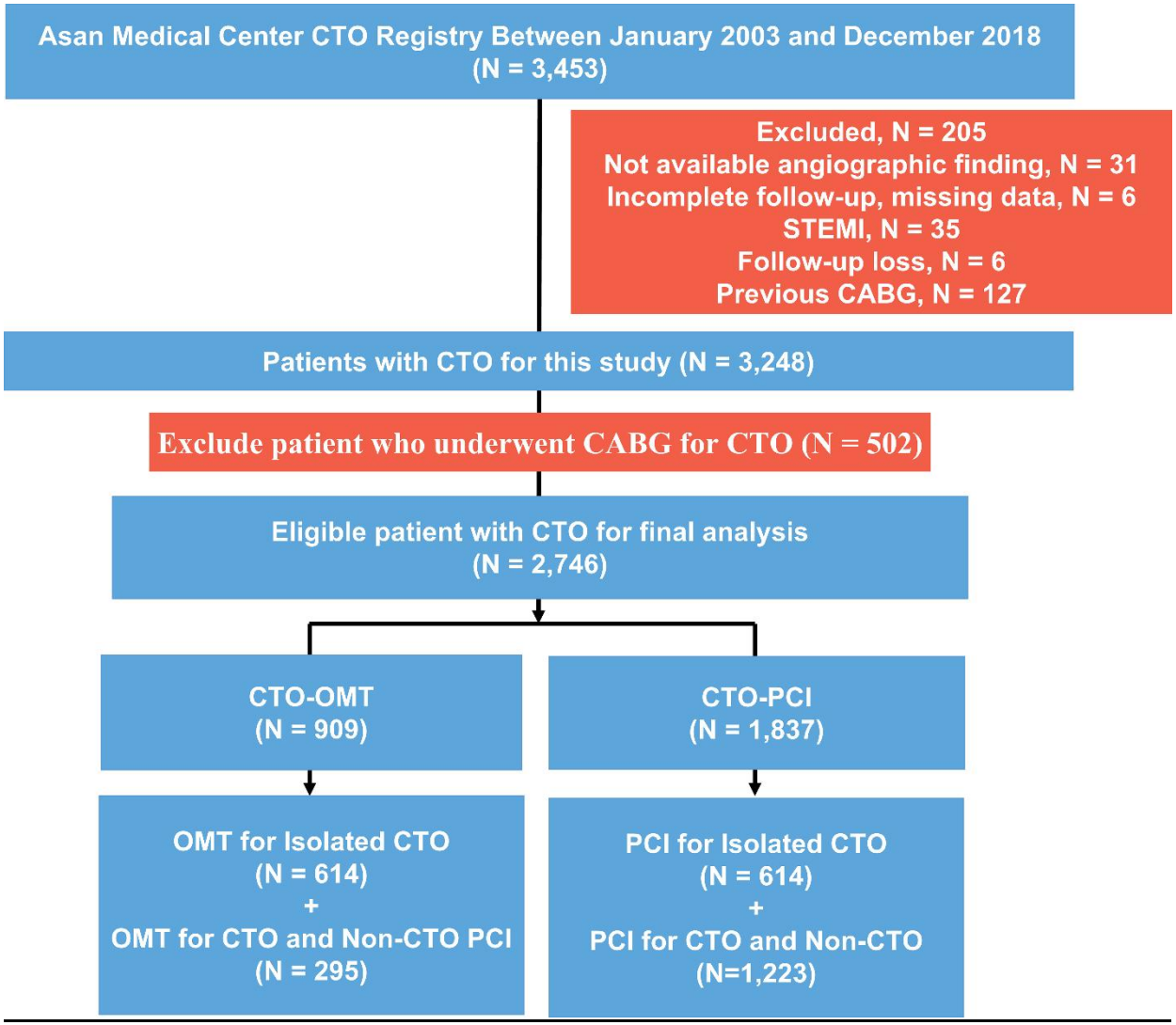


Figure 2. **Risks of the Primary Composite Outcome According to Initial Strategy**

