OPEN

Impact of periprocedural myocardial injury on long-term clinical outcomes of chronic total occlusion patients undergoing percutaneous coronary intervention: a systematic review and meta-analysis

Mei-Jun Liu, Chao-Feng Chen, Xiao-Fei Gao, Xiao-Hua Liu and Yi-Zhou Xu

Background: **Several studies have evaluated the long-term clinical outcomes of periprocedural myocardial injury for chronic total occlusions patients. However, the results of these studies were inconsistent. To determine whether the periprocedural myocardial injury has adverse effects on long-term clinical outcomes in chronic total occlusion patients undergoing percutaneous coronary intervention.**

Methods: **We searched Cochrane Library, PubMed, and Embase for eligible articles from their date of inception up to March 2019. Long-term clinical outcomes included major adverse cardiac events, all-cause death, cardiac death, myocardial infarction, and target vessel revascularization. Odds ratios with 95% confidence intervals were calculated as summary statistics by using Review Manager software.**

Results: **A total of 8 observational studies involving 5879 chronic total occlusions patients were included in this meta-analysis. These results of this meta-analysis indicated that periprocedural myocardial injury was associated with a higher risk of major adverse cardiac events (odds ratio, 1.94; 95% confidence interval, 1.22–3.08; $P = 0.005$), a higher risk of all-cause death (odds ratio, 1.30; 95% confidence interval, 1.02–1.64; $P = 0.03$), a higher risk of cardiac death (odds ratio, 2.59; 95% confidence interval, 1.41–4.78; $P = 0.002$), a higher risk of myocardial infarction (odds ratio, 3.07; 95% confidence interval, 1.90–4.98; $P < 0.00001$), and a higher risk of target vessel revascularization (odds ratio, 2.07; 95% confidence interval, 1.35–3.16; P=0.0008) than non-periprocedural myocardial injury.**

Conclusion: **Periprocedural myocardial injury was associated with significantly increased risk of major adverse cardiac events, all-cause death, cardiac death, myocardial infarction, and target vessel revascularization in chronic total occlusion patients undergoing percutaneous coronary intervention at long-term follow-up.** *Coron Artery Dis* **31: 208–214 Copyright © 2019 The Author(s). Published by Wolters Kluwer Health, Inc.**

Coronary Artery Disease 2020, **31**:208–214

Keywords: chronic total occlusion, meta-analysis, outcomes, percutaneous coronary intervention, periprocedural myocardial injury

Department of Cardiology, Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China

Correspondence to Yi-Zhou Xu, MD, Department of Cardiology, Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine, 261# Huansha Road, Hangzhou, Zhejiang 310006, China
Tel: +8613357109696; e-mail: hzsykyzsci@163.com

Received 6 May 2019 **Accepted** 7 September 2019

Introduction

Percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) remains one of the most challenging percutaneous procedures owing to angiographic and procedural complexities, which is considered to be the final frontier of PCI for interventional cardiologists. However, the success rates of PCI for CTO lesion have improved over the last decade because of the development of novel devices and procedural techniques as well as accumulated operator experience [1,2]. Previous studies have demonstrated that a successful revascularization of CTO lesion was associated with better clinical outcomes compared to a failed procedure or conservative therapy [3–6]. Nevertheless, on the other hand, given the complex nature of the CTO-PCI procedure, periprocedural complications are unavoidable and jeopardize patient prognosis. Periprocedural myocardial injury (PMI) is one of the most common complications of CTO-PCI procedure.

PMI is a well-known complication of PCI procedures and is frequently observed in a considerable proportion of patients who underwent PCI procedure [7–9]. Previous studies have shown that PMI was associated with adverse clinical outcomes in unselected populations undergoing PCI [10–12]. However, based on the existing limited data, the clinical significance of PMI in CTO patients who underwent PCI remains controversial. Therefore, we performed this meta-analysis to systematically evaluate whether the occurrence of PMI has a negative impact on long-term prognosis in CTO-PCI patients.

