Lesion Characteristics and Procedural Complications of Chronic Total Occlusion Percutaneous Coronary Intervention in Patients with Prior Bypass Surgery: A Meta-analysis

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Abstract

BACKGROUND: Coronary artery bypass graft (CABG) accelerates the prevalence of native coronary chronic total occlusion (CTO), and this kind of CTO shows more advanced and complex atherosclerotic pathology. As a result, the procedural success rate of percutaneous coronary intervention (PCI) is inferior to another kind of lesions. The present meta-analysis aims to compare the lesion characteristics and procedural complications of CTO-PCI in patients with or without prior CABG.

METHODS: A total of 8 studies, comprising of 13439 patients, published from inception to August 2021 were included in this meta-analysis. Results were pooled using random effects model and are presented as odds ratio (OR) with 95% confidence intervals (95% CIs).

RESULTS: From the 13439 patients enrolled, 3349 (24.9%) patients had previous CABG and 10090 (75.1%) formed the control group in our analysis. For the clinical characteristic, compared to the non-CABG patents, prior CABG patients were older (OR, 3.98; 95% CI, 3.19-4.78; P<0.001; I^2=72%), had more male (OR, 1.30; 95% CI, 1.14-1.49; P<0.001; I^2=6%), diabetes mellitus (OR, 1.54; 95% CI, 1.36-1.73; P<0.001; I^2=37%), dyslipidemia (OR, 1.89; 95% CI, 1.33-2.69; P<0.001; I^2=81%), hypertension (OR, 1.88; 95% CI, 1.46-2.41; P<0.001; I^2=71%), previous myocardial infarction (OR, 1.94; 95% CI, 1.48-2.56; P<0.001; I^2=85%), and previous PCI (OR, 1.74; 95% CI, 1.52-1.98; P<0.001; I^2=22%). Non-CABG patents had more current smoker (OR, 0.45; 95% CI, 0.27-0.74; P<0.001; I^2=91%). BMI (OR, -0.01; 95% CI, -0.07-0.06; P=0.85; I^2=36%) were similar in both groups. For lesions location, the right coronary artery (RCA) was predominant target vessel in both groups (50.5% vs 48.7%; P□0.49), although, the left circumflex (LCX) was more frequently CTO in the prior CABG group (27.3% vs 18.9%; P□0.01), while left anterior descending artery (LAD) in non-CABG ones (16.0% vs 29.1%; P□0.01). For lesions characteristics, prior CABG patients had more blunt stump (OR, 1.71; 95% CI, 1.46-2.00; P<0.001; I^2=40%), proximal cap ambiguity (OR, 1.45; 95% CI, 1.28-1.64; P<0.001; I^2=0.0%), severe calcifications (OR, 2.91; 95% CI, 2.19-3.86; P<0.001; I^2=83%), more bending (OR, 3.07; 95% CI, 2.61-3.62; P<0.001; I^2=0%), lesion length > 20 mm (OR, 1.59; 95% CI, 1.10-2.29; P=0.01; I^2=83%), inadequate distal landing zone (OR, 1.95; 95% CI, 1.75-2.18; P□0.001; I^2=0.0%), distal cap at bifurcation (OR, 1.65; 95% CI, 1.46-1.88; P<0.001; I^2=0.0%), and higher J-CTO score (SMD, 0.52; 95% CI, 0.42-0.63; P<0.001; I^2=65%). But side branch at proximal entry (OR, 0.88; 95% CI, 0.72-1.07; P=0.21; I^2 =45%), in-stent CTO (OR, 0.99; 95% CI, 0.86-1.14; P=0.88; I^2=0.0%), lack of interventional collaterals (OR, 0.80; 95% CI, 0.55-1.15; P=0.23; I^2=78%), and previously failed attempt (OR, 0.73; 95% CI, 0.48-1.11; P=0.14; I^2=89%) were similar in both groups. For complication, prior CABG patients had more perforation with need for intervention (OR, 1.91; 95% CI, 1.36-2.69; P<0.001; I^2=34%), contrast-induced nephropathy (OR, 3.40; 95% CI, 1.31-8.78; P=0.01; I^2=0.0%). Non-CABG patents had more tamponade (OR, 0.25; 95% CI, 0.09-0.72; P=0.01; I^2=0.0%), and the major bleeding complication (OR, 1.18; 95% CI, 0.57-2.44; P=0.65; I^2=0%) were no significant difference in both groups.

CONCLUSION: Patients undergoing CTO-PCI with prior CABG have more complex lesion characteristics, though procedural complication rates were comparable.

Introduction

Coronary chronic total occlusion (CTO) is characterized by a complete occlusion of anterograde blood flow (TIMI grade 0 flow) in coronary artery, present more than 3 months. The prevalence of CTO in patients with known coronary artery disease is between 30–50%, and identified in 20% of all coronary angiographies. CTO percutaneous coronary intervention (PCI) represents one of the most challenging field of interventional cardiology. Owing to the complexity of CTO-PCI, only 10–15% of CTO patients attempted to receive interventional revascularization, and more patients are undergoing coronary artery bypass grafting (CABG) surgery[1]. CABG significantly improved the long-term clinical outcomes for the treatment of complex coronary lesions indeed. On the other hand, CABG itself can accelerate the development of atherosclerosis of native coronary arteries, leading to development of a new CTO in up to 43% of the bypassed native arteries as early as 1 year after CABG. And the prevalence of native artery CTO in patients undergoing coronary angiography reaches 54% in the post-CABG population, higher than in patients without CABG[2]. However, repeat CABG was associated with worse long-term clinical outcomes as compared to initial CABG. And saphenous vein graft PCI also have high rates of failure. Therefore, for these cases, PCI of the native arteries CTO was preferred as revascularization strategy.

However, several reports have identified previous CABG as a predictor of procedural failure in CTO-PCI. In particular, patients who have undergone previous CABG have exhibit extensive calcification, fibrosis, inflammation and negative remodeling compared with CTO in CABG-naïve patients for pathologic examination[3]. As such, previous CABG has consequently been included as a risk factor for technical failure in the Registry of CrossBoss and Hybrid procedures in France, the Netherlands, Belgium, and United Kingdom (RECHARGE) score[4]. Therefore, prior studies have found that CTO-PCI in post-CABG patients were associated with higher complexity, lower success rates and higher rates of complications compared with CABG-naïve patients. Over the past decade, thanks to the remarkable development of contemporary algorithms, revascularization techniques, and devices in CTO-PCI procedures, CTO-PCI success rates have approached 90% for experienced operators currently[5]. Thus, successful revascularization by PCI has emerged as a promising alternative treatment for CTO lesions in post-CABG patients.

However, the long-term outcomes of CTO-PCI for a native coronary artery in previous CABG status have been sparsely studied, and it remains unclear whether the higher procedural difficulty encountered during CTO-PCI in patients who have undergone CABG is also mirrored by worse outcomes at follow-up. Some recent studies investigated the clinical outcomes of CTO-PCI in previous CABG patients; however, the results were inconsistent. Thus, whether the higher procedural complexity encountered during CTO-PCI in previous CABG patients translated into poor clinical outcomes is yet to be clarified. Given the increasing prevalence of patients with bypass graft failure, along with the implementation of novel interventional approaches, characterization and risk stratification of these patients gained further importance. To shed further light on this issue, we conducted a systematic review and meta-analysis to assess clinical and procedural characteristics as well as in-hospital major complications of CTO-PCI in patients with and without CABG.

Methods

Study objectives

We conducted a meta-analysis of observational studies according to established methods and standards recommended by the Cochrane collaboration. The aim of this systematic review and meta-analysis was to compare the angiographic characteristics and clinical outcomes of CTO-PCI in patients with and without prior CABG.

2.1. Data sources and search strategy

Two investigators (Yuchen Shi and Songyuan He) independently performed a comprehensive search of the PubMed, Embase and Cochrane Library databases from inception to August 15, 2021 using the following search terms: (1) coronary occlusion, chronic total occlusion, and CTO; (2) percutaneous coronary intervention and PCI; (3) coronary artery bypass, coronary bypass, bypass surgery and CABG.

2.2. Study selection

Studies were included when the following were satisfied: (1) studies with patients treated for coronary CTO by PCI, in which CTO was defined as a TIMI grade 0 flow in coronary artery for more than 3 months; (2) studies with comparisons of CTO-PCI in patients with and without prior CABG; (3) studies that reported the angiographic characteristics and in-hospital clinical outcomes in both groups. For duplicate publications, if the duplicate reports reflecting the same population, we selected the report with longer follow-up duration. And case reports, reviews, notes, letters, commentaries, and editorials were excluded.

2.3. Endpoints

The angiographic characteristics of the enrolled studies included blunt stump, degree of calcification, bending, lesion length, previously failed attempt, proximal cap ambiguity, situation of interventional collaterals, side branch at proximal entry, in-stent CTO, inadequate distal landing zone, distal cap at bifurcation and J-CTO score. The in-hospital clinical complication included perforation with need for intervention, tamponade, major bleeding, and contrast-induced nephropathy.

