Systematic Review and Meta-Analysis

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Successful revascularization of noninfarct related artery with chronic total occlusion among acute myocardial infarction patients

A systematic review and meta-analysis

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Abstract

Background: Randomized trials and meta-analyses demonstrated that chronic total occlusion (CTO) in noninfarct related artery (n-IRA) was associated with increased all-cause mortality. Recently, several observational studies suggested that the successful revascularization of n-IRA with CTO decreased all-cause mortality.

Methods: A systematic search was performed in Cochrane Controlled Trials Registry, PubMed, MEDLINE, and EMBASE databases for relevant studies. Article assessing the prognostic role of revascularization of n-IRA with CTO was enrolled in this meta-analysis. Data and characteristics of each study were extracted. A meta-analysis was performed to generate pooled odds ratio (OR) and 95% confidence intervals (95% CIs) for outcomes. The primary outcome was major adverse cardiac events (MACE). Beg funnel plot was used to evaluate publication bias.

Results: Four observational studies and one randomized controlled trial involving 1083 patients were enrolled for analysis. Compared with nonreperfusion, the successful percutaneous coronary intervention (PCI) of n-IRA with CTO was related to decreased all-cause mortality (OR was 0.34, and 95% CI was 0.2–0.59; $P = .0001$).

Conclusions: Successful PCI of n-IRA with CTO could significantly decrease all-cause mortality, cardiac mortality, MACE, and stroke in acute myocardial infarction patients. In addition, it was not associated with the increased risk of repeat revascularization and myocardial infarction.

Abbreviations: ACS = acute coronary syndrome, AMI = acute myocardial infarction, CTO = chronic total occlusion, LVEDV = left ventricular end diastolic volume, LVEF = left ventricular ejection fraction, MACE = major adverse cardiac events, MVD = multivessel disease, n-IRA = noninfarct related artery, PCI = percutaneous coronary intervention, PTCA = percutaneous transluminal coronary angioplasty, STEMI = ST-segment elevation myocardial infarction, SVD = single vessel disease.

Keywords: acute myocardial infarction, chronic total occlusion (CTO), noninfarct-related coronary (n-IRA), PCI, revascularization

1. Introduction

Percutaneous coronary intervention (PCI) is one of the main coronary revascularization approaches in patients with stable coronary artery disease and acute coronary syndrome (ACS).[1] In addition, with the progress of percutaneous transluminal coronary angioplasty (PTCA) and coronary stent implantation during the treatment of acute myocardial infarction (AMI), the clinical prognosis of those patients has been improved significantly. However, AMI remains one of the major diseases threatening human health and a leading cause of deaths worldwide.[2]

Among AMI patients, about 50% have single vessel disease (SVD), while about 40% to 60% have multivessel disease (MVD) and near 10% have MVD with chronic total occlusion (CTO) in noninfarct related artery (n-IRA).[3,4] Moreover, the morbidity and mortality of AMI in patients with MVD are twice of those in patients with SVD.[5] The most severe manifestation of coronary artery disease is CTO. Up to 15% of the patients with ST-segment elevation myocardial infarction (STEMI) have CTO in the n-IRA.[4] A growing body of evidence shows that high mortality of AMI is closely related to concurrent CTO in n-IRA among patients with MVD.[6–9]

A recent systematic review and meta-analysis demonstrated that CTO in n-IRA was an independent predictor of clinical outcomes in patients with AMI.[10]

A randomized controlled trial named EXPLORE evaluated the effect of CTO revascularization in n-IRA on left ventricle systolic function and clinical outcomes after PCI for STEMI.[11] It was concluded that PCI of CTO within 1 week after the primary PCI was feasible and safe. Although the overall benefit of PCI of CTO in terms of left ventricular ejection fraction (LVEF) or left ventricular end diastolic volume (LVEDV) and major adverse cardiac events (MACE) rates was not found, several studies declared that successful revascularization of CTO in the n-IRA was associated with improved clinical outcomes in AMI patients undergoing PCI. The above results were inconsistent and the sample size in their studies was

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relatively small, which may skew the statistical analysis. In respect of this, we performed a meta-analysis examining the impact of revascularization of n-IRA with CTO on the mortality of AMI patients treated by the primary PCI.

2. Methods

2.1. Ethical approval

All analyses were based on previous published studies; thus, no ethical approval and patient consent are required.

