Percutaneous Intervention for Concurrent Chronic Total Occlusions in Patients With STEMI

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BACKGROUND

In 10% to 15% of patients with ST-segment elevation myocardial infarction (STEMI), concurrent coronary chronic total occlusion (CTO) in a non–infarct-related artery is present and is associated with increased morbidity and mortality.

OBJECTIVES

The EXPLORE (Evaluating Xience and Left Ventricular Function in Percutaneous Coronary Intervention on Occlusions After ST-Elevation Myocardial Infarction) trial evaluated whether patients with STEMI and concurrent CTO in a non–infarct-related artery benefit from additional percutaneous coronary intervention (PCI) of CTO shortly after primary PCI.

METHODS

From November 2007 through April 2015, we enrolled 304 patients with acute STEMI who underwent primary PCI and had concurrent CTO in 14 centers in Europe and Canada. A total of 150 patients were randomly assigned to early PCI of the CTO (CTO PCI), and 154 patients were assigned to conservative treatment without PCI of the CTO(no CTO PCI). Primary outcomes were left ventricular ejection fraction (LVEF) and left ventricular end diastolic volume(LVEDV) on cardiac magnetic resonance imaging after 4 months.

RESULTS

The investigator-reported procedural success rate in the CTO PCI arm of the trial was 77%, and the adjudicated success rate was 73%. At 4 months, mean LVEF did not differ between the 2 groups (44.1 +- 12.2% vs. 44.8 +- 11.9%, respectively; p= 0.60). Mean LVEDV at 4 months was 215.6 +-62.5 ml in the CTO PCI arm versus 212.8 +-60.1 ml in the no–CTO PCI arm (p = 0.70). Subgroup analysis revealed that patients with CTO located in the left anterior descending coronary artery who were randomized to the CTO PCI strategy had significantly higher LVEF compared with patients randomized to the no–CTO PCI strategy (47.2 +- 12.3% vs. 40.4 +- 11.9%; p = 0.02). There were no differences in terms of 4-month major adverse coronary events (5.4% vs. 2.6%; p = 0.25).

CONCLUSIONS

Additional CTO PCI within 1 week after primary PCI for STEMI was feasible and safe. In patients with STEMI and concurrent CTO, we did not find an overall benefit for CTO PCI in terms of LVEF or LVEDV. The finding that early CTO PCI in the left anterior descending coronary artery subgroup was beneficial warrants further investigation. (Evaluating Xience and Left Ventricular Function in Percutaneous Coronary Intervention on Occlusions After ST-Segment Elevation Myocardial Infarction; NTR1108)

針對合併慢性完全堵塞的 ST 段抬高心肌梗塞病患，比較介入與保守治療的療效

背景介紹

ST-segment elevation(STEMI) 病患中，約有一半的病患，除 infarct-related artery 有堵塞之外，還有其他冠狀動脈有嚴重狹窄，甚至 10-15% 的 STEMI 病患中，合併有其他冠狀動脈慢性完全堵塞 (chronic total occlusion(CTO)) 的現象。這類病患的死亡率或是併發症的機率也比一般 STEMI 病患高。理論上打通 CTO 可以改善心肌休眠現象，增加心臟收縮功能；另外若是心肌梗塞血管與 CTO 血管支配區域有重疊，打通 CTO 可能增加心肌梗塞受損區域邊緣的血流，減少心肌受損範圍。

EXPLORE 試驗 (Evaluating Xience and Left Ventricular Function in Percutaneous Coronary Intervention on Occlusions After ST-Elevation Myocardial Infarction) 是一個跨國、多中心、前瞻性的雙盲試驗，試圖證明 STEMI 病患合併有他條冠狀動脈 CTO，在成功進行 primary percutaneous coronary intervention(PCI) 後，相較於保守治療，打通 CTO 可以改善心臟功能或是重塑現象。

方法

本試驗收錄對象為 STEMI 的病患在症狀產生 12 小時內，成功完成 primary PCI，同時發現其他血管有 CTO 現象者（血管直徑必須大於 2.5mm）。隨機分成積極治療組 (CTO PCI) 或是保守治療組 (no CTO PCI)。積極治療組會在 primary PCI 完成七天之內將 CTO 打通；接受保守治療的病患，除非有嚴重症狀必須進行侵入性治療，否則持續藥物治療 4 個月。在 STEMI 發生四個月後會進行心臟核磁共振 (CMR) 檢查。試驗終點為 left ventricular ejection fraction (LVEF) 以及 left ventricular end-diastolic volume (LVEDV)