DOI: 10.1097/MCA.0000000000000813

Materials and methods

Search strategy

We searched Cochrane Library, PubMed, and EMBASE from their date of inception up to March 2019 for eligible trials. The following keywords were used: "chronic total occlusion or CTO" AND "periprocedural myocardial injury or periprocedural myocardial infarction or PMI". In addition, to retrieve the most eligible studies, we also scanned the reference list of relevant reviews and manually searched relevant eligible studies. The language of relevant reviews was restricted to English.

Inclusion and exclusion criteria

Studies were eligible for inclusion in this meta-analysis if (1) they compared PMI with non-PMI in CTO patients who treated with PCI; (2) they reported at least one of the following outcomes: all-cause death, cardiac death, myocardial infarction (MI), target vessel revascularization (TVR), and major adverse cardiac events (MACEs); and (3) they were observational studies. The following studies were excluded from this meta-analysis: (1) studies which included non-CTO patients or CTO patients who not treated with PCI; (2) studies which lacked a control group; (3) studies which had no available outcomes even after the corresponding authors was contacted; and (4) case reports, abstracts, reviews, editorials, letters, meta-analysis, and duplicate publications.

Endpoints and definitions

The clinical outcomes of this meta-analysis included MACEs, all-cause death, cardiac death, MI, and TVR. The definition of MACEs and PMI was defined by each study. All-cause death was defined as death from any cause. Cardiac death was defined as death from cardiac origin. TVR was defined as repeated revascularization of the target vessel by PCI or coronary artery bypass grafting.

Data extraction and quality assessment

Two investigators (M.-J.L. and C.-F.C.) independently extracted the following data using a standardized form: name of first author, publication year, country, ethnicity, type of study, number of patients, baseline features of the subjects (mean age, percentage of males, diabetes mellitus, hypertension, dyslipidemia, previous MI, and previous PCI), CTO lesion location, definition of PMI, and median follow-up duration. Any disagreements about the extracted data were resolved by consensus. The quality of the included studies in the meta-analysis was assessed using the Newcastle–Ottawa Scale.

Statistical analysis

Odds ratios (OR) with 95% confidence interval (CI) were calculated as summary statistics. The heterogeneity between studies was calculated using Cochran Q test and I^2 statistic, which was considered significant when $P < 0.10$ in the Q test, or $I^2 > 50\%$. The random-effects model (DerSimoniane-Laird method) was used to calculated the pooled ORs when the $I^2 > 50\%$; otherwise, the fixed-effect model with the Mantel-Haenszel method was used when the $I^2 < 50\%$. Subgroup analyses were performed according to the different ethnicity (Caucasian and Asian populations) to explore potential sources of heterogeneity. Sensitivity analyses were carried out by sequentially omitting each trial to verify the robustness of the overall results. All *P*-values were two-sided, and a *P*-value < 0.05 was considered statistically significant. All statistical analyses were conducted by using Review Manager 5.3 software (The Cochrane Collaboration, Copenhagen, Denmark).

Results

Characteristics of the included studies

As shown in Fig. 1, a total of 8 trials [13–20] involving 5879 patients were included in the meta-analysis. All of these studies included in the meta-analysis were observational study. The main characteristics of each study were summarized in Tables 1 through 3. Of the 8 studies, two studies were carried out in Korea, two in China, one in Canada, one in European Union, one in Poland, and one in Germany. From the perspective of the ethnicity, four studies assessed Caucasian population and four assessed Asian population. Among the 8 studies, the PMI of 3 studies was defined by troponin, and the rest was defined by the creatine kinase MB (CK-MB). The sample size of studies varied from 337 to 1909 patients. Additionally, the median follow-up duration of studies varying from 1 year to 64.8 months.

Long-term clinical outcomes

Major adverse cardiac events

Seven studies reported the incidence of MACEs. PMI was associated with a significant increase in the risk of MACEs compared with non-PMI (absolute risk, 15.7% vs. 15.5%; OR, 1.94; 95% CI, 1.22–3.08; $P = 0.005$) (Fig. 2a).

All-cause death

Seven studies reported the incidence of all-cause death. PMI was significantly associated with increased the risk of all-cause death compared with Non-PMI (absolute risk, 11.7% vs. 9.1%; OR, 1.30; 95% CI, 1.02–1.64; $P = 0.03$) (Fig. 2b).