2.2. Search strategy

We conducted searches through Cochrane Controlled Trials Registry, PubMed, MEDLINE, and EMBASE databases for published articles using the following predefined search terms, "hronic total occlusion" OR "hronic occlusion" AND "yocardial infarction" OR "acute myocardial infarction" AND "PCI." Abstracts from selected major scientific meetings of cardiology (American Heart Association, American College of Cardiology, European Society of Cardiology, and Transcatheter Cardiovascular Therapeutics) were reviewed. References from reviews and selected articles were also screened for potential relevant citations. There were no language restrictions.

2.3. Eligibility criteria

Selection criteria for inclusion in the meta-analysis were as follows: AMI patients of STEMI treated by the primary PCI or non-ST elevation MI (NSTEMI) by the primary PCI; the diagnosis of CTO in n-IRA was made by coronary angiography; either a single-group cohort or a controlled comparison between patients who had successful PCI in n-IRA with CTO and those who had no or failed PCI; the time of PCI for CTO was 1 week or longer after PCI; available data on all-cause mortality and cardiac mortality or MACE; trials that reported outcomes of more than 3 months.

Definition of successful PCI was core lab-defined final TIMI flow grade ≥2, residual stenosis <50%, and no loss of a major side branch.

Full-text articles and meeting abstracts were included.

Redundant reports and ongoing studies were excluded. Data extraction was performed independently by 2 reviewers. Discrepancies were resolved by reaching a consensus between the 2 reviewers.

2.4. Data extraction

Two independent reviewers screened the data from the included studies using a predefined checklist for each study. Disagreements between reviewers were resolved by discussion until a consensus was reached. Data extraction and presentation for this article followed the recommendations of the PRISMA group. The primary efficacy end point was all-cause mortality. Secondary end points included cardiac mortality, MACEs, and nonfatal myocardial infarction. Stroke and repeat revascularization were also assessed. Outcomes were evaluated based on the longest follow-up period for each study. The Newcastle-Ottawa Scale (NOS) was employed as an assessment tool.

2.5. Data analysis

The meta-analysis was conducted in accordance with the general guidelines in the Cochrane Handbook for Systematic Reviews of Interventions, version 5.0.2. The Cochrane Q statistic and the I^2 statistic were used to assess the heterogeneity across different trials. A Cochrane Q statistic with P-value ≤.1 was considered significant. The I^2 statistic was used to measure the consistency among different trials, and 25%, 50%, and 75% indicated low, moderate, and high heterogeneity, respectively. A funnel plot was used to assess publication bias by plotting the standard error against the log risk ratio. Analyses were conducted using the RevMan software, version 5.3.

3. Results

3.1. Studies characteristics

As is shown in Fig. 1, 55 articles were identified, of which 42 were excluded based on the abstract review. Thirteen full articles were

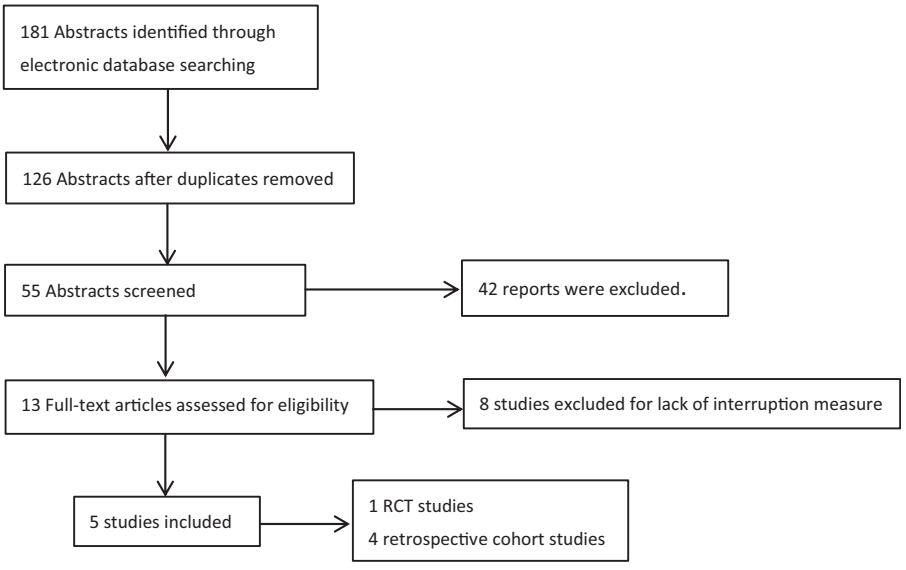

Figure 1. Process of screening articles, and finally we have incorporated 5 articles.

Table 1

Review of included studies.