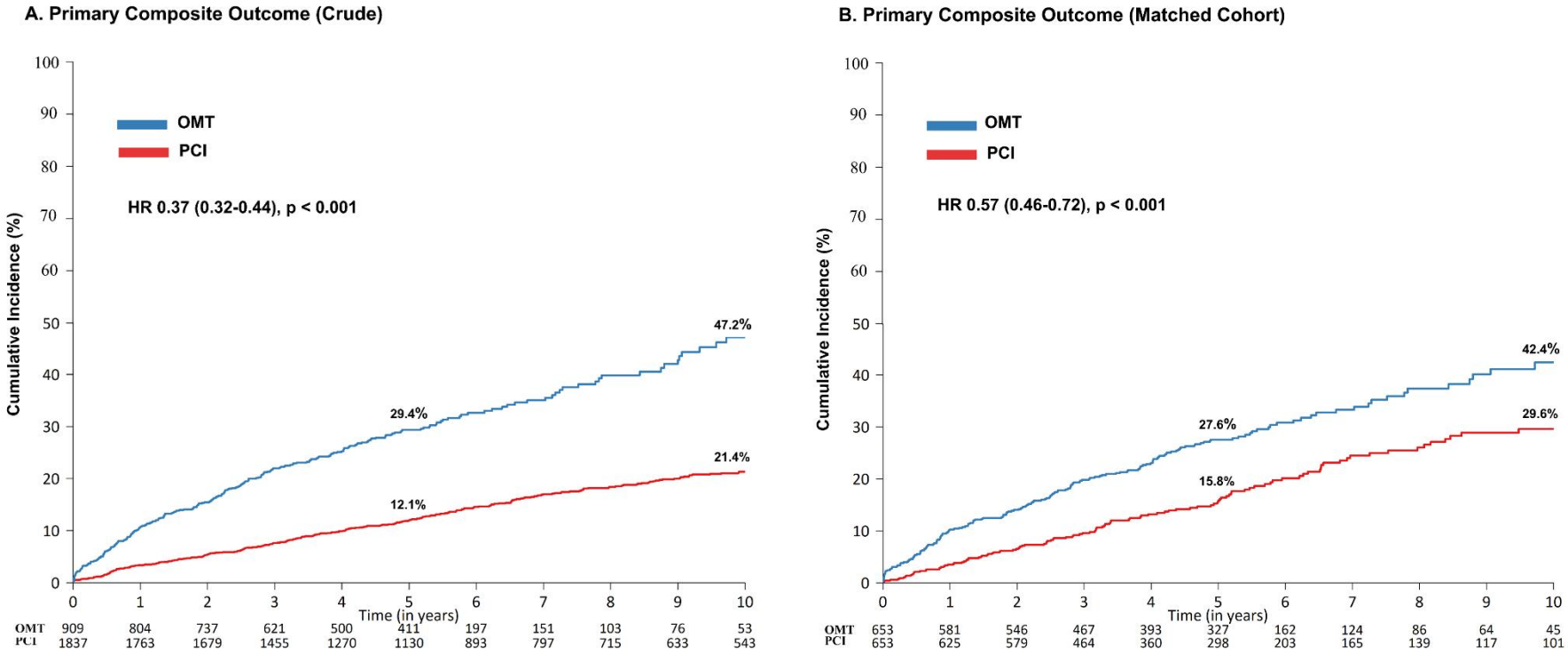


Figure 3. Risks of the All-cause or Cardiac Death According to Initial Strategy

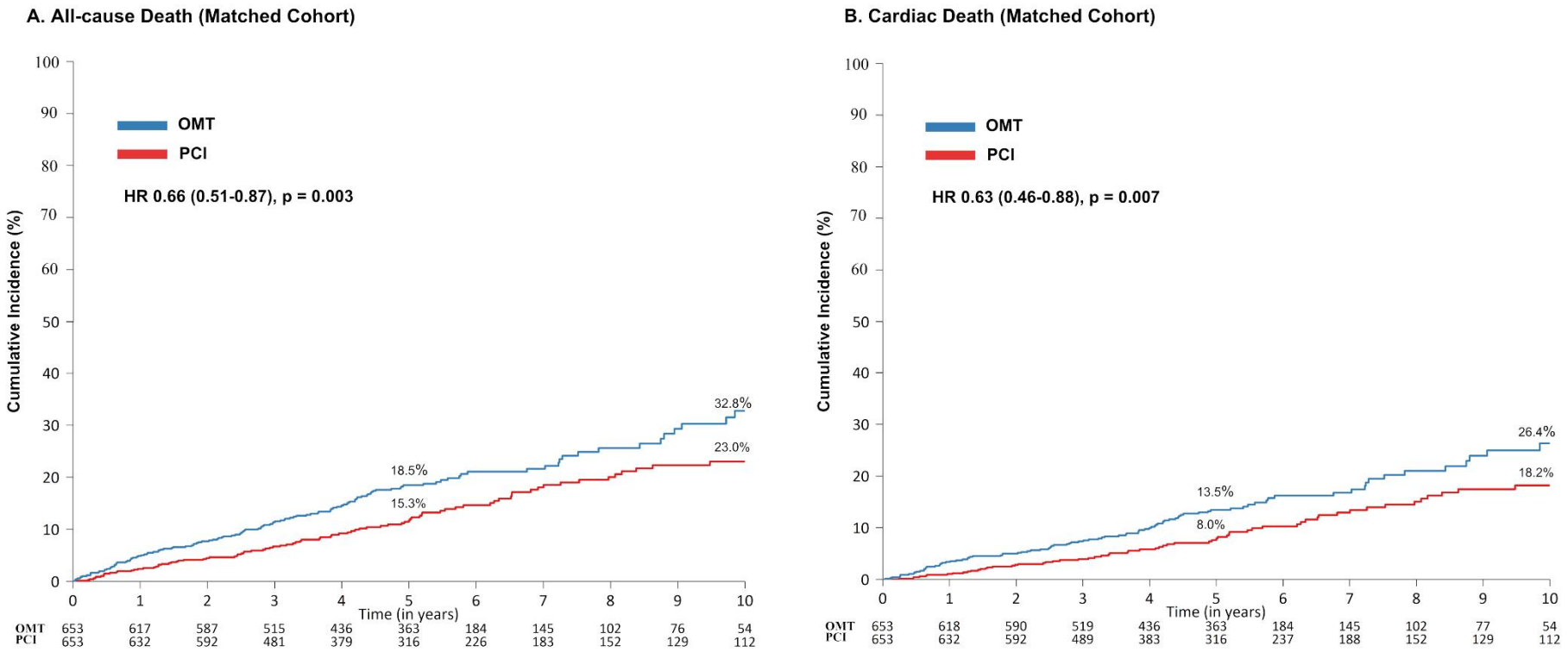
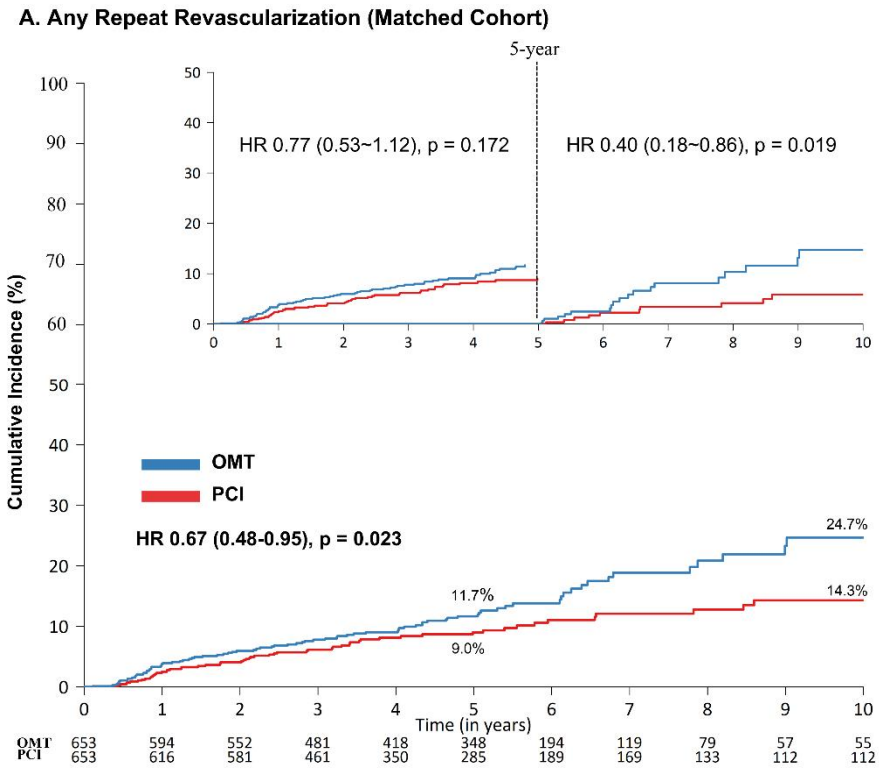


