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Original Research

Long-Term Outcomes of Chronic Total Occlusion Percutaneous Coronary Intervention Among Medicare Beneficiaries

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ABSTRACT

Background: Chronic total occlusion (CTO) percutaneous coronary interventions (PCIs) represent 4% of all PCIs for stable angina in the United States and have been associated with lower success and higher in-hospital event rates compared with non-CTO PCIs. We aimed to examine long-term outcomes of CTO PCI compared with non-CTO PCI, including prespecified subgroups of high-risk non-CTO PCI (atherectomy/saphenous vein graft/unprotected left main).

Methods: Among 551,722 patients in the National Cardiovascular Data Registry CathPCI Registry linked to Medicare (July 2009-December 2016), we evaluated in-hospital events and long-term major adverse cardiovascular events of CTO PCIs (N = 29,407) compared with non-CTO PCIs (N = 522,315). We then evaluated similar outcomes between CTO PCIs and high-risk non-CTO PCIs (N = 53,662). We excluded patients with ST-elevation myocardial infarction and non–ST-elevation myocardial infarction.

Results: Patients undergoing CTO PCI were more likely to be younger and male. CTO PCI was associated with a higher risk of in-hospital events compared with non-CTO PCI (7.0% vs 4.2%; $P < .001$) and high-risk non-CTO PCI (7.0% vs 6.5%; $P = .008$). In addition, CTO PCI was associated with a slightly higher risk of long-term repeat revascularization compared with non-CTO PCI (adjusted hazard ratio [aHR], 1.09; 95% CI, 1.05-1.13). However, compared with high-risk non-CTO PCIs, CTO PCIs were associated with a slightly lower risk of long-term major adverse cardiovascular events (aHR, 0.87; 95% CI, 0.84-0.90) and readmission (aHR, 0.87; 95% CI, 0.84-0.90).

Conclusions: In this study, CTO PCI was associated with higher risk of both in-hospital and out-of-hospital events but a slightly lower risk of long-term events compared with high-risk non-CTO PCIs. These findings shed light on the complexity of various PCI procedures that can inform clinicians and patients of expected outcomes.

Introduction

Chronic total occlusions (CTOs) are present in 14.7% to 52% of patients undergoing coronary angiography depending on the underlying cohort.[1,2] The presence of a CTO is associated with angina, decreased quality of life, and even depression.[3] However, in part because of the technical challenges associated with percutaneous coronary intervention (PCI) of CTO lesions in addition to the lower success rate, uncertain benefit, and a higher rate of complications, CTO PCIs represent a small proportion (~4%) of the PCIs performed for stable angina in the United States.[4]

Observational studies have demonstrated angina relief, improved exercise tolerance, increased left ventricular ejection fraction, and in some cases, improved survival associated with successful CTO PCI.[5-8] However, these results, particularly with regard to "hard" end points, have not been replicated in the small number of randomized clinical trials conducted to date.[9,10] In addition, the differences in techniques between CTO and non-CTO PCI, including extraplaque navigation,

Abbreviations: aHR, adjusted hazard ratio; CABG, coronary artery bypass grafting; CTO, chronic total occlusion; MACE, major adverse cardiovascular event; MI, myocardial infarction; PCI, percutaneous coronary intervention; SVG, saphenous vein graft; ULM, unprotected left main.

Keywords: atherectomy; chronic total occlusion; left main coronary artery; outcomes; percutaneous coronary intervention; saphenous vein graft.

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longer total stent length, and other procedural factors, also raise questions about long-term outcomes and patency even after successful CTO PCI. Thus, it is critical to understand the long-term outcomes postdischarge after CTO PCI compared with non-CTO PCI.

In addition, although outcomes of CTO PCIs have been compared with non-CTO PCIs, comparative outcomes relative to high-risk non-CTO PCIs, such as those requiring atherectomy, unprotected left main (ULM) PCI, or saphenous vein graft (SVG) PCI, have been limited. A single-center study suggested that patients undergoing CTO PCI had higher procedural complications but similar long-term outcomes compared with high-risk non-CTO PCIs.[11] However, these findings have not been validated in a large multicenter study.

In this study, we examined the in-hospital and long-term outcomes after CTO PCI in the American College of Cardiology National Cardiovascular Data Registry (NCDR) CathPCI Registry and compared the outcomes with other forms of high-risk non-CTO PCI procedures, such as rotational atherectomy, ULM interventions, and SVG interventions.

Methods

Study population

All patients aged ≥65 years who underwent PCI between July 1, 2009 and December 31, 2016 in the American College of Cardiology NCDR CathPCI Registry were included in this study.[12] Data elements are prospectively collected from the medical record using standardized forms and definitions (Version 4). We aimed to capture outcomes associated with elective PCI; as such, we excluded initial presentations of ST segment elevation myocardial infarction (MI), non-ST segment elevation MI, preprocedure cardiogenic shock, and patients who experienced cardiac arrest. Patients were categorized as CTO PCI if the index lesion was categorized as 100% with thrombolysis in MI score 0 flow and coded as CTO in the CathPCI Registry. All other patients were classified as non-CTO PCI. In patients with >1 PCI, the first procedure was considered the index procedure. Using direct patient identifiers, patients were linked to the CathPCI registry data with administrative claims data from Centers for Medicare and Medicaid Services fee for services inpatient and outpatient claims data between 2009 and 2017 as well as the Centers for Medicare and Medicaid Services beneficiary enrollment data, which provided long-term outcomes with at least 1 year of follow-up.

Covariates and outcomes

The primary exposure of interest was CTO PCI vs non-CTO PCI. Covariates of interest in the study included demographic characteristics (including age, sex, and race/ethnicity), prior medical history (including diabetes mellitus, hypertension, current dialysis, dyslipidemia, prior MI, prior cerebrovascular disease, prior peripheral arterial disease, prior heart failure, prior valve surgery/procedure, and prior revascularization), and procedural and lesion characteristics (including symptoms at presentation, cardiogenic shock at the start of the procedure [this is collected separately in the American College of Cardiology NCDR CathPCI Registry from intraprocedural and postprocedural cardiogenic shock], PCI indication, coronary anatomy, bifurcation lesion, lesion in a graft, lesion calcification, CTO, stent type, total stent length, minimum stent diameter, highest lesion location [using the following order: left main (highest), proximal left anterior descending artery, proximal right coronary artery, medial left anterior descending artery, and proximal circumflex artery], and use of intra-aortic balloon pump).

