

Major In-Hospital Complications During Contemporary Chronic Total Occlusion Percutaneous Coronary Intervention: A Multicenter Turkish Registry

ABSTRACT

Objective: To examine the incidence, predictors, and strategy-specific patterns of major in-hospital complications during contemporary chronic total occlusion percutaneous coronary intervention (CTO PCI) in a multicenter Turkish registry.

Methods: This retrospective analysis of a prospective multicenter registry included 2375 consecutive CTO PCI procedures performed from January 2020 to February 2026. The primary endpoint comprised death, myocardial infarction (MI), stroke, treatment-requiring coronary perforation, donor-vessel complication, emergency repeat percutaneous coronary intervention, or emergency coronary artery bypass grafting. Myocardial infarction and stroke were based on site-reported fields without central adjudication. Predictors were evaluated using logistic regression, with 500 bootstrap resamples for internal validation.

Results: Major complications occurred in 87 procedures (3.7%) and in-hospital death in 14 (0.6%). Event rates ranged from 1.3% in Japanese-Chronic Total Occlusion (J-CTO) 0-1 lesions to 7.3% in J-CTO ≥ 4 lesions and were 2.3% vs. 7.1% in planned antegrade-only vs. planned retrograde or hybrid procedures. With actual retrograde involvement, the complication rate was 8.1% vs. 2.2% without retrograde use ($P < .001$). Treatment-requiring perforation occurred in 52 procedures and donor-vessel complications in 22. The primary multiple logistic regression model yielded odds ratio (OR) of 1.02 per year for age ($P = .042$, 95% CI: 1.00-1.05); OR of 1.23 per 10 mm for CTO length ($P = .002$, 95% CI: 1.08-1.40); and OR of 1.92 for moderate or severe calcification ($P = .005$, 95% CI: 1.22-3.03). Model discrimination was area under the curve (AUC) of 0.668 ($P < .001$, 95% CI: 0.614-0.722); bootstrap optimism-corrected AUC = 0.643.

Conclusion: Major complications occurred in 3.7% of procedures, with rates varying across J-CTO strata and planned strategy groups. These findings may inform preprocedural counseling and procedural planning.

Keywords: Complications, coronary occlusion, myocardial infarction, percutaneous coronary intervention, vascular calcification

INTRODUCTION

Over the past decade, chronic total occlusion percutaneous coronary intervention (CTO PCI) has evolved substantially. Use of hybrid and retrograde strategies has expanded, dedicated devices have become more widely available, and intravascular imaging has become more firmly embedded in routine practice. These developments have coincided with improved procedural success in experienced centers.¹⁻³ Nevertheless, CTO PCI remains technically demanding and entails greater procedural intensity, radiation exposure, and complication risk than non-CTO PCI.⁴⁻⁶

Most recent CTO PCI studies have concentrated on procedural success, crossing strategies, lesion complexity, or longer-term symptomatic benefit.^{1-3,7,8} In contrast, major in-hospital safety events have received less direct attention, particularly in broad multicenter cohorts that reflect everyday practice.⁴⁻⁶

ORIGINAL INVESTIGATION

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Understanding the incidence and predictors of major in-hospital complications is important for case selection, patient counseling, bailout preparedness, and team planning. Reporting complication burden alongside procedural success and across strategy strata may offer a more clinically useful perspective on CTO PCI safety than success metrics alone.^{2,4,6}

In this study, the authors used a contemporary multicenter CTO PCI registry to quantify the incidence and components of major in-hospital complications, describe strategy-specific event rates, and estimate adjusted odds ratios (ORs) for prespecified clinical-anatomic variables.

METHODS

Study Design and Population

This study was a retrospective analysis of a prospective multicenter CTO PCI registry and included consecutive CTO PCI procedures performed between January 2020 and February 2026 at 3 university hospitals. The analysis was conducted at the procedure level. Because the registry was organized around procedures rather than unique longitudinal patient episodes, each CTO PCI entry was treated as a separate observation, and repeat procedures, when present, were retained as distinct entries. This approach was considered appropriate for the present analysis of periprocedural safety. Clinical, angiographic, procedural, and in-hospital outcome variables were extracted from the registry database. All procedures were performed in tertiary referral hospitals by dedicated chronic total occlusion (CTO) operators within these programs. Based on operator-level procedural-activity records from the participating primary CTO operators, 2 operators performed more than 150 CTO PCI procedures per year, and the third performed more than 60 CTO PCI procedures per year. In addition, annual non-CTO PCI volume exceeded 300 procedures for each of these operators. Thus, all participating primary CTO operators met or exceeded the EuroCTO Club volume criterion of at least 50 CTO PCI procedures per year for experienced CTO practice.⁹

HIGHLIGHTS

- Most chronic total occlusion percutaneous coronary intervention reports emphasize procedural success, whereas multicenter data specifically addressing in-hospital complications remain limited.
- Among 2375 procedures performed in Türkiye, major in-hospital complications occurred in 3.7%, whereas in-hospital mortality was 0.6%.
- Major complication rates rose from 1.3% in Japanese Chronic Total Occlusion (J-CTO) 0-1 lesions to 7.3% in J-CTO ≥ 4 lesions and were 2.3% vs. 7.1% according to planned strategy.
- With actual retrograde involvement, the major complication rate was 8.1% vs. 2.2% without retrograde use ($P < .001$); donor-vessel complications occurred in 3.8% vs. 0.0% and treatment-requiring perforation in 3.5% vs. 1.8%.

Clinical presentation at the time of CTO PCI referral/procedure was recorded separately from CTO chronicity. Clinical indications for CTO PCI were based on symptoms, acute clinical presentation, angiographic suitability, and available CTO-territory assessment. In procedures without recorded angina, selection for revascularization was based on clinical judgment, angiographic suitability, and available CTO-territory assessment, including electrocardiographic (ECG) findings, ECG segmental wall-motion findings, and previous myocardial infarction (MI) in the CTO territory. Dedicated non-invasive ischemia or viability imaging was not systematic and was therefore not used as a main analytic variable (Supplementary Table 1).

