Master of Medicine

Short versus Long Duration Dual Antiplatelet Therapy after Drug-Eluting Stent for Coronary Chronic Total Occlusion Lesions

관동맥 만성폐색병변에서 약물방출스텐트 치료 후 이중 항혈소판제제의 단기 및 장기 사용에 대한 연구

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Short versus Long Duration Dual Antiplatelet Therapy after Drug-Eluting Stent for Coronary Chronic Total Occlusion Lesions

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ABSTRACT

BACKGROUND The optimal duration of dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) in patients with chronic total lesion (CTO) is still controversial.

METHODS From Feb 2003 to May 2015, consecutive patients who underwent CTO-PCI with drug-eluting stents in Asan medical center were analyzed. The primary outcome was a major cardiovascular adverse event (MACE, composite of death, myocardial infarction, stent thrombosis, target vessel revascularization). Propensity-score matching with a 1:3 ratio was used for between-group comparison.

RESULTS A total of 1119 CTO patients treated with drug-eluting stents was evaluated. Among excluding 169 patients who were followed up for less than 2 years, a total of 950 patients were included in the analysis. DAPT was used for 6 months or less and more than 6 months in 83 patients and 867 patients, respectively. In the matched cohort, the 5-year risk of MACE for long DAPT, as compared with the short DAPT, was not significantly different (hazard ratio [HR] 0.68, 95% confidence interval [CI]: 0.41-1.13; P=0.14). Similarly, there were no significant differences in the risk of death (HR 0.64, 95% CI, 0.27-1.50, P=0.31], myocardial infarction (HR:0.82, 95% CI 0.49-1.37, p=0.45), and target vessel revascularization (HR: 0.67, 95% CI 0.35-1.28 P=0.23). However, the risk of stent thrombosis was significantly higher with shorter DAPT (HR: 0.06, 95% CI 0.01-0.55, P=0.01).

CONCLUSION After CTO-PCI with drug-eluting stents, there was no significant difference in major clinical outcomes between short and long DAPT. However, long DAPT strategy may be preferred considering the increased risk of stent thrombosis.

Key Words: atherosclerosis, chronic total lesion, percutaneous coronary intervention, dual antiplatelet therapy

ABBREVIATIONS

CAD = coronary artery disease

CTO = chronic total lesion

CI = confidence interval

DES = drug-eluting stent

HR = hazard ratio

MI = myocardial infarction

PCI = percutaneous coronary intervention

TVR = target vessel revascularization

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INTRODUCTION

The optimal duration of dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) is still debate. Longer-duration over 30 months DAPT after stent implantation was associated with the risk reduction of stent thrombosis and major cardiovascular and cerebrovascular events but with increasement of bleeding.[1] With second-generation drug-eluting stent (DES) implantation, 6 months of DAPT showed non-inferiority compared with the incidence of cardiac and bleeding events at 12 months.[2] In 2016 American College of Cardiology/ American Heart Association guideline recommended that patients with stable ischemic heart disease treated with DES, DAPT therapy should be given for at least 6 months.[3] In this guideline, extended DAPT over 6months is considered in patients with increased ischemic risk which did not cover chronic total lesion (CTO). In contrast, 2017 European Society of Cardiology focused update on DAPT suggested prolonged DAPT duration may be considered in complex PCI including CTO lesion.[4] Although major recent randomized trials report advantages related with DAPT beyond 12 months, which were accompanied by an increased number of bleeding events, several earlier studies suggested that there is no net clinical benefit of DAPT beyond 12 months after drug-eluting stent (DES) implantation to ischemic and bleeding events.[5-7] Longer DAPT after complex PCI significantly reduced the cardiac ischemic events. However, as high-risk procedural subsets, CTO lesion did not increase the major adverse event, coronary thrombotic events, stent thrombosis, and myocardial infarction.[8] For this reason, it is necessary to decide whether to exclude CTO lesion from complex PCI for identifying optimal DAPT duration after CTO PCI. A network meta-analysis of DAPT and DES was published recently and they consistently concluded that short term duration of DAPT was non-inferior for ischemic outcomes compared with 12 months.[9] The usage of DAPT longer than 6 months is recommend for patients with an increased risk of ischemia and stent thrombosis without high bleeding risk, but authors did not mention about the patients who underwent PCI in CTO lesion. Previously two retrospective studies evaluated the optimal DAPT duration of CTO patients treated with DES.[10,11] These reports showed inconsistent results. In one study, long-term use of DAPT for more than 12 months showed benefit, while other study did not. We compared two groups

with a DAPT duration of less than 6 months and a prolonged group over 6 months after successfully revascularization of CTO lesions.

METHODS

Study Population

This study was retrospective analysis with CTO registry in Asan medical center. From February 2003 through May 2015, patients aged over 20 years or older with CTO and underwent successful revascularization with DES were included. In this analysis, selecting patients with follow-up of more than 2 years were included. The duration of DAPT was determined by clinicians. The reasons for this differential treatment of extended DAPT regimen may be according to the patient's individual risk of bleeding and ischemic risk. We also performed a retrospective electric health record review of all patients to assess prescription history. Clinical, laboratory and outcome data were collected by a trained study coordinator using a standardized case report form and protocol.

Study Outcomes

The end point of the study was major cardiovascular adverse event (MACE) which is consist of death, myocardial infarction (MI), target vessel revascularization (TVR), and stent thrombosis (ST). Major bleeding was defined by the International Society of Thrombosis and Hemostasis (ISTH) criteria: clinically overt bleeding accompanied by a decrease in the hemoglobin level of $\geq$ 2g/dL or transfusion of at least 2 units of packed red cells or resulting in death. The definite cause of death was confirmed by the electric recorded hospital data classified by the International Classification of Disease or National Health Insurance Service system of South Korea.