結果

在 2007 年 11 月到 2015 年 4 月之間共收集 304 位病患，分為隨機分為兩組，基本資料無差異，如表一。CTO PCI 成功率約 77%。CMR 結果如表二，在心肌梗塞四個月後，兩組平均 LVEF 為 44.1 +-12.2% vs. 44.8 +-11.9% (p = 0.60)；平均 LVEDV 為 215.6 +- 62.5 ml (CTO PCI 組) 與 212.8 +-60.3 ml (no–CTO PCI 組) (p = 0.70)，如圖一。臨床心血管事件也無顯著差異 (5.4% vs. 2.6%; p=0.25)（表三）（圖二）。在亞組分析方面，相較於保守治療，打通 left anterior descending coronary artery (LAD) CTO 者，LVEF 明顯較高（圖三）。

討論

以往已經有臨床試驗（如 PRAMI, CvLPRIT）證實，分階段 PCI 對於 STEMI 合併多條血管病變會有幫助，但都排除 non-infarct-related artery 有 CTO 的情形。一些回溯性研究顯示，積極打通此類病患的 CTO 會改善 LVEF。EXPLORE 是第一個大規模前瞻研究併有 CTO 的 STEMI 病患的治療方式的臨床試驗，雖然本試驗無法證實打通 CTO 對於 STEMI 病患有所助益，但本試驗謹限於一些病況穩定，較低風險的族群，同樣結論是否適用於 STEMI 併休克、或嚴重心律不整等高危險病患，仍屬未知。另外本試驗的 power 也不足以驗證兩種治療對臨床終點的影響。未來研究方向可以針對高危險族群或是 non-LAD STEMI 病患合併 LAD CTO，比較積極介入與保守治療的效果。

結論

EXPLORE 試驗證實，在成功做完 primary PCI 後七天內例行進行 CTO PCI 是可行而安全，但對於 LVEF 與 LVEDV 並無助益。

表一

TABLE 1 Baseline Characteristics and Discharge Medication

	CTO PCI (n = 148)	No CTO PCI (n = 154)
Age, yrs	60 ± 10	60 ± 10
Men	131 (89)	126 (82)
Diabetes	22 (15)	25 (16)
Hypertension	59 (40)	69 (45)
Family history of coronary artery disease	66 (45)	64 (42)
Hypercholesterolemia or receiving statin therapy	51 (35)	52 (34)
Current smoker	77 (52)	76 (49)
Previous myocardial infarction	19 (13)	24 (16)
Previous PCI	9 (6)	16 (10)
Previous stroke	5 (3)	6 (4)
Primary PCI		
Infarct-related artery		
Right coronary artery	46 (31)	47 (31)
Left circumflex artery	30 (20)	43 (28)
Left anterior descending artery	72 (49)	64 (42)
TIMI flow pre-PCI 0/1	101 (68)	97 (63)
TIMI flow post-PCI 2/3	148 (100)	154 (100)
Stent placement	146 (99)	154 (100)
Drug-eluting stent	88 (59)	103 (67)
Triple-vessel disease (>70% stenosis)	62 (42)	67 (44)
MI SYNTAX score I (pre-PCI)	29 ± 8	29 ± 10
MI SYNTAX score II (wiring/balloon/aspiration)	27 ± 8	27 ± 10
Infarct size		
Peak CK-MB	130 (39–272)	111 (43–256)
Peak troponin T	3.1 (1.1–7.8)	3.3 (0.9–6.0)
LVEF before randomization*	41 ± 11	42 ± 12
CTO characteristics during primary PCI (adjudicated)		
Patients with multiple CTOs†	13 (9)	22 (14)
CTO-related artery		
Right coronary artery	64 (43)	78 (51)
Left circumflex artery	48 (32)	37 (24)
Left anterior descending artery	36 (24)	39 (25)
TIMI flow		
0	132 (89)	139 (90)
1	15 (10)	14 (9)
2	1 (1)	1 (1)
Total J-CTO score	2 ± 1	2 ± 1
Previously failed lesion	2 (1)	4 (3)
Blunt stump	33 (22)	45 (29)
Bending	98 (66)	108 (70)
Calcification	115 (78)	132 (86)
Occlusion length ≥20 mm	60 (41)	68 (44)
Discharge medication		
Aspirin	148 (100)	152 (99)
Clopidogrel, prasugrel, or ticagrelor	148 (100)	154 (100)
Beta-blocker	138 (93)	139 (90)
ACE inhibitor or ARB	133 (90)	121 (79)
Lipid-lowering drugs	144 (97)	147 (96)

