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Association of Acute Procedural Results with Long-term Outcomes After CTO-PCI

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Tweet/handle: @ajaykirtane, @rwyeh, and @esbrilakis; The retrospective analysis of a large cohort of CTO-PCI population showed that suboptimal acute procedural results were associated with worse long-term prognosis and higher costs compared with optimal or failed CTO interventions.

ABSTRACT

OBJECTIVES. To determine the association of procedural outcomes with long-term mortality and myocardial infarction (MI) after chronic total occlusion (CTO) percutaneous coronary intervention (PCI).

BACKGROUND. The association between acute procedural results and subsequent outcomes has received limited study.

METHODS. Between January 2010 and December 2013, a total of 2,659 CTO-PCI patients were consecutively enrolled at our center. Procedural results were categorized into 3 groups: 1) optimal recanalization, with reperfusion of the occluded vessel and side branches (if any) with TIMI 3 flow; 2) suboptimal recanalization, meeting any of the following criteria: persistence of significant side branch occlusion, final TIMI flow of 1/2, or residual % diameter stenosis >30%; and 3) procedural failure, i.e., failure to cross a lesion with a balloon angioplasty catheter. The primary outcome was the 5-year composite endpoint of cardiac death and MI.

RESULTS. Overall, optimal recanalization was achieved in 1,562 (58.7%) patients, suboptimal recanalization in 399 (15.0%) patients, and recanalization failed in 698 (26.3%) patients. The 5-year incidence of the primary outcome was significantly higher in the suboptimal recanalization group compared with the optimal recanalization and the failure groups (10.1% vs. 6.5% vs. 6.3%, p=0.046), which was mainly driven by higher risk of MI. In subgroup analysis, significant side branch occlusion was associated with numerically higher risk of 5-year MI (hazard ratio: 1.55, 95% confidence intervals: 0.99-2.43, p=0.054).

CONCLUSIONS. In this large cohort of CTO-PCI, suboptimal recanalization was associated with significantly higher long-term incidence of cardiac death and MI compared with optimal recanalization or procedural failure.

KEY WORDS: chronic total occlusion, acute results, suboptimal recanalization, long-term outcomes, percutaneous coronary intervention

CONDENSED ABSTRACT

The present study investigated the association of suboptimal procedural results with long-term mortality and MI after CTO-PCI among 2,659 consecutive patients. Suboptimal recanalization criteria included persistence of significant side branch occlusion, final TIMI 1/2 flow, or residual diameter stenosis >30%. The primary outcome of 5-year cardiac death

and MI occurred significantly more often in the suboptimal recanalization group compared with both the optimal recanalization and the failure group (10.1% vs. 6.5% vs. 6.3%, p=0.046), which was mainly driven by higher risk of MI. Suboptimal CTO recanalization was associated with worse long-term outcomes compared with both optimal and failed CTO recanalizations.

ABBREVIATIONS AND ACRONYMS

CI = confidence intervals

CTO = chronic total occlusions

DS = diameter stenosis

MI = myocardial infarction

PCI = percutaneous coronary intervention

SCAI = Society for Cardiovascular Angiography and Interventions

SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery

TIMI = Thrombolysis In Myocardial Infarction

TLR = target lesion revascularization

TVR = target vessel revascularization

INTRODUCTION

Chronic total occlusions (CTOs) are identified in 33% to 52% of patients undergoing coronary angiography(1). However, CTO percutaneous coronary intervention (PCI) constitutes less than 5% of PCI in contemporary practice globally(2). Most observational studies reported better outcomes with CTO revascularization versus medical treatment(3,4), and with successful versus failed CTO-PCI(5,6). In contrast, two recently published randomized trials, DECISION-CTO (Drug-Eluting Stent Implantation Versus Optimal Medical Treatment in Patients with Chronic Total Occlusion)(7) and EuroCTO (Randomized Multicenter Trial to Evaluate the Utilization of Revascularization or Optimal Medical Therapy for the Treatment of Chronic Total Coronary Occlusions)(8), did not demonstrate improvement in hard clinical outcomes despite high CTO-PCI success rates. Thus, the impact of CTO-PCI on hard clinical outcomes continues to be debated.

CTO-PCI may sometimes have a suboptimal acute result, the impact of which on subsequent clinical outcomes has received limited study. The present study sought to determine the association of suboptimal procedural results with the long-term incidence of cardiac death and MI after CTO-PCI in a large cohort of consecutive patients.

METHODS

Patient Population

All patients who underwent PCI with at least one CTO lesion between January 2010 and December 2013 at Fu Wai Hospital, Beijing, China were consecutively enrolled. CTO was defined as 100% occlusion with TIMI (Thrombolysis In Myocardial Infarction) 0 flow for > 3 months. Lesions with bridging collaterals but unknown occlusion duration were classified as CTO lesions. A planned PCI procedure for multi-CTO disease or a failed CTO recanalization was decided by each operator, for patients with multiple procedures during a single hospitalization, only the final procedure was included in the analysis. All baseline patient demographics, comorbidities, laboratory examinations, and periprocedural data including stenting information were prospectively recorded in a dedicated database. Clinical follow-up via office visit or telephone contact at 1 month, 6 months, 1 year, and annually up to 5 years were performed by research staff in an independent office in Fu Wai hospital. The study was approved by the Institutional Review Board of Fu Wai hospital. All eligible patients provided electronic informed consent by telephone interview or clinical visit during follow-up.

Intervention

Coronary angioplasty was performed using standard techniques through femoral or radial artery access. Antegrade wiring was most commonly used in the present population, while retrograde approach was still in an early learning period at this center. In case of single wire technique failure, the parallel wire technique was applied. Antegrade dissection and re-entry was mainly performed when the vessel was ambiguous within the occluded segment. Retrograde crossing via collateral pathways was reserved for second attempts after antegrade failure or as a strategy of choice for complex cases and was mainly performed by certified specialists. Guide catheter selection and stent type, as well as intravascular imaging utilization was left to the discretion of the operators. Before the procedure, patients were prescribed daily aspirin (100 mg once daily) and clopidogrel (75 mg once daily) for at least 6 days, or a loading dose (aspirin 300 mg, clopidogrel 600 mg) before the procedure. After PCI, pharmacological treatments were at each operator’s discretion, with most patients maintained on aspirin (100 mg once daily) indefinitely and clopidogrel (75 mg once daily) for at least 1 year.

Angiographic Analysis

Lesion angiographic data, including Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) score and Multicenter CTO Registry in Japan (J-CTO) score, and procedural characteristics were retrospectively evaluated by an independent core laboratory (Interventional Cardiovascular Imaging Core Laboratory, National Center for Cardiovascular Diseases, Beijing, China). A significant side branch occlusion was defined as TIMI 0 or 1 final flow in branches ≥ 1.5mm in diameter.

Grouping

Patients were classified into three groups according to CTO procedural acute results. Optimal recanalization was defined as reperfusion of occluded vessel and its side branch (if any) with TIMI-3 flow recovery. Suboptimal recanalization was defined as reperfusion of occluded main vessel, and any of the following: 1) persistence of significant side branch occlusion; 2) final TIMI flow of 1/2; or 3) residual % diameter stenosis (DS) > 30%. Procedural failure was defined as failure to cross a lesion with a balloon angioplasty catheter. Patients with more than one CTO lesion treated were categorized into the failure group if they had at least one unsuccessfully recanalized CTO. Similarly, patients with reperfusion of all treated CTOs with suboptimal recanalization of at least one CTO lesion were categorized into suboptimal recanalization group.

