Austin Journal of Clinical Cardiology

Open Access

Austin Publishing Group

Research Article

# Impact of Successful Recanalization of Chronic Total Occlusions Using Coronary Stents on Long-Term Clinical Outcomes: A Meta-Analysis

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**Received:** December 12, 2016; **Accepted:** January 18, 2017; **Published:** January 24, 2017

## Abstract

**Background and Objectives:** Although coronary stent implantation dramatically reduced the occurrences of restenosis and the needs for repeat revascularization, there is still uncertainty as to the prognostic impact of successful recanalization of Chronic Total Occlusion (CTO) lesion. The objective of this study was to determine the impact of successful CTO recanalization using coronary stent deployment on clinical outcomes.

**Subjects and Methods:** Databases were searched for clinical studies that compared outcomes after successful recanalization of CTO lesions using coronary stent deployment with those of unsuccessful recanalization from January 2003 to March 2016. The end points of this study were mortality; Myocardial Infarction (MI); Major Adverse Cardiac Events (MACE); the need for Coronary Artery Bypass Graft Surgery (CABG); and angina relief at the longest follow-up.

**Results:** Nineteen studies encompassing 12,598 patients with a median follow-up period of 12-60 months after successful vs. unsuccessful CTO recanalization using coronary stent were identified. There were 455 (5.0%) deaths of 9,041 patients after successful recanalization compared to 339 (10.3%) among 3,280 patients after unsuccessful recanalization (odds ratio [OR] 0.48, 95% Confidence Interval [CI] 0.38 to 0.61). Successful CTO recanalization significantly reduced the incidence of MI (OR 0.67, 95% CI 0.46 to 0.97) and MACE (OR 0.55, 95% CI 0.42 to 0.73). Successful CTO recanalization was associated with a lower need for subsequent CABG and higher angina relief.

**Conclusion:** Successful recanalization of CTO lesions using coronary stents deployment appears to be associated with improvement in mortality and reduced needs for CABG as compared with unsuccessful PCI.

**Keywords:** Chronic total occlusion; Percutaneous coronary intervention; Stents

## Introduction

Percutaneous Coronary Intervention (PCI) for Chronic Total Occlusion (CTO) of coronary arteries accounts for 10% to 20% of all PCI [1]. Increasing experience and advanced interventional technologies have increased success rate of CTO intervention up to 90% if performed by experts [2,3]. Moreover, successful recanalization of CTO reduces anginal symptom, risk of periprocedural Myocardial Infarction (MI), mortality, improve left ventricular function, and diminish subsequent needs for Coronary Artery Bypass Grafting (CABG) [3-6].

Although coronary stents implantation dramatically reduced the occurrence of restenosis and the need for repeat revascularization, there is still uncertainty as to the prognostic impact of successful CTO recanalization using coronary stents. Several previous studies evaluating long-term outcomes after CTO intervention have shown conflicting results regarding the benefit of opening CTO lesion [5,7-10]. Recent publication of several observational studies of CTO using coronary stents [11-15] have provided substantial evidences, suggesting the need for an updated meta-analysis to confirm the benefits of successful recanalization and attempting of PCI for CTO lesions.

## Subjects and Methods

The investigator followed the PRISMA statement for meta-analysis in health care interventions [16] and performed the analysis in accordance with the Meta-Analysis of Observational Studies in Epidemiology guidelines in describing all stages design, implementation, and reporting of this meta-analysis [17].

### Data sources and searches

Relevant studies were identified through electronic searches of MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials from 2003 through to 31 March 2016.Medical subject headings and keyword searches included chronic total occlusion, stent, angioplasty, and percutaneous coronary intervention. Reference lists of selected articles were reviewed for other potentially relevant citations.




**Citation:** Jang JS. Impact of Successful Recanalization of Chronic Total Occlusions Using Coronary Stents on Long-Term Clinical Outcomes: A Meta-Analysis. Austin J Clin Cardiolog. 2017; 4(1): 1054.