Source	EXPLORE[18]	Careggi[19]	Korea[20]	Ruijin[21]	Guangzhou[22]
Design	RCT	Retrospective cohort study	Retrospective cohort study	Retrospective cohort study	Retrospective cohort study
No. of patients, N	304	169	324	136	150
Follow-up, mo	4	36	60	24	36
Mean age ($\bar{x} \pm s$)	60 ± 10	64 ± 10	62.7 ± 12.9	66 ± 11	NA
Female, N (%)	11	15	30.6	18	22
Diabetes, N (%)	15	17	32.9	36	23
Prior MI, N (%)	13	19	5.3	26	28
Prior PCI, N (%)	6	NA	5.9	NA	28
Cardiac shock, N (%)	3	16	4.7	NA	22
SVD%	58	41	NA	0	0
MVD%	42	59	NA	100	100
Clinical endpoints	Death LVEDV, cardiac mortality, MACE, myocardial infarction, CABG, stroke, bleeding	Death, cardiac mortality, stroke, CABG, revascularization, LVEF	Death, MACE, cardiac mortality, stroke, revascularization	Death, MACE, Cardiac mortality, myocardial infarction, revascularization, rehospitalization due to heart failure	Death, MACE, cardiac mortality, myocardial infarction, revascularization, rehospitalization due to heart failure

CABG = coronary artery bypass grafting, LVEDV = left ventricular end-diastolic volume, LVEF = left ventricular ejection fraction, MACE = major adverse cardiac events, MVD = multivessel disease, PCI = percutaneous coronary intervention, RCT = randomized controlled trial, SVD = single vessel disease.

assessed for eligibility. Of them, 8 studies were excluded because they investigated the impact of concurrent CTO in n-IRA on mortality.[4,12–17] Finally, 5 studies containing a total of 1083 patients were included in the analysis, of which there was 1 randomized controlled trial,[11] and 4 observational studies.[18–21] Details and baseline characteristics of the included studies are listed in Tables 1–5. The quality of the enrolled studies was assessed using the Newcastle-Ottowa scale in Table 2.

3.2. Quantitative synthesis results

In the global analysis of all studies, successful PCI for n-IRA with CTO was associated with lower all-cause mortality during a median follow-up of 36 months (interquartile range, 19–42 months) compared with CTO (the absolute risk was 9.38% vs 19.50%; the odds ratio [OR] was 0.34, and the 95% confidence interval [CI] was 0.2–0.59; $P = .0001$) (Fig. 2).

Long-term cardiac mortality was reported in the above 5 studies.[11,18–21] Successful revascularization of CTO was closely linked with decreased long-term cardiac mortality (the absolute risk was 6.02% vs 12.55%; OR: 0.36, 95% CI: 0.19–0.68; $P = .002$).

MACEs were reported in 3 studies.[20–22] There was a significant correlation between successful PCI of CTO and the lower incidence of MACEs (the absolute risk was 21.85% vs 43.48%; OR: 0.35, 95% CI: 0.24–0.5; $P < .00001$).

The nonfatal myocardial infarction and repeat revascularization were evaluated in all included studies,[11,18–21] and there was no evidence suggesting that the successful PCI of CTO may affect their incidence. This conclusion was similar regarding to MI (the absolute risk was 3.19% vs 3.47%; OR: 0.78, 95% CI: 0.36–1.70; $P = .54$) and repeat revascularization (the absolute risk was 18.58% vs 17.18%; OR: 1.11, 95% CI: 0.43–2.87; $P = .83$).

Stroke was reported in only 4 studies,[11,19–21] and its incidence in the population who underwent successful PCI of CTO was significantly lower (the absolute risk was 1.26% vs 3.41%; OR: 0.36, 95% CI: 0.13–0.97; $P = .04$).

4. Discussion

The present meta-analysis demonstrated an important association between the successful revascularization of n-IRA with CTO and the survival rate in AMI patients treated by PCI. In the global comparison of data collected from 1083 patients, it was observed that the successful PCI for n-IRA with CTO was related to lower all-cause mortality and cardiac mortality as well as lower incidence of MACE and stroke. In addition, it was proved that the successful PCI was not related to the increased risk of repeat revascularization and nonfatal myocardial infarction.

The EXPLORE trial reported heart function and MACE rates, and a significantly lower rate was not found, but a subgroup analysis suggested that PCI for n-IRA with CTO

Table 2

Newcastle-Ottawa Scale assessment of the included studies.