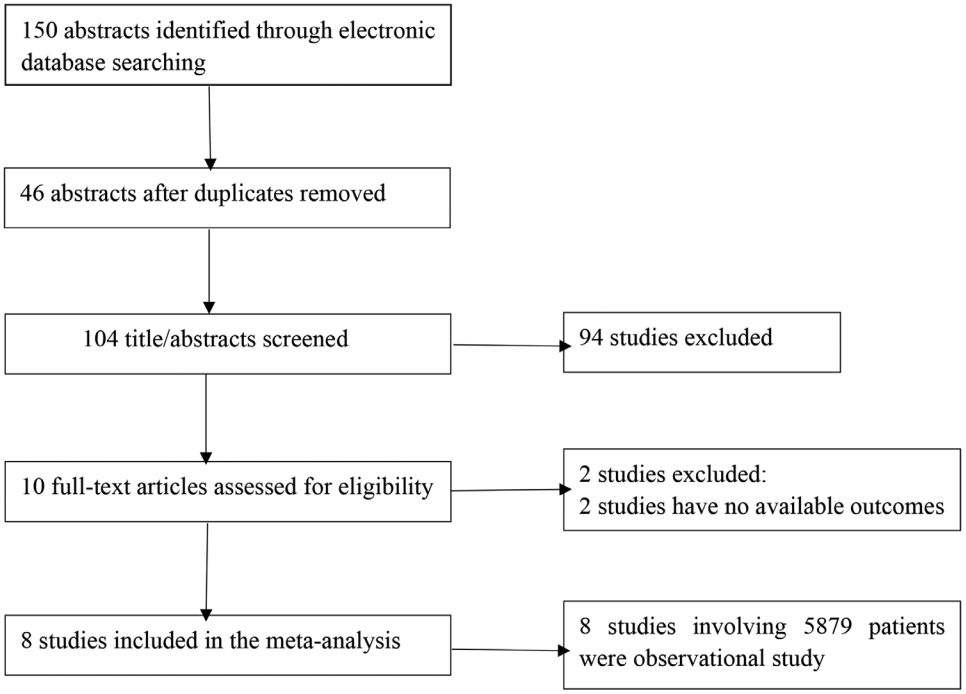
Cardiac death

Five studies reported the incidence of cardiac death. PMI was associated with a higher risk of cardiac death compared with non-PMI (absolute risk, 4.3% vs. 2.6%; OR, 2.59; 95% CI, 1.41–4.78; $P = 0.002$) (Fig. 2b).

Myocardial infarction

The incidence of MI was reported in seven studies. PMI can significantly increase the risk of MI compared with non-PMI (absolute risk, 5.2% vs. 3.5%; OR, 3.07; 95% CI, 1.90–4.98; P < 0.00001) (Fig. 2b).

Fig. 1



Flow diagram of study selection.

Table 1 Main characteristics of studies included in this meta-analysis

					No. of patients (n)		Mean age (years)		Male gender (%)	
Study	Year	Country	Ethnicity	Type of study	PMI	Non-PMI	PMI	Non-PMI	PMI	Non-PMI
Dautov	2018	Canada	Caucasian	Observational	156	299	69	65	80	81
Di Serafino	2016	EU	Caucasian	Observational	133	195	64	64	86	78
Jaguszewski	2017	Poland	Caucasian	Observational	52	1058	67	63	15	24
Jang	2016	Korea	Asian	Observational	59	501	62	62	87	83
Kim	2017	Korea	Asian	observational	23	314	61	62	83	87
Toma	2017	Germany	Caucasian	observational	484	1425	68	65	85	84
Zhang	2016	China	Asian	observational	115	514	65	65	78	84
Zhong	2015	China	Asian	observational	80	357	65	62	79	83

EU, European Union; PMI, periprocedural myocardial injury.

Target vessel revascularization

The incidence of TVR was reported in five studies. PMI was significantly associated with increased the risk of TVR compared with non-PMI (absolute risk, 9.1% vs. 4.0%; OR, 2.07; 95% CI, 1.35–3.16; $P = 0.0008$) (Fig. 2b).