Endpoints

The primary outcome was the composite of cardiac death or myocardial infarction (MI) at 5 years. Secondary outcomes included 30-day outcomes, individual components of the primary endpoint, as well as all-cause death, target vessel MI, rehospitalization for heart failure, any ischemia-driven (ID) revascularization or ID-target vessel revascularization (TVR), and ID-target lesion revascularization (TLR). Periprocedural MI was adjudicated by the Society for Cardiovascular Angiography and Interventions (SCAI) definition(9) , and Academic Research Consortium (ARC)-2(10) and 4th universal definition(11). ID were defined as a restenotic lesion with angiographic diameter stenosis ≥50% with ischemic evidence or ≥70% irrespective of the presence of ischemic evidence. TVR was defined as any repeat percutaneous intervention or surgical bypass of any segment of the target treated CTO vessel. TLR was defined as any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target treated CTO lesion. Costs during procedure and hospitalization for each patient were collected based on a dedicated Electronic Medical Record and were adjusted to 2020 US dollars. All adverse events were adjudicated by an independent clinical events committee.

Statistical Analysis

Categorical variables are reported as percentage (counts) and were compared using chi-square or Fisher exact test. Continuous data are presented as mean ± standard deviation (SD) and were compared using a 2-sample t-test. We compared costs between groups using the nonparametric Mann-Whitney *U* test. A p value < 0.05 was considered statistically significant. Survival curves were constructed for time-to-event variables with the Kaplan-Meier method and compared using the log-rank test. Cox regression analysis was performed to identify long-term risk in terms of primary or secondary endpoint between suboptimal recanalization group and either optimal recanalization group or failure group. Logistic regression was used to obtain odds ratio for possible predictors of suboptimal results. Variables with $p < 0.1$ on univariable analysis (Supplementary Table I) and mandatory variables that might be related with suboptimal clinical results from clinical were included in multivariate analysis. All statistical analyses were performed with SAS 9.4 (Cary, NC, United States).

RESULTS

Baseline and Procedural Characteristics

Data from 2,659 consecutively enrolled CTO-PCI patients with 2,735 lesions were analyzed (Figure 1). Within the study cohort, optimal recanalization was achieved in 1,562 (58.7%) patients and suboptimal recanalization in 399 (15.0%), while guidewire crossing failed in 698 (26.3%) patients. In the suboptimal recanalization group, 275 patients were identified with significant side branch occlusion, final TIMI flow 1/2 was observed in 39 patients, and 101 patients had residual DS% > 30% (Figure 1).

Baseline patient demographics were similarly distributed among 3 groups (Table 1). As shown in Table 2, more in-stent restenosis CTOs were observed in the suboptimal recanalization group. Lesion length in the suboptimal recanalization group was longer compared with the optimal recanalization group (18.3mm vs. 15.6mm, $p < 0.0001$), but shorter compared with the failure group (18.3mm vs. 21.5mm, $p < 0.0001$). The SYNTAX score was slightly higher in patients with suboptimal recanalization compared with optimal recanalization (20.3 vs. 18.9, $p = 0.003$), while the prevalence of patients with J-CTO score ≥ 2 were similar between suboptimal and optimal recanalization groups (43.5% vs. 39.0%, p =

0.22). Parallel wire and antegrade dissection and re-entry technique were performed in a minority of cases and suboptimal results were observed in patients using those techniques. Use of intravascular ultrasound guidance was low and more common in patients in the suboptimal recanalization group. The incidence of procedural complications was significantly higher in the suboptimal recanalization group.

A multivariable analysis showed that moderate or severe vessel tortuosity, in-stent lesion, frequently changing CTO guidewire (more CTO guidewire used per unit time), as well as during procedural dissection (type C to F) were independently associated with suboptimal results (Supplementary Table II).

Costs

We retrospectively collected the total costs charged in the index hospitalization (Supplementary Table III), the mean in-hospital and procedural costs in the suboptimal recanalization group were significantly higher than those in the optimal recanalization group (costs during hospitalization: \$14,940 ± 7,181 vs. \$11,905 ± 5,420, $p < 0.0001$; procedural costs: \$11,459 ± 6,476 vs. \$9,144 ± 3,338, $p < 0.0001$) and in the failed recanalization group (costs during hospitalization: \$14,940 ± 7,181 vs. \$8,259 ± 2,055, $p < 0.0001$; procedural costs: \$11,459 ± 6,476 vs. \$4,118 ± 2,734, $p < 0.0001$).

Thirty-Day Outcomes

At 30 days, the incidence of the composite endpoint of cardiac death or MI was similar among 3 groups (suboptimal group: 1.3% vs. optimal group: 1.5% vs. failure group: 0.9%, $p = 0.49$). All-cause death occurred in 1 patient and myocardial infarction in 5 patients in the suboptimal recanalization group, which were similar compared with other groups. In the sensitivity analysis, the incidence of periprocedural MI was similar among 3 groups according to SCAI definition, numerically higher with suboptimal recanalization according to the ARC-2 definition, and significantly higher with optimal (15.5%) and suboptimal (14.0%) recanalization compared with the failure group (9.2%), with a p value < 0.0001 based on 4th universal definition (Supplementary Table IV). The incidence of repeat ID-revascularization was similar among 3 groups, while ID-TVR was higher with failure group (Table 3).

Five-Year Outcomes

Finally, a total of 2,407 (90.5%) patients completed 5-year clinical follow-up, with a median duration of 5.1 (5.1, 5.1) years. The primary endpoint of 5-year cardiac death or MI occurred in 37 (10.1%) patients in the suboptimal recanalization group, which was significantly higher than the optimal recanalization group (10.1% vs. 6.5%, hazard ratio [HR]: 1.56, 95% confidence intervals [CI]: 1.06 to 2.28, p = 0.02) as well as the failure group (10.1% vs. 6.3%, HR: 1.63, 95%CI: 1.04 to 2.54, p = 0.03). The increased risk was driven by significantly higher MI rates in patients with suboptimal recanalization as compared with those who had optimal recanalization (9.7% vs. 5.7%, p = 0.005), or failed CTO PCI (9.7% vs. 5.3%, p = 0.005). The MI incidence curve in the suboptimal recanalization group started to diverge during the first year post PCI but separated the most between 3 and 5 years from PCI (Figure 2). Time-to-event curves also demonstrated that for the composite endpoint, the separation of KM curves after the third year was primarily driven by the significant increased risk of MI, and to a lesser extent by numerically increased cardiac death. The curve of the suboptimal recanalization group diverges in the first year until the end of 5-year follow-up (Figure 2). All-cause death and cardiac death were numerically higher with suboptimal recanalization, but the differences did not achieve statistical significance. The 5-year incidence of ID-revascularization including ID-TVR and ID-TLR was significantly higher with suboptimal recanalization as compared with optimal recanalization (ID-revascularization: 22.8% vs. 15.0%, $p < 0.0001$; ID-TVR: 12.1% vs. 6.7%, $p < 0.0001$; ID-TLR: 10.8% vs. 6.0%, $p = 0.001$, respectively), but were significantly lower with the failure group (Table 3).