2.4. Statistical analysis

For dichotomous data, the random-effects model with the Mantel-Haenszel method was used as a summary statistic to calculate the pooled odds ratio (OR) with the 95% confidence intervals (95% CIs). For continuous data, standard mean differences (SMD) calculated according to the inverse-variance method was used. Statistical heterogeneity was assessed using Cochrane's Q via the chi-square test and further quantified with the I^2 statistic. And 25%, 50%, and 75% indicated low, moderate, and high heterogeneity, respectively. All statistical analyses were conducted using Review Manager 5.4.1 version (RevMan, The Cochrane Collaboration, Copenhagen, Denmark).

Results

1. Characteristics of the studies and patients included

Figure 1 shows the flowchart of the study selection. As a result, a total of 2838 studies were identified through the electronic searches. Then, 2829 studies were excluded after reading the titles and abstracts. The remaining 9 studies were assessed by reading the full texts. Eventually, 8 studies comprising a total of 13439 patients met the inclusion criteria, and were included in qualitative synthesis and meta-analysis[6-12]. The baseline characteristics of the studies included in this meta-analysis are summarized in Tables 1. Out of the 13439 patients enrolled, 3349 (24.9%) presented with previous CABG and 10090 (75.1%) formed the control group for the present analysis. Patients who had undergone CABG were older □68.0±8.8 years vs 64.3±10.3 years; $P<0.001$□, were mostly men□87.2% vs 84.0%; $P<0.001$□, but the BMI had no different □29.6±5.4 vs 29.2±6.0; $P=0.85$□. For past medical history, there were more previous myocardial infarction□54.7% vs 36.7%; $P<0.001$□and previous PCI □65.7% vs 48.1%; $P<0.001$□. For risk factors, post-CABG patients had a higher prevalence of diabetes mellitus□45.2% vs 33.8%; $P<0.001$□, hypertension□88.3% vs 76.7%; $P<0.001$□and dyslipidemia□89.4% vs 76.5%; $P<0.001$□,but the current smoking prevalence was lower □13.6% vs 24.5%; $P=0.002$□.

2. Angiographic characteristics

2.1 Lesions location

All studies reported the lesions location, which involved 3422 lesions in post-CABG group and 10430 lesions in no-CABG group. The CTO lesions ratio distributions are shown in Table 2. The right coronary artery (RCA) was the main target vessel in both groups (50.5% vs 48.7%; P□0.49), although, the left circumflex (LCX) was more frequently CTO in the prior CABG group (27.3% vs 18.9%; P□0.01), while left anterior descending artery (LAD) in non-CABG patients (16.0% vs 29.1%; P□0.01).

2.2 Blunt stump

4 studies involving a total of 1914 patients in prior CABG group and 5352 patients in non-CABG patients, reported the incidence of blunt stump in those allocated to pCABG 56.1% (1074 of 1914) or nCABG 44.2% (2367 of 5352) treatment. The pooled outcomes revealed that patients with prior CABG undergoing CTO PCI often have severe blunt stump compared with no-CABG group (OR = 1.71, 95% CI: 1.46-2.00, P□0.001). And low heterogeneity was found among these trials (I^2= 40%, P = 0.17; Fig. 2)

2.3 Side branch at proximal entry

Figure 3 pooled analysis of 3 studies from 5208 patients revealed 2507 events (48.1%): per treatment, the event rate was 48.1% (728 of 1513) in the prior CABG group and 48.1% (1779 of 3695) in the non-

CABG group. No significant difference was observed between the two groups and the overall OR was 0.88 (95% CI: 0.72-1.07, P=0.21), with moderate heterogeneity (I^2 =45%, P=0.16).

2.4 Proximal cap ambiguity

Proximal cap ambiguity in angiographic makes PCI more complex. Only 3 studies involved 5208 participants and 1849 events (35.5%), but a positive result was found. Regarding treatment, 41.5% (628 of 1513) occurred in prior CABG group and 33.0% (1221 of 3695) in non-CABG treated group. The results were OR = 1.45 and 95% CI: 1.28-1.64 ($P<0.001$), with no heterogeneity (I^2 = 0.0%, P = 0.47; Fig. 4)

2.5 Moderate or severe calcifications

A total of 6 studies reported the degree of calcification in both groups, which involved 10905 patients. Figure 2 includes data on the moderate or severe calcifications in both groups. Pooled data analysis revealed 4613 calcification (overall rate 42.3%). Regarding treatment, calcification occurred in 60.0% (1447 of 2412) of prior CABG treated patients and 37.3% (3166 of 8493) of non-CABG treated patients. The overall OR was 2.91 (95% CI: 2.19-3.86, $P<0.001$), and high degree of heterogeneity was found among these trials (I^2 =83%, $P<0.001$; Fig. 5)

2.6 Bending

Only 3 studies involving a total of 1211 patients reported 4613 bending (overall rate 42.3%) in both groups. Regarding treatment, bending occurred in 53.6% (425 of 793) of prior CABG treated patients and 26.3% (786 of 2987) of non-CABG treated patients. The pooled outcomes revealed the OR was 2.91 (95% CI: 2.19-3.86, $P<0.001$), and no heterogeneity was found for bending incidence(I^2 = 0.0%, P = 0.8; Fig. 6)

2.7 Lesion length

Lesion length > 20 mm have been well recognized as an unfavorable characteristic in angiographic. 4 studies reported this characteristic, which involved 5782 patients and 3553 events in both groups (overall rate 61.4%). Among these patients, 67.8% (736 of 1085) occurred in prior CABG treated group and 60.0% (2817 of 4697) in non-CABG treated group. The pooled outcomes revealed the OR was 1.59 (95% CI: 1.10-2.29, P=0.001), with high heterogeneity (I^2 =83%, $P<0.001$; Fig. 7).

2.8 In-stent CTO

In-stent CTO was reported in 5 studies from 8903 patients and 1242 (overall rate 14.0%) was found. However, no significant difference was found between the two groups: per treatment, the event rate was

14.3% (304 of 2120) in the prior CABG group and 13.8% (938 of 6783) in the non-CABG group. The pooled OR value was 0.99 (95% CI: 0.86-1.14, P=0.88; Fig. 8), and there was no heterogeneity (I^2 = 0.0%, P=0.44).

2.9 Lack of interventional collaterals

The outcome occurred in 2013 events among 5208 participants (38.7%) from 3 studies, finding a negative result. Among these patients, 36.8% (557 of 1513) in the prior CABG treated patients and 39.4% (1456 of 3695) in non-CABG treated patients (OR: 0.80, 95% CI: 0.55-1.15, P=0.23), with high heterogeneity (I^2 =78%, P=0.01; Fig. 9).

2.10 Inadequate distal landing zone

A total of 7266 patients were included in 4 studies reporting this event. And the incidence was 33.7% (2448 of 7266) in overall rate. Compared with treatment method, 44.1% (844 of 1914) in the prior CABG group and 30.0% (1604 of 5352) in the non-CABG group. The pooled OR value was 1.95 (95% CI: 1.75-2.18, $P<0.001$; Fig. 10), and there was no heterogeneity (I^2 = 0.0%, P=0.54).

2.11 Distal cap at bifurcation

For bifurcation at the distal cap during CTO PCI, only 3 studies were included, reporting 1646 events among 5208 individuals (overall rate 31.6%), but finding a positive result. The incidence was significantly higher in patients with prior CABG (40.0%, 605 of 1513), when compared with non-CABG patients (28.2%, 1041 of 3695). The pooled outcomes revealed the OR was 1.65 (95% CI: 1.46-1.88, $P<0.001$), with no heterogeneity (I^2 = 0.0%, P = 0.49; Fig. 11)

2.12 Previously failed attempt

Previously attempted but failed were more common among harder CTO cases. Five studies provided this data, reporting 1677 events among 8573 individuals (19.6%). Regarding treatment, 18.0% (417 of 2313) occurred in prior CABG group and 20.1% (1260 of 6260) in non-CABG treated group. The pooled outcomes revealed that the rate of previously failed attempt did not vary significantly between two groups (OR: 0.73 [95% CI, 0.48-1.11], P=0.14; I^2 = 89%, heterogeneity $P<0.001$; Fig. 12).

2.13 J-CTO score

Four studies provided data regarding the comparison of J-CTO score between the two groups which involved 7255 patients: 26.3% (1914 of 7255) in the prior CABG group and 73.7% (5352 of 7255) in the non-CABG group. The score was significantly higher in patients with prior CABG, when compared with non-CABG group (2.74±1.24 vs 2.02±1.26; $P<0.001$). The pooled SMD value was 0.52 (95% CI: 0.42-0.63, $P<0.001$; Fig. 13), with moderate heterogeneity (I^2 =65%, P=0.04).