Statistical analysis

Continuous variables were compared with Student's *t*-test or the Wilcoxon rank-sum test, and categorical variables were compared with the χ^2 test or Fisher's exact test (expected frequency: <5). Cumulative event rates were calculated using the Kaplan-Meier estimates, with event or censoring times calculated from the date of enrollment. Event rates were based on Kaplan-Meier estimates in time-to-first-event analyses and were compared using the log-rank test. Variables associated with MACE (all-cause mortality, MI, TVR, and stent thrombosis) were included in multiple cox-regression analyses. The propensity score is the conditional probability of receiving treatment given a set of baseline and procedure related characteristics. The propensity score was estimated using a logistic regression model,

with the treatment group of short duration DAPT as the dependent variable and the baseline and procedural characteristics outlined in Table 1, Table 2 as covariates.

RESULTS

Baseline Characteristics

Between Feb 2003 to May 2015, a total of 1119 CTO patients was evaluated. Follow up for less than 2 years was excluded and 950 patients were analyzed. The number of patients with DAPT duration less than 6 months was 83(8.7%), more than 6 months was 867(91.3%). The baseline demographic characteristics are summarized in Table1. and angiographic and procedural characteristics are described in Table 2. Before propensity score matching, there are several differences between two groups. Generally, patients who received short DAPT had lower incidence of dyslipidemia and current use of statin and had a higher proportion of previous generation DES use. There were no significant differences in CTO lesions, length, diameter, and numbers of stents. After matching, standardized differences were less than 0.1 for most variables excepts congestive heart failure without severe LV dysfunction, history of atrial fibrillation. In procedural characteristics, several variables such as lesions, generation of DES, total fluro-time still showed a difference of more than 0.10. Especially, the difference between the percentage of 1st generation DES was 39.4% (vs 66.3%) 6mo< DAPT group before matching and changed to 70.7% (vs 66.3%) after matching. Distribution of propensity score after match is shown at Figure 5.

Clinical Outcomes According to DAPT duration

The median follow-up duration was 5.57years (interquartile range, 3.46 to 7.74). The group that treated with over 6-months DAPT therapy have a significant lower incidence of MACE compared with under 6-months DAPT therapy (hazard ratio [HR]: 0.60; 95% confidence interval [CI]:0.38-0.95; P=0.03). There was no significant difference between all-cause mortality (HR: 0.68; 95% CI: 0.32-1.43; P=0.31) and cardiac death (HR:0.95; 95% CI: 0.29-3.15; P=0.94). MI also did not demonstrate obvious difference according to DAPT duration. However, significantly higher incidences were observed in short-duration DAPT group at target vessel revascularization (10.8% in the ≤ 6mo group, and 6.4% in the 6mo< group; HR: 0.53, P=0.04) and stent thrombosis (4.9% in the ≤ 6mo group, and 1.1% in the 6mo< group; HR: 0.06, P=0.01) (Table 5, Figure 2).

In the matched cohort, the rate of composite of all-cause mortality, MI, target vessel revascularization, and stent thrombosis at 5 years were similar between two groups. (21.1% in the ≤ 6mo group and 13.7% in the 6mo < group; adjusted hazard ratio [HR]: 0.68; CI: 0.41-1.13; P=0.14). The individual components of primary outcomes were also indifferent except stent thrombosis. The incidence of stent thrombosis remained higher in short duration DAPT group than over 6-month duration DAPT group. (4.9% in the ≤ 6mo group and 0.5% in the 6mo < group; aHR: 0.06; CI: 0.01-0.55; P=0.14 (Table 6, Figure 3).

There were no substantial interactions between DAPT duration and baseline, lesions and procedural characteristics to the MACE, as demonstrated in the forest plots in Figure 4.

Table 1. Baseline Characteristics

	DAPT Duration		
	≤ 6mo	**6mo <**	**p-test**
	(n=83)	**(n=867)**	
Age (mean (SD))	59.17 (9.77)	59.32 (10.33)	0.896
Male sex (%)	64 (77.1)	722 (83.3)	0.205
BMI (mean (SD))	25.35 (3.09)	25.41 (3.07)	0.877
Current Smoker (%)	17 (20.5)	221 (25.5)	0.382
Hypertension (%)	47 (56.6)	514 (59.3)	0.724
Diabetes (%)	30 (36.1)	246 (28.4)	0.173
- Requiring Insulin (%)	6 (7.2)	41 (4.7)	0.46
Dyslipidemia (%)	41 (49.4)	592 (68.3)	0.001
Chronic kidney disease (%)	2 (2.4)	18 (2.1)	1.000
Previous PCI (%)	15 (18.1)	222 (25.6)	0.167
Previous CABG (%)	2 (2.4)	29 (3.3)	0.893
Previous MI (%)	3 (3.6)	85 (9.8)	0.097
Stroke (%)	5 (6.0)	56 (6.5)	1.000
PVD (%)	5 (6.0)	20 (2.3)	0.096
COPD (%)	3 (3.6)	20 (2.3)	0.714
CHF (%)	6 (7.2)	77 (8.9)	0.76
- Ejection fraction (mean (SD))	58.52 (9.65)	57.94 (8.13)	0.544
- LV dysfunction <40% (%)	6 (7.2)	40 (4.6)	0.428
Atrial fibrillation	7 (8.4)	11 (1.3)	<0.001
Statin (%)	60 (72.3)	735 (84.8)	0.005

Beta blocker (%)	62 (74.7)	623 (71.9)	0.672
ACE/ARB (%)	26 (31.3)	297 (34.3)	0.677
CCB (%)	67 (80.7)	681 (78.5)	0.747

Values are n (%) or mean ± SD.