Procedural strategy was planned by the treating CTO operator after angiographic review and lesion-complexity assessment. Antegrade-only PCI was generally selected for less complex anatomy. Planned retrograde or hybrid involvement was selected for more complex lesions, including cases with prior failed attempts, ambiguous or unfavorable caps, long occlusions, severe calcification, or suitable collateral channels. Intraprocedural strategy change or escalation was left to operator judgment. The common clinical and procedural pathway used across the centers is shown in Supplementary Figure 1. Intravascular imaging was used selectively rather than routinely. Intravascular ultrasound (IVUS) was recorded as a structured registry variable, whereas OCT use was not captured as a separate structured registry variable.

Endpoints and Definitions

The primary endpoint was a composite of major in-hospital complications, defined as in-hospital death, MI, stroke, severe coronary perforation requiring treatment, donor-vessel complication, emergency repeat percutaneous coronary intervention (PCI), or emergency coronary artery bypass grafting (CABG). Death, treatment-requiring perforation, donor-vessel complication, emergency repeat PCI, and emergency CABG were identified from procedural and in-hospital registry records. Myocardial infarction and stroke were identified from prespecified in-hospital registry event fields recorded at each site; no central adjudication process was available for retrospective reclassification. Individual component counts were not mutually exclusive, and a single procedure could contribute to more than 1 component event; however, the composite endpoint was counted once per procedure. Severe coronary perforation requiring treatment included covered stent implantation, tamponade-related intervention, coil embolization, percutaneous treatment, or surgical treatment. It was included in the primary composite because it represents a major intraprocedural safety event with immediate therapeutic consequences.

A secondary extended in-hospital complication composite, which additionally included site-reported hemodynamic instability, treated collateral perforation, and vascular complications, was retained for supplementary descriptive reporting only. Endpoint definitions are summarized in Supplementary Table 2, and selected operational coding rules for component-level fields are summarized in Supplementary Table 3.

For strategy-specific component analyses, actual retrograde involvement was defined by documented retrograde use in the retrograde-result field, regardless of the initially planned procedural strategy. This operational definition was used to distinguish procedures with actual retrograde involvement from antegrade-only procedures for descriptive component-level reporting.

Candidate Predictors

The prespecified primary clinical-anatomic multiple logistic regression model included age, sex, diabetes mellitus, previous CABG, in-stent CTO, visually estimated CTO length, and moderate or severe calcification. Planned retrograde or hybrid involvement was analyzed descriptively as a procedural planning variable and was not entered into the primary multiple logistic regression model.

Statistical Analysis

Normality of continuous variables was assessed within the major-complication groups using the Shapiro–Wilk test. Because at least 1 comparison group showed a departure from normality for each continuous variable, continuous variables are presented as median [interquartile range] and were compared using the Mann–Whitney *U*-test. Categorical variables are presented as counts and percentages and were compared using the chi-square test or Fisher's exact test, as appropriate. For component-level stratification by actual retrograde involvement, proportions were compared using Fisher's exact test. Univariate and multiple logistic regression analyses were performed for the primary endpoint. Because only 87 primary events occurred, the main model was limited to prespecified, clinically plausible covariates to reduce the risk of overfitting. No imputation was performed. Completeness exceeded 99.9% for variables used in the analytic models after harmonization of registry fields. The largest missing proportions occurred in descriptive procedural burden metrics, which were summarized using available-case data. Missing-data patterns are summarized in Supplementary Table 4. A compact model incorporating the J-CTO score was examined as a sensitivity analysis. To address potential non-independence from repeated observations, identifiable within-registry repeat procedures were assessed using center, anonymized patient code, birth date, sex, and procedure date; an additional sensitivity analysis excluded later repeat entries from patients with more than 1 procedure date in the registry (Supplementary Table 5). Exploratory stratified analyses according to J-CTO category and planned procedural strategy were also performed, with interaction testing interpreted cautiously because of the limited number of major complication events (Supplementary Table 6). Model performance for the primary multiple logistic regression model was assessed using the area under the receiver-operating characteristic curve (AUC). The 95% CI and *P* value for the apparent AUC were calculated using the DeLong method, with an AUC of 0.50 as the null hypothesis. Calibration was assessed using the calibration intercept and slope and a decile-based calibration plot. Internal validation of discrimination was performed with 500 bootstrap resamples to estimate the optimism-corrected AUC. All tests were 2-sided, and *P* < .05 was considered statistically significant.

Statistical analyses were performed using Python version 3.11 (Python Software Foundation, Wilmington, Del, USA). Data handling and statistical analyses were conducted using the pandas, NumPy, SciPy, statsmodels, and scikit-learn libraries.

Ethics

This study was approved by the Local Ethics Committee (approval number: 2026/6397; date: March 13, 2026) and was conducted in accordance with the Declaration of Helsinki. Given the retrospective design, the requirement for written informed consent was waived.

RESULTS

A total of 2375 CTO PCI procedures were included in the analysis. Major in-hospital complications occurred in 87 procedures (3.7%), whereas in-hospital death occurred in 14 procedures (0.6%). The supplementary extended in-hospital complication composite was observed in 146 procedures (6.1%) and is reported in the Supplementary Material. Because individual component counts were not mutually exclusive, the sum of component events exceeded the number of procedures with a composite event. Individual components of the major in-hospital complication composite are detailed in Table 1, which also presents component-level stratification according to actual retrograde involvement. The distribution of component counts per procedure is shown in Supplementary Table 7; a fuller component breakdown, including the extended composite, is provided in Supplementary Table 8; and Figure 1 summarizes the overall absolute event counts.