**Table 1:** Characteristics of included studies.

| Study | Year | Study period | Subject number | Design | Definition of CTO | Successful PCI | Type of stents | Primary outcomes | Follow-up (months) |
|---|---|---|---|---|---|---|---|---|---|
| Olivari, et al. [5] | 2003 | 1999~2000 | 286/83 | Multicenter, prospective | TIMI 0 or 1, duration >30 days | TIMI 2 or 3, RS <50%, no MACE | BMS | Success, MACE, Symptom status | 12 |
| Hoye, et al. [4] | 2005 | 1992~2002 | 567/304 | Single center, retrospective | TIMI 0 or 1, duration >1 month | RS <50% | Stent in the majority | MACE (death, non-fatal AMI, and repeat revascularization | 60 |
| Arslan, et al. [24] | 2006 | 1999~2003 | 117/115 | Single center, retrospective | TIMI 0, duration >3 months | NA | Stents (91.5%) | All-cause death | 32 |
| Aziz, et al. [25] | 2007 | 2000~2004 | 377/166 | Single center, retrospective | TIMI 0 or 1, duration >3 months | RS <30%, TIMI 3, no dissection | BMS (80.5%), DES (17.3%) | All-cause death | 24 |
| Valenti, et al. [31] | 2008 | 2003~2006 | 344/142 | Single center, retrospective | TIMI 0, duration >3 months | RS <30%, TIMI 3, no complication | SES (42%), PES (58%) | Cardiac survival | 24 |
| de Labrioll, et al. [27] | 2008 | 2003~2005 | 127/45 | Single center, retrospective | TIMI 0, duration ≥3 months | TIMI 3, RS <30% | Stents (93.7%), DES (64.1%) | Success, In-hospital complications, MACE (death, MI, TVR) | 24 |
| Chen, et al. [26] | 2009 | 2004~2005 | 132/20 | Multicenter, prospective | TIMI 0 or 1, duration >3 months | TIMI 3, RS <20% | DES (95.5%) | MACE (cardiac death, MI, and TVR) | 36 |
| Mehran, et al. [29] | 2011 | 1998~2007 | 1226/565 | Multicenter, retrospective | TIMI 0, duration >3 months | RS <50%, TIMI ≥2 | BMS (34.1%), DES (65.9%) | MACE (all-cause death, MI, or TVR) | 60 |
| Lee, et al. [8] | 2011 | 2003~2006 | 251/82 | Multicenter, retrospective | TIMI 0, duration ≥3 months | TIMI 3, RS <30% | SES (75.7%), PES (24.3%) | MACE (death, MI, or TVR) | 36 |
| Niccoli, et al. [13] | 2012 | 2005~2009 | 196/121 | Multicenter, retrospective | TIMI 0, duration >3 months | TIMI 3, RS <30% | SES (60%), PES (40%) | MACE (cardiac death, MI, and repeat revascularization) | 36 |
| Jones, et al. [12] | 2012 | 2003~2010 | 582/254 | Single center, retrospective | TIMI 0, duration ≥3 months | TIMI≥ 2, RS ≤30% | BMS (23.9%), DES (76.1%) | Long-term mortality, further revascularization | 60 |
| Borgia, et al. [11] | 2012 | 2003~2009 | 237/65 | Single center, retrospective | TIMI 0, duration >3 months | TIMI ≥2 | DES (98.2%) | Cardiac death, MACE (cardiac death, MI, TVR) | 48 |
| Jolicoeu, et al. [19] | 2012 | 1999-2008 | 213/133 | Single center, retrospective | TIMI 0 or 1, duration >7 days | RS <40%, TIMI 3, no complication | BMS (50.7%), DES (51.6%) | Composite endpoint of death and cardiovascular rehospitalization | 60 |
| Yang, et al. [14] | 2013 | 2005~2008 | 87/49 | Single center, retrospective | TIMI 0 | RS <20%, TIMI 3, no complication | DES | Cardiac mortality, MACE (death, recurrent MI, repeat revascularization), HF rehospitalization | 24 |
| Ciećwierz, et al. [18] | 2013 | 2005~2007 | 138/139 | Single center, retrospective | TIMI 0 or 1, duration ≥1 month | TIMI 3, RS <10% | DES, BMS | Death, non-fatal MI and MACE (death, non-fatal MI, and symptom driven-revascularization) | 24 |
| Yamamoto, et al. [20] | 2013 | 2005~2007 | 1192/332 | Multicenter, retrospective | TIMI 0 or 1, duration >1 month | TIMI 2 or 3, RS <50% | BMS (22%), DES (78%) | All-cause death | 36 |
| Kim, et al. [28] | 2014 | 2007~2009 | 2045/524 | Multicenter, retrospective | TIMI 0, duration >3 months | TIMI≥ 2, RS ≤30% | SES (35.5%), PES (30%), ZES (21.9%), EES (12.7%) | Composite of cardiac death and MI | 24 |
| Valenti, et al. [30] | 2014 | 2003~2012 | 58/111 | Single center, retrospective | TIMI 0, duration >3 months | TIMI 3, RS <30% | DES | 1-year and 3-year cardiac survival | 36 |
| Lee, et al. [15] | 2016 | 2003~2014 | 1004/169 | Single center, retrospective | TIMI 0, duration ≥3 months | TIMI 3, RS <30% | DES (1st 46.1%, 2nd 53.9%) | All-cause mortality, composite of all-cause death or MI | 60 |

Data are presented as success/failure.