We evaluated in-hospital procedural events, including procedural success rate defined as <50% angiographic stenosis with thrombolysis in MI flow grade 3 following the procedure without any major events (death, urgent coronary artery bypass graft surgery [CABG], stroke, or cardiac tamponade), MI based on biomarker assessment, intraprocedure and postprocedural cardiogenic shock as defined in the American College of Cardiology NCDR CathPCI Registry, heart failure, stroke (ischemic and hemorrhagic), cardiac tamponade, new requirement for dialysis, other vascular complications requiring treatment, bleeding event within 72 hours (with subtypes), and in-hospital death.

The primary outcome was major adverse cardiovascular event (MACE), which was defined as the composite of death from any cause after discharge, repeat revascularization (any vessel), and MI. Secondary outcomes included the individual components of the primary composite outcome and readmission, including MI or stroke-related readmission. These were identified using previously validated *International Classification of Diseases, Ninth Revision, Clinical Modification* and *Procedure Coding System* codes for MI, stroke, and revascularization (Supplemental Table S1).[13-16] Deaths were ascertained using vital status information in the Master Beneficiary Summary files and was complete for all individuals. Readmission was defined as any inpatient admission following the index PCI. Readmission related to MI or stroke was defined as the presence of an inpatient readmission with an *International Classification of Diseases* code for MI or stroke in the principal position.

Statistical analysis

Baseline patient, procedural characteristics, and in-hospital procedural events were obtained from the American College of Cardiology NCDR CathPCI Registry and compared between patients with non-CTO PCI and patients with CTO PCI using independent sample *t* tests or Mann–Whitney *U* tests for continuous variables as indicated based on data normality. Categorical variables were compared using either χ^2 tests or Fisher exact tests as appropriate. We used the Kaplan–Meier method to estimate the cumulative incidence of the primary and secondary outcomes and the log-rank statistic to compare the differences between groups. Multivariate analyses were performed using a Cox proportional hazards regression model that included possible confounders selected a priori and listed in Table 1, which include age, sex, race, ethnicity, presence of diabetes mellitus, chronic kidney disease, hypertension, hyperlipidemia, known reduced left ventricular ejection fraction, symptoms at presentation, PCI indication, presence of prior stent, as well as procedure and device variables (stent length and diameter, bare metal stent vs drug-eluting stent, calcification, bifurcation involvement, intra-aortic balloon pump use). To account for the competing risk of death when assessing the individual nonfatal components of the primary composite outcome, we used the method described by Fine and Gray[17] to estimate the subdistribution hazard ratio of CTO vs non-CTO PCI for these events. A *P* value of ≤0.05 is considered statistically significant without adjustment for multiplicity.

In order to put the results within a more clinically relevant context, we performed the same analyses in prespecified subgroups comparing CTO PCI long-term outcomes with patients undergoing PCI of other high-risk lesions (atherectomy use in PCI, ULM PCI, and SVG PCI). Statistical analyses were performed using SAS software version 9.4 (SAS Institute). The institutional review board of the Beth Israel Deaconess Medical Center exempted this study from review.

Results

Baseline characteristics

Of the 1,990,847 patients aged ≥64 years who underwent PCI between July 1, 2009 and December 31, 2016, 551,722 (27.7%) were included in the cohort (Figure 1). The main reasons for exclusion were:

Table 1. Baseline characteristics of patients undergoing percutaneous coronary intervention.

	CTO PCI	Non-CTO PCI	*P*	Standardized differences
N	29,407	522,315		
Demographics				
Age, y, mean ± SD	73.7 ± 6.5	74.5 ± 6.6	<.001	11.85
>70 y	18,244 (62.0%)	348,084 (66.6%)	<.001	9.75
Female	8954 (30.5%)	192,570 (36.9%)	<.001	13.34
Race/ethnicity			<.001	.
White	26,781 (91.1%)	478,035 (91.5%)		1.62
Black	1447 (4.9%)	27,565 (5.3%)		1.60
Other	1179 (4.0%)	16,715 (3.2%)		−4.57
Comorbidities				
BMI, kg/m^2, mean ± SD	29.3 ± 5.9	29.2 ± 5.9	.223	−0.73
Prior MI	9856 (33.5%)	144,128 (27.6%)	<.001	−13.21
Prior heart failure	4843 (16.5%)	82,683 (15.8%)	.004	−1.75
Cerebrovascular disease	4538 (15.4%)	88,266 (16.9%)	<.001	3.92
Peripheral arterial disease	4675 (15.9%)	86,011 (16.5%)	.010	1.54
Prior valve surgery/procedure	591 (2.0%)	12,030 (2.3%)	.001	1.96
Prior revascularization				
Prior PCI	11,856 (40.3%)	209,294 (40.1%)	.401	−0.50
Prior CABG	7331 (24.9%)	123,780 (23.7%)	<.001	−2.89
Family history of premature CAD	5640 (19.2%)	104,705 (20.1%)	<.001	2.17
Diabetes mellitus	10,779 (36.7%)	192,869 (36.9%)	.348	0.56
IDDM	3728 (12.7%)	66,850 (12.8%)	.636	0.36
Hypertension	25,565 (86.9%)	464,537 (88.9%)	<.001	6.36
Dyslipidemia	24,962 (84.9%)	444,730 (85.2%)	.220	0.73
Current use of tobacco	3600 (12.2%)	59,586 (11.4%)	<.001	−2.62
GFR, mean ± SD	70.1 ± 27.3	70.8 ± 28.9	<.001	−2.48
Currently on dialysis	585 (2.0%)	11,406 (2.2%)	.026	1.33
Chronic lung disease	4671 (15.9%)	93,107 (17.8%)	<.001	5.09
Cath laboratory visit				
CAD presentation			<.001	
No symptom, no angina	3025 (10.3%)	53,390 (10.2%)		−0.20
Symptom unlikely to be ischemic	1290 (4.4%)	24,844 (4.8%)		1.74
Stable angina	7887 (26.8%)	126,217 (24.2%)		−6.19
Unstable angina	17,196 (58.5%)	317,687 (60.8%)		4.81
Anginal classification within 2 wk			<.001	
No symptoms	3836 (13.0%)	67,338 (12.9%)		−0.45
CCS I	1610 (5.5%)	31,408 (6.0%)		2.27
CCS II	6570 (22.3%)	116,259 (22.3%)		−0.20
CCS III	12,624 (42.9%)	226,017 (43.3%)		0.69
CCS IV	4689 (16.0%)	79,970 (15.3%)		−1.76
NYHA class within 2 wk			<.001	
Class I	364 (1.2%)	6386 (1.2%)		3.42
Class II	1118 (3.8%)	19,272 (3.7%)		−0.14
Class III	1646 (5.6%)	25,633 (4.9%)		−0.59
Class IV	696 (2.4%)	10,840 (2.1%)		−3.18
Antianginal medications within 2 wk	22,534 (76.6%)	398,059 (76.2%)	.101	−2.04
Heart failure within 2 wk	3833 (13.0%)	62,321 (11.9%)	<.001	−3.39
Cardiomyopathy or left ventricular systolic dysfunction	4612 (15.7%)	63,093 (12.1%)	<.001	−10.99
IABP	400 (1.4%)	2317 (0.4%)	<.001	−13.10
Diagnostic cath procedure				
Diagnostic cath status			<.001	
Elective	16,314 (55.5%)	302,849 (58.0%)		5.07
Urgent	8012 (27.3%)	149,879 (28.7%)		3.21
Emergency	763 (2.6%)	3798 (0.7%)		−20.65
Salvage	6 (<0.1%)	26 (<0.1%)		-2.03
Coronary anatomy				
Left main	1692 (5.8%)	32,528 (6.2%)	<.001	1.40
LAD	16,929 (57.6%)	295,215 (56.5%)	<.001	−5.05
Circ	13,695 (46.6%)	212,178 (40.6%)	<.001	−14.51
RCA	17,880 (60.8%)	262,284 (50.2%)	<.001	−22.78
PCI procedure				
PCI status			<.001	
Elective	18,356 (62.4%)	326,596 (62.5%)		0.22
Urgent	10,114 (34.4%)	191,420 (36.7%)		4.68
Emergency	895 (3.0%)	4021 (0.8%)		−24.23
Salvage	22 (<0.1%)	88 (<0.1%)		−4.11
Pre-PCI left ventricular ejection fraction, %, mean ± SD	51.1 ± 13.0	54.4 ± 12.2	<.001	23.33
Cardiogenic shock at start of the procedure	193 (0.7%)	1822 (0.4%)	<.001	−5.10
PCI indication			<.001	
PCI for unstable angina	14,903 (50.7%)	270,838 (51.9%)		2.35
Staged PCI	1785 (6.1%)	26,335 (5.0%)		−4.67
PCI for stable CAD	12,713 (43.2%)	224,929 (43.1%)		−0.34