Name	Design	Selection	Comparability	Outcome	Total
Korea[20]	Cohort	****	**	***	9
Ruijin[21]	Cohort	****	**	**	8
Guangzhou[22]	Cohort	****	**	***	9
Explore[18]	RCT	****	**	***	9
Careggi[19]	Cohort	****	**	***	9

Each asterisk is equivalent to 1 point. The maximum score is 9 (**** for selection, ** for comparability, ***for outcome).
RCT = randomized controlled trial.

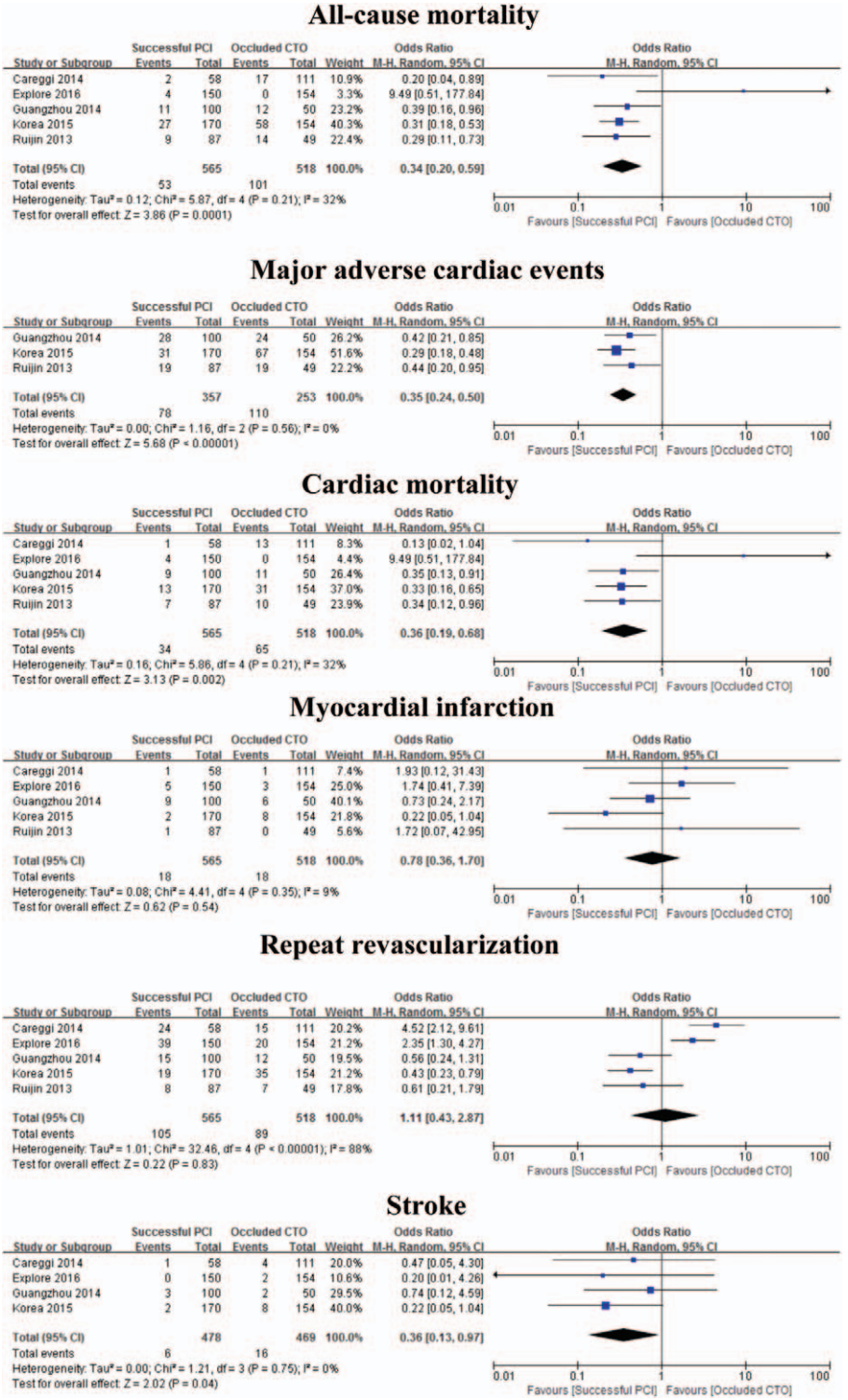

Figure 2. Forest plot of each result. And it illustrates successful PCI of n-IRA with CTO could significantly decrease all-cause mortality, cardiac mortality, major adverse cardiac events (MACE), and stroke in acute myocardial infarction patients.