3. Complication

3.1 Perforation with need for intervention

8544 patients from four studies were included in the analysis of this event and the incidence was 4.24% (362 of 8544) in overall rate. For treatment method, the incidence of perforation was significantly higher in prior CABG patients (5.55%, 124 of 2236), as compared with non-prior CABG patients (3.77%, 238 of 6308). The pooled OR value was 1.91 (95% CI: 1.36-2.69, $P<0.001$), with lower heterogeneity (I^2 = 34%, P = 0.21; Fig. 14)

3.2 Tamponade

A total of 4 studies reported the incidence of tamponade, which involved 7266 participants and 57 events (0.78%). The pooled results indicated that the non-CABG group may have a higher incidence of coronary perforation (0.99%, 53 of 5352), when compared with the prior CABG group (0.21%, 4 of 1914), during the perioperative period of CTO PCI (OR = 0.25, 95% CI 0.09-0.72, P=0.01) with no heterogeneity across studies (I^2 = 0.0%, P = 0.64; Fig. 15).

3.3 Major bleeding

A total of 4 studies were included for the major bleeding, which involved 5143 participants and 44 events (0.86%), and no heterogeneity was found for the incidence (I^2 = 0.0%, P = 0.67). Furthermore, there was no significant difference between the prior CABG (0.77%, 10 of 1301) and non-CABG group (0.89%, 34 of 3842) regarding major bleeding (OR = 1.18, 95% CI 0.57-2.44, P = 0.65; Fig. 16).

3.4 Contrast-induced nephropathy

Only 20 events among 3780 patients from 3 studies analysis this event and get a positive result. The prior CABG treatment (1.4%, 11 of 793) was significantly associated with higher risks of contrast-induced nephropathy, compared to non-CABG treatment (0.30%, 9 of 2987). And the pooled OR value was 3.40 (95% CI: 1.31-8.78, P=0.001), with no heterogeneity (I^2 = 0.0%, P = 0.64; Fig. 17).

Discussion

Over the past years, CTO recanalization has received much attention as one of the major frontiers of PCIs, and advisory documents highlighting technical and organizational aspects have been published.

Management of CTO by PCI or CABG or medical therapy has been controversial for a very long time[13]. The summary statistic shows that of these patients, 11% undergo PCI, 40% undergo CABG, and 49% had medication. In patients without CTO, 36% undergo PCI, 28% undergo CABG, and 35% had medication[14].

Some experts believe that CABG should be performed on patients with CTO. Patients with CTO often have high scores in the SYNTAX scoring system and also have a high probability of combining multiple comorbidities. Multiple risk factors make patients highly variable in clinical and cardiac characteristics. CABG surgery is capable to offer complete revascularization for both proximal and distal segments, consistent with the 2 trials by DECISION-CTO and EuroCTO[15, 16]. In addition, as technology advances in recent years, the long-term patency rate of graft vascular are higher. Not only the left internal mammary artery instead of LAD is very efficient, but also the long-term patency of CTO using saphenous vein is greater than 50%, with an average of 75%, which bring a better outcome for CABG long-term follow-up[14].

Although the use of PCI or CABG for the first choose to treat CTO is still a topic of debate[17]. PCI of native-vessel CTO for patients with previous CABG is often the favored revascularization strategy compared with redo CABG. Repeat CABG has often been associated with a greater risk of adverse events than initial CABG. Whereas, CTO-PCI for previous CABG patients is also a difficulty for interventional cardiologists that many score and study regard previous CABG as an independent risk factor for CTO-PCI.

In our meta-analysis,13439 CTO patients from 8 studies was included, which contained 3349 (24.9%) pCABG patients and 10090 (75.1%) nCABG patients. The main findings of this meta-analysis demonstrated that: (1) patients with history of CABG occupied a significant proportion in those undergoing CTO-PCI that one in every four patients had previous CABG; (2) compared to nCABG patients, pCABG patients were older and had more comorbidities; (3) patients with prior CABG had higher angiographic complexity; (4) the two groups complication rates were comparable.

First, we analyzed the characteristics of patient- rather than lesion specific factors between patients with or without CABG. Compared to nCABG patients, pCABG patients were older, more frequently male, and had more comorbidities such as diabetes mellitus, hypertension and dyslipidemia. Also, they had more previous myocardial infarction and PCI history. However, a pleasant surprise is that they had lower current smoker, which may attribute to better patient education and self-management.

Next, we analyzed the CTO target vessel location in both groups. Some multicenter CTO registry studies have reported that in the whole CTO, 47% CTO was located in the RCA, with the others 20% in the LAD, 16% in the LCX or 17% multiple locations. Consistent with previous studies, our meta-analysis showed that the RCA was the most common CTO vessel no matter the CABG history. While the LCX was more frequent target CTO vessel in post-CABG patients, whereas the LAD was more frequently located in CABG-naïve patients, presumably because of the high patency rates of left internal mammary artery. Furthermore, in the past studies, it has been questioned whether the CTO target vessel location associated with the success rate of recanalization. And some previous studies have proposed that LCX-CTO is associated with lower recanalization success rate, less efficiency, and higher complications rate. Even the PROGRESS-CTO (Prospective Global Registry for the Study of CTO Intervention) score has included LCX-CTO as an independent predictor of technical failure[18]. Although, a more recent multicenter study reported similar success rates in all arteries, the patients with successful recanalization of LCX-CTO showed a higher cardiac long-term mortality compared to other arteries[19]. The lower success rate for LCX-CTO target vessel is likely related to the increased tortuosity of this vessel and the less frequent presence of interventional collaterals.

Knowledge of potential caveats in treating CTO might cause patient selection; however, the decision of revascularization is done based on clinical need, not anatomical characteristics. Therefore, we further analyzed the lesion morphology of CTO target vessel.

The CTO lesion starts at the proximal cap. The proximal cap morphology, clarity and whether there is a side branch at proximal entry decided the starting place to probe the occlusion with a wire[20]. The CTO stump has two types which are tapered tip stump and blunt stump. While the CTO exhibits two types of histological vascular channels that span the occluded segment which are endothelialized microchannel and micro capillary. The endothelialized microchannel, termed histologically recanalized segment, is a 160–230 um diameter neovascularization that connects the CTO from the proximal to distal cap. The micro capillary, termed non-recanalized segment, is a <100 um diameter capillary that passes into the small side branch or into the vasa vasorum which cannot span the CTO from the proximal to distal cap. The tapered tip stump CTO is more likely associated with a histologically recanalized segment and less likely to have a major side branch. In contrast, the blunt stump CTO is more likely to have a non-recanalized micro capillary, which means it will be more difficult to open the CTO lesion[21]. In our meta-analysis, patients with prior CABG undergoing CTO-PCI have more blunt stump and proximal cap ambiguity, but the side branch at proximal entry has no significant difference between the two groups. The association between having undergone CABG and accelerated atherosclerosis progression was well documented in many studies. Especially in the proximal vessel, the competitive flow generated by the graft vascular itself may play a dominant role. Moreover, it has been hypothesized that the exposure of the distal cap to arterial pressure in a grafted CTO vessel may even promote adverse remodeling and blunt rather than tapered morphology.

Once the wire crosses the proximal cap, it will enter the body of the CTO lesion. In each body of the CTO lesion, its complexity and difficulty depend on the degree of calcification, tortuosity, and lesion length. In particular, the length of the occluded segment is the most important factor impacting the success of crossing a CTO. The longitudinal continuity of microchannels extends to approximately 85% of the total CTO length[22]. These pathological characteristics provide the basis for many of the CTO PCI techniques. Length greater than 20 mm was a stronger predictor of failure to cross the occlusion than calcification, tortuosity, and blunt stump. In our meta-analysis, prior CABG is associated with more severe calcification, more tortuosity and longer length of CTO, due either to the shrinkage of the occluded bypass graft or vessel distortion at the time of grafting. Blood stasis and low shear stress resulting from competitive flow between native vessel and bypass graft may also constitute the mechanism of greater calcification in the native arteries. These characteristics are all considered as challenges in the CTO-PCI process.

Collateral channels originate as arterioles connecting the vascular beds of visible coronary arteries. With increased chronicity of an occlusion, these small arteriole collaterals undergo remodeling to become muscular arteries known as arteriogenesis[23]. For appropriate interventional collaterals, the collateral channels can be septal, epicardial connections but also can be graft vascular (either venous or arterial)[24]. The success rate of CTO-PCI has improved to >90% in the hands of CTO masters with proper retrograde approach that essentially uses the backdoor to pass the guidewire from the donor artery via collateral channels to penetrate the distal CTO cap[25]. In our meta-analysis, the number of interventional collaterals has no significant difference between the two groups. However, On the other hand, bypass grafts can be used as conduits (even when occluded) that can facilitate CTO intervention via the retrograde approach. Data showed the most commonly used collaterals for the retrograde approach in prior CABG patients were septal collaterals (43%), followed by epicardial collaterals (34%), saphenous vein graft (30%), and left internal mammary artery grafts (3%)[10].