(*continued on next page*)

Table 1. (*continued*)

	CTO PCI	Non-CTO PCI	*P*	Standardized differences
High-risk PCI groups	3053 (10.4%)	54,413 (10.4%)	-	
Atherectomy	778 (2.7%)	11,612 (2.2%)	<.001	−5.93
ULM PCI	251 (0.9%)	4833 (0.9%)	.210	0.75
SVG PCI	2024 (6.9%)	37,968 (7.3%)	.013	1.49
High-risk lesion (SCAI lesion class)			<.001	
Class I	0 (0%)	258,668 (49.5%)		101.80
Class II	0 (0%)	263,647 (50.5%)		103.76
Class III	6745 (22.9%)	0 (0%)		−236.31
Class IV	22,662 (77.1%)	0 (0%)		−793.95
Highest lesion location			<.001	
pRCA/mLAD/pCIRC	11,465 (39.0%)	210,528 (40.3%)		2.69
pLAD	12,540 (42.6%)	202,766 (38.8%)		−7.84
Left main	4458 (15.2%)	90,654 (17.4%)		5.82
Other	863 (2.9%)	16,867 (3.2%)		1.67
Access site			.0032	
Radial	4688 (15.9%)	87,826 (16.8%)		2.34
Femoral	24,615 (83.7%)	432,527 (82.8%)		−2.38
Brachial	81 (0.3%)	1559 (0.3%)		0.42
Discharge location				
Home	27,847 (94.7%)	503,435 (96.4%)	<.001	8.95
Extended care/TCU/rehabilitation	680 (2.3%)	9264 (1.8%)		−4.05
Other acute care hospital	160 (0.5%)	1415 (0.3%)		−5.12
Nursing home	330 (1.1%)	4923 (0.9%)		−1.85
Hospice	43 (0.2%)	471 (0.1%)		−1.84
Other	31 (0.1%)	470 (0.1%)		−0.51
Left against medical advice	27 (0.1%)	381 (0.1%)		−0.69
Follow-up, d, mean ± SD	1478 ± 796.7	1546 ± 787.1	<.001	8.7
Follow-up, d, median [IQR]	1533 [1411]	1634 [1367]	<.001	8.7

Values are n (%) unless otherwise specified.
BMI, body mass index; CABG, coronary bypass grafting; CAD, coronary artery disease; CTO, chronic total occlusion; GFR, glomerular filtration rate; IDDM, insulin dependent diabetes mellitus; IQR, interquartile range; LAD, left anterior descending artery; MI, acute myocardial infarction; mLAD, medial left anterior descending artery; PCI, percutaneous coronary intervention; pCIRC, proximal circumflex; pLAD, proximal left anterior descending artery; pRCA, proximal right coronary artery; RCA, right coronary artery; SD, standard deviation; SVG, saphenous vein graft; TCU, transitional care unit; ULM, unprotected left main.

38.1% had ST-elevation MI or non–ST-elevation MI on hospital presentation, 0.4% had preprocedure cardiogenic shock or cardiac arrest within 24 hours, and 33.8% were unable to be linked to Medicare. There were no clinically significant differences between successfully linked patients and those unable to be linked (Supplemental Table S2).