Clinical presentation and CTO-territory findings are summarized in Supplementary Table 1. Clinical presentation was considered separately from CTO chronicity. Angina was recorded in 1774 procedures (74.7%), including stable angina in 1653 (69.6%) and unstable angina in 121 (5.1%). Acute MI was recorded as a separate clinical presentation in 39 procedures (1.6%). No angina was recorded in 557 procedures (23.5%), and clinical presentation was unknown in 5 procedures (0.2%). Among procedures without recorded angina, available CTO-territory assessment showed no Q waves in 487 of 557 (87.4%), segmental wall-motion abnormality in the CTO-related territory in 317 of 557 (56.9%), and documented evidence of formal ischemia in 113 of 557 (20.3%). Formal non-invasive ischemia or viability testing was available only in a limited subset, including myocardial scintigraphy in 170 procedures (7.2%), PET in 24 (1.0%), and cardiac MRI in 10 (0.4%).

Clinical and lesion characteristics according to major complication status are summarized in Table 2. Median age was 63.9 vs. 61.4 years (*P* = .029), median CTO length was 30 vs. 25 mm (*P* < .001), moderate or severe calcification was present in 60.9% vs. 42.0% (*P* < .001), blunt or absent stump morphology in 59.8% vs. 38.9% (*P* < .001), and median J-CTO score was 3 vs. 2 (*P* < .001) in procedures with vs. without major complications. Major complication rates were 1.3% in J-CTO 0-1, 3.4% in J-CTO 2, 5.2% in J-CTO 3, and 7.3% in J-CTO ≥4 (Figure 2).

Procedural planning, burden, and success according to major complication status are summarized in Table 3. Planned retrograde or hybrid involvement was present in 54.0% of

Table 1. Individual Components of the Major In-hospital Complication Composite According to Actual Retrograde Involvement

Complication Component	Overall, n (%)	Antegrade-only (n = 1798)	Actual Retrograde Involvement (n = 577)	P
In-hospital death	14 (0.6)	3 (0.2)	11 (1.9)	<.001
Myocardial infarction	11 (0.5)	6 (0.3)	5 (0.9)	.150
Stroke	2 (0.1)	2 (0.1)	0 (0.0)	1.000
Severe coronary perforation requiring treatment	52 (2.2)	32 (1.8)	20 (3.5)	.021
Donor-vessel complication	22 (0.9)	0 (0.0)	22 (3.8)	<.001
Emergency repeat PCI	5 (0.2)	2 (0.1)	3 (0.5)	.096
Emergency CABG	4 (0.2)	0 (0.0)	4 (0.7)	.003
Major in-hospital complication composite	87 (3.7)	40 (2.2)	47 (8.1)	<.001

Values are presented as n (%). Individual component counts are non-mutually exclusive; composite endpoints were counted once per procedure. Antegrade-only denotes procedures without documented retrograde use; actual retrograde involvement denotes procedures with documented retrograde use. Percentages are calculated using column denominators. *P*-values compare antegrade-only vs. actual retrograde involvement. CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

procedures with major complications and 26.9% without major complications, whereas actual retrograde involvement was recorded in 54.0% and 23.2%, respectively (both $P < .001$). The absolute major complication rate was 2.3% in planned antegrade-only cases and 7.1% in procedures with planned retrograde or hybrid involvement, corresponding to an absolute risk difference of 4.8 percentage points (Figure 3). In procedures with vs. without major complications, median procedure duration was 150 vs. 75 minutes, fluoroscopy time 76 vs. 34 minutes, contrast volume 350 vs. 230 mL, air kerma 4584 vs. 2661 mGy, and dose-area product 23200 vs. 14200 cGy·cm² (all $P < .001$). IVUS use was 8.0% vs. 9.1% ($P = 1.000$).

Treatment-requiring coronary perforation occurred in 52 procedures (2.2%), and donor-vessel complications occurred in 22 (0.9%). With actual retrograde involvement vs. no retrograde use, donor-vessel complications occurred in 3.8% vs. 0.0% ($P < .001$), emergency CABG in 0.7% vs. 0.0% ($P = .003$), treatment-requiring perforation in 3.5% vs. 1.8% ($P = .021$),

and in-hospital death in 1.9% vs. 0.2% ($P < .001$) (Table 1). Overall, in-hospital death occurred in 14 procedures (0.6%).

Among the 87 procedures with a major in-hospital complication, 14 involved in-hospital death, 5 required emergency repeat PCI, and 4 required emergency CABG. Severe treatment-requiring perforation was documented in 52 procedures, donor-vessel complication in 22, MI in 11, and stroke in 2. Because component events were not mutually exclusive, these numbers describe the in-hospital clinical burden rather than mutually exclusive patient trajectories.

Results of the primary clinical-anatomic multiple logistic regression model are shown in Table 4. The adjusted estimates were OR=1.02 per year for age, $P = .042$, 95% CI: 1.00-1.05; OR=1.23 per 10 mm for CTO length, $P = .002$, 95% CI: 1.08-1.40; and OR=1.92 for moderate or severe calcification, $P = .005$, 95% CI: 1.22-3.03. Planned retrograde or hybrid involvement was analyzed descriptively and was not included in the primary model. Model discrimination was AUC=0.668,