Adequate distal landing zone was defined as a distal vessel segment with a diameter larger than 2.0 mm, and without diffuse lesion[10]. An adequate landing zone represents a favorable feature for antegrade true-to-true lumen approach and dissection/re-entry techniques. Whereas bifurcation at the distal cap represents a favorable feature for retrograde approach. In our meta-analysis, for inadequate distal landing zone, prior CABG is related to significantly higher incidences, and for distal cap at bifurcation, to our pleasant surprise, the incidence was significantly higher in patients with prior CABG which means they will have a good change for retrograde approach[26].

These characteristics of CTO target vessel are also taken into account by risk scores for technical failure, such as the J-CTO (multicenter CTO registry in Japan) score[27]. The J-CTO score is currently the most widely used score predicting successful guidewire crossing through native coronary CTO lesions within 30 minutes. The J-CTO score takes into account 5 characteristics of the CTO, which are associated with procedural challenges: blunt stump, moderate/ severe calcifications, > 45° bending, length > 20 mm, and retry CTO -PCI. And the score defined all lesions into 4 difficulty groups: easy (J-CTO score of 0), intermediate (score of 1), difficult (score of 2), and very difficult (score of ≥3). In our meta-analysis, the score was significantly higher in patients with prior CABG (2.74±1.24), when compared with non-CABG group (2.02±1.26)($P<0.001$). The scoring model not only quantitatively measures the difficulty and the probability of CTO-PCI revascularization success rate but also objectively evaluates the anatomic and clinical complexity, which can aid the interventionalist in making optimal clinical decisions for each CTO patient.

The CTO-PCI is considered as one of the last frontiers for interventional cardiologist. Although the success rate for it has improved over the years with the update of new techniques and available equipment, the procedural complication is still an unavoidable risk[28]. In our meta-analysis, we analyzed 4 main complications those are perforation with need for intervention, tamponade, major bleeding, and contrast-induced nephropathy. And to our pleasant surprise, the procedural complications are rare in the both groups and the rates of complications in prior CABG group remains comparable to patients in non-CABG group. Notably, perforation with need for intervention, even tamponade, which is a fatal complication for CTO-PCI[29]. Our meta-analysis demonstrates that CTO-PCI in prior CABG patients is associated with a higher rate of perforation, but lower rate of pericardial tamponade. A possible explanation of this result may be attributed to the commonly held belief that the potential protective effect of pericardial adhesion in pCABG patients[30]. However, patients who have undergone CABG are not immune to tamponade, as previously thought. First, after cardiac surgery the pericardium may be repaired by itself, especially in young patients[31]. Furthermore, the pericardium is left open creating a pseudo-pericardial space commonly[32]. In this space, the risk of pericardial tamponade, which occurs in around 40% of all patients with coronary artery perforation, is still present despite the history of CABG[33]. Last but not least, it is well known that in patient with previous CABG a dry tamponade may occur with localized fluid collection around one cavity. The loculated hematomas can compress the atria or the ventricles, potentially progressing to cardiogenic shock. Even more dire is the tamponade without detection of relevant pericardial effusion at common echocardiographic examination. Given the potentially catastrophic complications of coronary perforations in prior CABG patients, the experts recommended immediate drainage or surgery treatment.

Conclusions

In the previous study, successful PCI for CTO was related to improved survival rate in both patients with and without previous CABG, and interaction analyses suggested a similar revascularization benefit in both patient groups. These findings extend our knowledge about mortality benefits associated with successful CTO revascularization to the high-risk patient subgroup with previous CABG and underline the importance to offer PCI for CTO to this complex lesion and patient subgroup. According to our findings, CTO-PCI is frequently performed in patients with history of prior CABG. Nevertheless, CTO-PCI for patients who have undergone CABG is still a challenging intervention and is associated with higher angiographic complexity such as blunt stump, proximal cap ambiguity, severe calcifications, bending and lesion length > 20 mm. Even in the PROGRESS scores, the presence of previous CABG represents an independent marker of patient complexity. Taking those specificities into account, some experts encourage that the retrograde approach should be accepted more widely, and performed appropriately[26]. And to our pleasant surprise, the rate of complications in prior CABG group remains comparable to patients without prior CABG, which makes interventionalists are motivated to update their techniques and equipment.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used during the study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Yuchen Shi, Songyuan He, and Jinghua Liu conceived the study and designed the protocol. Yuchen Shi and Songyuan He integrated the data and drafted the manuscript. Wen Jiana and Xueqian Shen were responsible for the study selection, data extraction, and assessment of study quality. Jesse Luo and Jinghua Liu revised the manuscript critically. All authors read and approved the final manuscript.

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References

1. Pereg D, Fefer P, Samuel M, Wolff R, Czarnecki A, Deb S, Sparkes J, Fremes S, Strauss B. Native coronary artery patency after coronary artery bypass surgery. JACC Cardiovascular interventions. 2014;7(7):761–7.
2. Fefer P, Knudtson M, Cheema A, Galbraith P, Osherov A, Yalonetsky S, Gannot S, Samuel M, Weisbrod M, Bierstone D, et al. Current perspectives on coronary chronic total occlusions: the Canadian Multicenter Chronic Total Occlusions Registry. J Am Coll Cardiol. 2012;59(11):991–7.
3. Sakakura K, Nakano M, Otsuka F, Yahagi K, Kutys R, Ladich E, Finn AV, Kolodgie FD, Virmani R. Comparison of pathology of chronic total occlusion with and without coronary artery bypass graft.

Eur Heart J. 2014;35(25):1683–93.

4. Maeremans J, Spratt JC, Knaapen P, Walsh S, Agostoni P, Wilson W, Avran A, Faurie B, Bressollette E, Kayaert P, et al. Towards a contemporary, comprehensive scoring system for determining technical outcomes of hybrid percutaneous chronic total occlusion treatment: The RECHARGE score. Catheter Cardiovasc Interv. 2018;91(2):192–202.
5. Tajti P, Karmpaliotis D, Alaswad K, Jaffer FA, Yeh RW, Patel M, Mahmud E, Choi JW, Burke MN, Doing AH, et al. The Hybrid Approach to Chronic Total Occlusion Percutaneous Coronary Intervention: Update From the PROGRESS CTO Registry. JACC Cardiovasc Interv. 2018;11(14):1325–35.
6. Azzalini L, Ojeda S, Karatasakis A, Maeremans J, Tanabe M, La Manna A, Dautov R, Ybarra L, Benincasa S, Bellini B, et al. Long-Term Outcomes of Percutaneous Coronary Intervention for Chronic Total Occlusion in Patients Who Have Undergone Coronary Artery Bypass Grafting vs Those Who Have Not. Can J Cardiol. 2018;34(3):310–8.
7. Budassi S, Zivelonghi C, Dens J, Bagnall A, Knaapen P, Avran A, Spratt J, Walsh S, Faurie B, Agostoni P. **Impact of prior coronary artery bypass grafting in patients undergoing chronic total occlusion-percutaneous coronary intervention**: **Procedural and clinical outcomes from the REgistry of Crossboss and Hybrid procedures in FrAnce**, **the NetheRlands**, **BelGium**, **and UnitEd** Kingdom (**RECHARGE**). *Catheterization and cardiovascular interventions: official journal of the Society for Cardiac Angiography & Interventions* 2021, **97**(1):E51-E60.
8. Dautov R, Manh Nguyen C, Altisent O, Gibrat C, Rinfret S. **Recanalization of Chronic Total Occlusions in Patients With Previous Coronary Bypass Surgery and Consideration of Retrograde Access via Saphenous Vein Grafts**. *Circulation Cardiovascular interventions* 2016, 9(7).
9. Michael T, Karmpaliotis D, Brilakis E, Abdullah S, Kirkland B, Mishoe K, Lembo N, Kalynych A, Carlson H, Banerjee S, et al. Impact of prior coronary artery bypass graft surgery on chronic total occlusion revascularisation: insights from a multicentre US registry. Heart. 2013;99(20):1515–8.
10. Tajti P, Karmpaliotis D, Alaswad K, Jaffer F, Yeh R, Patel M, Mahmud E, Choi J, Burke M, Doing A, et al. In-Hospital Outcomes of Chronic Total Occlusion Percutaneous Coronary Interventions in Patients With Prior Coronary Artery Bypass Graft Surgery. Circulation Cardiovascular interventions. 2019;12(3):e007338.
11. Teramoto T, Tsuchikane E, Matsuo H, Suzuki Y, Ito T, Ito T, Habara M, Nasu K, Kimura M, Kinoshita Y, et al. Initial success rate of percutaneous coronary intervention for chronic total occlusion in a native coronary artery is decreased in patients who underwent previous coronary artery bypass graft surgery. JACC Cardiovascular interventions. 2014;7(1):39–46.
12. Toma A, Stähli B, Gick M, Colmsee H, Gebhard C, Mashayekhi K, Ferenc M, Neumann F, Buettner H. Long-Term Follow-Up of Patients With Previous Coronary Artery Bypass Grafting Undergoing Percutaneous Coronary Intervention for Chronic Total Occlusion. The American journal of cardiology. 2016;118(11):1641–6.
13. Azzalini L, Carlino M, Bellini B, Marini C, Pazzanese V, Toscano E, Gramegna M, Moscardelli S, Bognoni L, Montorfano M. Long-Term Outcomes of Chronic Total Occlusion Recanalization Versus

Percutaneous Coronary Intervention for Complex Non-Occlusive Coronary Artery Disease. The American journal of cardiology. 2020;125(2):182–8.