Table 2. Procedural Characteristics

	DAPT Duration		
	≤ 6mo	**6mo <**	**p-test**
	(n=83)	**(n=867)**	
Denovo lesion (%)	76 (91.6)	807 (93.1)	0.772
Lesion (%)			0.431
LM	0 (0.0)	4 (0.5)	
LAD	40 (48.2)	375 (43.3)	
- Di	1 (1.2)	3 (0.3)	
LCX	16 (19.3)	116 (13.4)	
- OM	0 (0.0)	8 (0.9)	
RCA	27 (32.5)	368 (42.4)	
- PDA	0 (0.0)	1 (0.1)	
- PL	0 (0.0)	4 (0.5)	
Ri	0 (0.0)	1 (0.1)	
SVG	0 (0.0)	3 (0.3)	
Multivessel CTO (%)	6 (7.2)	67 (7.7)	1.000
Number of CTO vessels (%)			0.825
- 1	77 (92.8)	800 (92.3)	
- 2	6 (7.2)	63 (7.3)	
- 3	0 (0.0)	4 (0.5)	
Multivessel disease (%)	47 (56.6)	479 (55.2)	0.9
Generation of DES (%)			<0.001
1st generation	55 (66.3)	342 (39.4)	

2nd generation	25 (30.1)	521 (60.1)	
Others	3 (3.6)	4 (0.5)	
Number of stents (%)			0.357
- 1	40 (48.2)	338 (39.0)	
- 2	34 (41.0)	366 (42.2)	
- 3	8 (9.6)	140 (16.1)	
- 4	1 (1.2)	21 (2.4)	
- 5	0 (0.0)	2 (0.2)	
Multivessel stents (%)	36 (43.4)	293 (33.8)	0.103
Length (mean (SD))	47.73 (22.93)	52.72 (25.44)	0.086
- Long stents (40mm≤) (%)	42 (50.6)	522 (60.2)	0.113
Diameter (mean (SD))	3.12 (0.30)	3.16 (0.33)	0.231
Total fluorotime (mean (SD))	43.74 (25.40)	41.43 (34.32)	0.716
Total contrast (mean (SD))	465.06 (185.81)	446.72 (210.92)	0.45

Table 3. Baseline Characteristics after Propensity Score Matching

	DAPT Duration		
	≤ 6mo	**6mo <**	**SD**
	(n=83)	**(n=249)**	
Age (mean (SD))	59.17 (9.77)	59.48 (10.28)	0.031
Male sex (%)	64 (77.1)	194 (77.9)	0.019
BMI (mean (SD))	25.35 (3.09)	25.20 (2.86)	0.051
Current Smoker (%)	17 (20.5)	56 (22.5)	0.049
Hypertension (%)	47 (56.6)	146 (58.6)	0.041
Diabetes (%)	30 (36.1)	94 (37.8)	0.033
- Requiring Insulin (%)	6 (7.2)	18 (7.2)	<0.001
Dyslipidemia (%)	41 (49.4)	123 (49.4)	<0.001
Chronic kidney disease (%)	2 (2.4)	4 (1.6)	0.057
Previous PCI (%)	15 (18.1)	49 (19.7)	0.041
Previous CABG (%)	2 (2.4)	7 (2.8)	0.025
Previous MI (%)	3 (3.6)	10 (4.0)	0.021
Stroke (%)	5 (6.0)	15 (6.0)	<0.001
PVD (%)	5 (6.0)	10 (4.0)	0.092
COPD (%)	3 (3.6)	5 (2.0)	0.097
CHF (%)	6 (7.2)	30 (12.0)	0.164
- Ejection fraction (mean (SD))	58.52 (9.65)	57.27 (9.20)	0.133
- LV dysfunction <40% (%)	6 (7.2)	18 (7.2)	<0.001
Atrial fibrillation	7 (8.4)	3 (1.2)	0.342
Statin (%)	60 (72.3)	183 (73.5)	0.027

Beta blocker (%)	62 (74.7)	182 (73.1)	0.037
ACE/ARB (%)	26 (31.3)	85 (34.1)	0.06
CCB (%)	67 (80.7)	203 (81.5)	0.021

Values are n (%) or mean ± SD.

Balance between the groups was assessed by calculating standardized differences, for which a difference of less than 0.10 was considered to indicate good balance.

Table 4. Procedural Characteristics after Propensity Score Matching

	DAPT Duration		
	≤ 6mo	**6mo <**	**SD**
	(n=83)	**(n=249)**	
De novo lesion (%)	76 (91.6)	228 (91.6)	<0.001
Lesion (%)			0.237
LM	0 (0.0)	1 (0.4)	
LAD	40 (48.2)	104 (41.8)	
- Di	1 (1.2)	0 (0.0)	
LCX	16 (19.3)	41 (16.5)	
- OM	0 (0.0)	4 (1.6)	
RCA	27 (32.5)	101 (40.6)	
- PL	0 (0.0)	2 (0.8)	
- Ri	0 (0.0)	1 (0.4)	
SVG	0 (0.0)	1 (0.4)	
Multivessel CTO	6 (7.2)	18 (7.2)	<0.001
Number of CTO vessels			
- 1	76 (92.8)	228 (92.8)	<0.001
- 2	6 (7.2)	18 (7.2)	<0.001
Multivessel disease	47 (56.6)	142 (57.0)	0.008
Generation of DES			0.143
1st generation DES	55 (66.3)	176 (70.7)	
2nd generation DES	25 (30.1)	69 (27.7)	
Others	3 (3.6)	4 (1.6)	