Among the 551,722 patients included in the study, 5.3% (n = 29,407) underwent CTO PCI and 9.7% (n = 53,662) underwent high-risk non-CTO PCI, of which 21.6% (n = 11,612) included atherectomy, 9.0% (n = 4833) included ULM PCI, and 70.8% (n = 37,968) included SVG PCI. Patients undergoing CTO PCI were younger, more often male, and more likely to have a history of prior MI or prior CABG. Furthermore, patients who underwent CTO PCI presented more often with stable angina (26.8% vs 24.2%; $P < .001$) and more often had a cardiomyopathy or left ventricular dysfunction (15.7% vs 12.1%; $P < .001$) as compared with patients undergoing non-CTO PCI (Table 1). On the other hand, patients with non-CTO PCI were more likely to have a history of cerebrovascular disease, peripheral arterial disease, chronic lung disease, and hypertension. Similar findings were noted with additional differences in baseline characteristics among patients undergoing high-risk non-CTO PCI and its subgroups (Supplemental Tables S3-S6).

Procedural characteristics

There were several differences in procedural characteristics between the 2 groups. Patients undergoing CTO PCI were more likely to

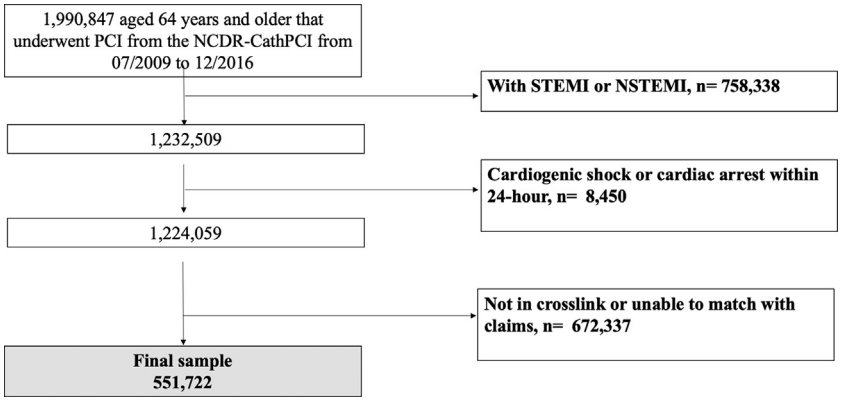


Figure 1.
Exclusion cascade for analytic sample in the study. We included patients aged ≥64 years that underwent PCI from the NCDR CathPCI and were successfully linked to claims for the years July 2009 to December 2016. We excluded patients with STEMI or NSTEMI, preprocedure cardiogenic shock or cardiac arrest within 24 hours of PCI. NCDR, National Cardiovascular Data Registry; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

have required an intra-aortic balloon pump (1.4% vs 0.4%; $P < .001$), more likely to have an emergency diagnostic catheterization (2.6% vs 0.7%; $P < .001$), and more likely to have staged PCI. The most common discharge location in both groups was home. Similar findings were noted with additional differences in procedural characteristics among patients undergoing high-risk non-CTO PCI and its subgroups (Supplemental Tables S3-S6).

Procedural events

Procedural success rates were significantly lower among patients undergoing CTO PCI compared with non-CTO PCI (76.0% vs 96.1%; $P < .001$). Following the procedure, patients undergoing CTO PCI were more likely to have an in-hospital event (7.0% vs 4.2%; $P < .001$), driven by periprocedural MI based on biomarker assessment (3.4% vs 1.9%; $P < .001$), bleeding within 72 hours (2.2% vs 1.3%; $P < .001$), intraprocedural and postprocedural cardiogenic shock (1.2% vs 0.3 %; $P < .001$), and in-hospital death (1.0% vs 0.4%; $P < .001$) (Table 2). There were also small increases in procedure-related heart failure, stroke, tamponade, new dialysis, and other vascular complications requiring treatment among patients undergoing CTO PCI.

Compared with high-risk non-CTO PCI, CTO PCI was associated with a significantly lower procedural success rate (76.0% vs 95.7%; $P < .001$). This was consistent across the subgroups of high-risk non-CTO PCI (Supplemental Table S7). In addition, CTO PCI was associated with a slightly higher risk of in-hospital events (7.0% vs 6.5%; $P = .008$), driven by intraprocedural and postprocedural cardiogenic shock (1.2% vs 0.8%; $P < .001$), cardiac tamponade (0.4% vs 0.2%; $P < .001$), and bleeding within 72 hours (2.2% vs 1.9%; $P = .032$). However, among the subgroups of high-risk non-CTO PCI, CTO PCI was associated with a lower risk of in-hospital events compared with non-CTO atherectomy PCI (7.0% vs 9.1%: $P < .001$) and non-CTO ULM PCI (7.0% vs 12.5%; $P < .001$) but higher risk compared with non-CTO SVG PCI (7.0% vs 5.1%; $P < .001$). These were primarily driven by differences in the incidence of periprocedural MI, intraprocedural and postprocedural cardiogenic shock, and bleeding within 72 hours (Supplemental Table S7).

Although CTO PCI without atherectomy, ULM, and/or SVG intervention was associated with a significantly lower procedural success rate than CTO PCI with atherectomy, ULM, and/or SVG intervention (75.6% vs 80.0%; $P < .001$), it was also associated with lower in-hospital event rates (6.6% vs 10.5%; $P < .001$), driven by intraprocedural and postprocedural cardiogenic shock (1.0% vs 2.5%; $P < .001$), periprocedural MI (3.2% vs 5.3%; $P < .001$), and bleeding within 72 hours (2.1% vs 3.0%; $P < .001$) (Supplemental Table S8).

Long-term outcomes of CTO PCI vs non-CTO PCI

After a median follow-up time of 1629 days (IQR, 1371), 48.8% of the entire cohort experienced the primary MACE outcome and 28.6% died (0.4% of deaths were in-hospital) (Table 3, Figure 2A-D). Patients undergoing CTO PCI were slightly more likely to experience the composite outcome (49.9% vs 48.8%; $P < .001$), driven by repeat revascularization (24.4% vs 22.3%; $P < .001$). However, they were less likely to experience death postdischarge (27.8% vs 28.6%; $P = .004$) and all-cause readmission (64.0% vs 68.5%; $P < .001$).

After multivariable adjustment, CTO PCI was associated with no significant difference in the primary MACE outcome (adjusted HR [aHR], 1.02; 95% CI, 0.99-1.15) but lower risk of death post discharge (aHR, 0.95; 95% CI, 0.91-0.98) and all-cause readmission (aHR, 0.91; 95% CI, 0.89-0.94), with a higher risk of repeat revascularization (aHR 1.09; 95% CI, 1.05-1.13) (Table 4, Central Illustration).