14. Tong J, Yu Q, Li C, Shao X, Xia Y. Successful revascularization of noninfarct related artery with chronic total occlusion among acute myocardial infarction patients: A systematic review and meta-analysis. Medicine. 2018;97(3):e9655.
15. Galassi AR, Tomasello SD, Reifart N, Werner GS, Sianos G, Bonnier H, Sievert H, Ehladad S, Bufe A, Shofer J, et al: **In-hospital outcomes of percutaneous coronary intervention in patients with chronic total occlusion**: **insights from the ERCTO** (**European Registry of Chronic Total Occlusion**) **registry**. *EuroIntervention* 2011, **7**(4):472-479.
16. Brilakis E, Mashayekhi K, Burke M. How DECISION-CTO Can Help Guide the Decision to Perform Chronic Total Occlusion Percutaneous Coronary Intervention. Circulation. 2019;139(14):1684–7.
17. Head S, Milojevic M, Daemen J, Ahn J, Boersma E, Christiansen E, Domanski M, Farkouh M, Flather M, Fuster V, et al. Mortality after coronary artery bypass grafting versus percutaneous coronary intervention with stenting for coronary artery disease: a pooled analysis of individual patient data. Lancet. 2018;391(10124):939–48.
18. Christopoulos G, Kandzari D, Yeh R, Jaffer F, Karmpaliotis D, Wyman M, Alaswad K, Lombardi W, Grantham J, Moses J, et al. Development and Validation of a Novel Scoring System for Predicting Technical Success of Chronic Total Occlusion Percutaneous Coronary Interventions: The PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) Score. JACC Cardiovascular interventions. 2016;9(1):1–9.
19. Mitomo S, Naganuma T, Jabbour R, Sato K, Takebayashi H, Kobayashi T, Obata J, Sakamoto K, Tsujita K, Kugiyama K, et al. Impact of target vessel on long-term cardiac mortality after successful chronic total occlusion percutaneous coronary intervention: Insights from a Japanese multicenter registry. Int J Cardiol. 2017;245:77–82.
20. Ojeda S, Luque A, Pan M, Bellini B, Xenogiannis I, Lostalo A, Montorfano M, Hidalgo F, Venuti G, La Manna A, et al. Percutaneous coronary intervention in aorto-ostial coronary chronic total occlusion: outcomes and technical considerations in a multicenter registry. Revista espanola de cardiologia (English ed). 2020;73(12):1011–7.
21. Dash D. Coronary chronic total occlusion intervention: A pathophysiological perspective. Indian heart journal. 2018;70(4):548–55.
22. Tran P, Phan H, Shah S, Latif F, Nguyen T. Applied Pathology for Interventions of Coronary Chronic Total Occlusion. Curr Cardiol Rev. 2015;11(4):273–6.
23. Allahwala U, Kott K, Bland A, Ward M, Bhindi R. Predictors and Prognostic Implications of Well-Matured Coronary Collateral Circulation in Patients with a Chronic Total Occlusion (CTO). Int Heart J. 2020;61(2):223–30.
24. Xenogiannis I, Gkargkoulas F, Karmpaliotis D, Krestyaninov O, Khelimskii D, Jaffer F, Khatri J, Kandzari D, Wyman R, Doing A, et al. Retrograde Chronic Total Occlusion Percutaneous Coronary Intervention via Saphenous Vein Graft. JACC Cardiovascular interventions. 2020;13(4):517–26.

25. Allahwala U, Ekmejian A, Mughal N, Brieger D, Nour D, Ciofani J, Weaver J, Ward M, Bhindi R. **Impact of coronary artery bypass grafting (CABG) on coronary collaterals in patients with a chronic total occlusion (CTO)**. *The international journal of cardiovascular imaging* 2021.
26. Kinnaird T, Gallagher S, Cockburn J, Sirker A, Ludman P, de Belder M, Smith E, Anderson R, Strange J, Mamas M, et al. Procedural Success and Outcomes With Increasing Use of Enabling Strategies for Chronic Total Occlusion Intervention. Circulation Cardiovascular interventions. 2018;11(10):e006436.
27. Morino Y, Abe M, Morimoto T, Kimura T, Hayashi Y, Muramatsu T, Ochiai M, Noguchi Y, Kato K, Shibata Y, et al. Predicting successful guidewire crossing through chronic total occlusion of native coronary lesions within 30 minutes: the J-CTO (Multicenter CTO Registry in Japan) score as a difficulty grading and time assessment tool. JACC Cardiovasc Interv. 2011;4(2):213–21.
28. Karacsonyi J, Vemmou E, Nikolakopoulos I, Ungi I, Rangan B, Brilakis E. Complications of chronic total occlusion percutaneous coronary intervention. Netherlands heart journal: monthly journal of the Netherlands Society of Cardiology the Netherlands Heart Foundation. 2021;29(1):60–7.
29. Kinnaird T, Anderson R, Ossei-Gerning N, Cockburn J, Sirker A, Ludman P, de Belder M, Johnson T, Copt S, Zaman A, et al: **Coronary Perforation Complicating Percutaneous Coronary Intervention in Patients With a History of Coronary Artery Bypass Surgery: An Analysis of 309 Perforation Cases From the British Cardiovascular Intervention Society Database**. *Circulation Cardiovascular interventions* 2017, 10(9).
30. Azzalini L, Poletti E, Ayoub M, Ojeda S, Zivelonghi C, La Manna A, Bellini B, Lostalo A, Luque A, Venuti G, et al. Coronary artery perforation during chronic total occlusion percutaneous coronary intervention: epidemiology, mechanisms, management, and outcomes. EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2019;15(9):e804–11.
31. Danek B, Karatasakis A, Tajti P, Sandoval Y, Karmpaliotis D, Alaswad K, Jaffer F, Yeh R, Kandzari D, Lembo N, et al. Incidence, Treatment, and Outcomes of Coronary Perforation During Chronic Total Occlusion Percutaneous Coronary Intervention. The American journal of cardiology. 2017;120(8):1285–92.
32. Adusumalli S, Morris M, Pershad A. Pseudo-Pericardial Tamponade From Right Ventricular Hematoma After Chronic Total Occlusion Percutaneous Coronary Intervention of the Right Coronary Artery: Successfully Managed Percutaneously With Computerized Tomographic Guided Drainage. Catheterization cardiovascular interventions: official journal of the Society for Cardiac Angiography Interventions. 2016;88(1):86–8.
33. Wu K, Huang Z, Zhong Z, Liao H, Zhou Y, Luo B, Zhang B. Predictors, treatment, and long-term outcomes of coronary perforation during retrograde percutaneous coronary intervention via epicardial collaterals for recanalization of chronic coronary total occlusion. Catheterization cardiovascular interventions: official journal of the Society for Cardiac Angiography Interventions. 2019;93:800–9.

Tables

Due to technical limitations, tables are only available as a download in the Supplemental Files section.