Figure 4 Risks of the Repeat Revascularization According to Initial Strategy



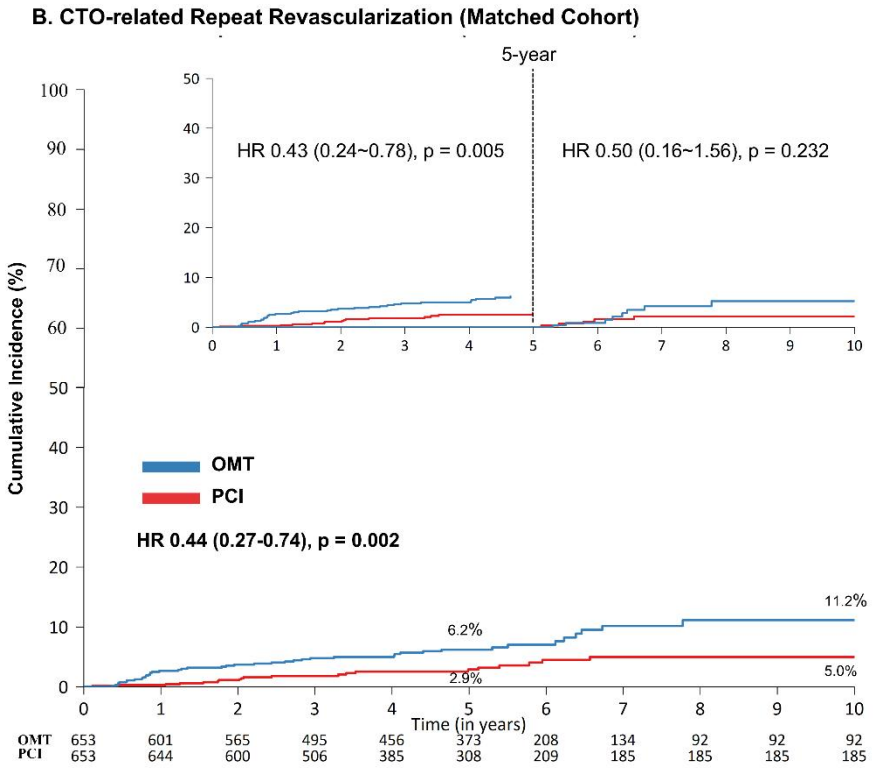
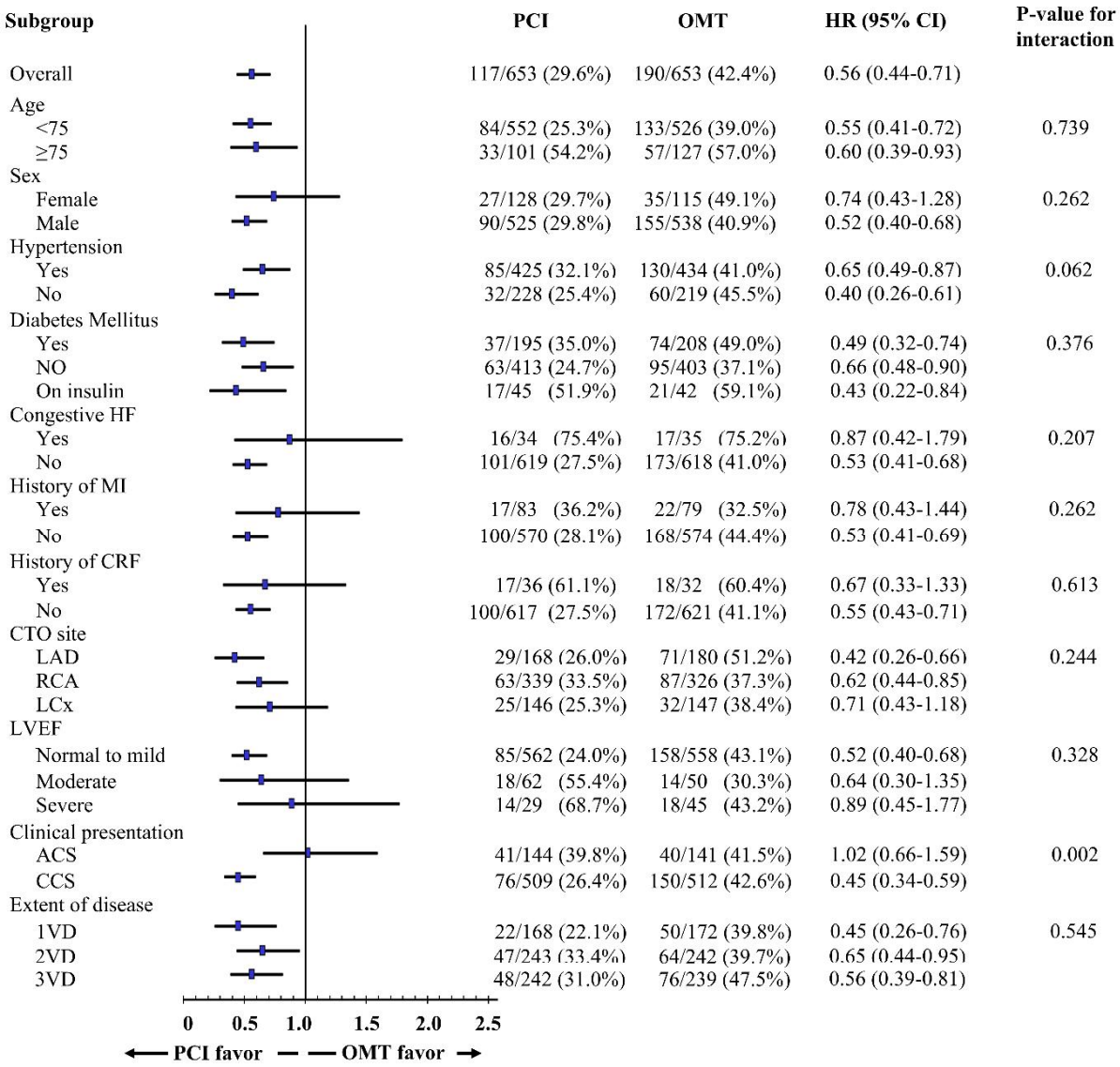
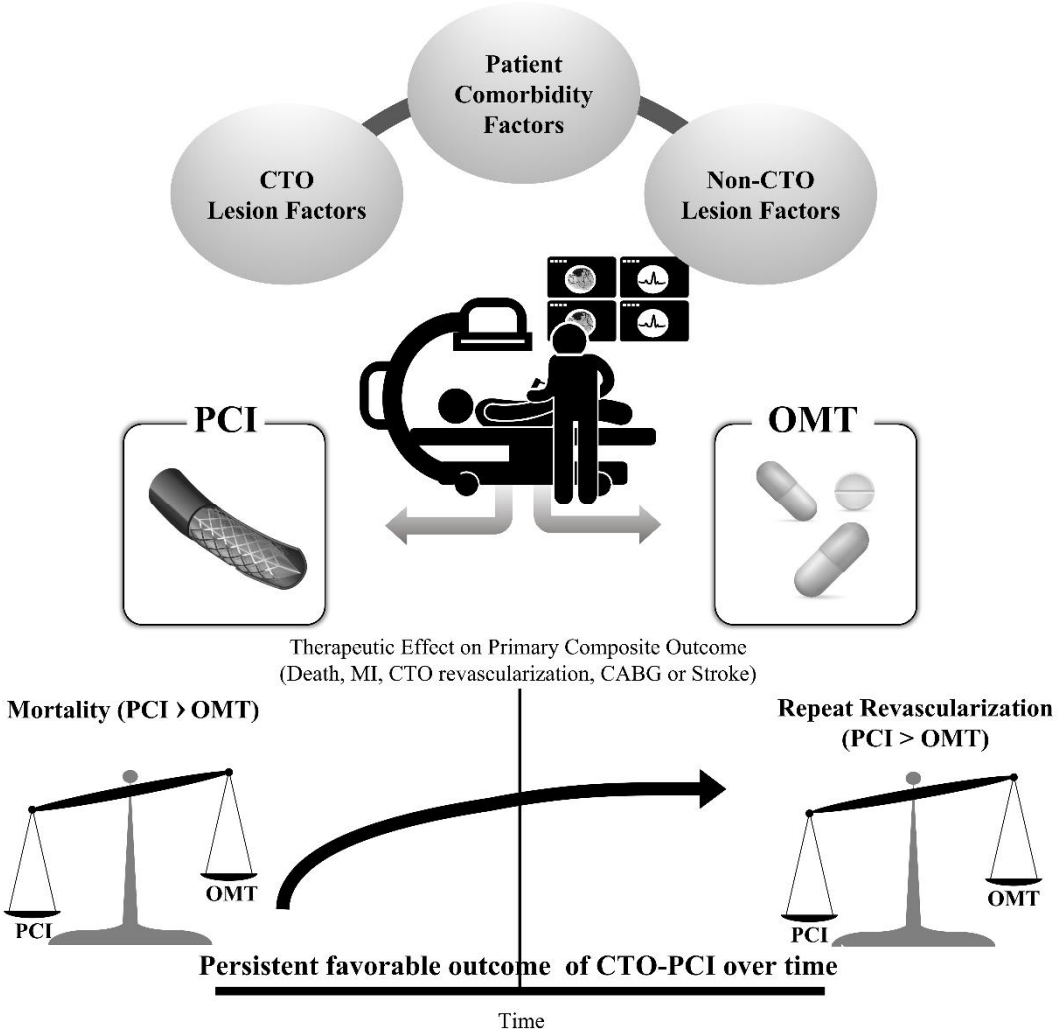