Heterogeneity analysis

As for MACEs, significant heterogeneity between studies included in the meta-analysis were observed ($I^2 = 60\%$). Therefore, subgroup analysis was performed to identify the sources of the heterogeneity observed across the studies. The result indicated that the heterogeneity was significantly decreased in Caucasian populations ($I^2 = 0\%$); however, the heterogeneity was still significant in Asian populations ($I^2 = 70\%$).

Sensitivity analysis

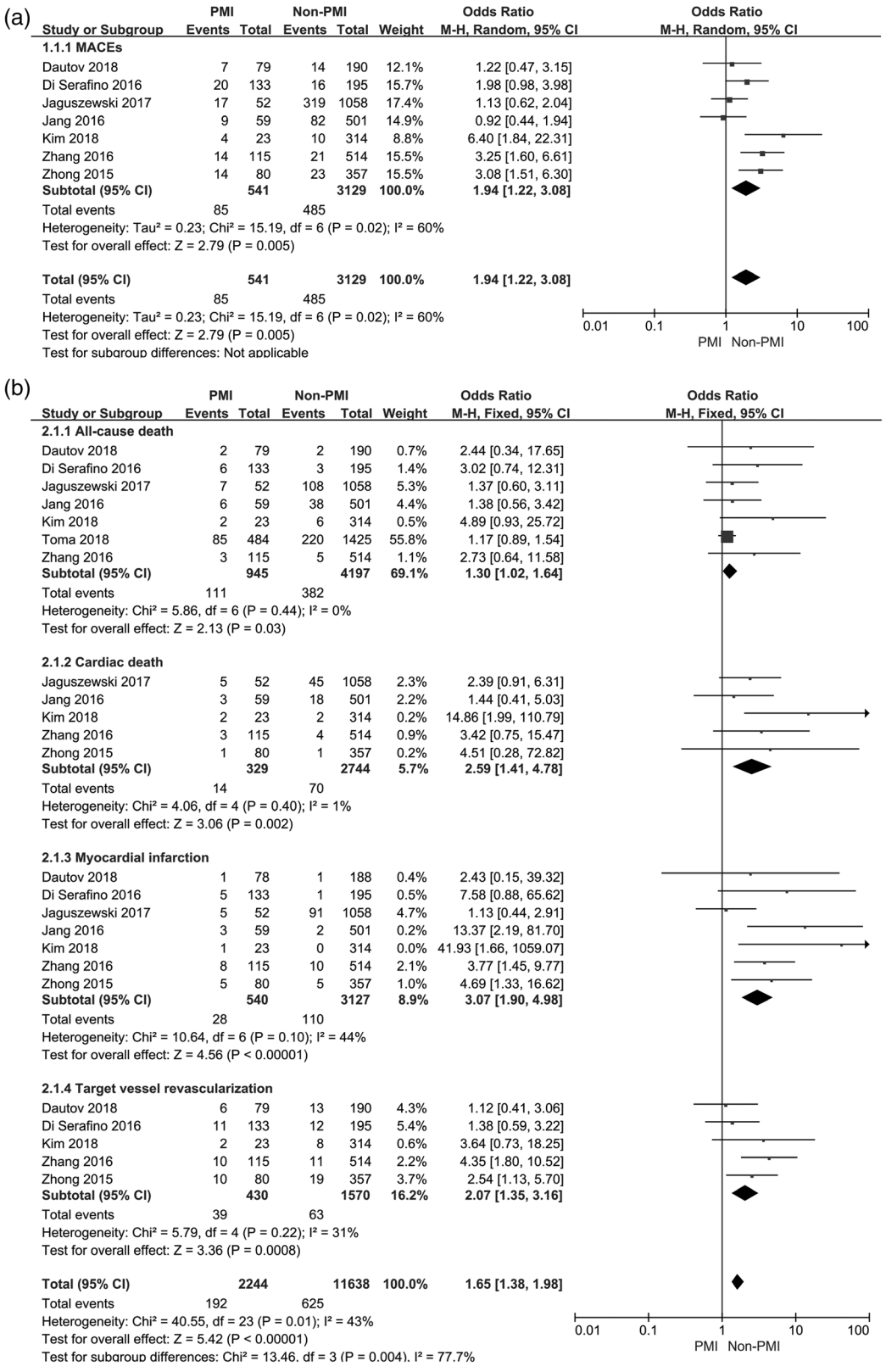
To evaluate the reliability of the results of this meta-analysis, sensitivity analysis was performed by omitting each individual study one by one to evaluate whether or not each study changed the results. The result of sensitivity analysis indicated that all these outcomes were reliable.