表二

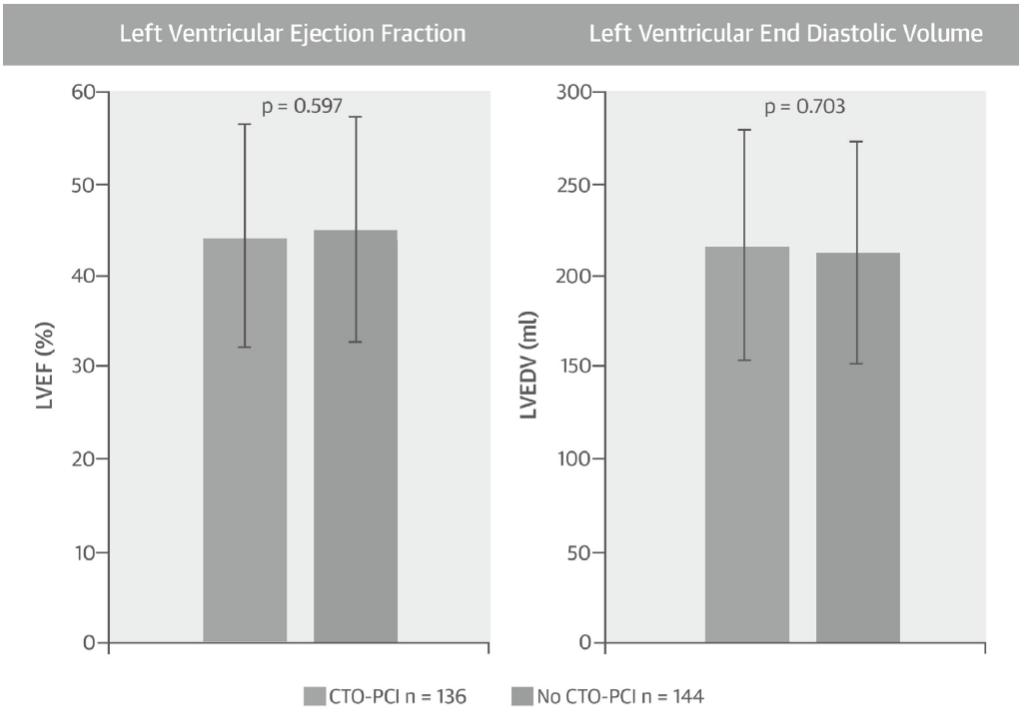
TABLE 3 Imaging Outcomes

	CTO PCI	No CTO PCI	Difference (95% CI)	p Value
Primary endpoint	136	144		
Left ventricular ejection fraction, %	44.1 (12.2)	44.8 (11.9)	−0.8 (−3.6 to 2.1)	0.60
Left ventricular end-diastolic volume, ml	215.6 (62.5)	212.8 (60.3)	2.8 (−11.6 to 17.2)	0.70
MRI or other imaging	132	143		
Left ventricular ejection fraction, %	45.1 (10.9)	45.1 (11.6)	0.1 (−2.7 to 2.7)	1.00
Left ventricular end-diastolic volume, ml	209.9 (53.8)	211.5 (58.3)	−1.6 (−14.9 to 11.8)	0.82
Left ventricular end-diastolic volume index, ml/m^2	102.9 (23.9)	104.3 (25.4)	−1.4 (−7.3 to 4.4)	0.63
Left ventricular end-systolic volume index, ml/m^2	57.9 (22.6)	58.9 (24.8)	−1.1 (−6.7 to 4.6)	0.71
MRI only	124	135		
Left ventricular ejection fraction, %	45.0 (10.6)	45.2 (11.5)	−0.2 (-2.9 to 2.5)	0.88
Left ventricular end-diastolic volume, ml	213.8 (51.8)	214.8 (56.4)	−1.0 (−14.2 to 12.3)	0.89
Left ventricular end-diastolic volume index, ml/m^2	104.9 (22.6)	105.9 (24.2)	−1.0 (−6.7 to 4.7)	0.73
Left ventricular end-systolic volume index, ml/m^2	59.0 (22.4)	59.7 (24.5)	−0.7 (−6.5 to 5.0)	0.81
Left ventricular end-diastolic mass index, g/m^2*	51.6 (9.2)	52.4 (12.0)	−0.8 (−3.5 to 2.0)	0.58
Dysfunctional segments, %*	58.0 (26.6)	61.5 (27.0)	−3.6 (−10.4 to 3.2)	0.30
Total infarct size, g†	7.6 (6.0)	7.2 (5.6)	0.4 (−1.1 to 2.0)	0.59