Figure 5


Subgroup
PCI
OMT
HR (95% CI)
P-value for interaction
Overall 117/653 (29.6%) 190/653 (42.4%) 0.56 (0.44-0.71)
Age
<75 84/552 (25.3%) 133/526 (39.0%) 0.55 (0.41-0.72) 0.739
≥75 33/101 (54.2%) 57/127 (57.0%) 0.60 (0.39-0.93)
Sex
Female 27/128 (29.7%) 35/115 (49.1%) 0.74 (0.43-1.28) 0.262
Male 90/525 (29.8%) 155/538 (40.9%) 0.52 (0.40-0.68)
Hypertension
Yes 85/425 (32.1%) 130/434 (41.0%) 0.65 (0.49-0.87) 0.062
No 32/228 (25.4%) 60/219 (45.5%) 0.40 (0.26-0.61)
Diabetes Mellitus
Yes 37/195 (35.0%) 74/208 (49.0%) 0.49 (0.32-0.74) 0.376
NO 63/413 (24.7%) 95/403 (37.1%) 0.66 (0.48-0.90)
On insulin 17/45 (51.9%) 21/42 (59.1%) 0.43 (0.22-0.84)
Congestive HF
Yes 16/34 (75.4%) 17/35 (75.2%) 0.87 (0.42-1.79) 0.207
No 101/619 (27.5%) 173/618 (41.0%) 0.53 (0.41-0.68)
History of MI
Yes 17/83 (36.2%) 22/79 (32.5%) 0.78 (0.43-1.44) 0.262
No 100/570 (28.1%) 168/574 (44.4%) 0.53 (0.41-0.69)
History of CRF
Yes 17/36 (61.1%) 18/32 (60.4%) 0.67 (0.33-1.33) 0.613
No 100/617 (27.5%) 172/621 (41.1%) 0.55 (0.43-0.71)
CTO site
LAD 29/168 (26.0%) 71/180 (51.2%) 0.42 (0.26-0.66) 0.244
RCA 63/339 (33.5%) 87/326 (37.3%) 0.62 (0.44-0.85)
LCx 25/146 (25.3%) 32/147 (38.4%) 0.71 (0.43-1.18)
LVEF
Normal to mild 85/562 (24.0%) 158/558 (43.1%) 0.52 (0.40-0.68) 0.328
Moderate 18/62 (55.4%) 14/50 (30.3%) 0.64 (0.30-1.35)
Severe 14/29 (68.7%) 18/45 (43.2%) 0.89 (0.45-1.77)
Clinical presentation
ACS 41/144 (39.8%) 40/141 (41.5%) 1.02 (0.66-1.59) 0.002
CCS 76/509 (26.4%) 150/512 (42.6%) 0.45 (0.34-0.59)
Extent of disease
1VD 22/168 (22.1%) 50/172 (39.8%) 0.45 (0.26-0.76) 0.545
2VD 47/243 (33.4%) 64/242 (39.7%) 0.65 (0.44-0.95)
3VD 48/242 (31.0%) 76/239 (47.5%) 0.56 (0.39-0.81)
0 0.5 1.0 1.5 2.0 2.5
PCI favor
OMT favor

HF = heart failure; MI = myocardial infart; CRF = chronic renal failure; CTO = chronic total occlusion; LAD = left anterior descending; RCA right coronary artery; LCx = left circumflex artery; LV = left ventricle; EF = ejection fraction; ACS = acute coronary syndrome; CCS = chronic coronary syndrome; VD = vessel disease.