Figures

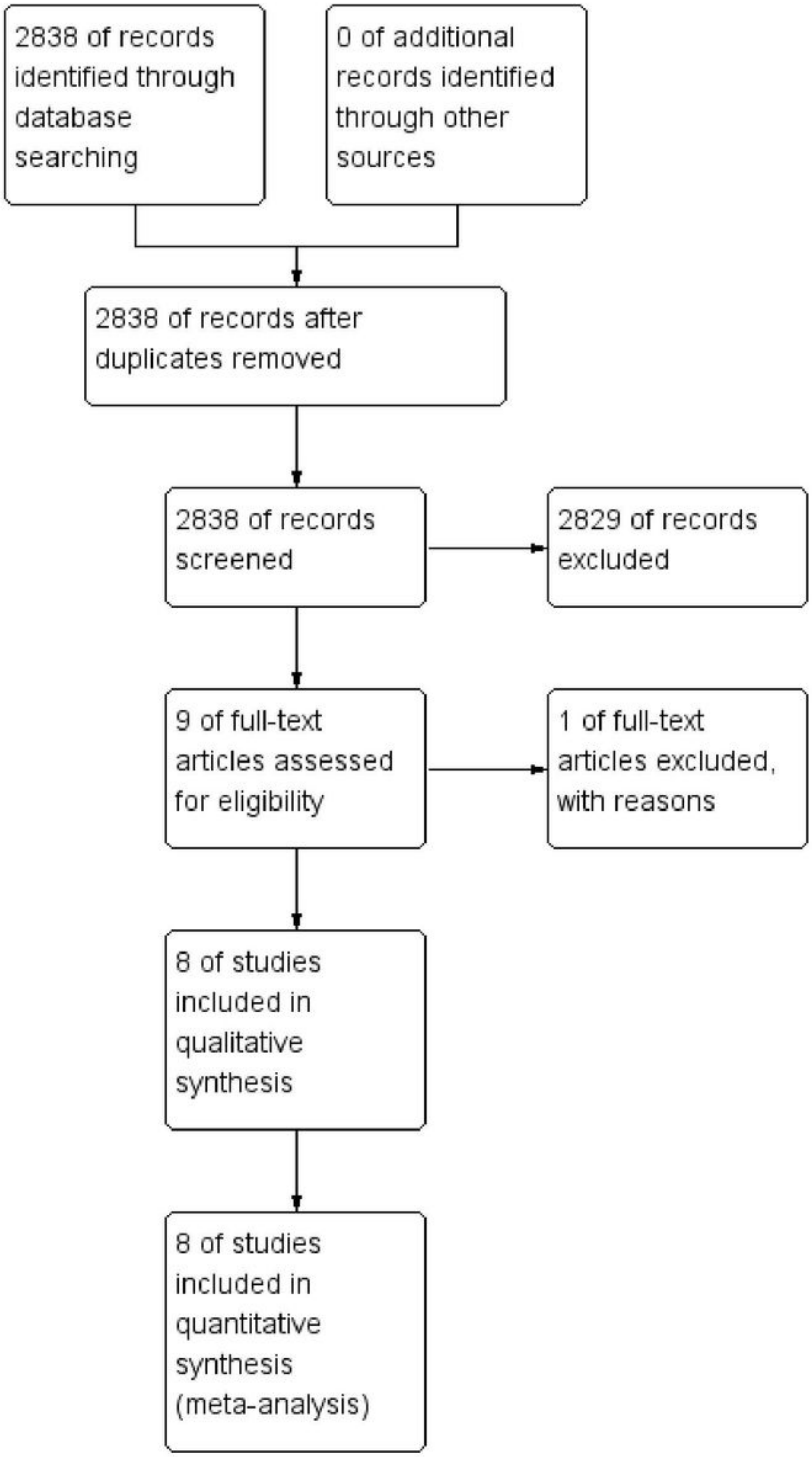

Figure 1

Flow diagram of study selection

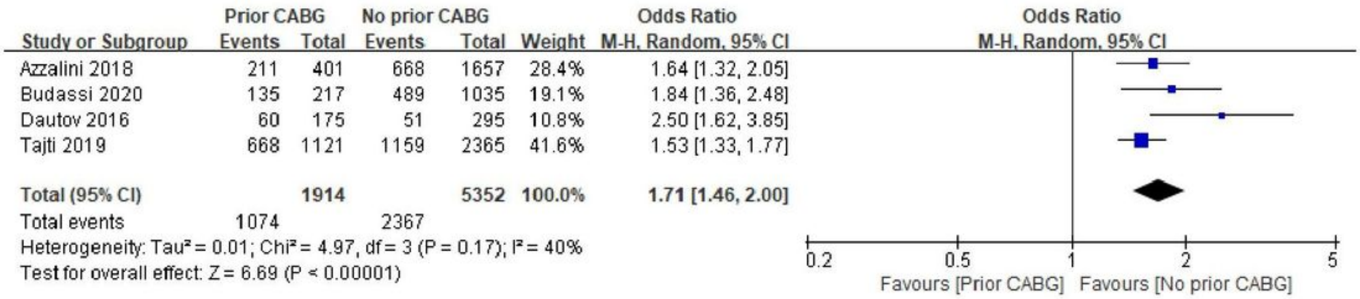

Figure 2

Forest plot demonstrating a pooled estimate of the blunt stump.

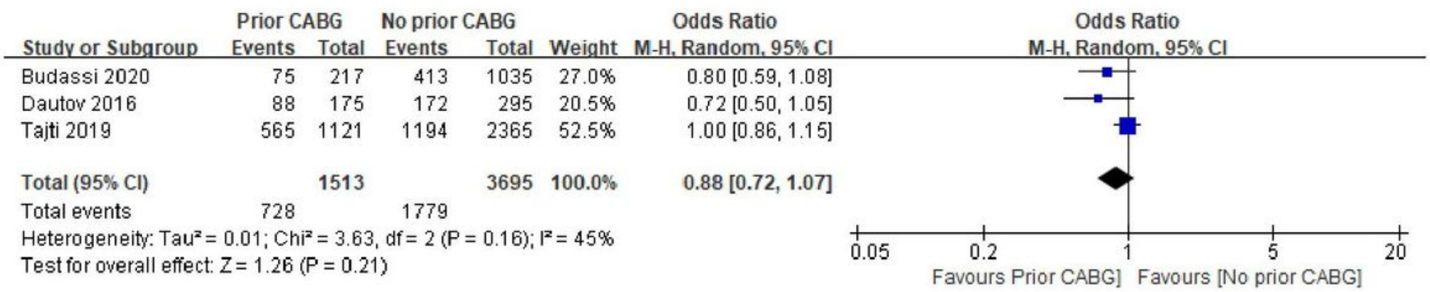

Figure 3

Forest plot demonstrating a pooled estimate of the side branch at proximal entry.

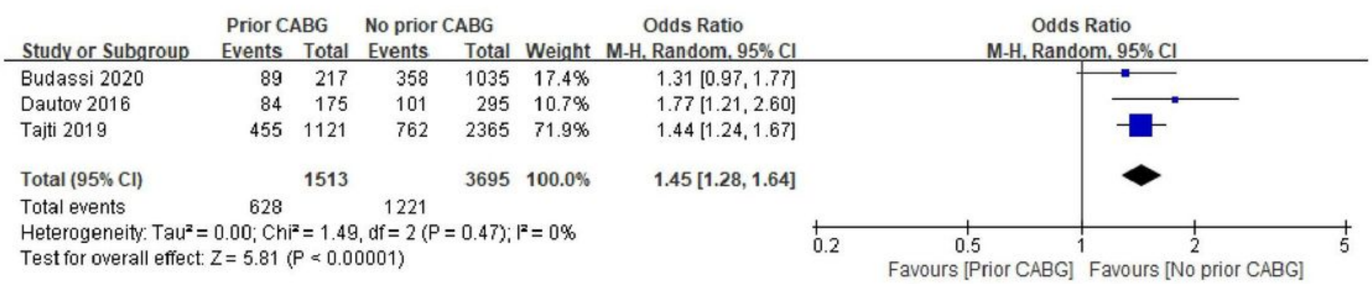

Figure 4

Forest plot demonstrating a pooled estimate of the proximal cap ambiguity.

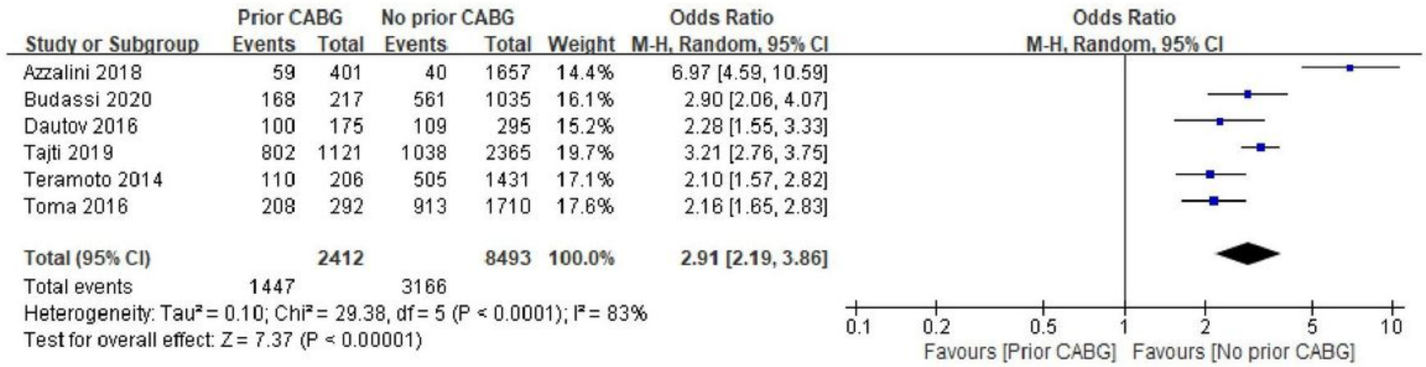

Figure 5

Forest plot demonstrating a pooled estimate of the moderate or severe calcifications.