BMS: Bare-Metal Stents; CTO: Chronic Total Occlusion; DES: Drug-Eluting Stents; EES: Everolimus-Eluting Stents; MACE: Major Adverse Cardiac Events; MI: Myocardial Infarction; NA: Not Available; PES: Paclitaxel-Eluting Stents; RS: Residual Stenosis; SES: Sirolimus-Eluting Stents; TIMI: Thrombolysis in Myocardial Infarction; TVR: Target Vessel Revascularization; ZES: Zotarolimus-Eluting Stents

## Study selection and data extraction

The investigator (J.-S.J.) conducted the literature search, data extraction, and quality assessment by using a standardized data extraction form. Selected publications were reviewed by the same investigators to assess if studies met the inclusion criteria: randomized or observational studies comparing clinical outcomes of successful versus unsuccessful recanalization of CTO lesions after coronary stent implantation. The minimum follow-up period required for inclusion was one year. Studies including patients treated with balloon angioplasty alone were excluded from the inclusion.

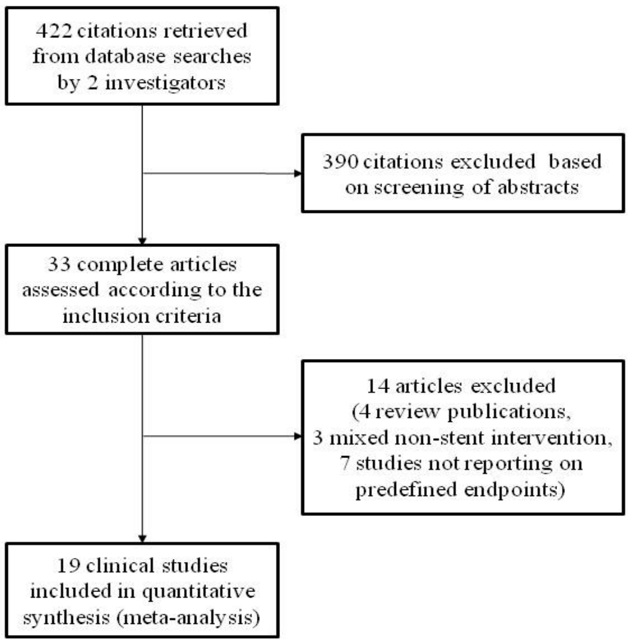


**Figure 1:** Trial flow chart shows number of studies retrieved by individual searches and number of trials included in review.

Relevant information was extracted from the articles including patient characteristics (mean age, gender distribution, risk factors), study period, study design, publication year, sample size, type of stent used, left ventricular ejection fraction, and duration of follow-up.

## End points

The end points of this study were all-cause mortality, Myocardial Infarction (MI), Major Adverse Cardiac Events (MACE), and incidence of Coronary Artery Bypass Surgery (CABG) at the available follow-up. CTO was defined as a complete obstruction of the vessel exhibiting Thrombolysis in Myocardial Infarction (TIMI) flow grade 0 or 1 and an estimated duration of ≥3 months except 5 study [4,5,18-20] which required from 7 to 30 days' occlusion for its definition. Death was defined as mortality from any cause. The trial-specific definitions of MI and MACE were used because of different definition across studies. Successful recanalization of CTO was defined as restoration of TIMI flow grade 2 or 3 with a residual stenosis ≤20~50% after stent implantation without procedural complications.

## Data synthesis and analysis

Random effects models were used to produce across-study summary Odds Ratios (ORs) with 95% Confidence Intervals (CIs). All p values were 2-tailed, with statistical significance set at 0.05. Statistical heterogeneity was assessed between trials with $I^2$ statistic, which is derived from Cochran's Q and the degree of freedom