Central Illustration (Figure 6)



Supplementary Appendix

This appendix is provided by the authors to provide readers with additional information about their work. Supplement to: TO Kim, PH Lee et al. "**Long-Term Outcomes of Percutaneous Coronary Intervention Versus Optimal Medical Treatment for Chronic Total Occlusion**"

Supplementary Table 1. Clinical Variables that Led to the Selection of Optimal Medical Treatment Over Percutaneous Coronary Intervention in Patients with Chronic Total Occlusion

Variable	Estimate	Standard Error	Wald Chi-Squared	Pr > Chi-Squared
Complete revascularization for Non-CTO lesion	1.7598	0.1585	123.3401	< 0.001
CTO site (LCx)	1.4958	0.1401	113.9279	< 0.001
Year of procedure (late year)	0.1235	0.013	89.6543	< 0.001
CTO site (RCA)	1.0063	0.1166	74.4708	< 0.001
History of cancer	1.5263	0.1824	69.9907	< 0.001
Disease extent (3 vessel disease)	0.8869	0.1323	44.9197	< 0.001
Severe LV dysfunction	-0.0342	0.00549	38.7758	< 0.001
Age (> 75 years)	0.0341	0.00609	31.3439	< 0.001
Previous MI	0.5703	0.1618	12.4259	< 0.001
Hyperlipidemia	0.4384	0.1318	11.063	< 0.001
Diabetes mellitus	0.2696	0.1081	6.221	0.0126
Chronic coronary syndrome	0.2517	0.1204	4.3665	0.0367
BMI	-0.0284	0.0157	3.2599	0.071
Hypertension	0.2002	0.108	3.4369	0.0638
Previous Stroke	0.2884	0.1696	2.8897	0.0891
Disease extent (2 vessel disease)	0.1914	0.1231	2.4173	0.12
Current Smoker	0.1519	0.1166	1.6978	0.1926
Estimated GFR	-0.00417	0.00337	1.5326	0.2157
Congestive heart failure	-0.2928	0.2641	1.2289	0.2676

Peripheral artery disease	0.262	0.2428	1.1637	0.2807
Previous PCI	0.1068	0.1184	0.8124	0.3674
Chronic renal failure	-0.3243	0.3904	0.6902	0.4061
Dialysis	0.2362	0.4607	0.2628	0.6082
Chronic lung disease	0.1177	0.3092	0.1449	0.7035
Sex, male	0.00905	0.1331	0.0046	0.9458
Atrial fibrillation	0.0145	0.2659	0.003	0.9566
Diabetes mellitus requiring insulin	-0.00745	0.2182	0.0012	0.9728

Propensity score-matched pairs were found using a greedy algorithm with a caliper of 0.2 standard deviations of the logit of the propensity score (c-statistic = 0.821; Hosmer-Lemeshow statistic = 8.4762; df = 8; p = 0.3884 supported the goodness of fit).

Supplementary Table 2. Procedural Characteristics According to the Initial Treatment Strategies for Chronic Total Occlusion*

Variable	Unadjusted			Propensity Score-Matched		
	PCI (N=1837)	OMT (N=909)	p Value	PCI (N=653)	OMT (N=653)	p Value
CTO lesion treatment†						
Failed PCI	106 (5.8%)					
CABG after failed PCI	12 (0.7%)			4 (0.6%)		
Medical treatment after failed PCI	94 (5.1%)			13 (2.0)		
Ballooning	91 (5.0%)			47 (7.2%)		
Stenting	1640 (89.3%)			565 (86.5%)		
Stent generation for CTO‡						
BMS	31 (1.7%)			11 (1.7%)		
1st DES	505 (27.5%)			71 (10.9%)		
2nd DES	1104 (60.1%)			483 (74.0%)		
No. of stents for CTO	2.0 (1.0–2.0)			2.0 (1.0–2.0)		
Stent diameter for CTO	3.1 (3.0–3.5)			3.1 (3.0–3.5)		
Total stent length for CTO	51.0 (33.0–66.0)			53.0 (33.0–74.0)		
Complete revascularization for CTO	1523 (82.9%)			556 (85.1%)		
Non-CTO lesion treatment	1,223 (66.6%)	295 (32.5%)		490 (75.0%)	213 (32.6%)	
Ballooning	1 (0.1%)ⁿ	13 (4.4%)ⁿ	<0.001	0	10 (4.7%)ⁿ	<0.001
stenting	1,222 (99.9%)ⁿ	282 (95.6) ⁿ		490 (100%)ⁿ	203 (95.3%)ⁿ	
Stent generation for Non-CTO						

BMS	21 (1.7%) [n]	6 (2.0%) [n]	<0.001	12 (2.4%)[n]	0	<0.001
1st DES	329 (26.9%) [n]	11 (3.7%) [n]		67 (13.7%) [n]	11 (5.2%) [n]	
2nd DES	872 (71.3%) [n]	265 (89.8%) [n]		411 (83.9%) [n]	192 (90.1%) [n]	
No. of stents for non-CTO	1.0 (1.0–2.0)	1.0 (1.0–2.0)	0.001	1.0 (1.0~2.0)	1.0 (1.0–2.0)	0.001
Stent diameter for non-CTO	3.25 (3.0–3.5)	3.5(3.0–3.5)	0.003	3.3 (3.0~3.5)	3.5 (3.0–3.5)	0.012
Total stent length for non-CTO	32.0 (23.0–40.0)	38.0 (24.0–52.0)	0.002	33.0 (23.0–45.0)	36 (23.3–52.0)	0.03
Complete revascularization for non-CTO	797 (65.2%)	217 (73.6%)	<0.001	407 (83.1%)	179 (84.0%)	0.56

Values are n (%) or median (interquartile range).