The sensitivity analysis excluding patients with side branch occlusion in suboptimal recanalization group showed a less pronounced difference in terms of cardiac death or MI among 3 groups ($p = 0.13$) (Supplementary Table V). Meanwhile, in the cohorts of patients with optimal or suboptimal recanalization, significant side branch occlusion was associated with numerically higher incidence of cardiac death or MI (9.5% vs. 7.0%, $p = 0.16$), mainly driven by higher incidence of MI (9.5% vs. 6.2%, $p = 0.054$) (Figure 3 and Supplementary Figure I).

A subgroup of in-stent occlusion versus *de novo* CTO population demonstrated that the higher risk of 5-year cardiac death or MI in suboptimal recanalization group was more pronounced in *de novo* CTO patients as compared with optimal recanalization (p for interaction = 0.005), but showed no between-group difference when compared with failure group (p for interaction = 0.30). However, in both in-stent restenosis and *de novo* CTO populations, TVR event rates with suboptimal recanalization were higher compared with the optimal recanalization group (p for interaction = 0.79), while lower compared with the failure group (p for interaction = 0.69) (Supplementary Table VI, Table VII, and Table VIII).

DISCUSSION

The main findings of this large-scale CTO-PCI cohort with long follow-up duration can be summarized as follows: 1) in one-sixth of patients, recanalization of the occluded vessels was suboptimal; 2) successful CTO-PCI was not associated with lower risk of long-term cardiac death and MI compared to failure; however, suboptimal recanalization was associated with significantly higher costs and worse clinical outcomes (Central Illustration); and 3) significant side branch occlusion was the most common reason for a suboptimal CTO-PCI result and was associated with numerically higher 5-year incidence of MI.

Remarkable success rates of CTO-PCI have been recently achieved catalyzed by advanced techniques and device innovation; however, recent trials reported no reduction in mortality or MI after CTO recanalization (7,8,12). As a result, CTO-PCI was recommended to be reserved for alleviation of symptoms in patients who fail medical management(13). However, in order to be of benefit to patients, it must be able to be performed with a low rate of complications. During CTO-PCI, vessel injury with significant side branch occlusion and less favorable angiographic results could potentially influence recovery of myocardial perfusion and may lead to worse outcomes.

One major adverse impact of suboptimal recanalization was the higher risk of both periprocedural and long-term spontaneous MI. Since the insensitive SCAI definition was used to adjudicate periprocedural MI for the primary outcome, myocardial injury might be underestimated. Sensitivity analysis showed that both optimal and suboptimal recanalizations were associated with higher rate of periprocedural MI by using 4^{th} universal definition. Side branch occlusion was a major reason for MI events in suboptimal group, consistent with prior reports(14,15), and confirmed by the sensitivity analysis with only low TIMI flow and higher residual narrowing patients. Also, lower TIMI flow accompanied by temporary ischemia, collateral channel trauma, or donor vessel injury might be associated with high risk of periprocedural MI due to incomplete protection from ischemia by pre-existing collateral network(16). The rates of MI for the suboptimal recanalization group started to separate from the other groups before 1 year and further accelerated after 3 years. Potential mechanisms for late MI might be outflow disease with worse runoff associated with restenosis and re-occlusion of the recanalized vessel(17). Persistent dissections and uncovered hematoma were more often observed in suboptimal group and might also be associated with poor recovery. On the other hand, after an arduous and lengthy attempt to CTO crossing, operators might pay less attention on stent optimization, which can potentially result in a higher restenosis risk(18).

As the present study shows, optimal CTO recanalization resulted in less need for repeat revascularization, while suboptimal recanalization was associated with worse prognosis compared with the failure group. Possible explanations include treatment of more non-CTO lesions in the failure group, which might reduce adverse ischemic events due to improved collateral circulation. Consistent with the recent ISCHEMIA trial(19), symptom improvement is the primary benefit of CTO-PCI. Although symptom-driven revascularization events were higher following a failed CTO recanalization, the long-term “hard endpoint” of cardiac death and MI was similar between the failure and optimal recanalization groups, and even lower in the failure group compared with the suboptimal group. Therefore, preprocedural risk assessment and planning are essential as has been emphasized previously(20,21). When a suboptimal result is anticipated after stenting, i.e. high risk of significant side branch occlusion, diffuse disease or large hematoma at distal vessel or failure of the guidewire to enter into the distal true lumen, etc., a contemporary "investment" strategy could be considered to increase the possibility of achieving an optimal result in the next procedure. As demonstrated in the present data, suboptimal CTO recanalization was not only associated with higher risk of long-term cardiac death and MI, even compared with patients with failed recanalization, but also had significantly higher costs. Considering “time-economy” of CTO-PCI, which is a major factor dissuading physicians in real clinical settings, it is necessary to systematically review the cases and conduct sufficient preprocedural planning before CTO-PCI using various prediction tools like the J-CTO score or coronary computed tomography angiography(22,23).

Limitations

The present study has several limitations. First, this is a retrospective single-center experience with potential selection bias. However, since randomized trials or other registries are often conducted by a selected group of very experienced investigators, similar results may be unattainable by “normal” operators without specific training (24). Second, the presented cases were performed during an early time period reflecting clinical practice 6 to 9 years ago, hence lesion complexity was low with comparatively less utilization of IVUS, bilateral injections, dissection re-entry or retrograde approach, particularly for those contemporary CTO techniques. The resultant overall success rate of the present study was relatively low as compared with other recent studies. Third, the lesion complexity confounding in the association between acute results and outcomes cannot be fully excluded despite application of appropriate statistical techniques. Those finding of higher risk of suboptimal results might be more likely apply to contemporary practice as well. Finally, the present study did not provide a quality of life comparison during long-term follow-up.

CONCLUSIONS

This large-scale CTO-PCI cohort study, with long follow-up duration, demonstrated that patients with suboptimal procedural results predefined as significant side branch occlusion, final TIMI flow 1/2, or residual DS% > 30% was achieved in 15% of patients and was associated with significantly higher long-term incidence of cardiac death and MI, compared with both optimal recanalization and procedural failure. Reducing complications especially significant side branch occlusion could decrease costs and also provide better clinical outcomes.

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PERSPECTIVES

WHAT IS KNOWN?

Successful CTO-PCI has been associated with better clinical outcomes.

WHAT IS NEW?

Compared with optimal or failed CTO interventions, suboptimal acute procedural results were associated with worse long-term prognosis and higher costs.

WHAT IS NEXT?

Future studies using contemporary techniques are warranted to investigate the long-term impact of CTO recanalization.

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FIGURE LEGENDS

Figure 1. Study Flowchart

Thirty-day follow-up includes a window of ± 7 days; 5-year follow-up includes a window of ± 30 days. CTO = chronic total occlusion; DS = diameter stenosis; TIMI = Thrombolysis In Myocardial Infarction.