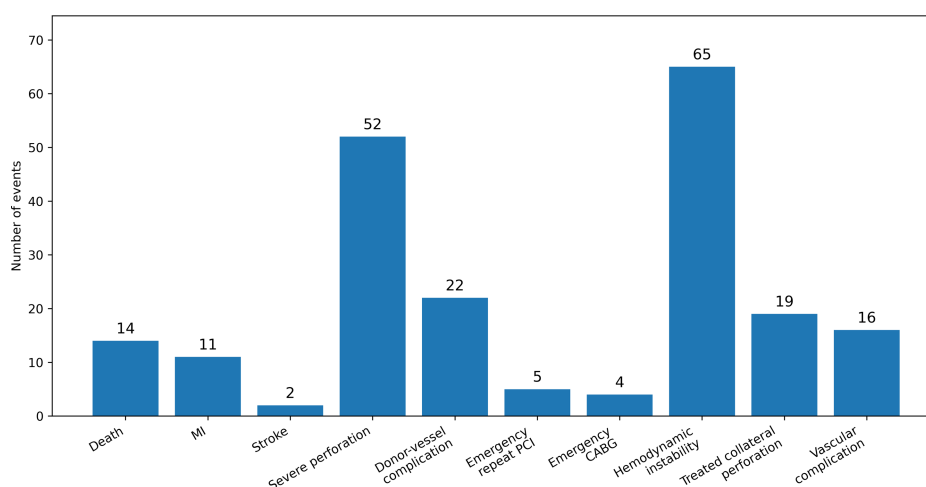


Figure 1. Individual in-hospital complication components. Bar chart showing the absolute event counts of the main complication components recorded in the registry. Component counts are non-mutually exclusive. CABG, coronary artery bypass grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 2. Clinical and Lesion Characteristics According to Major In-hospital Complication Status

Variables	Overall	No Major Complication	Major Complication	P
Age, years	61.4 [54.1-68.6]	61.4 [54.0-68.6]	63.9 [57.8-70.6]	.029
Female sex	363 (15.3)	349 (15.3)	14 (16.1)	.951
Diabetes mellitus	996 (41.9)	966 (42.2)	30 (34.5)	.185
Previous CABG	276 (11.6)	265 (11.6)	11 (12.6)	.894
In-stent CTO	296 (12.5)	284 (12.4)	12 (13.8)	.828
CTO length, mm	25 [16-30]	25 [15-30]	30 [25-40]	<.001
Moderate/severe calcification	1015 (42.7)	962 (42.0)	53 (60.9)	<.001
Blunt/absent stump	941 (39.6)	889 (38.9)	52 (59.8)	<.001
J-CTO score	2 [1-3]	2 [1-3]	3 [2-4]	<.001

Values are presented as median [interquartile range] or n (%).

CABG, coronary artery bypass grafting; CTO, chronic total occlusion; J-CTO, Japanese Chronic Total Occlusion score.

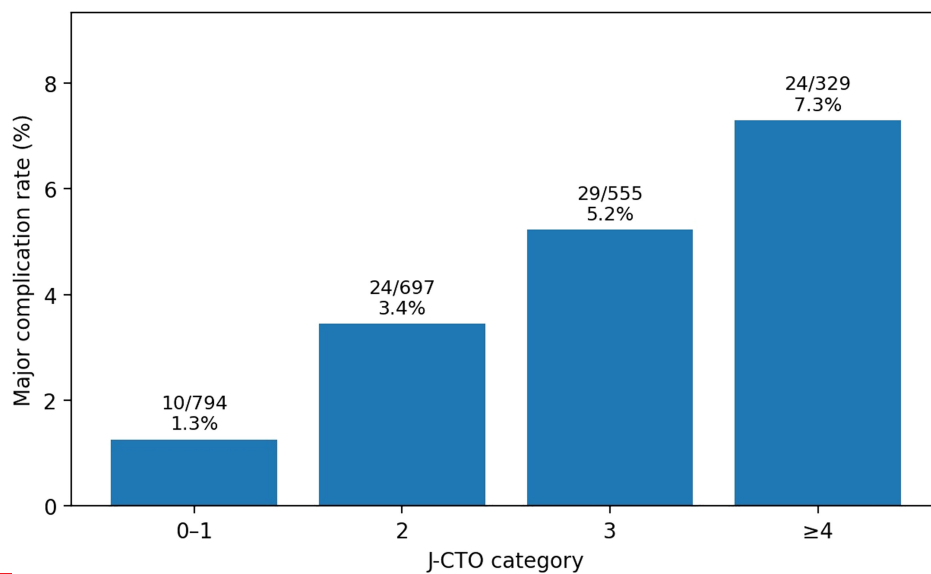


Figure 2. Major in-hospital complication rates according to J-CTO category. Bar chart illustrating the stepwise increase in major in-hospital complication rates across J-CTO strata. J-CTO, Japanese Chronic Total Occlusion score.

$P < .001$, 95% CI: 0.614-0.722; bootstrap optimism-corrected AUC=0.643. The apparent calibration intercept was approximately 0.00 and the calibration slope was approximately 1.00; decile-based calibration is shown in Supplementary Figure 2. In the compact sensitivity model, the adjusted estimates were

OR=1.03 per year for age, $P=.017$, 95% CI: 1.00-1.05, and OR=1.62 per J-CTO point, $P < .001$, 95% CI: 1.35-1.94 (Table 5).

In additional sensitivity analyses, the repeat-excluded estimates are presented in Supplementary Table 5. Exploratory

Table 3. Procedural Planning, Burden, and Success According to Major In-hospital Complication Status

Variables	Overall	No Major Complication	Major Complication	P
Planned retrograde/hybrid involvement	663 (27.9)	616 (26.9)	47 (54.0)	<.001
Actual retrograde involvement	577 (24.3)	530 (23.2)	47 (54.0)	<.001
IVUS use	215 (9.1)	208 (9.1)	7 (8.0)	1.000
Procedure time, min	76 [53-120]	75 [52-117]	150 [116-183]	<.001
Fluoroscopy time, min	36 [22-60]	34 [22-58]	76 [55-99]	<.001
Contrast volume, mL	240 [180-350]	230 [180-320]	350 [290-450]	<.001
Air kerma, mGy	2712 [1556-4685]	2661 [1520-4582]	4584 [2872-7968]	<.001
Dose-area product, cGy·cm ²	14470 [6770-24900]	14200 [6750-24600]	23200 [9800-33700]	<.001
Procedural success	2183 (91.9)	2125 (92.9)	58 (66.7)	<.001

Values are presented as median [interquartile range] or n (%).

IVUS, intravascular ultrasound.