Number of Stent (%)			0.152
- 1	40 (48.2)	115 (46.2)	
- 2	34 (41.0)	96 (38.6)	
- 3	8 (9.6)	33 (13.3)	
- 4	1 (1.2)	4 (1.6)	
- 5	0 (0.0)	1 (0.4)	
Multivessel stents (%)	36 (43.4)	106 (42.6)	0.016
Length (mean (SD))	47.73 (22.93)	49.29 (25.96)	0.063
- Long stents (40mm≤) (%)	42 (50.6)	132 (53.0)	0.048
Diameter (mean (SD))	3.12 (0.30)	3.12 (0.31)	0.009
Total fluorotime (mean (SD))	43.74 (25.40)	39.38 (30.04)	0.157
Total contrast (mean (SD))	465.06 (185.81)	458.08 (205.60)	0.036

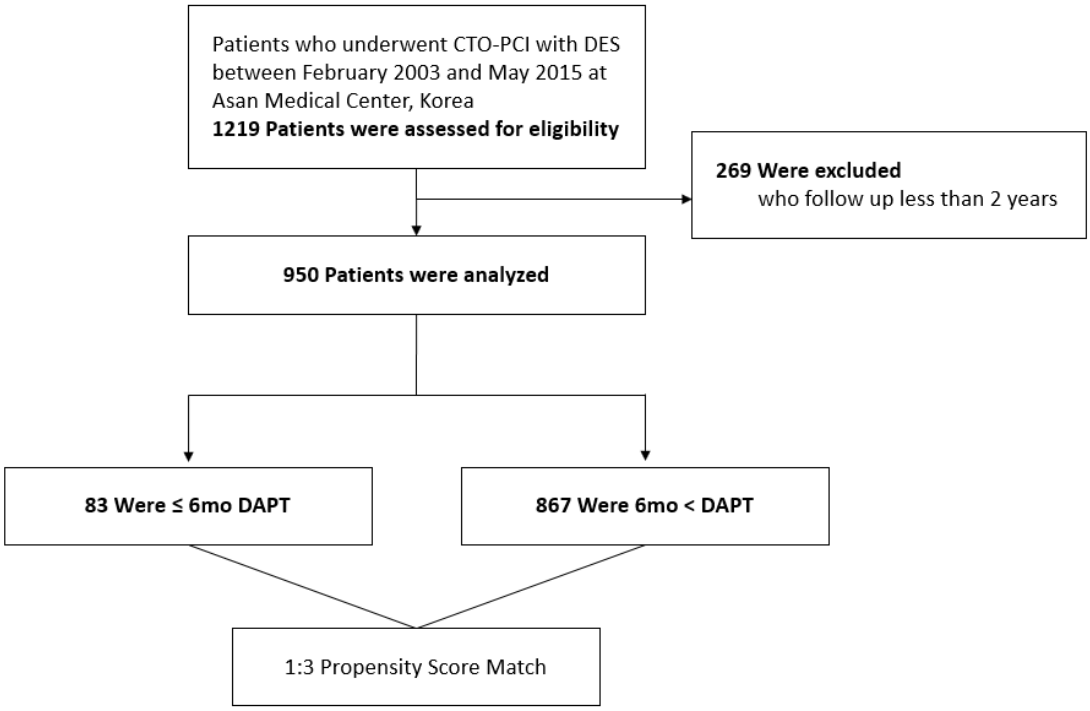
Table 5. Event Rate according to DAPT duration from index CTO-PCI

	DAPT Duration			
	≤ 6mo (n=83)	6mo < (n=867)	HR	p Value
Primary Outcomes				
MACE	16 (21.1%)	85 (11.1%)	0.60[0.38-0.95]	0.03
Bleeding events	5 (6.0%)	36 (4.4%)	0.65[0.27-1.55]	0.33
Secondary Outcomes				
Death from any cause	6 (8.2%)	21 (3.2%)	0.68[0.32-1.43]	0.31
Cardiac death	2 (2.8%)	14 (2.1%)	1.07[0.36-3.15]	0.90
Non-cardiac cause	4 (5.6%)	7 (1.0%)	0.36[0.12-1.06]	0.06
MI	12 (15.8%)	51 (7.2%)	0.93[0.59-1.49]	0.77
Target Vessel Revascularization	8 (10.8%)	51 (6.4%)	0.53[0.29-0.96]	0.04
Any revascularization	10 (13.5%)	82 (10.3%)	0.83[0.47-1.45]	0.51
Stent thrombosis	4 (4.9%)	8 (1.1%)	0.16[0.05-0.48]	<0.01
Stroke	1 (1.6%)	11 (1.6%)	2.67[0.35-20.38]	0.34

Table 6. Adjusted Clinical Outcomes According to DAPT duration from index CTO-PCI

	DAPT Duration			
	≤ 6mo (n=83)	6mo < (n=249)	HR	p Value
Primary Outcomes				
MACE	16 (21.1%)	32 (13.7%)	0.68[0.41-1.13]	0.14
Bleeding events	5 (6.0%)	11 (4.5%)	0.63[0.23-1.72]	0.37
Secondary Outcomes				
Death from any cause	6 (8.2%)	7 (3.3%)	0.64[0.27-1.50]	0.31
Cardiac death	2 (2.8%)	4 (1.2%)	0.95[0.29-3.15]	0.94
Non-cardiac cause	4 (5.6%)	3 (1.4%)	0.40[0.11-1.41]	0.15
MI	12 (15.8%)	15 (6.8%)	0.82[0.49-1.37]	0.45
Target Vessel Revascularization	8 (10.8%)	20 (8.3%)	0.67[0.35-1.28]	0.23
Any revascularization	10 (13.5%)	33 (13.6%)	1.03[0.56-1.88]	0.93
Stent thrombosis	4 (4.9%)	1 (0.5%)	0.06[0.01-0.55]	0.01
Stroke	1 (1.6%)	6 (2.7%)	2.99[0.37-24.18]	0.30

Figure 1. Patient Enrollment and Follow-up.