Long-term outcomes of CTO PCI vs high-risk non-CTO PCI subgroups

Compared with high-risk non-CTO PCI, CTO PCI was associated with a lower risk of the primary MACE outcome (49.9% vs 63.9%; $P < .001$), driven by death postdischarge (27.8% vs 39.2%; $P < .001$) and repeat revascularization (24.4% vs 31.1%; $P < .001$) (Table 3). In addition, CTO PCI was associated with a lower risk of all-cause readmission (64.0% vs 75.0%; $P < .001$), including readmission for MI (8.0% vs 15.1%; $P < .001$) or stroke (5.8% vs 7.2%; $P < .001$). These findings were consistent in nearly all individual subgroups of high-risk non-CTO PCI (Table 3).

In multivariable models comparing CTO PCI with high-risk non-CTO PCI (Table 4, Central Illustration), CTO PCI was associated with a significantly lower risk of the primary MACE outcome (aHR, 0.87; 95% CI, 0.84-0.90), death postdischarge (aHR, 0.86; 95% CI, 0.81-0.91), repeat revascularization (aHR, 0.89; 95% CI, 0.84-0.94), and all-cause

Table 2. In-hospital procedure-related events of patients undergoing percutaneous coronary intervention.

	Total	CTO PCI	Non-CTO PCI	High-risk non-CTO PCI	*P* CTO vs non-CTO PCI	*P* CTO vs high-risk non-CTO PCI
N	551,722	29,407	522,315	53,662	-	-
Procedural success	524,357 (95.0%)	22,362 (76.0%)	501,995 (96.1%)	51,372 (95.7%)	<.001	<.001
Any event	23,768 (4.3%)	2060 (7.0%)	21,708 (4.2%)	3500 (6.5%)	<.001	.008
Periprocedural MI (biomarker positive)	11,134 (2.0%)	995 (3.4%)	10,139 (1.9%)	1731 (3.2%)	<.001	.222
Intraprocedural and postprocedural cardiogenic shock	2055 (0.4%)	344 (1.2%)	1711 (0.3%)	440 (0.8%)	<.001	<.001
Heart failure	2728 (0.5%)	246 (0.8%)	2482 (0.5%)	461 (0.9%)	<.001	.735
Stroke	878 (0.2%)	74 (0.3%)	804 (0.2%)	121 (0.2%)	<.001	.456
Hemorrhagic stroke	117 (<0.1%)	9 (<0.1%)	108 (<0.1%)	13 (<0.1%)	.255	.589
Tamponade	576 (0.1%)	130 (0.4%)	446 (0.1%)	104 (0.2%)	<.001	<.001
New requirement for dialysis	675 (0.1%)	54 (0.2%)	621 (0.1%)	122 (0.2%)	.002	.190
Other vascular events requiring treatment	2349 (0.4%)	155 (0.5%)	2194 (0.4%)	311 (0.6%)	.006	.333
Bleeding event within 72 h	7559 (1.4%)	635 (2.2%)	6924 (1.3%)	1041 (1.9%)	<.001	.032
Bleeding at access site	2623 (0.5%)	245 (0.8%)	2378 (0.5%)	366 (0.7%)	<.001	.015
Hematoma at access site	3666 (0.7%)	245 (0.8 %)	3421 (0.7%)	437 (0.8%)	<.001	.774
Retroperitoneal bleeding	747 (0.1%)	47 (0.2%)	700 (0.1%)	82 (0.2%)	.242	.806
Gastrointestinal bleeding	880 (0.2%)	63 (0.2%)	817 (0.2%)	126 (0.2%)	.016	.552
Genital-urinary bleeding	255 (0.1%)	15 (0.1%)	240 (0.1%)	37 (0.1%)	.695	.323
Other bleeding	1266 (0.2%)	169 (0.6%)	1097 (0.2%)	211 (0.4%)	<.001	<.001
In-hospital death	2138 (0.4%)	286 (1.0%)	1852 (0.4%)	432 (0.8%)	<.001	.013

CTO, chronic total occlusion; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 3. Long-term outcomes of patients undergoing percutaneous coronary intervention.

	Total	CTO PCI	Non-CTO PCI	*P*
CTO PCI vs non-CTO PCI				
N	551,722	29,407	522,315	
MACE	269,308 (48.8%)	14,671 (49.9%)	254,637 (48.8%)	<.001
Death postdischarge	157,494 (28.6%)	8,180 (27.8%)	149,314 (28.6%)	.004
Readmission (all-cause)	376,582 (68.3%)	18,832 (64.0%)	357,750 (68.5%)	<.001
Readmission for AMI	44,811 (8.1%)	2346 (8.0%)	42,465 (8.1%)	<.001
Readmission for stroke	33,635 (6.1%)	1700 (5.8%)	31,935 (6.1%)	<.001
Repeat pevascularization	123,492 (22.4%)	7163 (24.4%)	116,329 (22.3%)	<.001
CTO PCI vs high-risk non-CTO PCI				
N	83,069	29,407	53,662	
MACE	48,968 (59.0%)	14,671 (49.9%)	34,297 (63.9%)	<.001
Death postdischarge	29,197 (35.2%)	8180 (27.8%)	21,017 (39.2%)	<.001
Readmission	59,082 (71.1%)	18,832 (64.0%)	40,250 (75.0%)	<.001
Readmission for MI	10,454 (12.6%)	2346 (7.8%)	8108 (15.1%)	<.001
Readmission for stroke	5565 (6.7%)	1700 (5.8%)	3865 (7.2%)	<.001
Repeat revascularization	23,849 (28.7%)	7163 (24.4%)	16,686 (31.1%)	<.001
CTO PCI vs non-CTO atherectomy PCI				
N	41,019	29,407	11,612	
MACE	20,951 (51.1%)	14,671 (49.9%)	6280 (54.1%)	<.001
Death postdischarge	12,100 (29.5%)	8180 (27.8%)	3920 (33.8%)	<.001
Readmission	26,823 (65.4%)	18,832 (64.0%)	7991 (68.8%)	<.001
Readmission for MI	3340 (8.1%)	2346 (8.0%)	994 (8.6%)	<.001
Readmission for stroke	2347 (5.7%)	1700 (5.8%)	647 (5.6%)	<.001
Repeat revascularization	9915 (24.1%)	7163 (24.4%)	12,752 (23.7%)	.161
CTO PCI vs non-CTO unprotected left main PCI				
N	34,240	29,407	4833	
MACE	17,667 (51.6%)	14,671 (49.9%)	2996 (62.0%)	<.001
Death postdischarge	10,429 (30.5%)	8180 (27.8%)	2249 (46.5%)	<.001
Readmission	22,375 (63.4%)	18,832 (64.0%)	3543 (73.3%)	<.001
Readmission for MI	2811 (8.2%)	2346 (8.0%)	465 (9.6%)	<.001
Readmission for stroke	1980 (5.8%)	1700 (5.8%)	280 (5.8%)	<.001
Repeat revascularization	8119 (23.7%)	7163 (24.4%)	956 (19.8%)	<.001
CTO PCI vs non-CTO saphenous vein graft PCI				
N	67,375	29,407	37,968	
MACE	40,188 (59.7%)	14,671 (49.9%)	25,517 (67.2%)	<.001
Death postdischarge	23,382 (34.7%)	8180 (27.8%)	15,202 (40.0%)	<.001
Readmission	48,099 (71.4%)	18,832 (64.0%)	29,267 (77.1%)	<.001
Readmission for MI	9103 (13.5%)	2346 (8.0%)	6757 (17.8%)	<.001
Readmission for stroke	4678 (6.9%)	1700 (5.8%)	2978 (7.8%)	<.001
Repeat revascularization	20,343 (30.2%)	7163 (24.4%)	13,180 (34.7%)	<.001