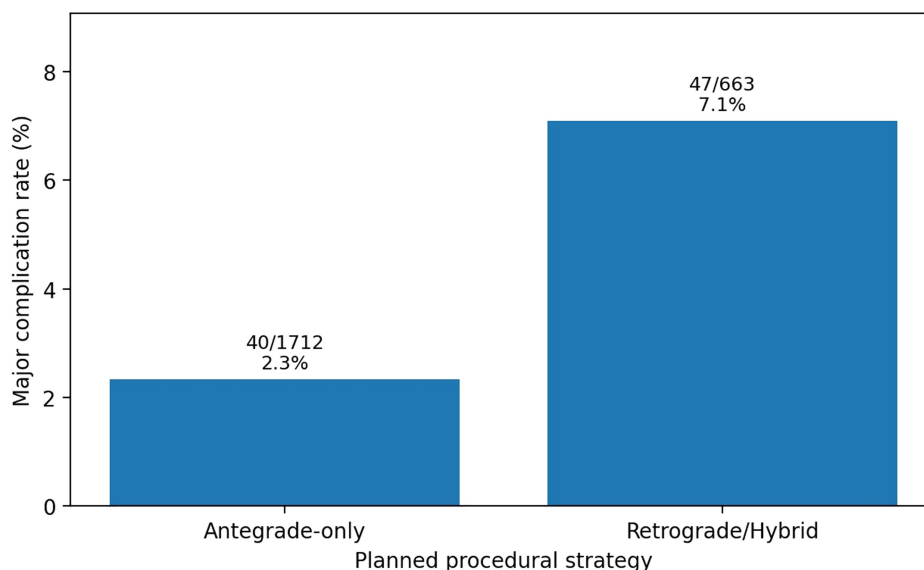


Figure 3. Major in-hospital complication rates according to planned procedural strategy. Bar chart comparing major in-hospital complication rates between planned antegrade-only procedures and procedures with planned retrograde or hybrid involvement.

Table 4. Univariate Predictors and Primary Clinical-Anatomic Multiple Logistic Regression Model for Major In-hospital Complications

Variables	Univariate OR (95% CI)	P	Adjusted OR (95% CI)	P
Age (per year)	1.03 (1.00-1.05)	.026	1.02 (1.00-1.05)	.042
Female sex	1.07 (0.60-1.91)	.827	1.16 (0.63-2.12)	.639
Diabetes mellitus	0.72 (0.46-1.13)	.150	0.65 (0.41-1.03)	.068
Previous CABG	1.10 (0.58-2.10)	.763	0.81 (0.42-1.59)	.543
In-stent CTO	1.13 (0.61-2.10)	.704	1.01 (0.53-1.93)	.983
CTO length (per 10 mm)	1.22 (1.09-1.38)	<.001	1.23 (1.08-1.40)	.002
Moderate/severe calcification	2.15 (1.39-3.33)	<.001	1.92 (1.22-3.03)	.005

CTO, chronic total occlusion; OR, odds ratio.

event rates were 6.0% in J-CTO ≥ 3 lesions vs. 2.3% in J-CTO 0-2 lesions. In planned retrograde or hybrid vs. planned antegrade-only procedures, event rates were 5.8% vs. 1.8% within J-CTO 0-2 and 7.6% vs. 4.1% within J-CTO ≥ 3 (Supplementary Table 6).

DISCUSSION

In this multicenter CTO PCI registry, major in-hospital complications occurred in 3.7% of procedures and in-hospital death in 0.6%. Event rates were 1.3%, 3.4%, 5.2%, and 7.3%

across successive J-CTO strata and 2.3% vs. 7.1% in planned antegrade-only vs. planned retrograde or hybrid procedures. These gradients identify the procedural settings in which additional preparation and bailout readiness may be considered.

The observed 3.7% event rate may reflect improvements in CTO PCI practice, including better equipment, greater operator experience, and more structured procedural planning.^{2,3,8,10} Even with this absolute rate, the recorded complications remain clinically relevant. These findings support safety planning and bailout readiness in contemporary CTO PCI practice.⁴⁻⁶

The findings can also be compared with recent international CTO PCI data. Periprocedural mortality was approximately 0.4% in the PROGRESS-CTO registry and 0.6% in this cohort.¹¹ In the contemporary ERCTO registry, major adverse cardiac and cerebrovascular events (MACCE) rates were 3.1% in retrograde cases and 1.2% in antegrade cases.¹² Although end-point definitions differ across registries, these values place the results within the range reported in contemporary real-world CTO PCI practice.

Table 5. Alternative Compact Clinical-Anatomic Model Using J-CTO Score

Variables	Adjusted OR (95% CI)	P
Age (per year)	1.03 (1.00-1.05)	.017
Female sex	1.22 (0.66-2.24)	.526
Diabetes mellitus	0.66 (0.42-1.05)	.082
Previous CABG	0.87 (0.45-1.69)	.686
In-stent CTO	1.14 (0.61-2.14)	.681
J-CTO score (per point)	1.62 (1.35-1.94)	<.001

J-CTO, Japanese Chronic Total Occlusion score; OR, odds ratio.

The primary adjusted model yielded OR=1.02 per year for age, $P=.042$, 95% CI: 1.00-1.05; OR=1.23 per 10 mm for CTO length, $P=.002$, 95% CI: 1.08-1.40; and OR=1.92 for moderate or severe calcification, $P=.005$, 95% CI: 1.22-3.03. The J-CTO event-rate gradient ranged from 1.3% to 7.3%. Planned retrograde or hybrid involvement was recorded in 54.0% of procedures with major complications and 26.9% without major complications. The comparison by planned strategy is descriptive and reflects case selection and lesion complexity. In the actual retrograde group, all 22 donor-vessel complications and all 4 emergency CABG events were recorded; treatment-requiring perforation occurred in 3.5% vs. 1.8% and in-hospital death in 1.9% vs. 0.2%. These findings support specific preparation for donor-vessel injury, perforation, and surgical bailout in procedures involving retrograde techniques.^{2,4-7}

For clinical use, these findings are better viewed as a simple procedural preparedness framework than as a formal externally validated prediction score. The absolute risk gradients across J-CTO category and planned strategy may help identify cases requiring more detailed consent, senior operator involvement, access and equipment planning, radiation and contrast minimization, and readiness for perforation, donor-vessel, and surgical bailout. The common clinical and procedural pathway used across participating centers is schematized in Supplementary Figure 1.