Figure 2. Kaplan-Meier Curves for 5-Year Cardiac Death or MI

The p values were calculated using the log-rank test. The HRs were reported for patients with suboptimal recanalization compared with those with either optimal recanalization or failure. HR = hazard ratio; other abbreviations as in Central Illustration.

Figure 3. Impact of Varying Suboptimal Recanalization Criterion on 5-Year Cardiac Death or MI

The analysis was based on a cohort of patients with optimal or suboptimal recanalization. The HRs were reported for patients with vs. without suboptimal recanalization criteria. Abbreviations as in Central Illustration, Figure 1 and Figure 2.

CENTRAL ILLUSTRATION. Association of In-Hospital Costs and Adverse Clinical Events with Acute Procedural Results

Mean costs include the total expenses during procedure and hospitalization. MI = myocardial infarction; ID-TVR = ischemia-driven target vessel revascularization.

Table 1. Baseline Demographic Characteristics Among Patients with Different Acute Results

	Optimal Recanalization (Patients, N=1,562)	**Suboptimal Recanalization (Patients, N=399)**	**Failure (Patients, N=698)**	**p Value** (Suboptimal vs. Optimal Recanalization)	**p Value** (Suboptimal vs. Failure Recanalization)	**p Value** (3-group Comparison)
Age, years	57.0 ± 10.5	57.6 ± 10.6	57.3 ± 10.5	0.34	0.67	0.73
Female	17.7% (277)	16.3% (65)	14.3% (100)	0.50	0.38	0.13
Diabetes	30.5% (477)	31.1% (124)	34.0% (237)	0.84	0.33	0.27
Hypertension	63.1% (985)	66.7% (266)	67.6% (472)	0.18	0.75	0.08
Hyperlipidemia	83.9% (1311)	86.0% (343)	84.1% (587)	0.32	0.41	0.60
Family history of coronary artery disease	11.5% (180)	12.8% (51)	13.6% (95)	0.49	0.70	0.36
Current smoker	38.7% (604)	43.9% (175)	45.8% (320)	0.06	0.53	0.02
Previous MI	42.6% (665)	46.9% (187)	36.8% (257)	0.12	0.001	0.003
Previous PCI	8.1% (127)	12.8% (51)	9.9% (69)	0.004	0.14	0.01
Previous CABG	3.5% (54)	2.5% (10)	3.7% (26)	0.34	0.28	0.55
Previous stroke	7.3% (114)	8.0% (32)	9.9% (69)	0.62	0.30	0.11
COPD	0.4% (6)	0% (0)	0.1% (1)	0.26	0.64	0.32
Creatinine clearance, ml/min	97.3 ± 29.9	96.0 ± 27.3	98.3 ± 29.9	0.42	0.21	0.08
LVEF, %	60.4 ± 8.3	60.6 ± 8.7	60.4 ± 8.2	0.66	0.63	0.45
LVEF ≤ 40%	3.6% (56)	3.0% (12)	3.4% (24)	0.57	0.70	0.85
Clinical presentation				0.80	0.04	0.15
Silence ischemia	12.5% (195)	12.3% (49)	14.9% (104)			
Stable angina	33.3% (520)	31.1% (124)	34.5% (241)			
Unstable angina	52.8% (825)	54.9% (219)	50.1% (350)			
Acute myocardial infarction	1.4% (22)	1.8% (7)	0.4% (3)			

Values are mean ± SD or % (n). CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Table 2. Angiographic and Procedural Characteristics Among Patients with Different Acute Results

	Optimal Recanalization (Patients, N=1,562 Lesions, N=1,625)	**Suboptimal Recanalization (Patients, N=399 Lesions, N=409)**	**Failure (Patients, N=698 Lesions, N=701)**	**p Value** (Suboptimal vs. Optimal Recanalization)	**p Value** (Suboptimal vs. Failure Recanalization)	**p Value** (3-group Comparison)
Angiographic findings				0.09	0.001	<0.0001
One-vessel disease	22.0% (344)	20.6% (82)	12.3% (86)			
Two-vessel disease	31.6% (493)	34.3% (137)	34.2% (239)			
Three-vessel disease	42.8% (668)	39.1% (156)	48.6% (339)			
Concomitant LM disease	3.6% (57)	6.0% (24)	4.9% (34)			
Numbers of CTO lesion				0.02	0.89	0.007
1	95.2% (1487)	91.7% (366)	91.7% (640)			
2	4.5% (70)	8.0% (32)	7.9% (55)			
3	0.3% (5)	0.3% (1)	0.4% (3)			
Target lesion location				0.11	<0.0001	<0.0001
Left main artery	0.2% (3)	0% (0)	0.1% (1)			
Left anterior descending artery	39.4% (641)	43.5% (178)	28.7% (201)			
Left circumflex artery/ramus	14.8% (241)	17.1% (70)	16.4% (115)			
Right coronary artery	45.5% (740)	39.4% (161)	54.8% (384)			
In-stent restenosis	7.4% (121)	14.2% (58)	4.9% (34)	<0.0001	<0.0001	<0.0001
Ostial CTO	1.8% (29)	2.4% (10)	2.7% (19)	0.38	0.79	0.32
Moderate or severe vessel tortuosity	20.1% (327)	23.2% (95)	29.0% (203)	0.17	0.04	<0.0001
Lesion bending > 45°	40.7% (662)	37.9% (155)	53.9% (378)	0.30	<0.0001	<0.0001
Lesion length	15.6 ± 10.1	18.3 ± 13.0	21.5 ± 14.9	<0.0001	<0.0001	<0.0001
≥ 20mm	32.6% (530)	41.8% (171)	53.8% (377)	<0.0001	<0.0001	<0.0001
Blunt stump	40.2% (653)	41.6% (170)	41.2% (289)	0.61	0.91	0.83
Moderate or severe calcification	11.0% (178)	14.4% (59)	17.7% (124)	0.05	0.16	<0.0001
Re-try lesion	2.6% (43)	3.9% (16)	5.1% (36)	0.17	0.35	0.009
Rentrop grade				0.01	0.18	0.001
0	6.8% (111)	4.6% (19)	3.1% (22)			