**Table 2**: Characteristics of patients.

| Study | Age | Male gender (%) | Hypertension (%) | Diabetes (%) | Hyperlipidemia (%) | Current smoker (%) | Prior MI (%) | Prior PCI (%) | Prior CABG (%) | ACS (%) | LVEF (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Olivari, et al. [5] | 58/59 | 86/85 | 53/54 | 17/20 | 59/56 | 37/30 | 69j/69 | 11/18 | 5/7 | 18/5 | 56/56 |
| Hoye, et al. [4] | 60/61 | 74/74 | 20/21 | 12/9 | 49/43 | NA | 56/49 | 24/23 | 9/10 | NA | NA |
| Arslan, et al. [24] | 61/60 | 75/75 | 27/24 | 26/24 | 27/24 | 35/38 | 40/45 | NA | NA | NA | 5050 |
| Aziz, et al. [25] | 59/59 | 76/81 | 48/57 | 14/9 | 91/88 | 18/21 | 58/58 | 3/5 | 4/7 | 12/19* | 53/53 |
| Valenti, et al. [31] | 67/70* | 81/83 | 57/57 | 24/21 | 50/51 | 20/22 | 45/54 | 25/30 | 8/18* | 39/32 | 42/41 |
| de Labrioll, et al. [27] | 61/64 | 72/87 | 82/80 | 19/41* | 94/80* | 21/11 | 21/22 | 24/29 | 12/16 | 58/53 | 50/48 |
| Chen, et al. [26] | 64/68 | 74/80 | 76/65 | 26/25 | 20/20 | 35/35 | 46/65 | NA | NA | 80/90 | 45/42 |
| Mehran, et al. [29] | 61/62 | 85/89* | 60/59 | 23/22 | 66/61* | 23/28* | 47/56* | NA/NA | 14/21* | NA/NA | 54/53* |
| Lee, et al. [8] | 59/64* | 77/71 | 50/50 | 31/31 | 22/28 | 34/32 | 18/29* | 16/33* | NA/NA | 41/31 | 56/55 |
| Niccoli, et al. [13] | 64/66 | 82/88 | 70/66 | 34/37 | 54/47 | 42/31 | 32/26 | NA/NA | 15/10 | NA/NA | NA/NA |
| Jones, et al. [12] | 63/64 | 76/79 | 64/67 | 27/29 | 56/61 | NA/NA | 32/36 | 21/36* | 7/17* | NA/NA | 56/54 |
| Borgia, et al. [11] | 64/65 | 82/82 | 60/61 | 26/31 | 75/89* | 36/36 (current or former) | 58/60 | 36/42 | 14/31* | 8/7 | 53/53 |
| Jolicoeu, et al. [19] | 58/61* | 70/79 | 70/74 | 33/26 | 66/71 | 53/50 | 21/29 | 24/18 | 18/28* | NA | 56/55 |
| Yang, et al. [14] | 66/69 | 82/82 | 70/76 | 36/37 | 20/22 | 39/37 | 26/33 | NA | NA | NA | 46/47 |
| Ciećwierz, et al. [18] | 62/62 | 80/80 | 62/57 | 23/19 | 38/33 | 12/12 | NA | NA | NA | NA | NA |
| Yamamoto, et al. [20] | 67/66 | 78/66 | 83/87 | 42/42 | NA | 33/36 | 32/24* | NA | NA | 9/19* | 56/54 |
| Kim, et al. [28] | 63/64* | 73/77 | 63/63 | 35/38 | 38/36 | 32/30 | 13/19* | 24/31* | 2/5* | 43/44 | NA |
| Valenti, et al. [30] | 64/69* | 85/73 | 55/67 | 17/15 | 36/41 | 50/30* | 19/29 | NA | 2/10 | 91/87 | 36/38 |
| Lee, et al. [15] | 59/61 | 83/83 | 60/65 | 31/32 | 64/59 | 27/23 | 8/14* | 20/21 | 3/4 | 27/21 | 58/58 |

Data are presented as success/failure. *p<0.05.

CABG: Coronary Artery Bypass Grafting; LVEF: Left Ventricular Ejection Fraction; MI: Myocardial Infarction; NA: Not Available; PCI: Percutaneous Coronary Intervention.

[100×(Q-df)/Q] [21]. $I^2$ values greater than 25%, 50%, and 75% were considered evidence of low, moderate, and severe statistical heterogeneity, respectively. In case of heterogeneity across the studies, I performed sensitivity analyses, serially excluding studies to determine the source of heterogeneity. The likelihood of publication bias was examined by visual inspection of constructed funnel plot for the all-cause mortality and mathematically by means of Egger's test (p for significant asymmetry <0.1) [22]. For specific evaluation of the presence and extent of publication bias, *I* used trim-and-fill method according to Duval and Tweedie [23], which imputes missing studies in the funnel plot based on symmetry assumptions. All statistical analyses were performed using the Review Manager Version 5.2 (The Nordic Cochrane Center, Copenhagen, Denmark) and MIX version 2.0 (Biostat XL, Sunnyvale, CA, USA).