could still improve the outcomes of high-risk patients.[11] However, it was shown that routine PCI of CTO did not result in higher LVEF and lower LVEDV at 4 months, and the reasons may be as follows: the complexity of the patients enrolled; lack of a specific protocol or technique for PCI of CTO; a lower successful rate of PCI of CTO; smaller sample size for evaluation of clinical endpoints. The presence of CTO led to a higher degree of complexity in the coronary artery diseases investigated in the study. In our study, 48.19% to 73.04% of patients had triple-vessel disease (TVD), and their percentage was higher compared to the EXPLORE trial, in which 43% of the patients had TVD.

Table 3

The characteristics of single studies.

Source	EXPLORE[18]	Careggi[19]	Korea[20]	Ruijin[21]	Guangzhou[22]
Study year	2016	2014	2015	2013	2014
Location	Europe and Canada	Florence	Korean	China	China
Number of patients	304	169	324	136	150
Study design	RCT	Retrospective cohort study	Retrospective cohort study	Retrospective cohort study	Retrospective cohort study
Primary endpoint	LVEF, LVEDV, MACE, other events	1-y and 3-y cardiac survival	All-cause mortality, MACE	MACE	MACE
Mortality reported	0.013	0.112	0.262	0.1586	0.155
Follow-up	4 mo	3 y	5 y	2 y	3 y
Lost to FU %	0	0	0	0.69	1.5

LVEDV = left ventricular end-diastolic volume, LVEF = left ventricular ejection fraction, MACE = major adverse cardiac events, MVD = multivessel disease, RCT = randomized controlled trial, SVD = single vessel disease.

According to the CREDO-Kyoto AMI registry, in AMI patients with MVD, the CTO in non-IRA was associated with an increased 5-year mortality.[17]

The PRAMI trial concluded that as compared with conservative treatments, preventive PCI of n-IRA was related to a lower risk of adverse cardiovascular events. In our study, CTO were all located at n-IRA and our data were consistent with those obtained from the previous study.[22]

Regrettably, the exact mechanisms of reduced mortality were not investigated, but some explanations might be inferred: First, patients with CTO might have a larger infarct size due to acute occlusion, thus CTO-PCI may save dying myocardium and prevent the infiltration area expansion.[23] Second, the decrease in electrical instability increased the tolerance for future coronary occlusion events by reducing the risk of fatal arrhythmia. Third, patients with successful treatment with CTO-PCI may enhance

Table 4

The definitions of the outcome in each of the studies.

Source	EXPLORE[18]	Careggi[19]	Korea[20]	Ruijin[21]	Guangzhou[22]
All-cause mortality	Not clearly defined	Not clearly defined	All clinical outcomes of interest were confirmed by source documents and were centrally adjudicated by a local events committee at the Cardiovascular Centre of Seoul St. Mary's Hospital and by an independent group of clinicians who were unaware of the patients' statuses. Information regarding death was matched with records from the National Population Registry of the Korea National Statistical Office with a unique personal identification number to validate the mortality follow-up data	Not clearly defined	Not clearly defined
Major cardiovascular events	The composite of cardiac death			Including cardiac death, recurrent myocardial infarction, repeat revascularization (PCI and/or CABG), and rehospitalization	Including cardiac death, recurrent myocardial infarction, repeat revascularization (PCI and/or CABG), and rehospitalization
Cardiac mortality	According to the ARC criteria			Any death with a demonstrable cardiac cause or any death that was not clearly attributable to a noncardiac cause	Not clearly defined
Myocardial infarction	According to the third universal definition of myocardial infarction criteria			A new occurrence of ischemic symptoms in the presence of electrocardiographic changes and rise of biochemical markers of myocardial necrosis	Not clearly defined
Repeat revascularization	Repeat PCI of the treated CTO lesion, PCI of non-CTO lesions in the CTO vessel, and PCI in non-CTO vessels according to ARC criteria.			Any clinically driven target or nontarget vessel reintervention by either PCI or CABG	Not clearly defined
Stroke	None			Not clearly defined	Not clearly defined

CABG = coronary artery bypass grafting, CTO = chronic total occlusion, PCI = percutaneous coronary intervention.

Table 5

Cochrane collaboration's tool for assessing risk of bias.