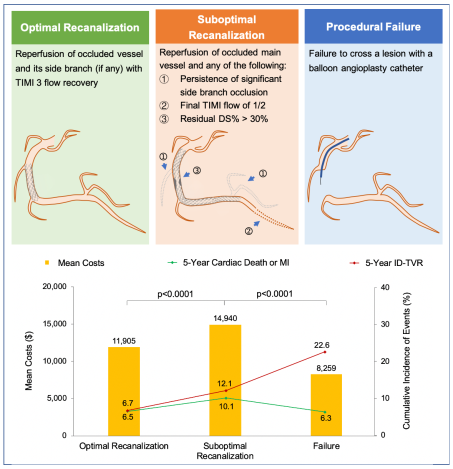
1	10.1% (164)	14.9% (61)	11.4% (80)			
2	35.7% (580)	37.7% (154)	39.9% (280)			
3	47.4% (770)	42.8% (175)	45.5% (319)			
SYNTAX score	18.9 ± 8.2	20.3 ± 9.0	19.7 ± 8.4	0.003	0.32	0.003
J-CTO score				0.22	<0.0001	<0.0001
0	23.1% (376)	20.5% (84)	14.3% (100)			
1	37.9% (616)	35.9% (147)	28.5% (200)			
≥2	39.0% (633)	43.5% (178)	57.2% (401)			
Transradial approach	84.6% (1374)	85.1% (348)	81.6% (572)	0.53	0.14	0.11
Guidance with IVUS	6.4% (104)	9.8% (40)	5.3% (37)	0.02	0.004	0.01
Bilateral angiography	27.8% (451)	36.4% (149)	34.2% (240)	0.001	0.46	<0.0001
Antegrade	98.1% (1594)	98.5% (403)	97.6% (684)	0.55	0.28	0.52
Parallel wire	16.9% (274)	24.7% (101)	28.4% (199)	<0.0001	0.18	<0.0001
ADR	0.7% (11)	1.7% (7)	1.4% (10)	0.05	0.71	0.08
Retrograde	1.9% (31)	1.5% (6)	2.4% (17)	0.55	0.28	<0.0001
Reverse CART	1.6% (26)	1.2% (5)	0.7% (5)	0.58	0.39	0.22
Stent implantation	98.0% (1593)	63.8% (261)	3.6% (25)	<0.0001	<0.0001	<0.0001
Number of stents (patient level)	2.27 ± 1.03	1.66 ± 1.42	0.49 ± 1.05	<0.0001	<0.0001	<0.0001
Number of stents (lesion level)	2.15 ± 0.95	1.44 ± 1.34	0.08 ± 0.43	<0.0001	<0.0001	<0.0001
Stent diameter, mm	2.96 ± 0.95	2.85 ± 0.37	2.94 ± 0.41	0.08	0.20	0.22
Stent length, mm	26.2 ± 5.20	25.7 ± 5.40	25.8 ± 7.10	0.16	0.93	0.36
Treating non-CTO lesion	10.1% (158)	14.5% (58)	29.1% (203)	0.01	<0.0001	<0.0001
PCI procedure duration, min	55.0 ± 37.9	54.7 ± 33.6	60.7 ± 38.2	0.91	0.009	0.002
PCI procedure duration > 60 min	28.0% (438)	32.1% (128)	34.1% (238)	0.11	0.50	0.01
Procedural complications	9.0% (146)	79.5% (325)	65.2% (457)	<0.0001	<0.0001	<0.0001
Dissection	8.4% (136)	42.1% (172)	44.2% (310)	<0.0001	0.48	<0.0001
Perforation	0.2% (4)	1.0% (4)	3.7% (26)	0.06	0.007	<0.0001
Slow/no flow	0.1% (2)	1.5% (6)	0.3% (2)	<0.0001	0.03	<0.0001
Side branch occlusion	0.1% (2)	41.8% (171)	29.8% (209)	<0.0001	<0.0001	<0.0001
Post-procedural TIMI 3 flow	100% (1625)	76.5% (313)	0% (0)	<0.0001	<0.0001	<0.0001
Residual SYNTAX score	7.12 ± 6.89	10.8 ± 8.89	17.0 ± 9.12	<0.0001	<0.0001	<0.0001
Residual SYNTAX score > 8	35.1% (548)	53.9% (215)	81.7% (570)	<0.0001	<0.0001	<0.0001

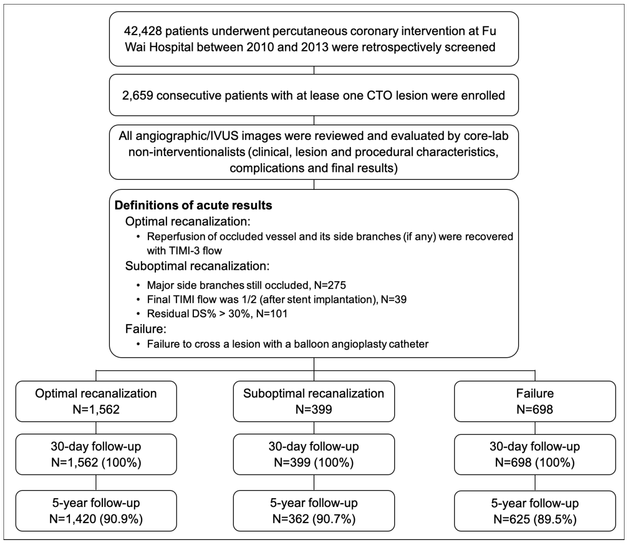
Values are mean ± SD or % (n). ADR = antegrade dissection and re-entry; CTO = chronic total occlusion; IVUS = intravascular ultrasound; LM = left main; SYNTAX = synergy between percutaneous coronary intervention with TAXUS and cardiac surgery; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

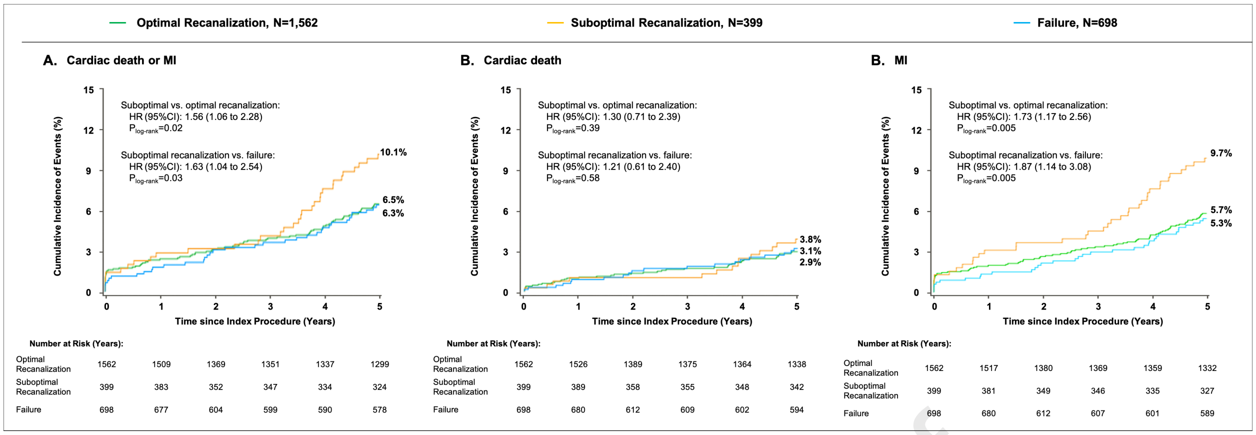
Table 3. Cumulative Event Rates Among Patients with Different Acute Results