## Results

A total of 422 publications were reviewed and 32 articles were selected for inclusion and further evaluation. Subsequently, 19 clinical studies were included into the final analysis (Figure 1) [4,5,8,11-15,18-20,24-31]. Characteristics of the included studies are summarized in (Table 1). Of the 12,598 patients, 9,179 patients comprised the successful PCI group and 3,419 patients comprised the unsuccessful PCI group. The success rate of CTO intervention was 72.9% in our study. Seven studies [5,8,13,20,26,28,29] were multicenter trials whereas the other studies [4,8,11,12,14,15,18,19,24,25,27,31] were single center trials. Baseline characteristics of patients are summarized in (Table 2). To identify possible differences between groups, preprocedural prevalence of risk factors (hypertension, diabetes, and hyperlipidemia), left ventricular ejection fraction, and proportion of patients with acute coronary syndrome were extracted and compared (Table 2). Proportion of patients with multivessel disease and location of involved coronary arteries were presented in (Supplementary Table 1).

### All-cause mortality

Eighteen studies reported all-cause mortality. There were 455 (5.0%) deaths of 9,041patients after successful CTO recanalization compared to 339 (10.3%) among 3,280 patients after unsuccessful CTO recanalization, corresponding to 52% relative reduction with successful recanalization (OR 0.48, 95% CI 0.38 to 0.61, p<0.001; (Figure 2)). The Number Needed to Treat (NNT) to prevent with 1 death with successful CTO recanalization of CTO was 20. Mild statistical heterogeneity was noted among the trials (heterogeneity $\chi^2$ = 30.35, $I^2$ = 43 %, p = 0.03). The sensitivity analysis limited to the 7 multicenter studies [5,8,13,20,26,28,29] did not change the significance of the overall estimates (OR 0.60, 95% CI 0.45-0.82, p = 0.001). The sensitivity analysis of the risk of mortality with successful recanalization after exclusion of one study at a time yielded effect sizes similar in magnitude and direction to the overall estimates.

### Myocardial infarction

Sixteen studies reported data on MI [4,5,8,11,13-15,19,20,24,26-31]. Two hundred fifty total MI occurred among the 8,082patients with successful CTO recanalization and 156 in the 2,860 patients with unsuccessful recanalization. The risk of MI at 12 to 60 months was significantly lower in successful PCI group (OR 0.67, 95% CI 0.46 to 0.97, p = 0.05; (Figure 3)). Statistical heterogeneity was noted among the included studies (heterogeneity $\chi^2$ = 26.87, $I^2$ = 48%, p = 0.02).

### Major adverse cardiac events

Sixteen studies including 9,694 patients were included for the analysis of MACE [4,5,8,11,13-15,18,19,24,26-31]. Overall, 1,071 among 7,028 patients with successful CTO recanalization developed MACE compared with 749 among 2,666 patients after unsuccessful recanalization. Successful CTO recanalization was associated with a significantly lower incidence of MACE compared to the patients with unsuccessful recanalization (OR 0.55, 95% CI 0.42 to 0.73, p<0.001; (Figure 4)). Statistical heterogeneity was observed across the studies (heterogeneity $\chi^2$ = 69.63, $I^2$=78%, p<0.001).

### Coronary Artery Bypass Graft Surgery (CABG) and angina relief

Fifteen studies reported CABG [4,5,11-15,18-20,25,28-31] and the pooled analysis showed a consistent 86% relative reduction in the incidence of CABG with successful recanalization of CTO lesions

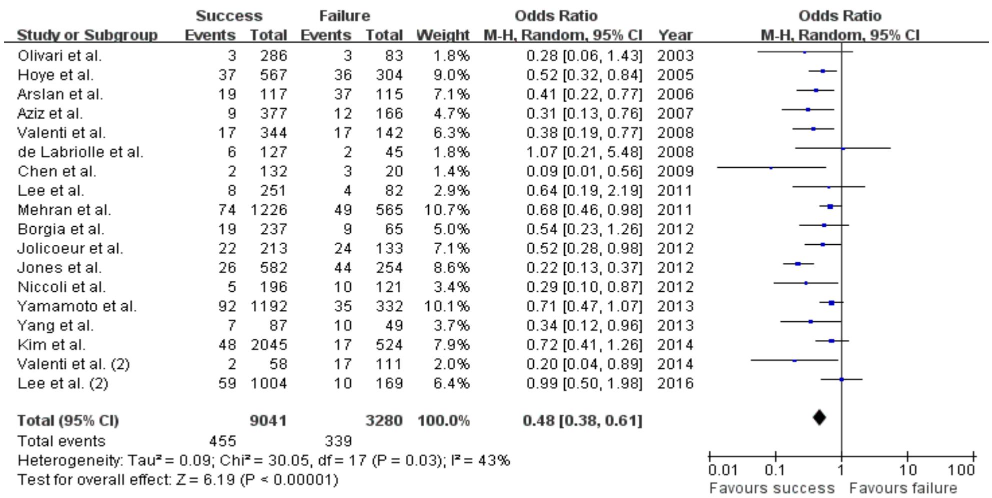


**Figure 2:** ORs for all-cause mortality with successful versus unsuccessful recanalization of CTO. The incidence of all-cause mortality was lower in successful recanalization group.