In procedures with vs. without major complications, median procedure duration was 150 vs. 75 minutes, fluoroscopy time 76 vs. 34 minutes, contrast volume 350 vs. 230 mL, air kerma 4584 vs. 2661 mGy, and dose-area product 23200 vs. 14200 cGy·cm² (all $P < .001$). Treatment-requiring perforation was recorded in 52 procedures and donor-vessel complications in 22. The authors did not use this endpoint as a conventional ischemic major adverse cardiovascular events (MACE) measure. The broader safety composite was chosen to include complications that directly affect CTO PCI management, especially perforation and donor-vessel complications. The components differ in mechanism and clinical importance. Therefore, the multiple logistic regression analysis was intended to support risk assessment, rather than to provide a formal prediction model for a homogeneous outcome. Model performance was AUC=0.668, $P < .001$, 95% CI: 0.614-0.722; bootstrap optimism-corrected AUC=0.643. Validation was limited to internal bootstrap resampling.

Study Limitations

Several limitations should be acknowledged. This was a retrospective analysis of registry data, and some event components—particularly MI and stroke—were based on site-coded fields without central adjudication or retrospective reclassification to standardized definitions. Accordingly, some between-center variation in ascertainment and potential misclassification are possible. In addition, component events were not mutually exclusive, so the counts were intended to reflect overall in-hospital event burden rather than discrete clinical categories.

The analysis was limited to the in-hospital period because systematic 30-day post-discharge outcomes were not

available for the full registry; therefore, the findings primarily address periprocedural risk and procedural preparedness. Selective reporting of only available post-discharge follow-up was avoided because it could introduce bias. Formal non-invasive ischemia or viability testing was not systematic. Therefore, patient selection, particularly in procedures without recorded angina, may have depended on local clinical judgment, angiographic suitability, and available CTO-territory ECG or echocardiographic findings. This should be considered when interpreting patient selection in procedures without recorded angina. The study was also conducted at the procedure level rather than the patient level. Previous-attempt status was not used as a proxy for repeated observations because it mainly reflected prior CTO attempts outside the present registry. Nine later identifiable within-registry repeat entries were found, and their exclusion did not materially alter the main findings. Only 3 tertiary referral centers with dedicated CTO programs and experienced CTO operators contributed data. The procedural-volume information reflected operator-level activity from the participating primary CTO operators, rather than systematically captured center-level annual volumes. This may introduce selection bias and limits direct generalizability to lower-volume centers or less experienced operators. Detailed center-level annual PCI volumes and non-CTO complex PCI subcategories were not systematically captured in the analytical registry. Selected procedural burden variables were summarized using available-case data, and no imputation was performed. The multiple logistic regression model was kept compact to reduce overfitting. Although the apparent calibration intercept and slope were approximately 0.00 and 1.00, respectively, validation was limited to bootstrap resampling, and no external cohort was available. Finally, comparisons based on actual retrograde involvement remain descriptive because of case selection and intraprocedural escalation.

CONCLUSION

Major in-hospital complications occurred in 3.7% of contemporary CTO PCI procedures, and in-hospital death occurred in 0.6%. Event rates ranged from 1.3% to 7.3% across J-CTO strata and were 2.3% vs. 7.1% in planned antegrade-only vs. planned retrograde or hybrid procedures. These results may inform preprocedural counseling, case selection, and procedural planning.

Ethics Committee Approval: This study was approved by the Ethics Committee of Necmettin Erbakan University University, (Approval No: 2026/6397, Date: 13.3.2026).

Informed Consent: The requirement for informed consent was waived due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

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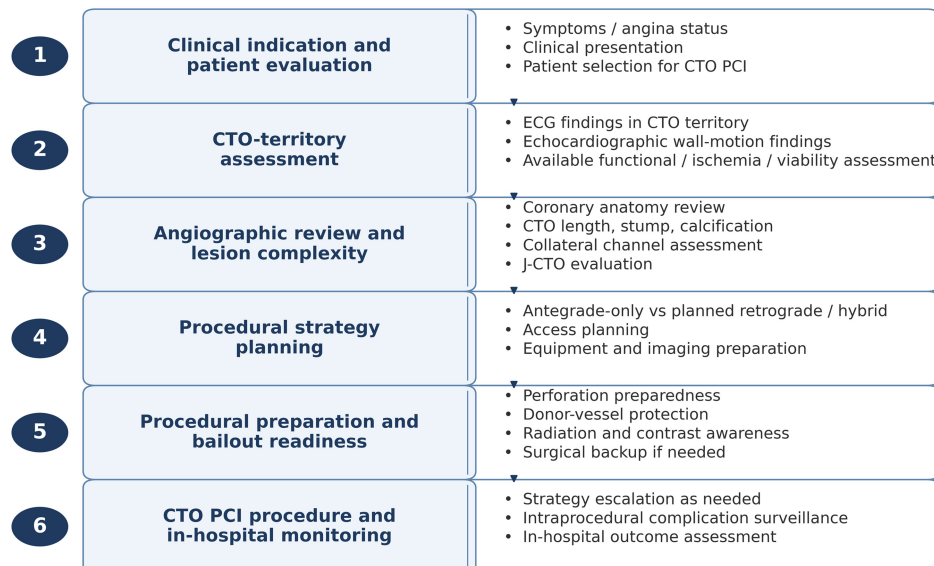
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Supplementary Material

Supplementary Table 1. Clinical presentation and CTO-territory assessment before CTO PCI	
Variables	Overall (n=2,375)
Stable angina	1,653 (69.6%)
Unstable angina	121 (5.1%)
Acute MI	39 (1.6%)
No angina recorded	557 (23.5%)
Unknown clinical presentation	5 (0.2%)
No Q waves in CTO territory	1,820 (76.6%)
Segmental wall-motion abnormality in the CTO-related territory	1,251 (52.7%)
Previous MI in the CTO territory	238 (10.0%)

Values are n (%). Clinical presentation categories are mutually exclusive; CTO-territory findings are not mutually exclusive. Formal ischemia/ viability imaging was not systematic. CTO, chronic total occlusion; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Common workflow from clinical indication to in-hospital safety monitoring.