	Optimal Recanalization (Patients, N=1,562)	**Suboptimal Recanalization (Patients, N=399)**	**Failure (Patients, N=698)**	**p Value** (Suboptimal vs. Optimal Recanalization)	**p Value** (Suboptimal vs. Failure Recanalization)	**p Value** (3-group Comparison)
At 30 days						
Cardiac death or MI	1.5% (23)	1.3% (5)	0.9% (6)	0.72	0.53	0.49
All-cause death	0.4% (7)	0.3% (1)	0.4% (3)	0.49	0.54	0.86
Cardiac death	0.4% (6)	0.3% (1)	0.3% (2)	0.57	0.70	0.89
Myocardial infarction	1.3% (21)	1.3% (5)	0.7% (5)	0.56	0.28	0.43
Periprocedural MI	1.2% (19)	1.3% (5)	0.7% (5)	0.56	0.28	0.54
Target-vessel related	1.3% (20)	1.3% (5)	0.7% (5)	0.60	0.28	0.49
Rehospitalization for heart failure	0% (0)	0% (0)	0% (0)	-	-	-
Any ID-revascularization	1.0% (15)	1.8% (7)	1.1% (8)	0.18	0.40	0.41
ID-TVR	0.3% (4)	0% (0)	0.9% (6)	0.31	0.06	0.04
ID-TLR	0.2% (3)	0% (0)	0.4% (3)	0.38	0.19	0.32
At 5 years						
Cardiac death or MI	6.5% (94)	10.1% (37)	6.3% (40)	0.02	0.03	0.046
All-cause death	5.2% (76)	5.7% (21)	4.7% (30)	0.76	0.50	0.78
Cardiac death	2.9% (42)	3.8% (14)	3.1% (20)	0.39	0.58	0.69
Myocardial infarction	5.7% (83)	9.7% (36)	5.3% (34)	0.005	0.005	0.009
Target-vessel related	5.0% (72)	8.7% (32)	4.7% (30)	0.007	0.01	0.01
Rehospitalization for heart failure	3.3% (47)	3.6% (13)	4.3% (27)	0.80	0.56	0.53
Any ID-revascularization	15.0% (220)	22.8% (86)	27.3% (183)	<0.0001	0.04	<0.0001
ID-TVR	6.7% (98)	12.1% (46)	22.7% (153)	<0.0001	<0.0001	<0.0001
ID-TLR	6.0% (88)	10.8% (41)	20.9% (141)	0.001	<0.0001	<0.0001

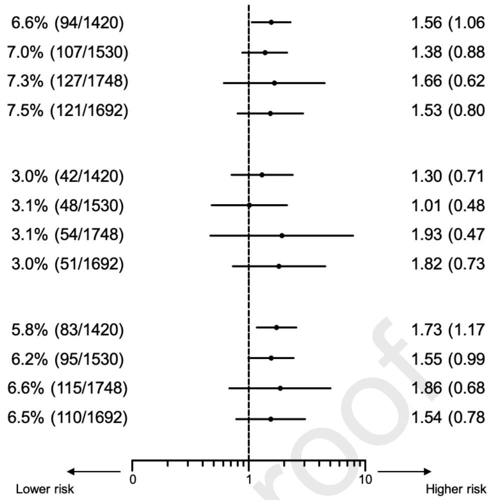
Percentages are Kaplan-Meier estimates and p values are calculated with the use of the log-rank test. ID = ischemic driven; TVR = target vessel revascularization; TLR = target lesion revascularization. Other abbreviations as in Table 1


Optimal Recanalization
Reperfusion of occluded vessel and its side branch (if any) with TIMI 3 flow recovery
Suboptimal Recanalization
Reperfusion of occluded main vessel and any of the following:
① Persistence of significant side branch occlusion
② Final TIMI flow of 1/2
③ Residual DS% > 30%
Procedural Failure
Failure to cross a lesion with a balloon angioplasty catheter
Mean Costs
5-Year Cardiac Death or MI
5-Year ID-TVR
Mean Costs ($)
Cumulative Incidence of Events (%)
p<0.0001
p<0.0001
11,905
14,940
8,259
22.6
12.1
10.1
6.7
6.5
6.3
Optimal Recanalization
Suboptimal Recanalization
Failure


42,428 patients underwent percutaneous coronary intervention at Fu Wai Hospital between 2010 and 2013 were retrospectively screened
2,659 consecutive patients with at lease one CTO lesion were enrolled
All angiographic/IVUS images were reviewed and evaluated by core-lab non-interventionalists (clinical, lesion and procedural characteristics, complications and final results)
Definitions of acute results
Optimal recanalization:
• Reperfusion of occluded vessel and its side branches (if any) were recovered with TIMI-3 flow
Suboptimal recanalization:
• Major side branches still occluded, N=275
• Final TIMI flow was 1/2 (after stent implantation), N=39
• Residual DS% > 30%, N=101
Failure:
• Failure to cross a lesion with a balloon angioplasty catheter
Optimal recanalization N=1,562
Suboptimal recanalization N=399
Failure N=698
30-day follow-up N=1,562 (100%)
30-day follow-up N=399 (100%)
30-day follow-up N=698 (100%)
5-year follow-up N=1,420 (90.9%)
5-year follow-up N=362 (90.7%)
5-year follow-up N=625 (89.5%)


Optimal Recanalization, N=1,562
Suboptimal Recanalization, N=399
Failure, N=698
A. Cardiac death or MI
Suboptimal vs. optimal recanalization:
HR (95%CI): 1.56 (1.06 to 2.28)
$P_{log-rank}$=0.02
Suboptimal recanalization vs. failure:
HR (95%CI): 1.63 (1.04 to 2.54)
$P_{log-rank}$=0.03
10.1%
6.5%
6.3%
Cumulative Incidence of Events (%)
Time since Index Procedure (Years)
Number at Risk (Years):
Optimal Recanalization 1562 1509 1369 1351 1337 1299
Suboptimal Recanalization 399 383 352 347 334 324
Failure 698 677 604 599 590 578
B. Cardiac death
Suboptimal vs. optimal recanalization:
HR (95%CI): 1.30 (0.71 to 2.39)
$P_{log-rank}$=0.39
Suboptimal recanalization vs. failure:
HR (95%CI): 1.21 (0.61 to 2.40)
$P_{log-rank}$=0.58
3.8%
3.1%
2.9%
Cumulative Incidence of Events (%)
Time since Index Procedure (Years)
Number at Risk (Years):
Optimal Recanalization 1562 1526 1389 1375 1364 1338
Suboptimal Recanalization 399 389 358 355 348 342
Failure 698 680 612 609 602 594
B. MI
Suboptimal vs. optimal recanalization:
HR (95%CI): 1.73 (1.17 to 2.56)
$P_{log-rank}$=0.005
Suboptimal recanalization vs. failure:
HR (95%CI): 1.87 (1.14 to 3.08)
$P_{log-rank}$=0.005
9.7%
5.7%
5.3%
Cumulative Incidence of Events (%)
Time since Index Procedure (Years)
Number at Risk (Years):
Optimal Recanalization 1562 1517 1380 1369 1359 1332
Suboptimal Recanalization 399 381 349 346 335 327
Failure 698 680 612 607 601 589