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was one to one with a block of size 6. The list of randomization was obtained using the SAS procedure plan at the data statistical analysis centre"
Allocation concealment (selection bias)	Low risk	Randomization was done in an open-label manner with an electronic Internet-based system in permuted blocks of varying size in each participating center
Blinding of participants and researchers (performance bias)	High risk	Open label
Blinding of outcome assessment (detection bias)	High risk	Open label
Incomplete outcome data (attrition bias)	Low risk	Losses to follow-up were disclosed and the analyses were conducted using, firstly, a modified intention to treat analysis in which missing failures, secondly, on an observed basis. Although the authors describe an intention to treat analysis, the 304 participants initially randomized were not all included; 2 were excluded. This is a reasonable attrition and not expected to affect results. Adequate sample size of 60 per group was achieved
Selective reporting (reporting bias)	Low risk	All prespecified outcomes were reported
Other bias	Unclear risk	No description of the uptake of the therapeutic drug monitoring recommendations by physicians, which could result in performance bias

SAS = statistics analysis system.

their care about health, leading to lifestyle and other changes that may decrease the risk of stroke. A recent meta-analysis comparing complete and incomplete coronary revascularization has suggested that the former is associated with a 30% reduction of cardiac mortality in patients with MVD,[24] whereas the main decisive factor for incomplete revascularization is known to be CTO.[25,26]

Complete revascularization is beneficial for long-term survival of patients treated with multivessel PCI in an elective setting.[25] Another meta-analysis of selective patients showed that the successful PCI for CTO was related to a 4.4% improvement in terms of absolute LVEF points.[27] Successful CTO-PCI is a prerequisite for complete revascularization. The vast majority patients who underwent successful CTO-PCI had complete coronary revascularization, and it has been shown that complete revascularization in MVD patients was associated with longer survival. Furthermore, previous reports have demonstrated the clinical benefit of complete revascularization in patients with MVD and CTO.[28,29]

At present, the time for PCI of n-IRA with CTO is not determined. Most experts agree that IRA PCI should be performed as soon as possible for AMI to save the dying myocardium, reduce the mortality rate in the acute phase; and elective intervention in the opening CTO to reduce long-term events. In the EXPLORE study,[11] staged CTO-PCI attempt was performed up to 7 days from primary PCI. And it proved that this approach is feasible and safe. Although the preliminary results of the study were not satisfactory, it still posed challenges and reflections for our conventional intervention strategy.

Does the difference between the methods for revascularization affect the outcome? Ascione and other professors from the Royal Institute of Cardiology, Royal College of Bristol, UK, believe that coronary artery bypass grafting (CABG) should be performed on patients with chronic total occlusion of the coronary artery (CTO). Patients with CTO have a high probability of combining multiple ailments and also have high scores in the SYNTAX scoring system. Multiple risk factors make patients very variable in clinical and cardiac characteristics. CABG surgery is capable of performing both proximal and distal segments, consistent with the 2 trials by DECISION-CTO and EuroCTO. In addition, CABG long-term follow-up results are good, graft vascular patency rate higher. The use of left internal mammary artery instead of anterior descending artery is very efficient, long-term patency rate is also very impressive. Long-term patency of CTOs using saphenous vein is greater than 50%, with an average of 75% in recent years as technology advances.

But professor Weintraub believes that although most of the patients with chronic coronary artery occlusive disease (CTO) are currently treated with CABG, the current evidence is not enough to prove that CABG is a common treatment for CTO. Of these patients with CTO, 11% had PCI, 40% had CABG, and 49% had medication. In patients without CTO, 36% had PCI, 28% had CABG, and 35% had medication. In one study from Canada, 18.4% of patients with nonurgent diagnosis of coronary heart disease had CTO. Of these, 25% reported Q wave conduction in the CTO blood supply area, most of them had normal left ventricular function. Almost half of CTO in the right coronary artery. Although only 30% of patients use PCI, the success rate is as high as 70%.

Although more patients currently use CABG to treat CTOs, the rapid development of PCI technology will allow more CTO patients to be treated with PCI. PCI can be effective in relieving angina pectoris, but there are few studies on the treatment of angina pectoris by CABG. In terms of increased survival, data on PCI versus CABG are not enough, and some low-risk patients are likely to increase their risk if CABG is routinely performed in all CTO patients. In the current CABG treatment of CTO literatures, some literature is not a randomized controlled trial and have some preferences. So we believe that at present, there are several factors that should be considered to determine which CTO patients should be treated with CABG and to study the long-term prognostic outcome of CABG therapy and that more rigorous trials should be conducted to compare treatments to determine the optimal CTO treatment method.