Discussion

The meta-analysis demonstrated that PMI was associated with significantly increased risk of MACEs, all-cause death, cardiac death, MI, and TVR in CTO patients undergoing PCI at long-term follow-up.

Previous several studies have shown that PMI following PCI was associated with worse adverse clinical events. Park *et al.* [21], found that PMI was associated

Fig. 2



(a) Comparison between PMI and non-PMI in the risk of major cardiac adverse events. (b) Comparison between PMI and non-PMI in the risk of all-cause death, cardiac death, myocardial infarction, and target vessel revascularization. PMI, periprocedural myocardial injury.

Table 2 Main characteristics of studies included in this meta-analysis

	DM (%)		Hypertension (%)		Dyslipidemia (%)		Previous MI (%)		Previous PCI (%)	
Study	PMI	Non-PMI	PMI	Non-PMI	PMI	Non-PMI	PMI	Non-PMI	PMI	Non-PMI
Dautov	35	40	88	79	NA	NA	51	58	67	72
Di Serafino	27	20	59	60	75	75	NA	NA	42	43
Jaguszewski	19	25	82	75	62	57	64	59	46	47
Jang	46	51	59	64	32	31	25	21	24	18
Kim	35	40	83	70	78	85	13	15	NA	NA
Toma	30	30	84	82	85	87	31	23	24	13
Zhang	34	33	88	92	41	38	27	25	10	7
Zhong	36	31	73	64	NA	NA	26	31	NA	NA

DM, diabetes mellitus; MI, myocardial injury; NA, not available; PCI, percutaneous coronary intervention; PMI, periprocedural myocardial injury.

Table 3 Main characteristics of studies included in this meta-analysis

	LAD CTO (%)		LCx and OM CTO (%)		RCA CTO (%)			
Study	PMI	Non-PMI	PMI	Non-PMI	PMI	Non-PMI	PMI definition	Median follow-up
Dautov	14	16	21	20	58	57	TnT or hsTnT > 5× ULN	396 days
Di Serafino	29	28	21	17	50	55	TnT > 5× ULN, or rise of Tn > 20% from elevated baseline	25 months
Jaguszewski	21.2	32.5	21.2	23.3	57.6	44.2	TNI ≥ 5× URL alone or associated with chest pain or ST-segment or T-wave changes	64.8 months
Jang	43.2	43.1	27.1	31.4	50	50.6	CK-MB ≥ 3× ULN	42 months
Kim	43.5	44.6	NA	NA	NA	NA	CK-MB ≥ 3× ULN	29.6 months
Toma	26.7	28.1	22.9	26	49.4	45.2	cTnT > 5× ULN	3.1 years
Zhang	33.9	57.4	9.6	11.1	56.5	31.9	CK-MB ≥ 3× ULN	1 year
Zhong	42.5	47.1	10	14	47.5	38.7	TnT > 5× ULN	763 days

CK-MB, creatine kinase MB; CTO, chronic total occlusion; hsTnT, high-sensitivity troponin T; LAD, left anterior descending; LCx, Left circumflex; NA, not available; OM, obtuse marginal; PMI, periprocedural myocardial injury; RCA, right coronary artery; TnT, troponin T; ULN, upper limit of normal; URL, upper reference limit.

with increased the risk of mortality. Prasad *et al.* [22], showed that isolated minor elevation in cardiac troponin T (cTnT) was independently associated with increased the risk of long-term mortality. A meta-analysis conducted by Feldman *et al.* [23], demonstrated that an elevation of cTnT or cardiac troponin I (cTnI) after nonemergent PCI was predictive of an increase in long-term mortality as well as the composite adverse events of all-cause mortality/MI. However, these studies did not evaluate CTO patients. In a study conducted by Lee *et al.* [24], the result showed that PMI was associated with an increased risk of long-term mortality after successful CTO-PCI. Moreover, this association between PMI and adverse clinical events was not reversed due to diverse definitions of PMI. Furthermore, Lo *et al.* [25], reported that PMI was associated with worse subsequent clinical outcomes in CTO patients who treated with PCI during median 2.3 years follow-up.