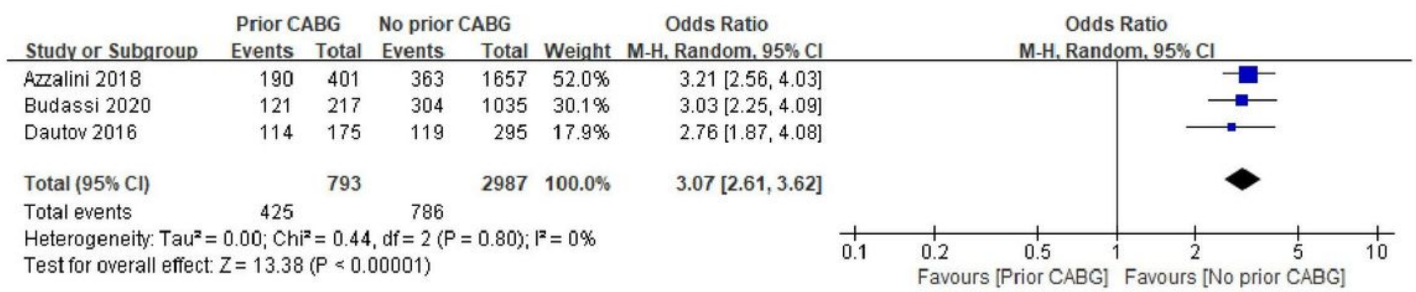

Figure 6

Forest plot demonstrating a pooled estimate of the bending.

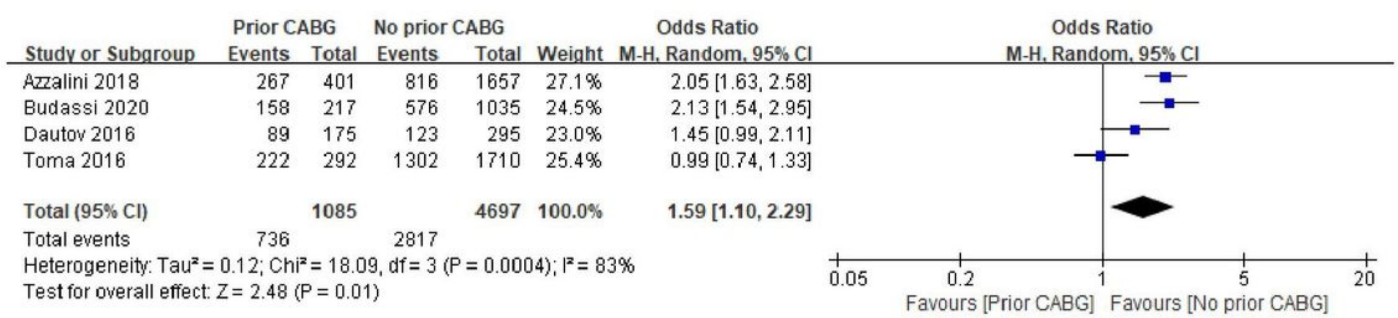

Figure 7

Forest plot demonstrating a pooled estimate of the lesion length.

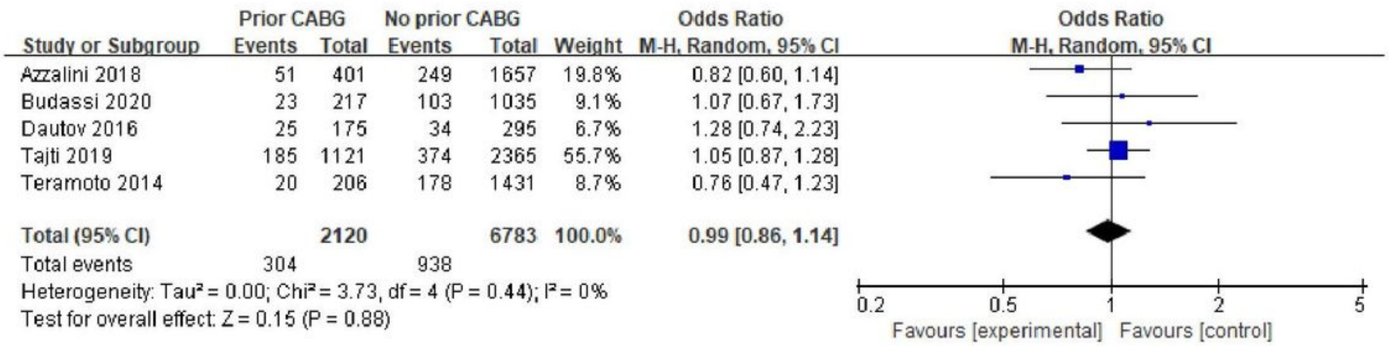

Figure 8

Forest plot demonstrating a pooled estimate of the in-stent CTO.

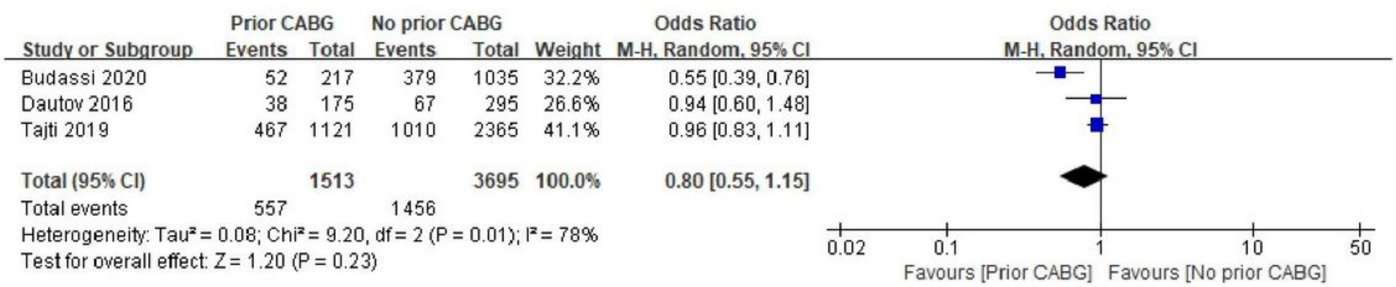

Figure 9

Forest plot demonstrating a pooled estimate of the lack of interventional collaterals.

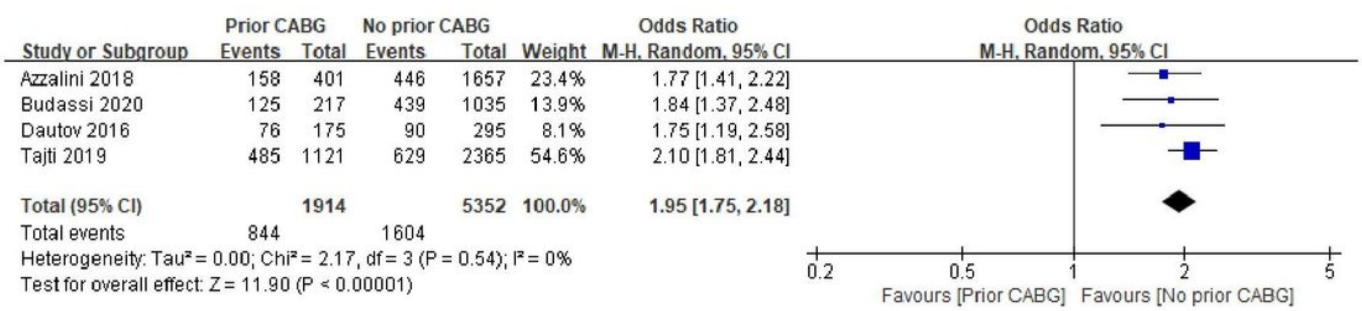

Figure 10

Forest plot demonstrating a pooled estimate of the inadequate distal landing zone.

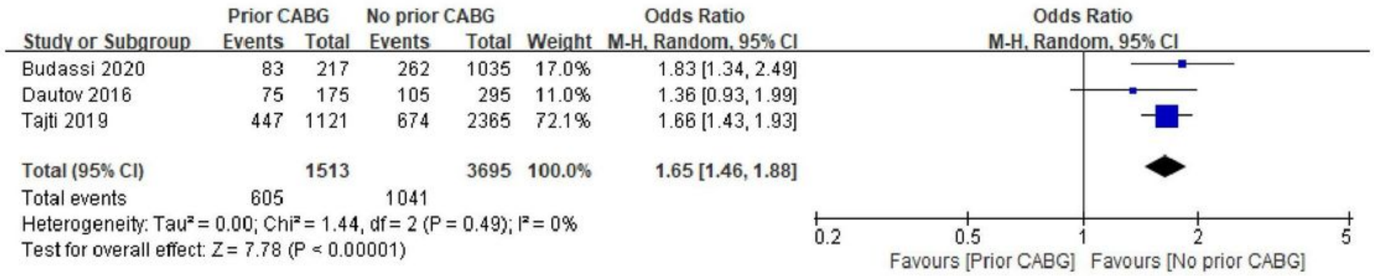

Figure 11

Forest plot demonstrating a pooled estimate of the distal cap at bifurcation.