Despite good outcomes after successful PCI, little is known about the outcomes after failed PCI. By reading the literature, it was found that patients with a failed CTO-PCI were much more likely to be referred for surgical revascularization, CABG. The possible reasons are as follows: First, mechanical trauma to a coronary artery resulted in frank perforation and required emergent cardiac surgery. Thus, the higher number of complications among the CTO failure group probably accounted for a higher number of emergent CABG in this group. Second, in some

patients with MVD and unsuccessful CTO-PCI, even absent complications prompted a need for bypass surgery.[30,31]

5. Conclusion

This meta-analysis suggested that successful revascularization of n-IRA with CTO could improve long-term outcomes of AMI patients who underwent the primary PCI. However, it remains unclear which kind of AMI patients benefit most. The findings are significant for interventional cardiologists. It is implied that when exploring the choice of revascularization modalities for patients with CTO of n-IRA, preference might be given to revascularization of n-IRA with CTO in addition to considering lesion complexity, functional significance, patient characteristics, and syntax scores in accordance with the current international recommendations.[32]

6. Limitation

Our study has some limitations. First, some retrospective studies were included and hence the results might be affected by unmeasured confounders and selection bias due to the retrospective, nonrandomized, and observational nature of the study design. Second, the lack of patient-level data prevented a comprehensive assessment to identify patient characteristics associated with the greatest clinical benefits, and subgroup analyses were not performed. Third, the number of patients in our study was small and STEMI and NSTEMI were not distinguished. Forth, the difference in body weight between the 2 groups was not analyzed and information about collateral circulation and viability/ischemia of the area supplied by the occluding artery was not provided.