CTO, chronic total occlusion; PCI, percutaneous coronary intervention; DES, drug eluting stent

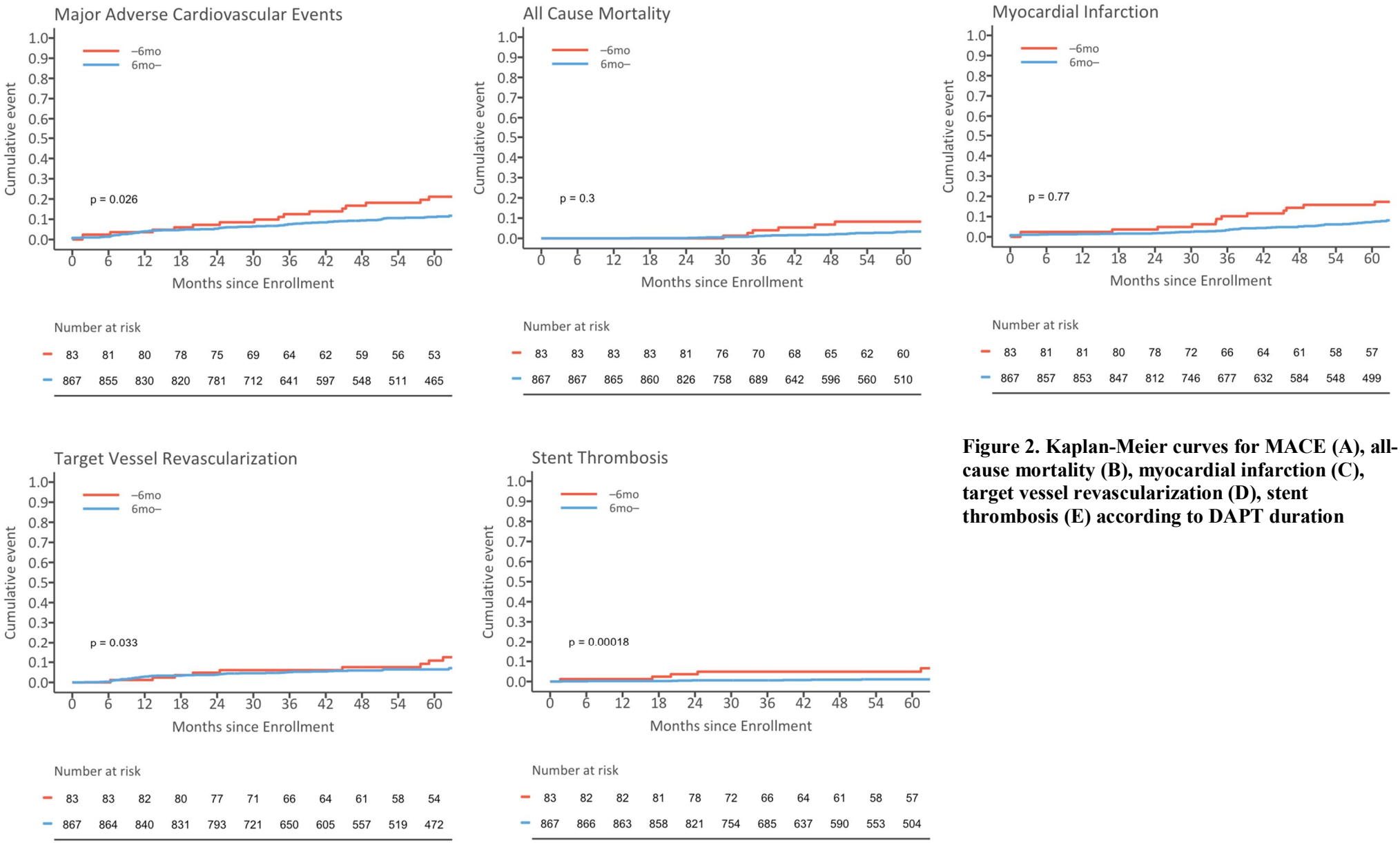


Figure 2. Kaplan-Meier curves for MACE (A), all-cause mortality (B), myocardial infarction (C), target vessel revascularization (D), stent thrombosis (E) according to DAPT duration