	Yes	No	HR (95%CI)	p Value
Cardiac death or MI				
Suboptimal recanalization	10.2% (37/362)	6.6% (94/1420)	1.56 (1.06 to 2.28)	0.02
Major side branches occlusion	9.5% (24/252)	7.0% (107/1530)	1.38 (0.88 to 2.14)	0.16
Final TIMI flow 1/2	11.8% (4/34)	7.3% (127/1748)	1.66 (0.62 to 4.50)	0.32
Residual % diameter stenosis > 30%	11.1% (10/90)	7.5% (121/1692)	1.53 (0.80 to 2.92)	0.20
Cardiac death				
Suboptimal recanalization	3.9% (14/362)	3.0% (42/1420)	1.30 (0.71 to 2.39)	0.39
Major side branches occlusion	3.2% (8/252)	3.1% (48/1530)	1.01 (0.48 to 2.13)	0.99
Final TIMI flow 1/2	5.9% (2/34)	3.1% (54/1748)	1.93 (0.47 to 7.91)	0.36
Residual % diameter stenosis > 30%	5.6% (5/90)	3.0% (51/1692)	1.82 (0.73 to 4.57)	0.20
MI				
Suboptimal recanalization	9.9% (36/362)	5.8% (83/1420)	1.73 (1.17 to 2.56)	0.006
Major side branches occlusion	9.5% (24/252)	6.2% (95/1530)	1.55 (0.99 to 2.43)	0.054
Final TIMI flow 1/2	11.8% (4/34)	6.6% (115/1748)	1.86 (0.68 to 5.03)	0.23
Residual % diameter stenosis > 30%	10.0% (9/90)	6.5% (110/1692)	1.54 (0.78 to 3.04)	0.21



Online Supplementary Appendix

Table I. Univariable Analysis of Predictors for Suboptimal Recanalization

Variables	Odds Ratio (95% CI)	p Value
Ad hoc PCI	0.94 (0.66 to 1.35)	0.75
Transradial approach	1.29 (0.95 to 1.76)	0.11
Bilateral angiography	1.10 (0.69 to 1.76)	0.68
Antegrade	1.42 (0.60 to 3.33)	0.43
Re-try lesion	1.16 (0.67 to 2.00)	0.60
Blunt stump	1.05 (0.84 to 1.29)	0.69
Lesion length ≥ 20mm	1.12 (0.91 to 1.39)	0.28
Moderate or severe vessel tortuosity	1.03 (0.80 to 1.32)	0.85
Moderate or severe calcification	1.13 (0.84 to 1.53)	0.43
In-stent lesion	2.31 (1.68 to 3.19)	<0.0001
J-CTO score > 2	0.96 (0.78 to 1.19)	0.73
Number of guiding wires per unit time	3.95 (1.44 to 10.9)	0.008
Dissection (type C to F)	2.08 (1.50 to 2.87)	<0.0001
Distal vessel implanted with stents (stent diameter ≤ 2.5 mm)	1.17 (0.83 to 1.63)	0.37

CI = confidence interval; CTO = chronic total occlusion; PCI = percutaneous coronary intervention.

Table II. Multivariable Logistic Regression Analysis for Predictors of Suboptimal Recanalization

Variables	Odds Ratio (95% CI)	p Value
Transradial approach	1.19 (0.88 to 1.62)	0.26
Re-try lesion	1.22 (0.70 to 2.14)	0.49
Blunt stump	0.98 (0.79 to 1.22)	0.87
Lesion length ≥ 20mm	1.06 (0.84 to 1.33)	0.63
Moderate or severe vessel tortuosity	1.48 (1.17 to 1.86)	0.001
Moderate or severe calcification	1.08 (0.79 to 1.48)	0.63
In-stent restenotic CTO lesion	2.45 (1.76 to 3.43)	<0.0001
Number of guiding wires per unit time	15.5 (1.05 to 228.9)	0.046
Dissection (type C to F)	2.38 (1.70 to 3.32)	<0.0001

Variables involved in multivariable analysis included those with $p<0.1$ in univariable analysis and mandatory variables that might be related with suboptimal clinical results. Abbreviations as in Table I.

Table III. Mean Costs in the Index Hospitalization

	Optimal Recanalization (Patients, N=1,562)		**Suboptimal Recanalization (Patients, N=399)**		**Failure (Patients, N=698)**		**p Value** (Suboptimal vs. Optimal Recanalization)	**p Value** (Suboptimal vs. Failure Recanalization)	**p Value** (3-group Comparison)
Total Costs	¥83,109 ± 37,854	$11,905 ± 5,420	¥104,297 ± 50,150	$14,940 ± 7,181	¥57,656 ± 14,354	$8,259 ± 2,055	<0.0001	<0.0001	<0.0001
Procedural costs	¥63,855 ± 23,317	$9,144 ± 3,338	¥80,023 ± 45,224	$11,459 ± 6,476	¥28,755 ± 19,098	$4,118 ± 2,734	<0.0001	<0.0001	<0.0001
Non-Procedural costs	¥19,254 ± 11,685	$2,757 ± 1,673	¥24,274 ±12,213	$3,476 ± 1,748	¥28,901 ± 28,357	$4,138 ± 4,060	<0.0001	<0.0001	<0.0001

The cost were adjusted to 2020 US dollars using the Consumer Price Index.

Table IV. Different Definition of Periprocedural Myocardial Infarction Among Patients with Different Acute Results

	Optimal Recanalization (Patients, N=1562)	**Suboptimal Recanalization (Patients, N=399)**	**Failure (Patients, N=698)**	**p Value** (Suboptimal vs. Optimal Recanalization)	**p Value** (Suboptimal vs. Failure Recanalization)	**p Value** (3-group Comparison)
SCAI definition	1.2% (19)	1.3% (5)	0.7% (5)	0.56	0.28	0.54
ARC-2 definition	2.6% (40)	3.3% (13)	2.3% (16)	0.44	0.34	0.62
4^{th} Uinversial definition	15.5% (242)	14.0% (56)	9.2% (64)	0.47	0.01	<0.0001

SCAI = Society for Cardiovascular Angiography and Interventions; ARC = Academic Research Consortium.

Table V. Sensitivity Analysis: Excluding Patients with Side Branch Occlusion in Suboptimal Recanalization Group

	Optimal Recanalization (Patients, N=1,837)	**Suboptimal Recanalization (Patients, N=124)**	**Failure (Patients, N=698)**	**p Value** (Suboptimal vs. Optimal Recanalization)	**p Value** (Suboptimal vs. Failure Recanalization)	**p Value** (3-group Comparison)
Cardiac death or MI	7.0% (118)	11.3% (13)	6.3% (40)	0.07	0.046	0.13
All-cause death	5.3% (90)	6.1% (7)	4.7% (30)	0.67	0.49	0.75
Cardiac death	2.9% (50)	5.2% (6)	3.1% (20)	0.16	0.24	0.37
Myocardial infarction	6.2% (107)	10.4% (12)	5.3% (34)	0.07	0.03	0.09
Target-vessel related	5.5% (94)	8.7% (10)	4.7% (30)	0.14	0.07	0.20
Rehospitalization for heart failure	3.5% (58)	1.8% (2)	4.3% (27)	0.36	0.22	0.36
Any ID-revascularization	16.1% (278)	24.3% (28)	27.3% (183)	0.02	0.30	<0.0001
ID-TVR	7.4% (128)	13.8% (16)	22.7% (153)	0.01	0.02	<0.0001
ID-TLR	6.6% (114)	12.9% (15)	20.9% (141)	0.007	0.03	<0.0001

Percentages are Kaplan-Meier estimates and p values are calculated with the use of the log-rank test. MI= myocardial infarction; ID = ischemic driven; TVR = target vessel revascularization; TLR = target lesion revascularization.