CI: Confidence Interval; OR: Odds Ratio; M-H: Mantel-Haenszel

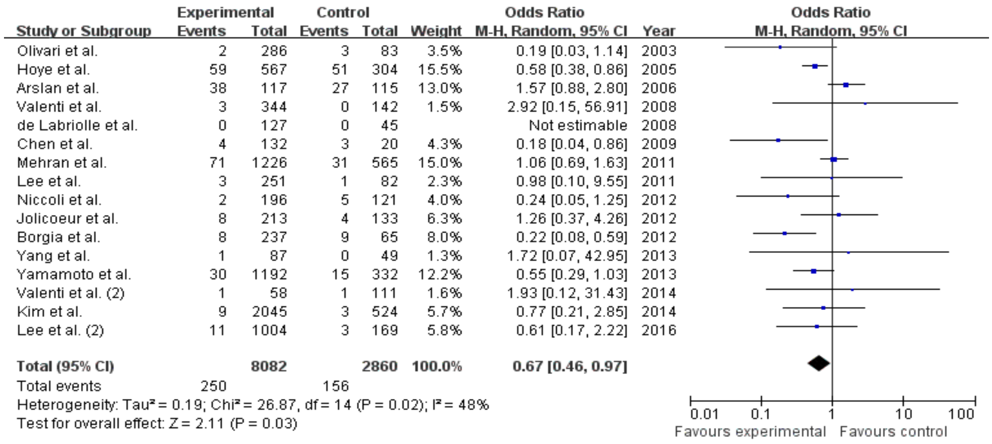


**Figure 3:** ORs for MI with successful versus unsuccessful recanalization of CTO. The risk of MI did not differ significantly between the two groups.
CI: Confidence Interval; OR: Odds Ratio; M-H: Mantel-Haenszel.

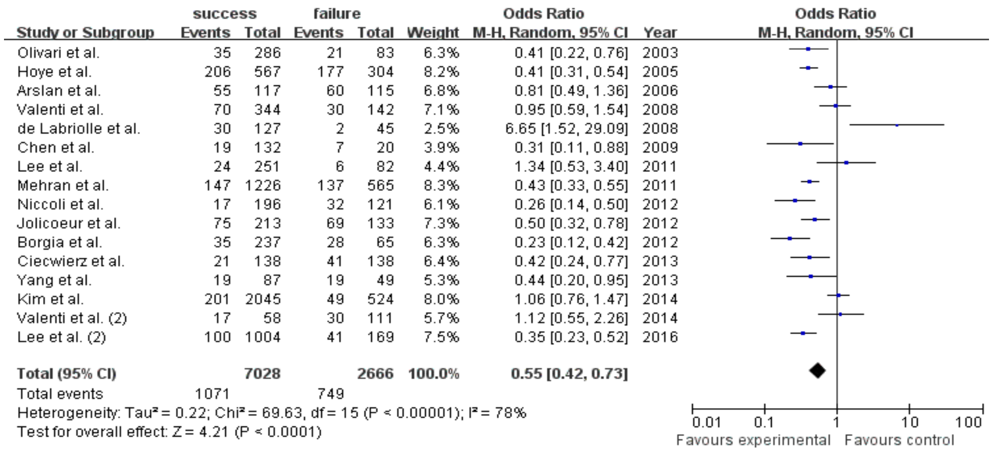


**Figure 4:** ORs for MACE with successful versus unsuccessful recanalization of CTO. Successful CTO recanalization was associated with a significantly lower incidence of MACE compared to the patients with unsuccessful recanalization.
CI: Confidence Interval; OR: Odds Ratio; M-H: Mantel-Haenszel.

(OR 0.14, 95% CI 0.10 to 0.20, p<0.001; (Figure 5)). Nine patients were needed to treat with successful CTO recanalization to prevent 1 CABG. Statistical heterogeneity was observed among the included studies (heterogeneity $\chi^2 = 38.61$, $I^2 = 64\%$, p<0.001). Data about relief of angina symptom by successful CTO recanalization was reported in 3 studies. Successful CTO PCI was associated with a significantly higher angina relief compared to the patients with unsuccessful recanalization (OR 7.47, 95% CI 2.43 to 22.93, p<0.001).

### Publication bias

Assessment of publication bias using OR of all-cause mortality of the included studies demonstrates a symmetric funnel plot with no evidence of publication bias (Figure 6), confirmed by means of a negative Egger's regression-based test (p=0.11). The trim-and-fill method indicated that 5 studies were needed to achieve a symmetrical funnel plot.