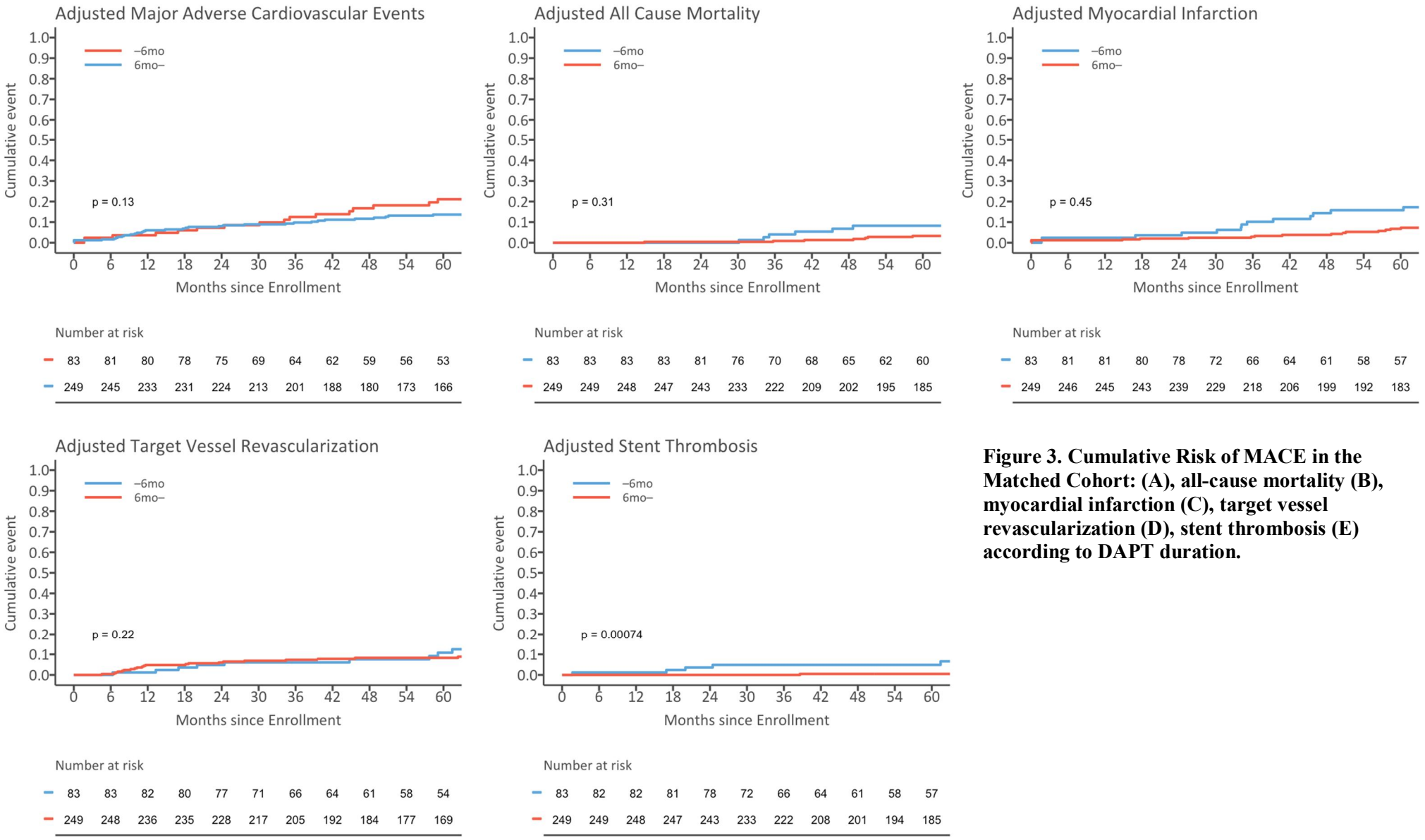


Figure 3. Cumulative Risk of MACE in the Matched Cohort: (A), all-cause mortality (B), myocardial infarction (C), target vessel revascularization (D), stent thrombosis (E) according to DAPT duration.

Figure 4. Subgroup Analysis of Major cardiovascular events.