Supplementary Figure 1. The schematic summarizes the common registry workflow from clinical indication and available functional/CTO-territory assessment to angiographic review, strategy planning, procedural preparation, and in-hospital safety monitoring.

Supplementary Table 2. Endpoint definitions and operational rules used in the safety analysis

Endpoint	Definition
Major in-hospital complication composite	Composite of in-hospital death, myocardial infarction, stroke, severe coronary perforation requiring treatment, donor-vessel complication, emergency repeat PCI, or emergency CABG.
In-hospital death	Counted when the in-hospital death field was explicitly coded positive in the registry.
Myocardial infarction	Counted when the in-hospital MI field was explicitly coded positive in the registry; this site-coded field was used as recorded at each site, without central adjudication or post hoc reclassification to a standardized definition.
Stroke	Counted when the in-hospital stroke field was explicitly coded positive in the registry as a site-reported in-hospital cerebrovascular event; no central event-adjudication process or post hoc neurologic reclassification was available.
Severe coronary perforation requiring treatment	Counted when the coronary perforation field documented a treatment-requiring category (covered stent, tamponade-related intervention, coil embolization, percutaneous treatment, or surgical treatment). Conservative or untreated perforations were excluded from the major in-hospital complication composite.
Donor-vessel complication/emergency repeat PCI / emergency CABG	Counted when the corresponding in-hospital registry field was explicitly coded positive.
Extended in-hospital complication composite	Secondary descriptive endpoint comprising the major in-hospital complication composite plus hemodynamic instability, treated collateral perforation, and vascular complications. Composite endpoints were counted once per procedure.
Hemodynamic instability / treated collateral perforation / vascular complication	Included in the extended composite when the corresponding site-coded in-hospital registry field was explicitly coded positive; treated collateral perforation required documentation beyond conservative management, and no central adjudication was performed.
Individual component counts are non-mutually exclusive; composite endpoints were counted once per procedure. PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; MI, myocardial infarction.	

Supplementary Table 3. Operational coding of selected complication fields used for component-level analyses

Variables	Operational rule
Severe coronary perforation requiring treatment	Counted as an event for treatment-requiring categories (covered stent, tamponade-related intervention, coil embolization, percutaneous treatment, or surgical intervention).
Treated collateral perforation	Included in the extended composite when treatment beyond conservative management was documented.
In-hospital myocardial infarction/stroke	Counted as an event when the corresponding in-hospital registry field was explicitly coded positive; these site-coded fields were used as recorded at each site, without central adjudication or post hoc reclassification to standardized definitions.
Hemodynamic instability / vascular complication	Hemodynamic instability was counted as an event when the corresponding site-coded registry field contained a positive in-hospital entry. Vascular complications were counted when the vascular-complication field contained any documented entry; both were retained only in the extended composite, without central adjudication.
Donor-vessel complication/emergency repeat PCI / emergency CABG	Counted as an event when the corresponding in-hospital registry field was explicitly coded positive.
PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.	

Supplementary Table 4. Missing-data pattern for key variables

Variables	Non-missing, n (%)	Missing/unknown, n (%)
Age	2,374 (100.0%)	1 (0.0%)
Sex	2,375 (100.0%)	0 (0.0%)
Diabetes mellitus positive indicator after harmonization	2,375 (100.0%)	0 (0.0%)
Previous CABG positive indicator	2,375 (100.0%)	0 (0.0%)
In-stent CTO positive indicator	2,375 (100.0%)	0 (0.0%)
CTO length	2,375 (100.0%)	0 (0.0%)
Moderate/severe calcification indicator	2,375 (100.0%)	0 (0.0%)
J-CTO score	2,375 (100.0%)	0 (0.0%)
Planned retrograde/hybrid positive indicator	2,375 (100.0%)	0 (0.0%)
Previous-attempt status	2,360 (99.4%)	15 (0.6%)
Procedural time	2,371 (99.8%)	4 (0.2%)
Fluoroscopy time	2,329 (98.1%)	46 (1.9%)
Contrast volume	2,362 (99.5%)	13 (0.5%)
Air kerma	2,361 (99.4%)	14 (0.6%)
Dose-area product	2,317 (97.6%)	58 (2.4%)
CTO-territory wall-motion status	2,293 (96.5%)	82 (3.5%)

No imputation was performed. CABG, coronary artery bypass grafting; CTO, chronic total occlusion; J-CTO, Japanese Chronic Total Occlusion score. Percentages are rounded to one decimal place; very small amounts of missingness may therefore appear as 0.0%.