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References

[1] Iqbal J, Serruys PW, Taggart DP. Optimal revascularization for complex coronary artery disease. Nat Rev Cardiol 2013;10:635–47.
[2] O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2013;127: e362–425.
[3] Toma M, Buller CE, Westerhout CM, et al. Non-culprit coronary artery percutaneous coronary intervention during acute ST-segment elevation myocardial infarction: insights from the APEX-AMI trial. Eur Heart J 2010;31:1701–7.
[4] Claessen BE, Dangas GD, Weisz G, et al. Prognostic impact of a chronic total occlusion in a non-infarct-related artery in patients with ST-segment elevation myocardial infarction: 3-year results from the HORIZONS-AMI trial. Eur Heart J 2012;33:768–75.
[5] Park DW, Clare RM, Schulte PJ, et al. Extent, location, and clinical significance of non-infarct-related coronary artery disease among patients with ST-elevation myocardial infarction. JAMA 2014;312: 2019–27.
[6] Bataille Y, Dery JP, Larose E, et al. Prevalence, predictors and clinical impact of unique and multiple chronic total occlusion in non-infarct-related artery in patients presenting with ST-elevation myocardial infarction. Heart 2012;98:1732–7.
[7] Kim HY. The concurrent chronic total occlusion in a non-infarct artery strongly associate with poor long-term prognosis in patients with acute myocardial infarction and multivessel coronary disease. Korean Circ J 2012;42:83–5.
[8] Tajstra M, Gasior M, Gierlotka M, et al. Comparison of five-year outcomes of patients with and without chronic total occlusion of noninfarct coronary artery after primary coronary intervention for ST-segment elevation acute myocardial infarction. Am J Cardiol 2012;109:208–13.
[9] Chen HC, Tsai TH, Fang HY, et al. Benefit of revascularization in non-infarct-related artery in multivessel disease patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Int Heart J 2010;51:319–24.
[10] O'Connor SA, Garot P, Sanguineti F, et al. Meta-analysis of the impact on mortality of noninfarct-related artery coronary chronic total occlusion in patients presenting with ST-segment elevation myocardial infarction. Am J Cardiol 2015;116:8–14.
[11] Henriques JP, Hoebers LP, Ramunddal T, et al. Percutaneous intervention for concurrent chronic total occlusions in patients with STEMI: the EXPLORE trial. J Am Coll Cardiol 2016;68: 1622–32.
[12] Claessen BE, Hoebers LP, van der Schaaf RJ, et al. Prevalence and impact of a chronic total occlusion in a non-infarct-related artery on long-term mortality in diabetic patients with ST elevation myocardial infarction. Heart 2010;96:1968–72.
[13] Gierlotka M, Tajstra M, Gasior M, et al. Impact of chronic total occlusion artery on 12-month mortality in patients with non-ST-segment elevation myocardial infarction treated by percutaneous coronary intervention (from the PL-ACS Registry). Int J Cardiol 2013;168:250–4.
[14] Lesiak M, Cugowska M, Araszkiewicz A, et al. Impact of the presence of chronically occluded coronary artery on long-term prognosis of patients with acute ST-segment elevation myocardial infarction. Cardiol J 2017;24:117–24.
[15] Mizuguchi Y, Takahashi A, Hashimoto S, et al. Impact of the presence of chronic total occlusion in a non-infarct-related coronary artery in acute myocardial infarction patients. Int Heart J 2015;56:592–6.
[16] Suzuki M, Enomoto D, Mizobuchi T, et al. Impact of chronic total coronary occlusion on microvascular reperfusion in patients with a first anterior ST-segment elevation myocardial infarction. J Invasive Cardiol 2012;24:428–32.
[17] Watanabe H, Morimoto T, Shiomi H, et al. Chronic total occlusion in a non-infarct-related artery is closely associated with increased five-year mortality in patients with ST-segment elevation acute myocardial infarction undergoing primary percutaneous coronary intervention (from the CREDO-Kyoto AMI registry). EuroIntervention 2017;12:e1874–82.
[18] Zhang HP, Zhao Y, Li H, et al. Impact of chronic total occlusion in a noninfarct-related artery on clinical outcomes in patients with acute ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Medicine 2016;95:e2441.
[19] Valenti R, Marrani M, Cantini G, et al. Impact of chronic total occlusion revascularization in patients with acute myocardial infarction treated by primary percutaneous coronary intervention. Am J Cardiol 2014;114: 1794–800.
[20] Choi IJ, Koh YS, Lim S, et al. Impact of percutaneous coronary intervention for chronic total occlusion in non-infarct-related arteries in patients with acute myocardial infarction (from the COREA-AMI Registry). Am J Cardiol 2016;117:1039–46.
[21] Yang ZK, Zhang RY, Hu J, et al. Impact of successful staged revascularization of a chronic total occlusion in the non-infarct-related artery on long-term outcome in patients with acute ST-segment elevation myocardial infarction. Int J Cardiol 2013;165:76–9.
[22] Shi G, He P, Liu Y, et al. Evaluation of the effect of concurrent chronic total occlusion and successful staged revascularization on long-term mortality in patients with ST-elevation myocardial infarction. ScientificWorldJournal 2014;2014:756080.
[23] Tarantini G, Mojoli M, Capodanno D. [The PRAMI study]. G Ital Cardiol (Rome) 2014;15:199–204.
[24] Garcia S, Sandoval Y, Roukoz H, et al. Outcomes after complete versus incomplete revascularization of patients with multivessel coronary artery disease: a meta-analysis of 89,883 patients enrolled in randomized clinical trials and observational studies. J Am Coll Cardiol 2013;62:1421–31.
[25] Hannan EL, Racz M, Holmes DR, et al. Impact of completeness of percutaneous coronary intervention revascularization on long-term outcomes in the stent era. Circulation 2006;113:2406–12.
[26] Farooq V, Serruys PW, Garcia-Garcia HM, et al. The negative impact of incomplete angiographic revascularization on clinical outcomes and its association with total occlusions: the SYNTAX (Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) trial. J Am Coll Cardiol 2013;61:282–94.

[27] Hoebers LP, Claessen BE, Elias J, et al. Meta-analysis on the impact of percutaneous coronary intervention of chronic total occlusions on left ventricular function and clinical outcome. Int J Cardiol 2015;187:90–6.
[28] Valenti R, Migliorini A, Signorini U, et al. Impact of complete revascularization with percutaneous coronary intervention on survival in patients with at least one chronic total occlusion. Eur Heart J 2008;29:2336–42.
[29] Valenti R, Vergara R, Migliorini A, et al. Predictors of reocclusion after successful drug-eluting stent-supported percutaneous coronary intervention of chronic total occlusion. J Am Coll Cardiol 2013;61:545–50.
[30] Khan MF, Brilakis ES, Wendel CS, et al. Comparison of procedural complications and in-hospital clinical outcomes between patients with successful and failed percutaneous intervention of coronary chronic total occlusions: a meta-analysis of observational studies. Catheter Cardiovasc Interv 2015;85:781–94.
[31] Lee PH, Lee SW, Park HS, et al. Successful recanalization of native coronary chronic total occlusion is not associated with improved long-term survival. JACC Cardiovasc Interv 2016;9:530–8.
[32] Windecker S, Kolh P, Alfonso F, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2014;35:2541–619.