BMS = bare-metal stent; CABG = coronary artery bypass grafting; CTO = chronic total occlusion; DES = drug-eluting stent; PCI = percutaneous coronary intervention

[†]The sum of the ratio of each element for target CTO treatment is not 100% because there were 41 (2.2%) cases of missing data in the unmatched population and 24 (3.7%) cases in the matched population.

[‡]The sum of the ratio of each element for target CTO stent generation is not 100% because there were 197 (10.7%) cases of missing data in the unmatched population and 88 (13.5%) cases in the matched population.

[n]Percentages were calculated as the proportion of patients treated for Non-CTO lesions in each group.

Supplementary Table 3. Cardiac-Related Medications at Discharge According to the Initial Treatment Strategies for Chronic Total Occlusion

	Unadjusted			Propensity Score-Matched		
	PCI (N=1837)	OMT (N=909)	p Value	PCI (N=653)	OMT (N=653)	p Value
Aspirin	1582 (86.1%)	890 (94.6%)	0.003	622 (95.3%)	563 (86.2%)	<0.001
P2Y12 inhibitor	1568 (85.4%)	840 (92.4%)	0.004	617 (94.5%)	422 (64.6%)	<0.001
Clopidogrel	1549 (84.3%)	815 (89.7%)	0.006	605 (92.6%)	402 (61.6%)	<0.001
Dual antiplatelet therapy	1563 (85.1%)	838 (92.2%)	0.005	614 (94.0%)	400 (61.3%)	<0.001
Beta blocker	1187 (64.6%)	674 (74.1%)	<0.001	463 (70.9%)	486 (74.4%)	0.172
Calcium channel blocker	1259 (68.5%)	576 (63.4%)	0.007	470 (72.0%)	425 (65.1%)	0.009
ACE inhibitor/ ARB	677 (36.9%)	469 (51.6%)	<0.001	284 (43.5%)	325 (49.8%)	0.027
Nitrate	664 (36.1%)	260 (28.6%)	<0.001	177 (27.1%)	182 (27.9%)	0.804
Statin	1503 (81.8%)	826 (90.9%)	<0.001	600 (91.9%)	595 (91.1%)	0.691

Data are n (%).

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker.

Supplementary Table 4. Unadjusted event rates of the primary and secondary outcomes according to the initial treatment strategies

	Unadjusted				Propensity Score-Matched			
	Overall (n=2746)	**PCI (n=1837)**	**OMT (n=909)**	**p Value**	**Overall (n=1306)**	**PCI (n=653)**	**OMT (n=653)**	**p Value**
Primary composite of all cause death, spontaneous MI, stroke, or any repeat revascularization								
5-year	439 (17.8%)	197 (12.1%)	242 (29.4%)	<0.001	250 (21.9%)	85 (15.8%)	165 (27.6%)	<0.001
10-year	564 (28.1%)	286 (21.4%)	278 (47.2%)	<0.001	307 (35.8%)	117 (29.6%)	190 (42.4%)	<0.001
5–10 years	125 (12.6%)	89 (10.6%)	36 (25.2%)	<0.001	57 (17.8%)	32 (16.4%)	25 (20.5%)	0.777
All-cause death								
5-year	307 (12.6%)	129 (8.0%)	178 (22.0%)	<0.001	170 (15.3%)	62 (15.3%)	108 (18.5%)	0.001
10-year	405 (20.9%)	196 (15.0%)	209 (38.5%)	<0.001	217 (27.4%)	88 (23.0%)	129 (32.8%)	0.003
5–10 years	98 (9.5%)	67 (7.7%)	31 (21.2%)	<0.001	47 (14.3%)	26 (12.8%)	21 (17.5%)	0.811
Spontaneous MI								
5-year	42 (1.8%)	21 (1.3%)	21 (2.7%)	0.009	28 (2.5%)	9 (1.7%)	19 (3.3%)	0.075
10-year	52 (2.8%)	31 (2.5%)	21 (2.7%)	0.052	30 (3.3%)	11 (3.0%)	19 (3.3%)	0.143
5–10 years	10 (1.0%)	10 (1.2%)	0 (0.0%)	0.162	2 (0.8%)	2 (1.3%)	0 (0.0%)	NA‡
Stroke								
5-year	49 (2.0%)	22 (1.4%)	27 (3.4%)	<0.001	33 (2.9%)	8 (1.4%)	25 (4.3%)	0.006
10-year	58 (3.0%)	29 (2.2%)	29 (5.6%)	<0.001	34 (3.4%)	8 (1.4%)	26 (5.6%)	0.004
5–10 years	9 (1.0%)	7 (0.8%)	2 (2.3%)	0.579	1 (0.5%)	0 (0.0%)	1 (1.4%)	NA‡