The following mechanisms may explain this observation. First, studies showed that PMI was usually associated with procedural complications, such as side-branch occlusion, abrupt closure, distal embolization, disruption of collateral flow, or coronary dissection [11,21,26]. In addition, the MRI study indicated that about 20% of myocardial necrosis events were caused by micro-embolization not seen on angiography [27]. Thus, in the long-term, myocardial injury may impair left ventricular function and predispose to arrhythmias, resulting in increased the risk of adverse cardiovascular events. Second, patients with elevated cTnT or CK-MB were more likely to have more severe coronary artery disease, complex lesion morphology, congestive heart failure, peripheral vascular disease, and the need for more advanced coronary interventions. Therefore, an elevated cTnT or CK-MB represented the severity of coronary atherosclerosis lesions, and which has been proved to have a significant relationship with the worse prognosis [28,29]. Third, CK-MB and cTnI elevation after PCI may be a marker of the increased atherosclerotic plaque burden and inflammatory state [30,31]. Studies have showed that patients who received anti-inflammatory and antithrombotic drugs, such as statins and glycoprotein IIb/IIIa inhibitors, were associated with a lower incidence of myonecrosis after PCI and had better long-term clinical outcomes [32,33]. Fourth, patient characteristic such as drug resistance may be contributed to myocardial damage. Chen *et al.* [34], showed that patients with aspirin resistance were more likely to have a higher incidence of myonecrosis following nonurgent PCI and subsequently a worse outcome. However, further clinical trials are needed to investigate mechanisms linking myocardial injury to adverse clinical events.

Significant heterogeneity across studies was identified in terms of the endpoint of MACEs. Therefore, we conducted subgroup analysis according to the different ethnicity (Caucasian and Asian populations) to explore sources of heterogeneity. The result of heterogeneity analysis showed that heterogeneity was significantly decreased in Caucasian populations. Thus, ethnicity may

be sources of the heterogeneity. Additionally, other factors, such as age, gender, length of follow-up, may also contributed to the heterogeneity across studies.

Our meta-analysis was the first study to systematically evaluate the clinical significance of PMI in CTO patients undergoing PCI, and the results of the analysis indicated that PMI was closely associated with adverse clinical outcomes. On the basis of the results of our study, we believed that routine cardiac marker measurement with cardiac enzymes or troponins following PCI should be necessary. At the same time, from the clinical point of view, these results suggested that it will be important to develop stricter strategies, including risk factor management of patients, careful selection of candidates, use of longer dual antiplatelet drugs and higher intensity statins, and more advanced interventional procedures, should be taken to reduce PMI occurrence and subsequently improving clinical outcomes.

Limitations

There were several limitations of this meta-analysis. First, this meta-analysis included only 9 non-randomized, observational studies. Thus, the results may be affected by confounding factors. Second, a total of 5879 patients was enrolled this meta-analysis and the small sample size may not be able to accurately evaluate the associations between PMI and clinical outcomes. Third, the definition of PMI varied among the included studies and may affect the reliability of the results. Fourth, some latest studies were included in our meta-analysis, so these studies were limited by follow-up time and may not deeply assess the relationship between PMI and outcomes.

Conclusion

PMI was associated with significantly increased risk of MACEs, all-cause death, cardiac death, MI, and TVR in CTO patients undergoing PCI at long-term follow-up.

Acknowledgements

I would like to declare on behalf of my co-authors that the work described was original research that has not been published previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the manuscript that is enclosed. I sign for and accept responsibility for releasing this material on behalf of any and all co-authors.

Conflicts of interest

There are no conflicts of interest.