## Discussion

In the present meta-analysis, the investigator found that successful recanalization of CTO was associated with lower all-cause mortality and risk of MACE. In addition, successful CTO PCI reduced the need for a subsequent CABG by 86%. Our study includes the largest cohort to date and demonstrates statistically significant survival benefit in favor of successful recanalization of CTO using coronary stent implantation.

Because CTO is present in at least one coronary artery in approximately one third among patients undergoing PCI [2,32] improving symptoms and clinical outcomes through successful recanalization of these patients have been one of the major challenges of interventional cardiologists. The principal barrier to CTO PCI has been procedural failure due to a failure to cross the culprit lesion with guide wire or balloon catheter [2,33]. However, the remarkable development of devices and techniques in CTO PCI as well as increased operator experiences have led to higher rates of successful recanalization of CTO vessels [34-36]. Moreover, coronary stents significantly increased long-term patency of recanalized vessel and drug-eluting stents have further improved angiographic outcomes [37,38]. Pancholy, et al. [39] have performed a meta-analysis including 13 observational studies comparing successful versus

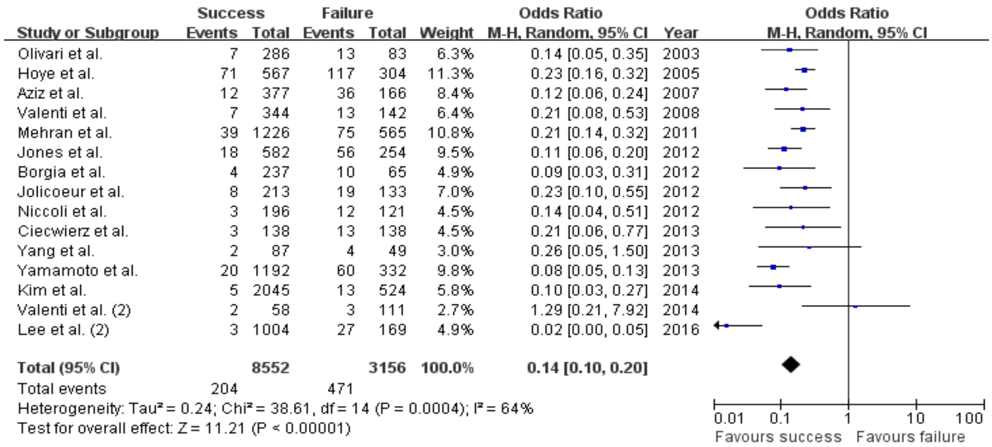


**Figure 5:** ORs for need of CABG with successful versus unsuccessful recanalization of CTO. Pooled analysis showed a consistent 86% relative reduction with successful recanalization of CTO lesions.
CI: Confidence Interval; OR: Odds Ratio; M-H: Mantel-Haenszel.

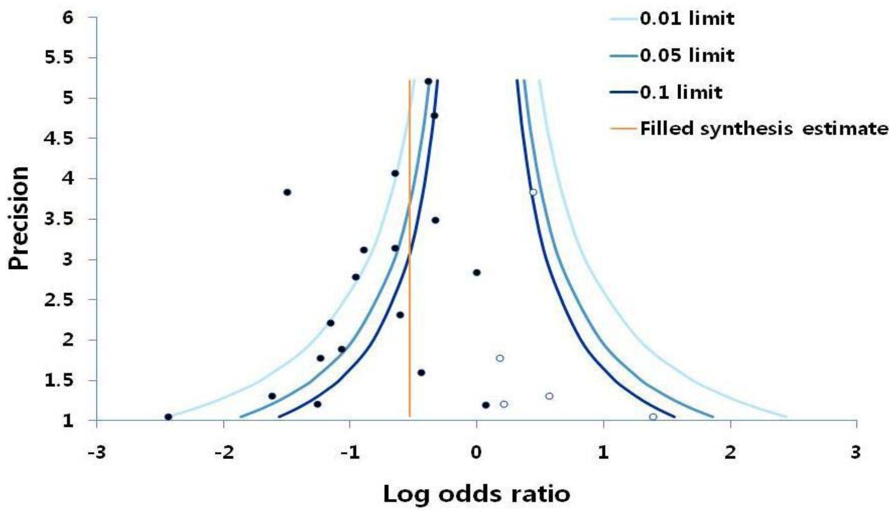


**Figure 6:** Funnel plots for assessment of publication bias. Assessment of publication bias using ORs of all-cause mortality illustrates a symmetrical funnel plots with no evidence of publication bias confirmed by negative Egger's test (p = 0.11). The trim-and-fill method indicated that 5 missing study was needed to achieve a symmetrical funnel plot.
CI: Confidence Interval; OR: Odds Ratio; M-H: Mantel-Haenszel.