Values are n or n (%), unless otherwise indicated. *Data available in n = 113/n = 130. †Data available in n = 95/n = 114.
CI = confidence interval; MRI = magnetic resonance imaging; other abbreviations as in Table 1.

圖一

CENTRAL ILLUSTRATION Left Ventricular Function at 4-Month Follow-Up in STEMI Patients Undergoing CTO PCI Versus no CTO PCI



Henriques, J.P.S. et al. J Am Coll Cardiol. 2016;68(15):1622-32.

Left ventricular ejection fraction (LVEF) **(left)** and left ventricular end-diastolic volume (LVEDV) **(right)** at 4-month follow-up. All analyses were performed on an intention-to-treat basis: core-laboratory-reported success rates of chronic total occlusion percutaneous coronary intervention were 73%; and operator-reported success rates were 77%. **Whiskers** indicate standard deviation. CTO = chronic total occlusion; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

表三

TABLE 4 Adjudicated Clinical Outcomes From Randomization to 4-Month Follow-Up

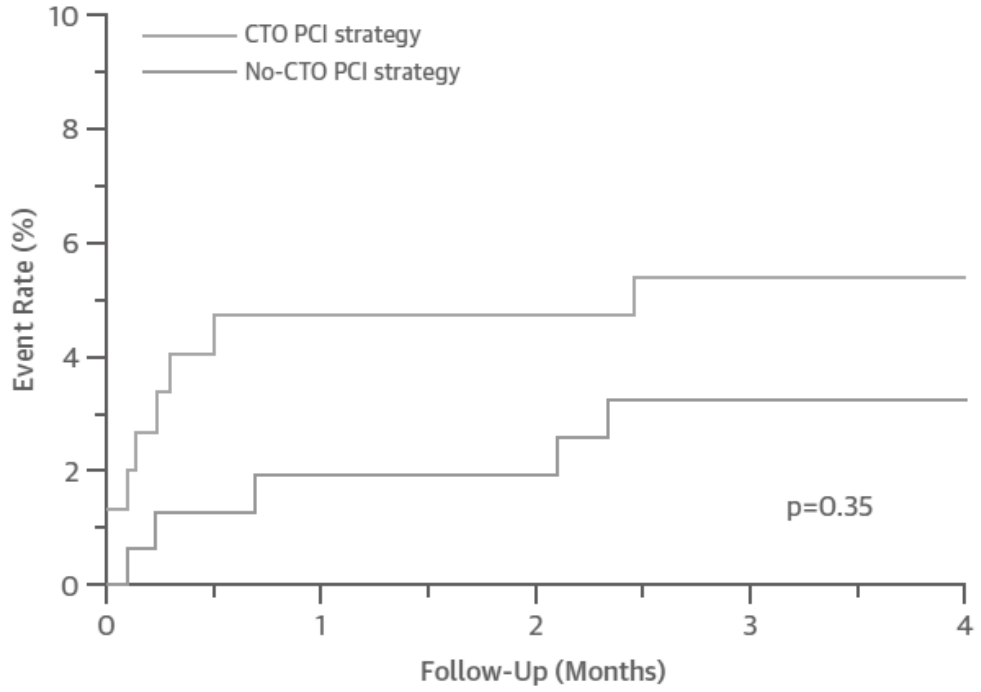
	CTO PCI (n = 148)	No CTO PCI (n = 154)	p Value
Major adverse cardiac events			
Cardiac death	4 (2.7)	0 (0.0)	0.056
Myocardial infarction	5 (3.4)	3 (1.9)	0.49
Periprocedural*	4 (2.7)	1 (0.6)	–
Spontaneous or recurrent	2 (1.4)	2 (1.3)	–
CABG operation	–	1 (0.6)	–
MACE	8 (5.4)	4 (2.6)	0.25
Other events			
PCI	39 (26.4)	20 (13.0)	0.004
CTO PCI	–	5 (3.2)	–
Repeat CTO PCI	2 (1.4)	0 (0.0)	–
Non-CTO PCI in CTO vessel	10 (6.8)	0 (0.0)	0.001
Before initial CTO procedure	1 (0.7)	–	–
During initial CTO procedure	9 (6.1)	–	–
Post-initial CTO procedure	–	–	–
PCI in non-CTO vessel	31 (20.9)	17 (11.0)	0.027
Before initial CTO procedure	0 (0.0)	–	–
During initial CTO procedure	26 (17.6)	–	–
Post-initial CTO procedure	5 (3.4)	–	–
Total stent thrombosis	5 (3.4)	3 (1.9)	0.49
Stent thrombosis CTO lesion	2 (1.4)	0 (0.0)	–
Definite	1 (0.7)	0 (0.0)	–
Probable	1 (0.7)	0 (0.0)	–
Timing of stent thrombosis CTO lesion			
Acute	0 (0.0)	0 (0.0)	–
Subacute	2 (1.4)	0 (0.0)	–
Stent thrombosis non-CTO lesion	4 (2.7)	3 (1.9)	0.72
Definite	3 (2.0)	3 (1.9)	–
Probable	1 (0.7)	0 (0.0)	–
Timing of stent thrombosis non-CTO lesion			
Acute	0 (0.0)	1 (0.6)	–
Subacute	3 (2.0)	2 (1.3)	–
Stroke†	0 (0.0)	2 (1.3)	–
Bleeding according to GUSTO-criteria	5 (3.4)	2 (1.3)	0.28
Mild	1 (0.7)	1 (0.6)	–
Moderate	3 (2.0)	1 (0.6)	–
Severe or life-threatening	1 (0.7)	0 (0.0)	–