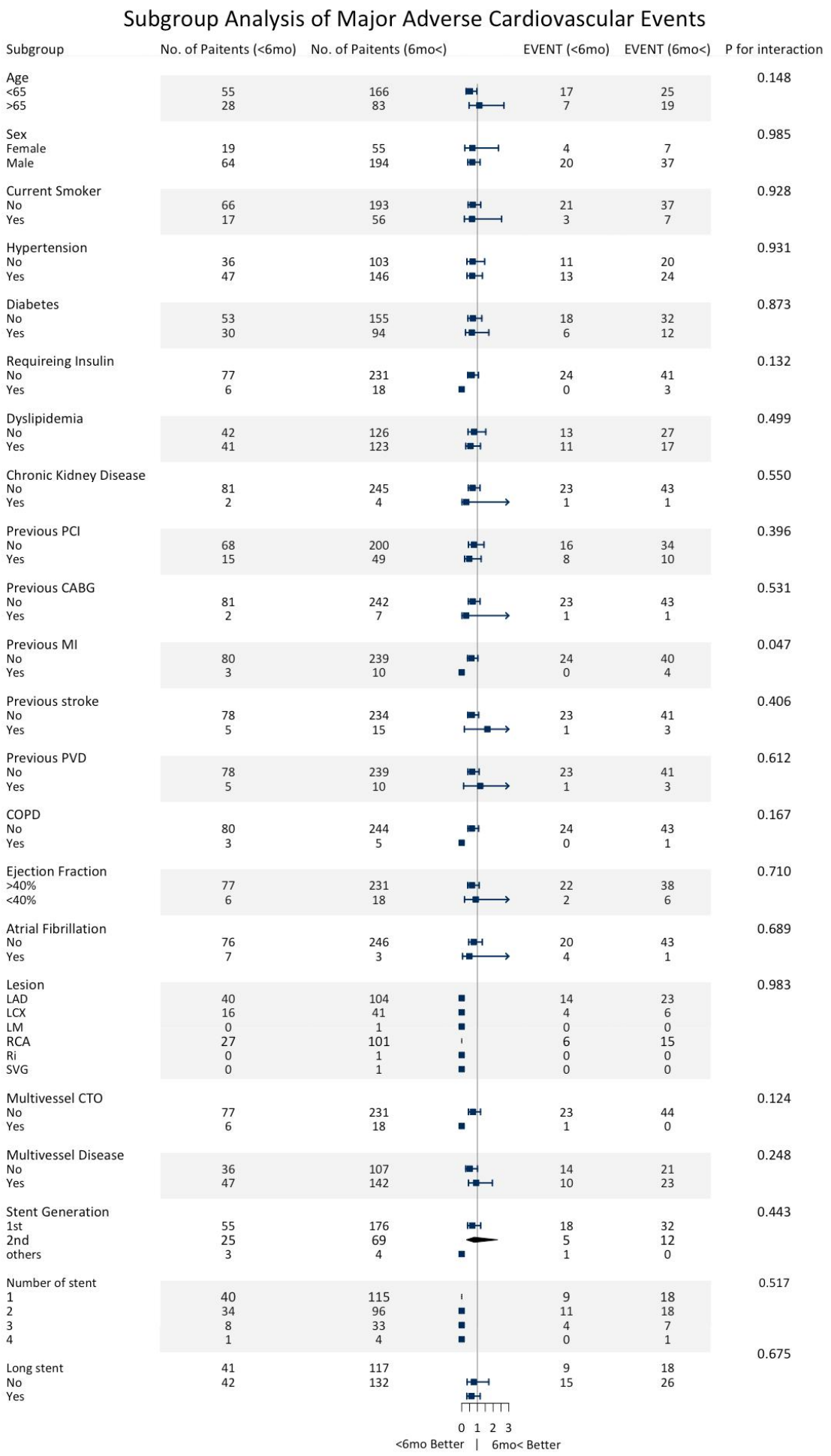
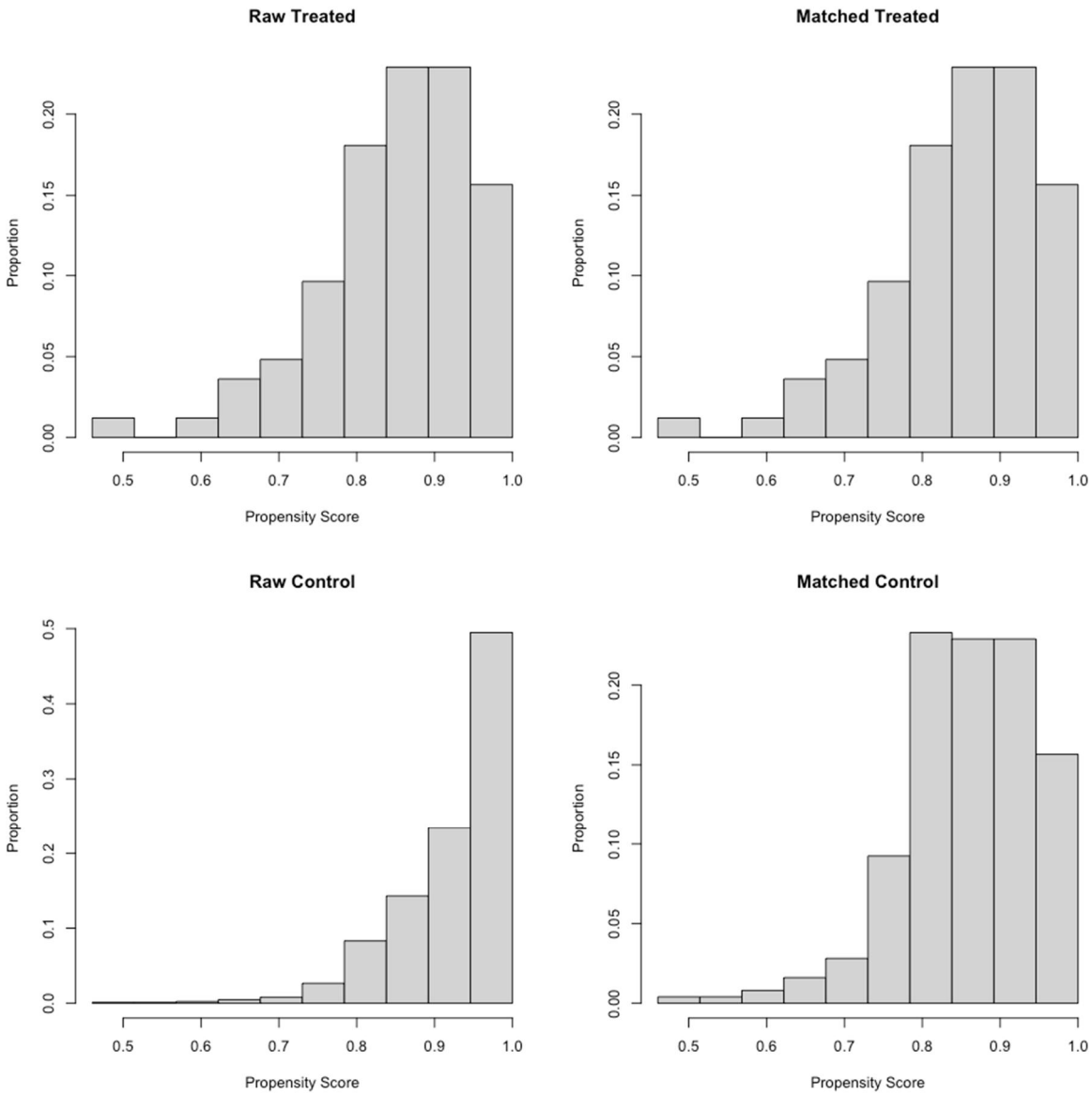


Figure 5. Distribution of Propensity Score after Match



DISCUSSION

Among patients with CTO receiving drug-eluting coronary stents, treatment with aspirin and thienopyridine over 6 months, as compared with under 6-month duration, did not reduce the risk of major adverse cardiovascular events. Also, the longer duration of DAPT was not associated with reduction in myocardial infarction, and target vessel revascularization, except stent thrombosis in propensity-score matched cohorts.

Chronic total occlusion is developed from occlusion of thrombus, organization, and tissue aging. Major histopathological features are calcification extent, inflammation, and neovascularization of CTO lesion.[12] It is difficult to perform successful revascularization due to these pathophysiological characteristics and technical complexity of the CTO lesion. In J-CTO registry (multicenter CTO registry in Japan) successful rates was reported 88.6% in the first attempt cases and 68.5% in the retry cases. Once the procedure is successful, it is essential to prevent future recurrence. Using aspirin is strongly recommended for recurrent event prevention after revascularization.[13] Optimal duration of thienopyridine with aspirin after revascularization therapy is continuously being discussed. Several prior investigations have concluded that extended DAPT has little clinical benefit.[14,15] Establishment of DAPT duration had trade-off between ischemia and bleeding and should be considered individually.[16] In United States, compared with non-CTO PCI, CTO PCI patients were to have more comorbidities like hypertension, dyslipidemia, current smoking and had a previous MI, PCI, and LV dysfunction. [17] Therefore, it is considered that the ischemic burden is higher than bleeding risk and DAPT duration is generally considered to be longer. However, with the development of coronary stent, concern about short duration DAPT use is emerging. Among patients at high risk for bleeding who underwent a polymer-free stent was superior used with an only one month DAPT.[18] In MASTER-DAPT study, one month of DAPT was noninferior to at least 2 additional months for net adverse clinical events and major adverse cardiac or cerebral events.[19] The trend of recent papers manifest that the early discontinuation of DAPT is noninferior to routine practice. However, 2016 ACC/AHA guideline suggest several factors which is associated with ischemic risk may favor longer duration DAPT. Procedure related high ischemic risk (also risk of stent thrombosis) is consist of stent undersizing, stent underdeployment, small stent diameter, greater stent length, bifurcation stents, and in-stent restenosis.[3] Due to the