MACE was defined as death, MI, or repeat revascularization.
AMI, acute myocardial infarction; CTO, chronic total occlusion; MACE, major adverse cardiovascular event; MI, myocardial infarction; PCI, percutaneous coronary intervention.

readmission (aHR, 0.87; 95% CI, 0.84-0.90), including readmission for MI (aHR, 0.86; 95% CI, 0.79-0.94) but no significant difference in readmission for stroke (aHR, 1.10; 95% CI, 0.98-1.24). These findings were consistent in nearly all individual subgroups of high-risk non-CTO PCI (Table 4, Central Illustration).

Discussion

In this large national cohort of patients undergoing PCI, we found that patients undergoing CTO PCI experienced lower procedural success rates and higher adverse events during the index hospitalization. These differences were driven by periprocedural MI based on biomarker assessment, bleeding within 72 hours of the procedure, and intraprocedural and postprocedural cardiogenic shock. However, these differences were less evident when comparing CTO PCI with high-risk non-CTO PCI and varied across the subgroups of high-risk non-CTO PCI. In addition, CTO PCI was associated with a similar long-term risk of the primary MACE outcome compared with non-CTO PCI. Despite being associated with a slightly lower risk of death postdischarge and all-cause readmission, CTO PCI was associated with a slightly higher risk of repeat revascularization. However, when compared with high-risk non-CTO PCI, CTO PCI was associated with a lower risk of the primary MACE outcome, death postdischarge, all-cause readmission, and repeat revascularization. The finding of lower risk of MACE and readmission persisted among all high-risk non-CTO PCI subgroups (atherectomy, ULM intervention, and SVG intervention). These findings highlight the comparative in-hospital and long-term outcomes of CTO PCI relative to non-CTO PCI specifically among high-risk non-CTO PCI procedures, which will inform both clinicians and patients. In addition, the study highlights an important subgroup of non-CTO PCIs that, similar to CTO PCI, may require special consideration to ensure optimal outcomes.

This study builds on prior work evaluating the outcomes of CTO PCI. In a prior analysis of the NCDR CathPCI Registry from 2009 to 2013, CTO PCIs accounted for 3.8% of all PCIs for stable coronary artery disease and were associated with a higher risk of in-hospital MACEs (1.6% vs 0.8%; $P < .001$).[4] Procedural success was noted to be 58.5% but was significantly higher (74.6% vs 53.1%) among operators with higher procedural volume (>10 CTO PCIs per year) compared with those with low volumes (<5). In addition, several predictors of lower success were identified: older age, current smoking, prior MI, prior CABG, prior peripheral artery disease, prior cardiac arrest, and right coronary artery CTO target vessel. In this updated analysis of the same registry, we observed a higher procedural success rate using the same definition. This likely reflects advances in technique and experience as we report on a more contemporary CTO cohort than was previously described. We similarly observed that patients undergoing CTO PCI (as