unsuccessful CTO PCI. They reported that successful recanalization of CTO was associated with a significant reduction in short (OR 0.218, 95% CI 0.095 to 0.498) and long-term mortality (OR 0.391, 95% CI 0.311 to 0.493) compared to unsuccessful CTO PCI. Although the authors intended to exclude studies with balloon angioplasty alone without stenting or studies using stents in <70% of patients, studies with limited use of stent-based PCI could not be completely excluded. Results of the present study correspond to those of the previous studies [39-41]. However, analyses of 19 clinical studies from the present work, including >12,000 patients, further support the benefits of successful CTO recanalization with an OR of 0.48 for all-cause mortality in favor of successful recanalization as compared with unsuccessful recanalization without profound heterogeneity or evidence of publication bias. In addition, coronary stents data were extracted exclusively from the included studies and excluded studies using stents in less than 70% of patients.

It is well known that the presence of a CTO in patients suffering from acute anterior MI increase mortality [42]. Hence, successful restoration of blood flow might have potential to reduce fatal complications during a subsequent infarct. In addition, the presence of a CTO is a risk factor for incomplete revascularization, which increase mortality compared to complete revascularization [43]. However, improved long-term survival from complete revascularization in the presence of CTO might not solely stem from higher recanalization rates itself, but also related with several other factors like patients' comorbidities, extent of viable myocardium, and global left ventricular function. Despite unclear prognostic implication, restoration of blood flow by successful recanalization of true lumen help improve left ventricular function, [10,44,45] decrease predisposition to fatal arrhythmias [2], and reduce risk of adverse clinical outcomes. However, it is still unclear whether increased rate of successful restoration of blood flow to the occluded true lumen may directly extrapolate into increased survival in patients with long-standing CTO lesion. Lee, et al. [15] reported that the survival and Q-wave MI rates during 4.6 years follow-up period were not significantly differ whether patients received a successful or failed CTO PCI in their longitudinal experience of consecutive CTO procedures over 11 years.

In this study, clinical outcomes of patients after successful recanalization of CTOs were better and our results further supports the evidence suggesting a survival advantage of successful recanalization compared with unsuccessful PCI. The result of our study corresponds to previous studies reporting similar incidence of MI [7,41]. However, benefits of opening CTO successfully by PCI might not be compared with PCI failure and the resultant ominous outcomes that frequently accompany several complications. There is an urgent need for randomized trials in view of the potential for medical treatment of CTO to reduce adverse clinical events when compared to the attempt to negotiate CTO lesions. The DECISION-CTO (Drug-Eluting Stent Implantation Versus Optimal Medical Treatment in Patients with Chronic Total Occlusion trial; NCT01078051) is currently underway and I expect this study might address the definitive proof of a beneficial effect of successful CTO PCI.

The present study has several limitations to be addressed. First, included studies are relatively small and heterogeneous in size. Second, I could not have access to patient-level data to predict which subgroup of patients could achieve better outcomes after successful recanalization of CTO. There might be wide variability in risk profile and lesion complexity of the included patients. Patients with unsuccessful recanalization are more likely to have heavy calcifications and long lesions [5,46]. Furthermore, there was no data comparing post-interventional medical treatment between patients with successful versus unsuccessful recanalization of CTO. Third, definitions of CTO, successful recanalization of CTO, and end points were different across the included studies. Fourth, some results of the present meta-analysis have significant heterogeneity, which is frequent in meta-analysis performed on global data. Thus, I tried to overcome heterogeneity by sensitivity analysis according to study design. Fifth, proportion of patients who received stents and types of used stents were different among the included studies. Finally, in spite of highly selective tools for retrieval of eligible studies from database search, some relevant studies might have been overlooked.

## Conclusion

This meta-analysis suggested that successful recanalization of CTO lesions using coronary stent is associated with improvement in all-cause mortality, and the need for subsequent CABG compared to unsuccessful CTO PCI. Adequately powered randomized trials to assess patient-oriented outcomes should be conducted in order to definitely assess the efficacy of CTO recanalization in participants with different risk profiles and lesion complexities.

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Austin J Clin Cardiolog - Volume 4 Issue 1 - 2017
**ISSN : 2381-9111** | www.austinpublishinggroup.com


**Citation:** Jang JS. Impact of Successful Recanalization of Chronic Total Occlusions Using Coronary Stents on Long-Term Clinical Outcomes: A Meta-Analysis. Austin J Clin Cardiolog. 2017; 4(1): 1054.