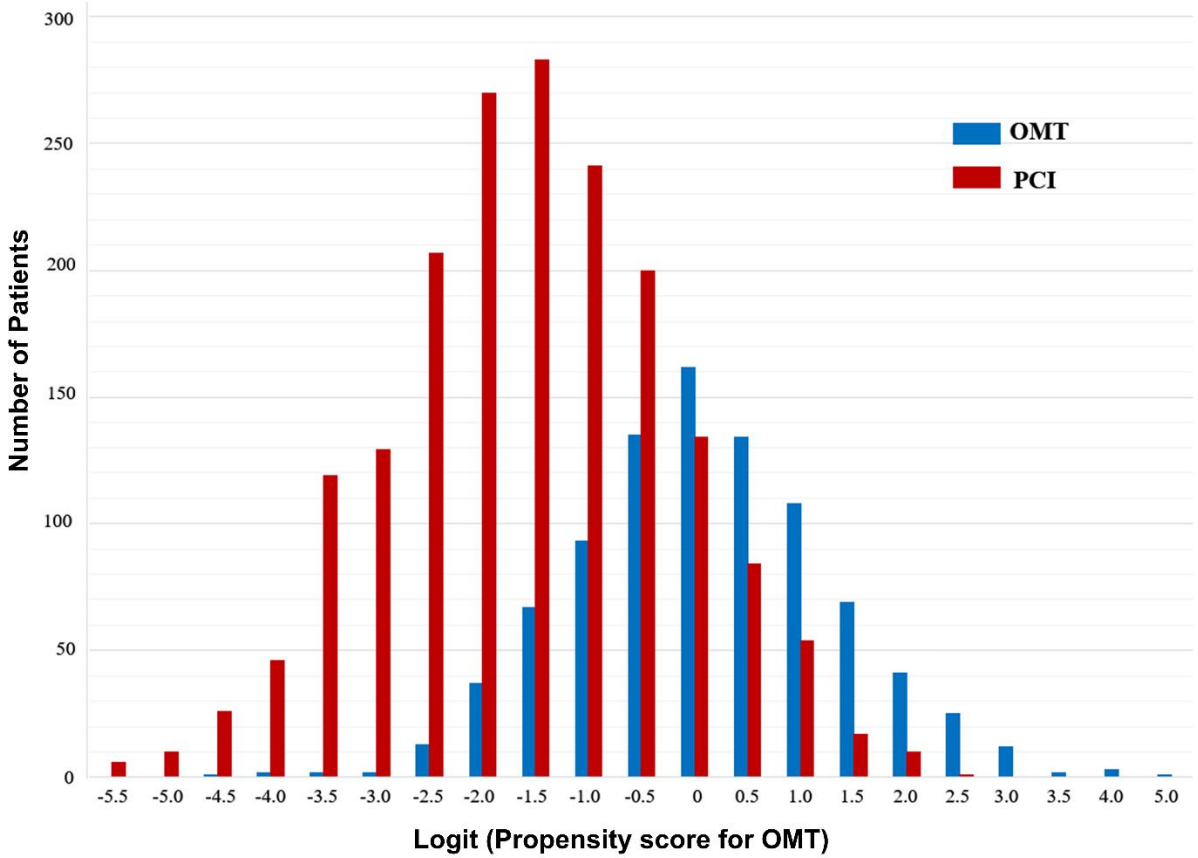
Any repeat revascularization								
5-year	217 (9.2%)	135 (8.2%)	82 (11.2%)	0.039	112 (10.4%)	48 (9.0%)	64 (11.7%)	0.172
10-year	284 (15.8%)	182 (14.0%)	102 (22.7%)	0.002	141 (18.9%)	58 (14.3%)	83 (24.7%)	0.023
5–10 years	67 (7.4%)	47 (6.3%)	20 (12.9%)	0.001	29 (9.5%)	10 (5.8%)	19 (14.8%)	0.019
Cardiac death								
5-year	214 (9.1%)	87 (5.5%)	127 (16.6%)	<0.001	115 (10.8%)	40 (8.0%)	75 (13.5%)	0.003
10-year	297 (16.4%)	142 (11.5%)	155 (31.5%)	<0.001	156 (22.0%)	62 (18.2%)	94 (26.4%)	0.007
5–10 years	83 (8.1%)	55 (6.4%)	28 (17.9%)	<0.001	41 (12.5%)	22 (11.2%)	19 (14.9%)	0.673
CTO-related repeat revascularization								
5-year	90 (3.8%)	45 (2.8%)	45 (6.0%)	<0.001	50 (4.6%)	15 (2.9%)	35 (6.2%)	0.005
10-year	115 (6.1%)	61 (4.6%)	54 (10.8%)	<0.001	63 (7.9%)	20 (5.0%)	43 (11.2%)	0.002
5–10 years	25 (2.4%)	16 (1.9%)	9 (5.1%)	0.01	13 (3.5%)	5 (2.2%)	8 (5.3%)	0.232

Data are n (%).

‡In the cases of spontaneous MI and stroke, P values between the two groups could not be derived after propensity matching due to the low outcome rate.

CI = confidence interval; MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting.

Supplementary Figure 1

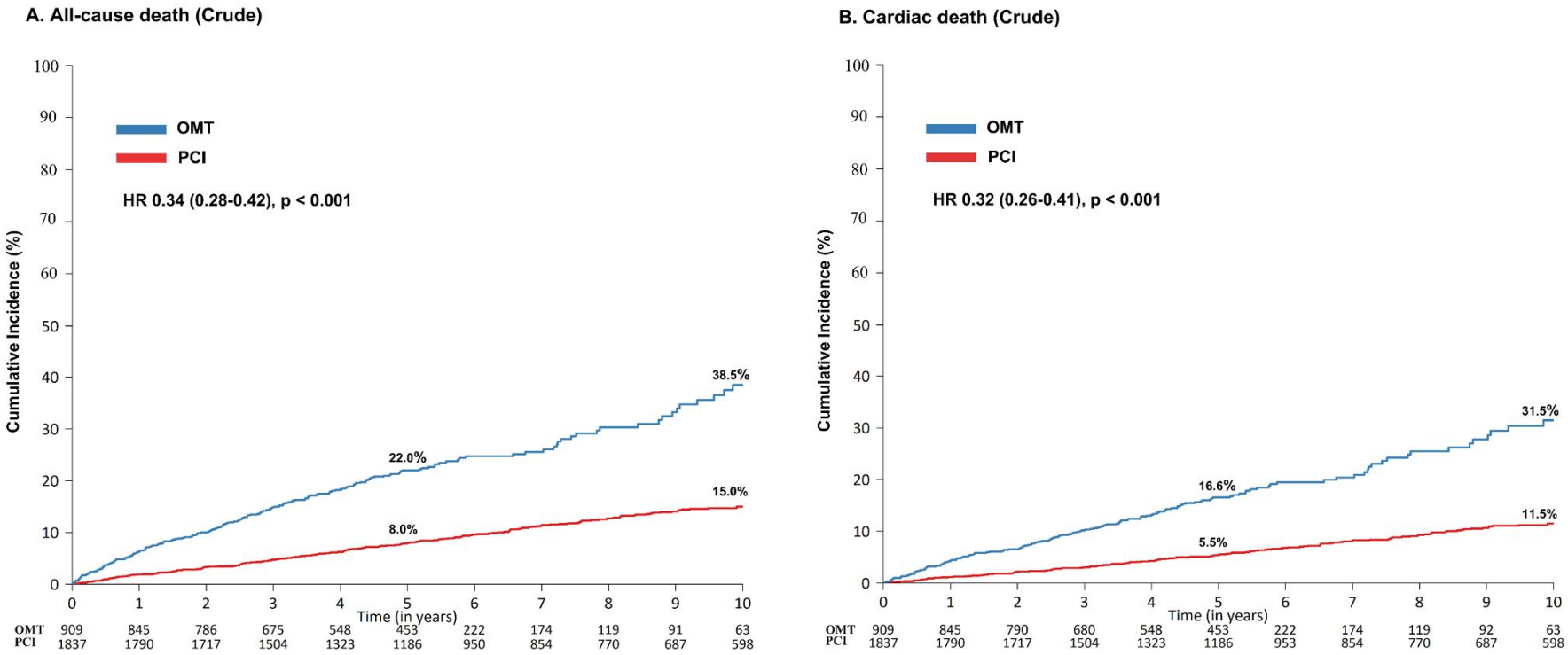


The propensity score for OMT is the probability, given the baseline variables, that any patient in either group would be selected for OMT.