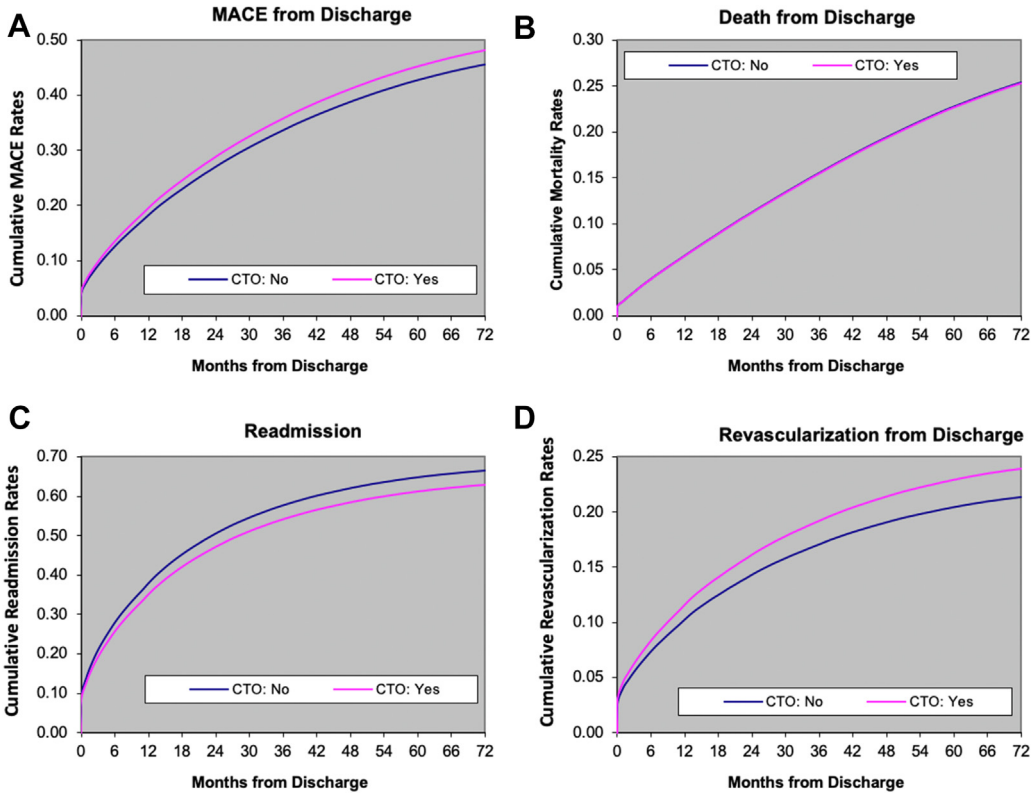


Figure 2.
Long-term outcomes of patient undergoing percutaneous coronary intervention. (**A**) Death from discharge. (**B**) Death from procedure. (**C**) Readmission. (**D**) Revascularization. Cumulative outcomes of patients undergoing PCI, including MACE, death following discharge, readmission, and revascularization. CTO, chronic total occlusion; MACE, major adverse cardiovascular events; PCI, percutaneous coronary intervention.

compared with patients undergoing non-CTO PCI) were more likely to develop periprocedural events, mainly periprocedural MI and bleeding requiring transfusion. Because these are unadjusted outcomes, they likely reflect differences in patient complexity and comorbidities. However, our study also shows that these differences were less evident when comparing CTO PCI with high-risk non-CTO PCI. In addition, among the various subgroups of high-risk non-CTO PCI, CTO PCI was associated with a lower risk of procedural events compared with non-CTO ULM PCI and non-CTO atherectomy PCI, but a higher risk compared with non-CTO SVG PCI. These differences in event rates reflect the risks associated with these procedures and the varied profiles of patients undergoing them. Overall, our study builds on the findings of the prior analysis by providing longer follow-up to assess the outcomes of CTO PCI relative to non-CTO PCI, inclusion of a broader definition for revascularization (PCI and CABG vs urgent CABG only) and providing additional insights into various high-risk subgroups, such as those requiring atherectomy, ULM PCI, or SVG PCI.

The findings comparing CTO PCI with high-risk non-CTO PCI highlight the complex nature of certain non-CTO PCI procedures. These findings, however, differ from a prior single-center study of 2396 patients undergoing PCI; 609 undergoing CTO PCI and 1787 undergoing high-risk non-CTO PCI that included atherectomy, SVG PCI, and ULM PCI. Similar to our study, the authors noted that patients undergoing CTO PCI had higher incidence of procedural events and lower success rate (74% vs 98%, $P < .001$). However, we show that these relationships differ when looking at the various subgroups of high-risk non-CTO PCI with both non-CTO ULM PCI and non-CTO atherectomy PCI having a higher associated risk of in-hospital events compared with CTO PCIs. On the other hand, unlike in our study, the authors showed no difference in long-term risk of MACEs. Several factors may have contributed to the differences in results, including the difference in cohort size, single-center design, shorter follow-up, and failure to adjust for competing risk of death. In addition, procedures, such as atherectomy PCI, ULM PCI, and SVG PCI, may carry their own risk regardless of CTO PCI status. Since these were included in the CTO cohort, future studies should evaluate the outcomes of CTO PCIs with and without these high-risk procedures to better understand the role they play in procedural risk of CTO PCIs.

The observations reported in our study shed light on an important comparison between CTO PCIs and high-risk non-CTO PCIs, emphasizing that CTO PCIs are only one type of high-risk PCI and that there are likely other types of high-risk interventions that may benefit from similar careful procedural considerations. Currently, some training programs and hospital systems provide special considerations for CTO PCI, including an additional of year training, specialized operators, and additional resources for the care of those patients. These considerations are not necessarily considered with all high-risk non-CTO PCIs, which may explain some of the differences in outcomes observed in our study. The findings of relatively higher event rates associated with high-risk non-CTO PCI compared with CTO PCI emphasizes the need for careful consideration to improve the outcomes of these procedures. These could include measures already being applied to CTO PCI with careful training considerations, specialized operators, and added resources for the care of these patients.

Limitations

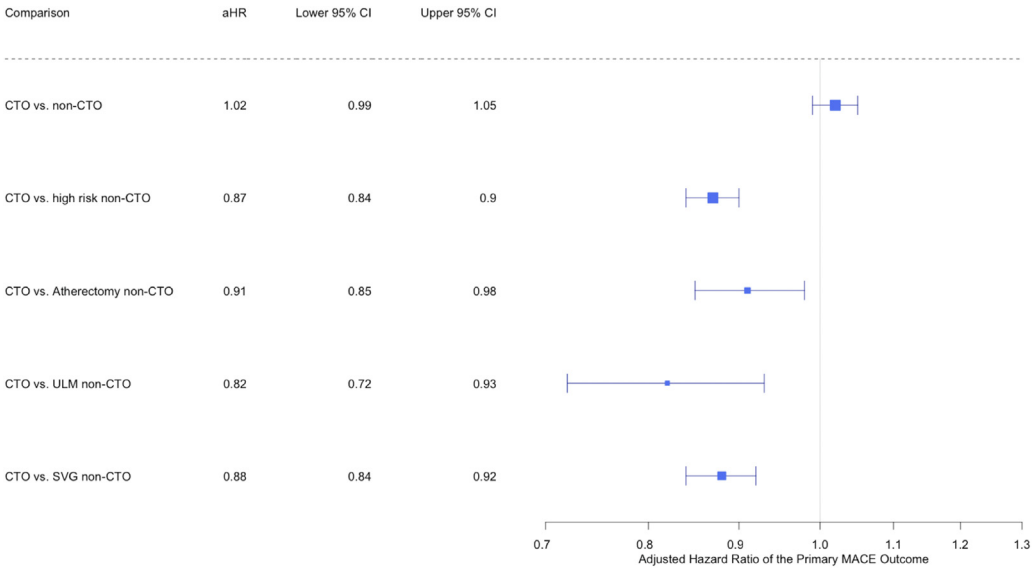
There are several strengths to this study. First, it includes a large multicenter national cohort undergoing PCI. Second, to our knowledge, it is the first multicenter study providing long-term follow-up on CTO PCI outcomes compared with high-risk non-CTO PCI. Third, our analysis takes into consideration the competing risk of death. Finally, the study

Table 4. Long-term outcomes of patients undergoing percutaneous coronary intervention adjusted for competing risk of death (censored at 6 years).