Table VI. Cumulative Event Rates Among Patients with Different Acute Results in In-stent Restenosis Subgroup

	Optimal Recanalization (Patients, N=119)	Suboptimal Recanalization (Patients, N=59)	Failure (Patients, N=34)	p Value (Suboptimal vs. Optimal Recanalization)	p Value (Suboptimal vs. Failure Recanalization)	p Value (3-group Comparison)
At 30 days						
Cardiac death or MI	2.5% (3)	1.7% (1)	0% (0)	0.73	0.45	0.64
All-cause death	1.7% (2)	1.7% (1)	0% (0)	0.99	0.45	0.75
Cardiac death	1.7% (2)	1.7% (1)	0% (0)	0.99	0.45	0.75
Myocardial infarction	1.7% (2)	1.7% (1)	0% (0)	0.99	0.45	0.75
Periprocedural MI	0.8% (1)	1.7% (1)	0% (0)	1.00	1.00	0.71
Target-vessel related	1.7% (2)	1.7% (1)	0% (0)	0.99	0.45	0.75
Rehospitalization for heart failure	0% (0)	0% (0)	0% (0)	-	-	-
Any ID revascularization	1.7% (2)	1.7% (1)	0% (0)	1.00	0.45	0.75
Ischemia-driven TVR	0.8% (1)	0% (0)	0% (0)	0.48	-	0.68
Ischemia-driven TLR	0.8% (1)	0% (0)	0% (0)	0.48	-	0.68
At 5 years						
Cardiac death or MI	11.4% (13)	14.9% (8)	6.2% (2)	0.55	0.22	0.48
All-cause death	4.3% (5)	5.5% (3)	3.1% (1)	0.77	0.59	0.87
Cardiac death	4.3% (5)	5.5% (3)	3.1% (1)	0.77	0.59	0.87
Myocardial infarction	9.7% (11)	12.9% (7)	3.1% (1)	0.52	0.13	0.32
Target-vessel related	8.1% (9)	11.3% (6)	3.1% (1)	0.51	0.19	0.41
Rehospitalization for heart failure	1.7% (2)	7.5% (4)	9.4% (3)	0.07	0.74	0.09
Any ID revascularization	14.0% (16)	16.5% (9)	33.1% (11)	0.68	0.04	0.01

Ischemia-driven TVR	4.4% (5)	12.9% (7)	30.1% (10)	0.048	0.02	<0.0001
Ischemia-driven TLR	4.4% (5)	11.0% (6)	24.1% (8)	0.11	0.07	0.001

Values are mean ± SD or % (n). Percentages are Kaplan-Meier estimates and p values are calculated with the use of the log-rank test. Abbreviations as in Table V.

Table VII. Cumulative Event Rates Among Patients with Different Acute Results in *De Novo* Lesion Subgroup

	Optimal Recanalization (Patients, N=1443)	**Suboptimal Recanalization (Patients, N=340)**	**Failure (Patients, N=664)**	**p Value** (Suboptimal vs. Optimal Recanalization)	**p Value** (Suboptimal vs. Failure Recanalization)	**p Value** (3-group Comparison)
At 30 days						
Cardiac death or MI	1.3% (20)	1.2% (4)	0.9% (6)	0.77	0.68	0.64
All-cause death	0.3% (5)	0% (0)	0.5% (3)	0.28	0.22	0.49
Cardiac death	0.3% (4)	0% (0)	0.3% (2)	0.33	0.31	0.61
Myocardial infarction	1.3% (19)	1.2% (4)	0.8% (5)	0.84	0.50	0.53
Periprocedural MI	1.2% (18)	1.2% (4)	0.8% (5)	0.92	0.50	0.60
Target-vessel related	1.2% (18)	1.2% (4)	0.8% (5)	0.92	0.50	0.60
Rehospitalization for heart failure	0% (0)	0% (0)	0% (0)	-	-	-
Any ID revascularization	0.9% (13)	1.8% (6)	1.2% (8)	0.16	0.47	0.37
Ischemia-driven TVR	0.2% (3)	0% (0)	0.8% (5)	0.40	0.11	0.07
Ischemia-driven TLR	0.1% (2)	0% (0)	0.5% (3)	0.49	0.22	0.22
At 5 years						
Cardiac death or MI	6.1% (81)	9.2% (29)	6.3% (38)	0.048	0.11	0.13
All-cause death	5.3% (71)	5.8% (18)	4.7% (29)	0.80	0.56	0.82
Cardiac death	2.8% (37)	3.5% (11)	3.1% (19)	0.51	0.78	0.78
Myocardial infarction	5.3% (72)	9.1% (29)	5.4% (33)	0.01	0.03	0.03
Target-vessel related	4.7% (63)	8.2% (26)	4.8% (29)	0.01	0.04	0.04
Rehospitalization for heart failure	3.4% (45)	2.9% (9)	4.0% (24)	0.64	0.39	0.65
Any ID revascularization	15.1% (204)	23.9% (77)	27.0% (172)	<0.0001	0.16	<0.0001

Ischemia-driven TVR	6.9% (93)	12.0% (39)	22.2% (142)	0.001	<0.0001	<0.0001
Ischemia-driven TLR	6.1% (83)	10.8% (35)	20.7% (133)	0.002	<0.0001	<0.0001

Values are mean ± SD or % (n). Percentages are Kaplan-Meier estimates and p values are calculated with the use of the log-rank test. Abbreviations as in Table V.

Table VIII. 5-Year Cardiac Death, MI, or TVR Among Patients with Different Acute Results in In-Stent Restenostic or *De Novo* Lesion Subgroup

	Suboptimal Recanalization	Optimal Recanalization	HR (95%CI)	p for Interaction
Cardiac death or MI				
In-stent restenositic CTO lesion	14.9% (8/59)	11.4% (13/119)	1.30 (0.54 to 3.15)	0.005
De novo CTO lesion	9.2% (29/340)	6.1% (81/1443)	1.53 (1.00 to 2.33)	
Ischemia-driven TVR				
In-stent restenositic CTO lesion	12.9% (7/59)	4.4% (5/119)	3.01 (0.96 to 9.50)	0.79
De novo CTO lesion	12.0% (39/340)	6.9% (93/1443)	1.86 (1.28 to 2.70)	
	Suboptimal Recanalization	**Failure**		
Cardiac death or MI				
In-stent restenositic CTO lesion	14.9% (8/59)	6.2% (2/34)	2.55 (0.54 to 12.0)	0.30
De novo CTO lesion	9.2% (29/340)	6.3% (38/664)	1.49 (0.92 to 2.41)	
Ischemia-driven TVR				
In-stent restenositic CTO lesion	12.9% (7/59)	30.1% (10/34)	0.34 (0.13 to 0.90)	0.69
De novo CTO lesion	12.0% (39/340)	22.2% (142/664)	0.49 (0.35 to 0.70)	

Abbreviations as in Tables I and V.

Figure I. Survival Curves for 5-Year Cardiac Death or MI in Suboptimal Recanalization Subgroups

HR = hazard ratio; CI = confidence interval. MI = myocardial infarction. HRs are patients with vs. without suboptimal recanalization criteria. Greater residual stenosis is defined as residual diameter stenosis > 30%.