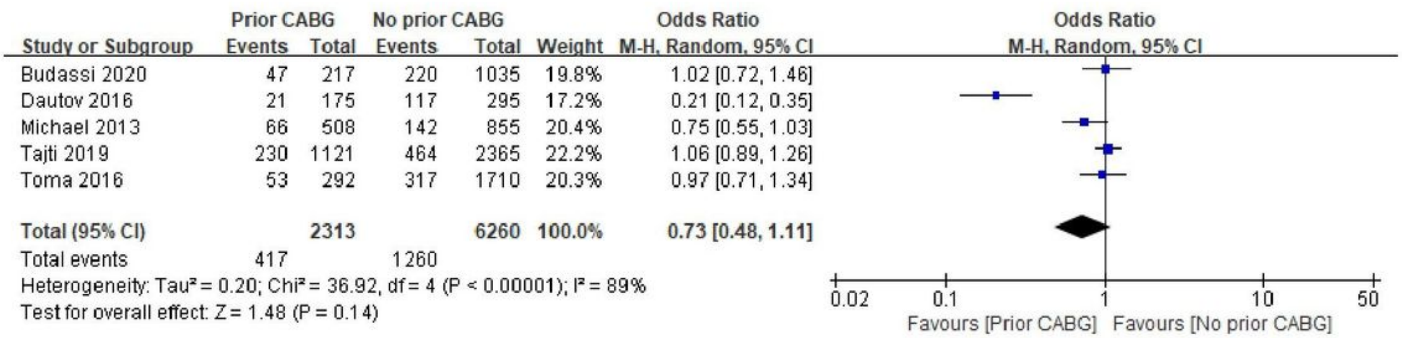

Figure 12

Forest plot demonstrating a pooled estimate of the previously failed attempt.

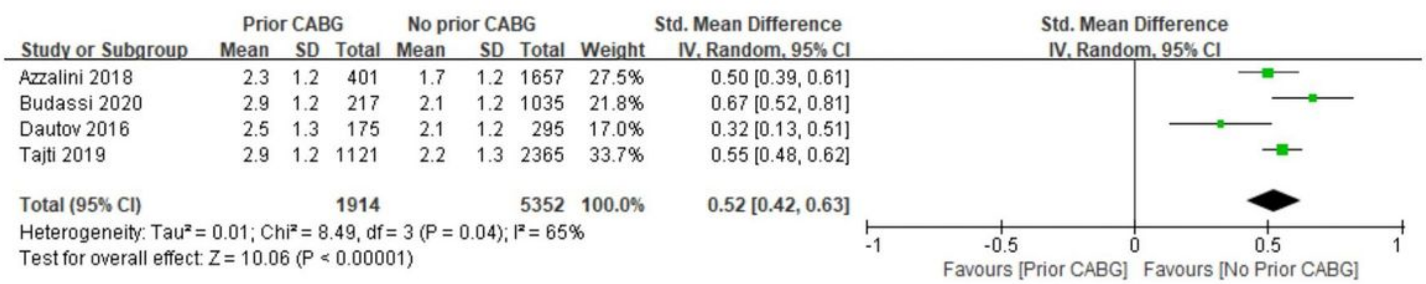

Figure 13

Forest plot demonstrating a pooled estimate of the J-CTO score

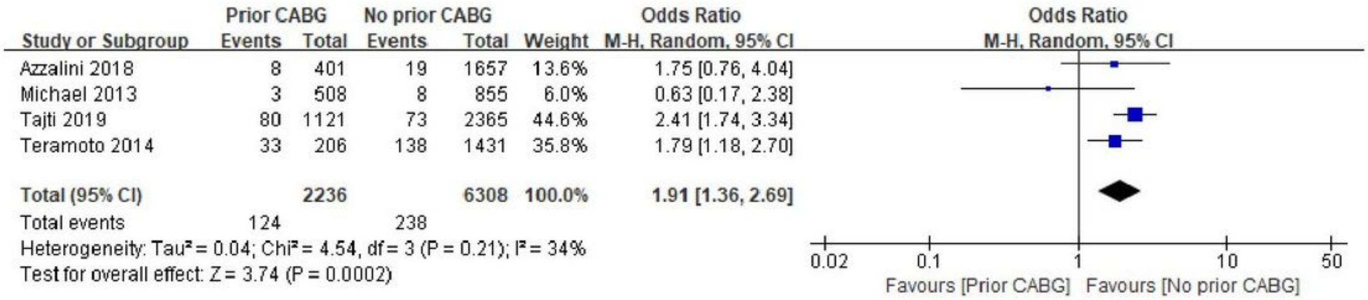

Figure 14

Forest plot demonstrating a pooled estimate of the perforation with need for intervention.

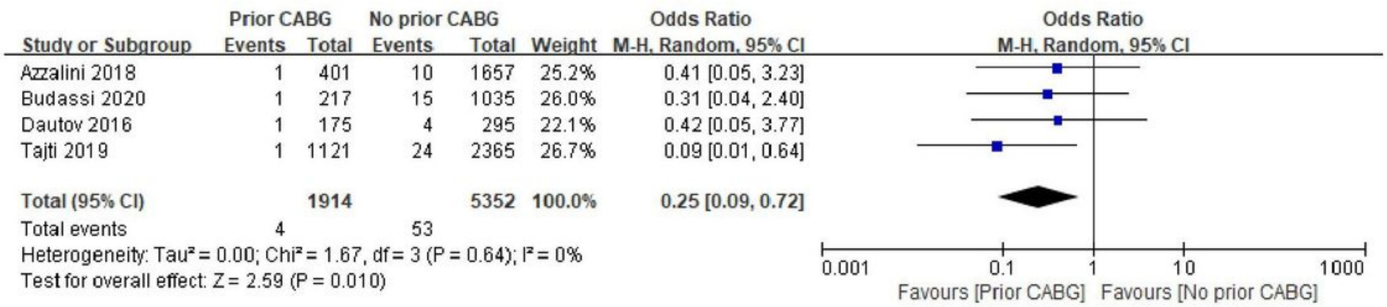

Figure 15

Forest plot demonstrating a pooled estimate of the tamponade.

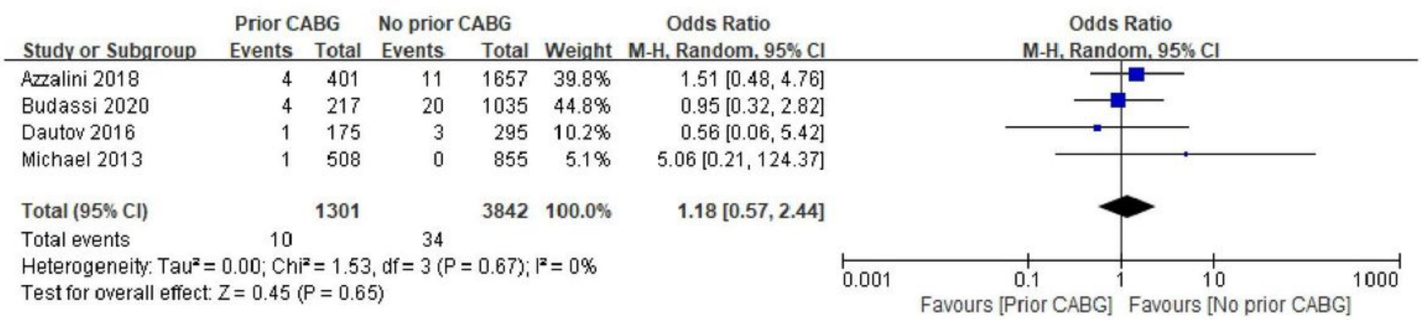

Figure 16

Forest plot demonstrating a pooled estimate of the major bleeding.

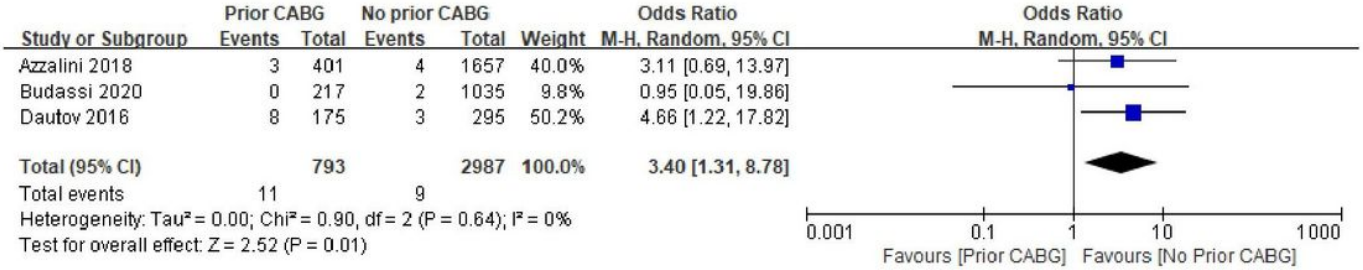

Figure 17

Forest plot demonstrating a pooled estimate of the contrast-induced nephropathy.

Supplementary Files

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- TAb1.png
- Tab2.jpg