	Unadjusted HR	95% CI	*P*	Adjusted HR[a]	95% CI	*P*
CTO PCI vs non-CTO PCI						
MACE	1.08	1.06-1.10	<.001	1.02	0.99-1.05	.211
Death postdischarge	0.99	0.97-1.02	.507	0.95	0.91-0.98	.005
Readmission	0.91	0.89-0.92	.000	0.91	0.89-0.94	<.001
Readmission for MI	0.98	0.94-1.02	.359	1.03	0.96-1.10	.416
Readmission for Stroke	0.95	0.90-1.00	.048	1.00	0.93-1.09	.916
Repeat revascularization	1.14	1.11-1.17	<.001	1.09	1.05-1.13	<.001
CTO PCI vs high-risk non-CTO PCI						
MACE	0.70	0.69-0.72	<.001	0.87	0.84-0.90	<.001
Death postdischarge	0.66	0.64-0.68	<.001	0.86	0.81-0.91	<.001
Readmission	0.75	0.74-0.76	<.001	0.87	0.84-0.90	<.001
Readmission for MI	0.50	0.48-0.52	<.001	0.86	0.79-0.94	.001
Readmission for stroke	1.11	1.05-1.18	<.001	1.10	0.98-1.24	.096
Repeat revascularization	0.77	0.74-0.79	<.001	0.89	0.84-0.94	<.001
CTO PCI vs non-CTO atherectomy PCI						
MACE	0.87	0.84-0.89	<.001	0.91	0.85-0.98	.014
Death postdischarge	0.76	0.73-0.79	<.001	0.91	0.82-1.01	.063
Readmission	0.84	0.82-0.87	<.001	0.88	0.83-0.94	<.001
Readmission for MI	0.89	0.83-0.97	.004	0.90	0.76-1.08	.274
Readmission for stroke	1.24	1.13-1.36	<.001	1.21	0.96-1.51	.102
Repeat revascularization	1.02	0.98-1.07	.362	0.91	0.82-1.02	.101
CTO PCI vs non-CTO unprotected left main PCI						
MACE	0.70	0.67-0.72	<.001	0.82	0.72-0.93	.003
Death postdischarge	0.48	0.46-0.50	<.001	0.80	0.67-0.96	.017
Readmission	0.72	0.70-0.75	<.001	0.76	0.67-0.86	<.001
Readmission for MI	0.78	0.70-0.86	<.001	0.82	0.59-1.15	.259
Readmission for Stroke	1.66	1.46-1.89	<.001	1.18	0.76-1.83	.462
Repeat revascularization	1.25	1.17-1.34	<.001	0.81	0.65-1.01	.060
CTO PCI vs non-CTO SVG PCI						
MACE	0.66	0.64-0.67	<.001	0.88	0.84-0.92	<.001
Death postdischarge	0.66	0.64-0.67	<.001	0.88	0.82-0.94	<.001
Readmission	0.72	0.71-0.74	<.001	0.88	0.85-0.92	<.001
Readmission for MI	0.42	0.40-0.44	<.001	0.87	0.79-0.97	.009
Readmission for Stroke	1.05	0.98-1.11	.160	1.06	0.92-1.22	.450
Repeat revascularization	0.68	0.66-0.70	<.001	0.86	0.80-0.92	<.001

MACE was defined as death, MI, or repeat revascularization
HR, hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention; SVG, saphenous vein graft.
[a] Adjusted for patient and procedural characteristics listed in Table 1.

uses a more clinically relevant reference in those undergoing PCI with high-risk non-CTO PCI, including atherectomy, ULM PCI, and SVG PCI. However, the study also has several limitations. First, the classification of CTO PCI was dependent on local physicians from hospitals participating in the registry with no core laboratory to evaluate the angiograms, and therefore, there is the risk of misclassification bias. Second, despite attempting to adjust for potential confounders, the study is observational and carries the risk of residual confounding.



Central Illustration.
Long-term outcomes of patients undergoing percutaneous coronary intervention. Primary MACE outcome of CTO PCI compared with non-CTO PCI, high-risk non-CTO PCI, and the various high-risk non-CTO subgroups. MACE was defined as death, MI, or repeat revascularization. Model was adjusted for patient and procedural characteristics listed in Table 1. aHR, adjusted hazard ratio; CTO, chronic total occlusion; MACE, major adverse cardiovascular event; MI, myocardial infarction; PCI, percutaneous coronary intervention; SVG, saphenous vein graft; ULM, unprotected left main.

Third, the study only included Medicare beneficiaries, and therefore, a third of the NCDR population was excluded, limiting the generalizability of our findings to these patients. However, the linked and non-linked (ie, excluded) participants had largely similar baseline characteristics (Supplemental Table S2). Fourth, although we did include the use of intra-aortic balloon pump, we did not have information on the use of other forms of mechanical circulatory support during the PCI, including the Impella device. Fifth, we included patients with cardiogenic shock at the start of the procedure, which is collected in the registry differently from intraprocedural cardiogenic shock. Although this occurred in <1% of the cohort, we are unable to determine if this led to higher rates of intraprocedural cardiogenic shock because these are collected separately in the registry. Finally, we did not include patients enrolled in Medicare Advantage plans because we are unable to accurately capture the outcomes of interest in that population.

Conclusion

In conclusion, CTO PCI was associated with an overall similar risk of long-term outcomes compared with non-CTO PCI but lower risk when compared with high-risk non-CTO PCIs. These findings shed light on the complexity of various PCI procedures that will inform clinicians and patients on the expected outcomes. In addition, it highlights an important subgroup of non-CTO PCIs that, similar to CTO PCIs, may require special consideration to ensure optimal outcomes.

Declaration of competing interest

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Ethics statement

The institutional review board of the Beth Israel Deaconess Medical Center exempted this study from review given the use of a national registry with no direct patient identifiers.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the *Journal of the Society for Cardiovascular Angiography & Interventions* at https://doi.org/10.1016/j.jscai.2023.100584.

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