Supplementary Table 5. Sensitivity analysis excluding later identifiable within-registry repeat entries

Variables	Primary model from Table 4 OR	p value	Repeat-excluded complete-case model	P
	(95% CI)		OR (95% CI)	
Age (per year)	1.02 (1.00–1.05)	0.042	1.02 (1.00–1.05)	0.043
Female sex	1.16 (0.63–2.12)	0.639	1.16 (0.63–2.13)	0.638
Diabetes mellitus	0.65 (0.41–1.03)	0.068	0.65 (0.41–1.03)	0.068
Previous CABG	0.81 (0.42–1.59)	0.543	0.81 (0.42–1.59)	0.545
In-stent CTO	1.01 (0.53–1.93)	0.983	1.01 (0.53–1.93)	0.982
CTO length (per 10 mm)	1.23 (1.08–1.40)	0.002	1.23 (1.08–1.40)	0.002
Moderate/severe calcification	1.92 (1.22–3.03)	0.005	1.93 (1.22–3.04)	0.005

Identifiable within-registry repeat procedures were assessed using center, anonymized patient code, birth date, sex, and procedure date. Nine later entries from patients with more than one procedure date were excluded. The repeat-excluded sensitivity model included 2,365 complete cases and 87 major in-hospital complication events. The model used the same clinical-anatomic covariates as the primary model. CABG, coronary artery bypass grafting; CI, confidence interval; CTO, chronic total occlusion; OR, odds ratio.

Supplementary Table 6. Exploratory complication rates according to J-CTO category and planned procedural strategy

Stratum	Planned antegrade-only	Planned retrograde/hybrid involvement
J-CTO 0–2	23/1,302 (1.8%)	11/189 (5.8%)
J-CTO ≥3	17/410 (4.1%)	36/474 (7.6%)
Overall, by the J-CTO category	J-CTO 0–2: 34/1,491 (2.3%)	J-CTO ≥3: 53/884 (6.0%)

Exploratory logistic regression yielded $p=0.219$ for the interaction between J-CTO category (0–2 vs. ≥3) and planned retrograde/hybrid involvement. These analyses were considered exploratory due to the limited number of major in-hospital complications. J-CTO, Japanese Chronic Total Occlusion score.

Supplementary Table 7. Distribution of the number of component events per procedure

No. of component events per procedure	Major in-hospital complication composite	Extended in-hospital complication composite
1	69 (79.3%)	101 (69.2%)
2	14 (16.1%)	33 (22.6%)
3	3 (3.4%)	8 (5.5%)
4 or more	1 (1.1%)	4 (2.7%)

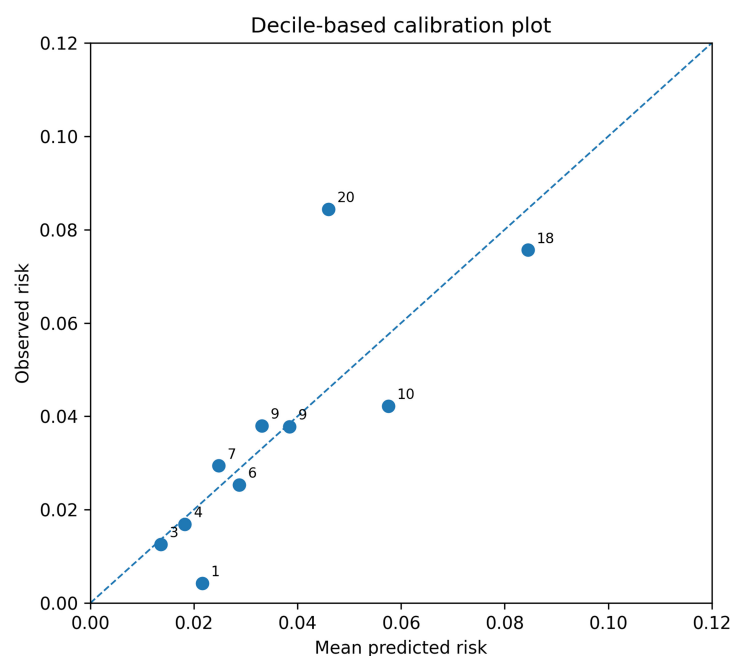
Differences between the primary and extended distributions reflect the addition of hemodynamic instability, treated collateral perforation, and vascular complications to the extended composite; therefore, procedures without a primary event could still contribute to the extended composite as single-component cases.

Note: Percentages are calculated across procedures that meet the corresponding definition of the composite endpoint.

Supplementary Table 8. Individual components and composite endpoints according to actual retrograde involvement

Complication component	Overall, n (%)	Antegrade-only (n=1,798)	Actual retrograde involvement (n=577)	P
In-hospital death	14 (0.6%)	3 (0.2%)	11 (1.9%)	<0.001
Myocardial infarction	11 (0.5%)	6 (0.3%)	5 (0.9%)	0.150
Stroke	2 (0.1%)	2 (0.1%)	0 (0.0%)	1.000
Severe coronary perforation requiring treatment	52 (2.2%)	32 (1.8%)	20 (3.5%)	0.021
Donor-vessel complication	22 (0.9%)	0 (0.0%)	22 (3.8%)	<0.001
Emergency repeat PCI	5 (0.2%)	2 (0.1%)	3 (0.5%)	0.096
Emergency CABG	4 (0.2%)	0 (0.0%)	4 (0.7%)	0.003
Hemodynamic instability	65 (2.7%)	23 (1.3%)	42 (7.3%)	<0.001
Treated collateral perforation	19 (0.8%)	3 (0.2%)	16 (2.8%)	<0.001
Vascular complication	16 (0.7%)	7 (0.4%)	9 (1.6%)	0.006
Major in-hospital complication composite	87 (3.7%)	40 (2.2%)	47 (8.1%)	<0.001
Extended in-hospital complication composite	146 (6.1%)	59 (3.3%)	87 (15.1%)	<0.001

Actual retrograde involvement refers to procedures with documented retrograde use. Percentages are calculated within each strategy subgroup. Individual component counts are non-mutually exclusive; composite endpoints were counted once per procedure. P values are from Fisher's exact test.



Supplementary Figure 2. Decile-based calibration plot for the primary multiple logistic regression model. The dashed diagonal line represents ideal agreement between predicted and observed risk. Points represent deciles of predicted risk, and numeric labels denote the number of major complication events within each decile. The apparent calibration intercept was approximately 0.00, and the calibration slope was approximately 1.00.