complexity and difficulty of the procedure at the time, it is often taken for granted to maintain longer DAPT duration, but the evidence for DAPT duration in CTO PCI is scanty. Considering longer duration DAPT in complex PCI was demonstrated.[8] In this study, complexity of PCI is consisted of chronic total lesion, longer stent length, bifurcation lesion, treated over three lesions, vessels, and stents. However, several results indicated that CTO lesions did not appear to increase the risk of MACE, which has not been studied further.

Before our study, two retrospective studies presented the duration of DAPT for CTO PCI. In a previous single-center study, authors reported that under 12-month DAPT duration is similar to long-term clinical of over 12-month.[10] Another multicenter retrospective study have reported conflicting results. Over 12 months of DAPT was associated with all-cause mortality without an increase in bleeding.[11]

Our study indicated that 6-month duration DAPT was inferior to major adverse cardiac event before propensity matching. In matched cohort, merely stent thrombosis was observed with higher incidence rate. As a result of our study, subtle advantage of the long-term use of DAPT in CTO PCI patients was observed. These results indicate that duration of DAPT was not strongly affected whether the degree of stenosis is totally occluded or not. Strategy for optimal thienopyridine duration with patients suffer from CTO treated with PCI should be focused on clinical manifestation and procedure-related factors (stent under sizing, stent under deployment, small stent diameter, greater stent length, bifurcation stents, and in-stent restenosis). In other words, although complex CTO procedures have been performed successfully, patients with stable angina and received 'ordinary-sized' stent, thienopyridine were worth being considered for 6 months just like non-CTO PCI patients.

CONCLUSION

Six months of dual antiplatelet therapy after placement of a drug-eluting stents in patients with CTO was not associated with reduced risk of major adverse cardiovascular event after propensity score matching.

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국문요약

연구배경 및 목적 약물 방출 스텐트(DES)를 이용한 관상동맥 중재시술 (PCI) 이후 이중항혈소판제제의 사용기간은 최소한 6 개월을 사용할 것을 권고하고 복잡한 병변의 경우 출혈 경향성을 고려하여 그 이상을 사용하는 것을 권장한다. 그러나 관상동맥 만성폐색병변(CTO) 환자에서 약물 방출 스텐트를 이용한 관상동맥 중재시술 이후 이중항혈소판제제의 최적의 사용기간은 여전히 근거가 부족하다. 이에 본 연구는 약물 방출 스텐트를 이용하여 관상동맥 중재 시술을 시행 받은 만성폐색병변 환자에서 이중항혈소판제제의 단기 요법의 효용성에 대하여 고찰하고자 하였다.

방법 2003 년 2 월부터 2015 년 5 월까지 서울아산병원에서 DES 를 이용하여 성공적인 재관류를 시행 받은 CTO PCI 환자들을 후향적으로 분석하였다. 1 차 평가지표는 주요 심혈관계 이상반응(모든 원인으로의 사망, 심근경색, 스텐트 내 혈전, 표적 혈관 재관류)으로 구성하였다. 1:3 의 성향 점수 매칭(propensity score matching)을 이용하여 두 그룹간 비교를 시행하였다.

결과 총 1119 명의 CTO 환자들을 평가하였고 그 가운데 169 명은 2 년 미만으로 추적관찰하였기 때문에 제외하였다. 950 명의 환자들이 분석에 포함되었으며 그 가운데 이중 항혈소판제제를 6 개월 미만으로 사용한 군이 83 명, 6 개월 이상 사용한 군이 867 명이었다. 매칭된 코호트 군에서 이중 항혈소판제제의 장기사용은 단기 사용과 비교하였을 때 5 년 주요 심혈관계 합병증은 위험비율(HR) 0.68(95% 신뢰구간(CI) 0.41-1.13; P=0.14)로 유의미하게 차이가 발생하지 않았다. 비슷하게 모든 원인으로의 사망 (HR 0.64, 95% CI, 0.27-1.50, P=0.31), 심근경색 (HR:0.82, 95% CI 0.49-1.37, P=0.45), 표적 혈관 재관류 (HR: 0.67, 95% CI 0.35-1.28 P=0.23)에서도 유의미한 차이를 보여주지 못하였다. 그러나 스텐트내 혈전은 이중 항혈소판제제의 장기사용에서 유의미하게 우월함을 보여주었다. (HR: 0.16, 95% CI 0.01-0.55, P=0.01)

결론 약물 방출 스텐트를 시행한 CTO-PCI 환자에서 이중 항혈소판제제의 단기 혹은 장기 사용은 주요 임상결과에 유의미한 차이를 보여주지 못하였다. 그러나 장기간의 이중 항혈소판제제 사용은 스텐트내 혈전 발생을 고려하였을 때 유의한 장점을 보였다.

중심단어: 죽상동맥경화증, 만성폐색병변, 경피적관상동맥중재술, 이중항혈소판요법