Values are number of events (%). The first event per patient is listed. *Periprocedural myocardial infarction was defined according to the third universal definition of myocardial infarction criteria. †1 patient had a fatal stroke; there were no other noncardiac deaths.

GUSTO = Global Use of Strategies to Open Occluded Coronary Arteries; MACE = a composite of cardiac death, myocardial infarction, and coronary artery bypass graft; other abbreviations as in Tables 1 and 2.

圖二

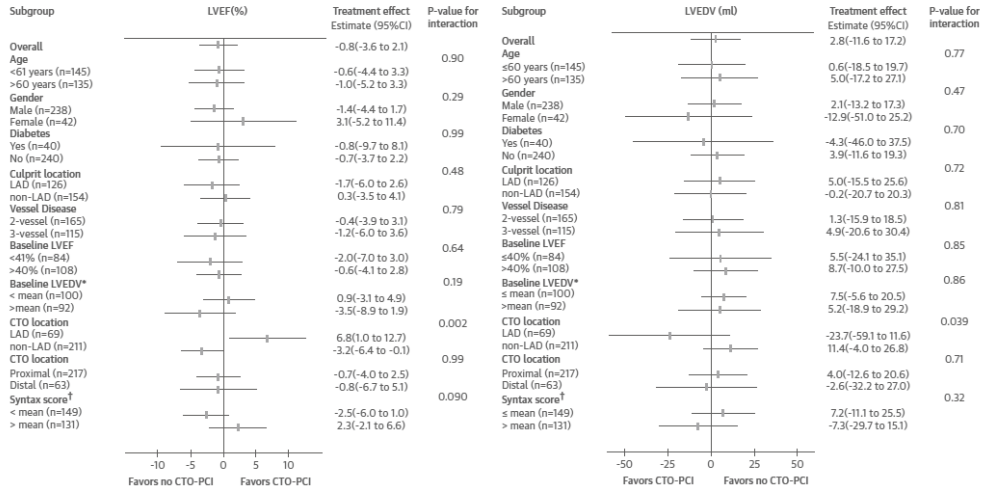
FIGURE 3 Major Adverse Cardiac Events Event Rates at 4-Month Follow-Up



Major adverse cardiac events consisted of cardiac death, myocardial infarction, and coronary artery bypass graft operation. Abbreviations as in Figure 1.

圖三

FIGURE 2 Forest Plots of Subgroup Analyses for the Primary Outcomes



*The mean left ventricular end-diastolic volume was 210.5 ml. †The mean SYNTAX score was 26.5. CI = confidence interval; LAD = left anterior descending coronary artery; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; other abbreviations as in Figure 1.