The logit of the propensity score has a value of – infinity to + infinity, and matches the probability value for OMT one-on-one.

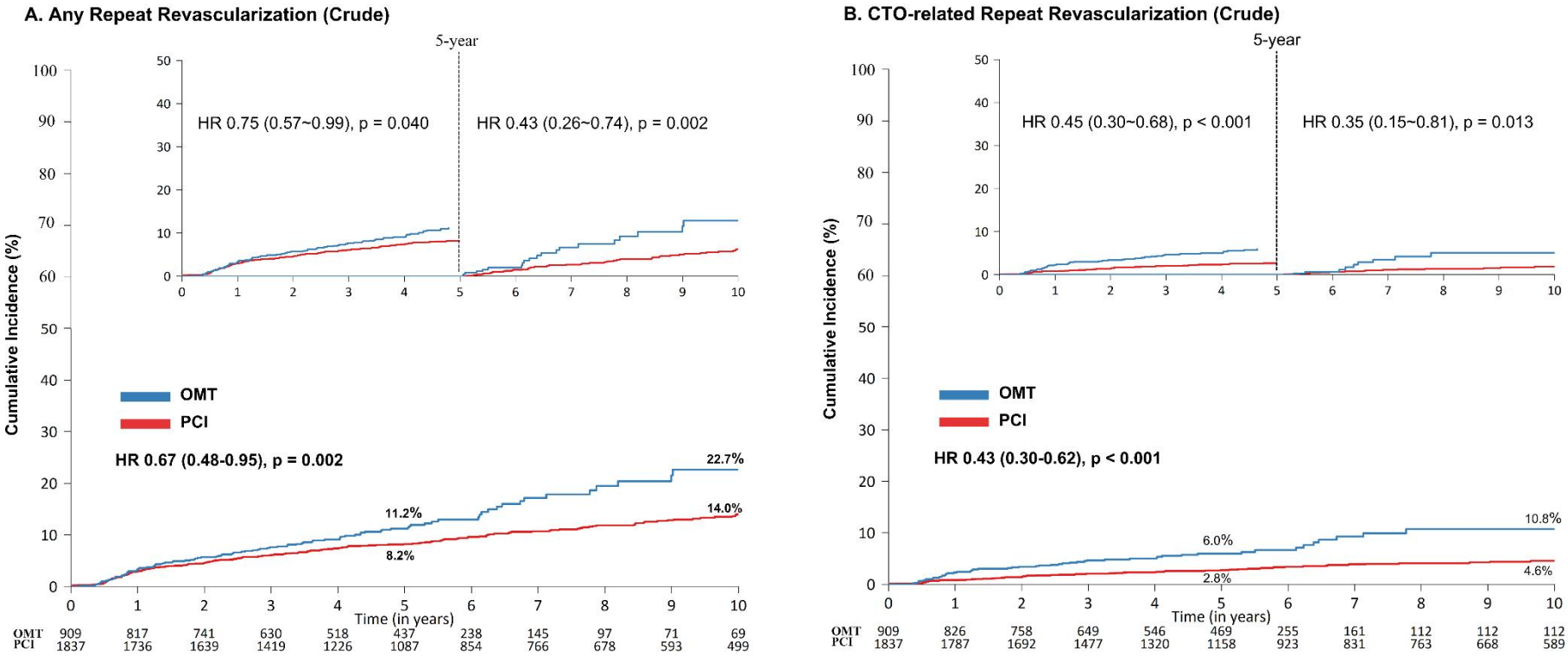
CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

Supplementary Figure 2.



OMT = optimal medical treatment; PCI = percutaneous coronary intervention

Supplementary Figure 3.



OMT = optimal medical treatment; PCI = percutaneous coronary intervention

국문요약

배경: 장기적 예후 측면에서 관상 동맥의 만성 완전 폐쇄 병변에 대한 관상 동맥 중재 시술의 이점은 논란이 있다.

목적: 본 연구는 관상 동맥의 만성 완전 폐쇄 병변에 대한 치료법으로 관상 동맥 중재 시술과 최적의 약물 치료의 장기간 예후를 비교하고자 한다.

방법: 2003년 1월부터 2018년 12월까지 총 3,248명의 관상동맥 만성 완전 폐쇄 병변을 가진 환자를 대상으로, 관상 동맥 우회 수술을 시행 받은 502명의 환자는 제외하고, 관상 동맥 중재 시술을 받은 1,837명과 최적의 약물을 받은 909명의 환자로 양분하여 분석을 진행하였다. 주 관심 결과는 사망, 자발성 심근 경색, 뇌경색, 혹은 반복적 재관류 시술의 합산이다. 성향 점수 보정을 통해 기본 특성이 비슷한 환자의 코호트를 구성하였다.

결과: 성향 점수 보정 이후 총 653 쌍의 환자군을 형성하였고, 주 관심 결과의 보정 위험도는 약물 치료군과 비교하여 관상동맥 중재시술 군에서 유의하게 낮았다. (위험도 0.57; 95% 신뢰도: 0.46~0.72, p 값 < 0.001). 이러한 치료 이득은 주로 사망률의 감소 (위험도: 0.66; 95% 신뢰도: 0.51~0.87, p값 0.003)과 반복적 재관류 시술의 감소(위험도: 0.67; 95% 신뢰도: 0.48~0.95, p값 0.023)에서 유발되었다. 만성 완전 폐쇄 병변에 대한 관상동맥 중재 시술의 이득은 고령, 고혈압, 당뇨병 및 진행된 관상동맥질환과 같은 주요 심혈관 질환의 위험 인자를 가진 하위 그룹 전반에 걸쳐 일관되게 관찰되었다.

결론: 초기 치료 전략으로, 관상동맥의 만성 완전 폐쇄 병변에 대한 관상 동맥 중재 시술은 장기간의 추적 관찰 중에 주요 심혈관 질환의 사건을 감소와 연관되었다.

중심 단어: 동맥 경화, 관상 동맥 질환, 만성 완전 폐쇄, 경도관 관상 동맥 중재시술, 최적의 약물 치료