References

1 Michael TT, Karmpaliotis D, Brilakis ES, Alomar M, Abdullah SM, Kirkland BL, *et al*. Temporal trends of fluoroscopy time and contrast utilization in coronary chronic total occlusion revascularization: insights from a multicenter united states registry. *Catheter Cardiovasc Interv* 2015; **85**:393–399.

2 Patel VG, Brayton KM, Tamayo A, Mogabgab O, Michael TT, Lo N, *et al*. Angiographic success and procedural complications in patients undergoing percutaneous coronary chronic total occlusion interventions: a weighted meta-analysis of 18,061 patients from 65 studies. *JACC Cardiovasc Interv* 2013; **6**:128–136.

3 Jones DA, Weerackody R, Rathod K, Behar J, Gallagher S, Knight CJ, *et al*. Successful recanalization of chronic total occlusions is associated with improved long-term survival. *JACC Cardiovasc Interv* 2012; **5**:380–388.

4 Khan MF, Wendel CS, Thai HM, Movahed MR. Effects of percutaneous revascularization of chronic total occlusions on clinical outcomes: a meta-analysis comparing successful versus failed percutaneous intervention for chronic total occlusion. *Catheter Cardiovasc Interv* 2013; **82**:95–107.

5 Lee SW, Lee JY, Park DW, Kim YH, Yun SC, Kim WJ, *et al*. Long-term clinical outcomes of successful versus unsuccessful revascularization with drug-eluting stents for true chronic total occlusion. *Catheter Cardiovasc Interv* 2011; **78**:346–353.

6 Aziz S, Stables RH, Grayson AD, Perry RA, Ramsdale DR. Percutaneous coronary intervention for chronic total occlusions: improved survival for patients with successful revascularization compared to a failed procedure. *Catheter Cardiovasc Interv* 2007; **70**:15–20.

7 Prasad A, Rihal CS, Lennon RJ, Singh M, Jaffe AS, Holmes DR Jr. Significance of periprocedural myonecrosis on outcomes after percutaneous coronary intervention: an analysis of preintervention and postintervention troponin T levels in 5487 patients. *Circ Cardiovasc Interv* 2008; **1**:10–19.

8 Cavallini C, Savonitto S, Violini R, Arraiz G, Plebani M, Olivari Z, *et al*; Italian 'Atherosclerosis, Thorombosis, and Vascular Biology' and 'Society for Invasive Cardiology-GISE' Investigators. Impact of the elevation of biochemical markers of myocardial damage on long-term mortality after percutaneous coronary intervention: results of the CK-MB and PCI study. *Eur Heart J* 2005; **26**:1494–1498.

9 Ioannidis JP, Karvouni E, Katritsis DG. Mortality risk conferred by small elevations of creatine kinase-MB isoenzyme after percutaneous coronary intervention. *J Am Coll Cardiol* 2003; **42**:1406–1411.

10 Roe MT, Mahaffey KW, Kilaru R, Alexander JH, Akkerhuis KM, Simoons ML, *et al*. Creatine kinase-MB elevation after percutaneous coronary intervention predicts adverse outcomes in patients with acute coronary syndromes. *Eur Heart J* 2004; **25**:313–321.

11 Tardiff BE, Califf RM, Tcheng JE, Lincoff AM, Sigmon KN, Harrington RA, *et al*. Clinical outcomes after detection of elevated cardiac enzymes in patients undergoing percutaneous intervention. IMPACT-II investigators. Integrilin (eptifibatide) to minimize platelet aggregation and coronary thrombosis-II. *J Am Coll Cardiol* 1999; **33**:88–96.

12 Prasad A, Herrmann J. Myocardial infarction due to percutaneous coronary intervention. *N Engl J Med* 2011; **364**:453–464.

13 Dautov R, Ybarra LF, Nguyen CM, Gibrat C, Joyal D, Rinfret S. Incidence, predictors and longer-term impact of troponin elevation following hybrid chronic total occlusion percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2018; **92**:E308–E316.

14 Di Serafino L, Borgia F, Maeremans J, Pyxaras SA, De Bruyne B, Wijns W, *et al*. Periprocedural myocardial injury and long-term clinical outcome in patients undergoing percutaneous coronary interventions of coronary chronic total occlusion. *J Invasive Cardiol* 2016; **28**:410–414.

15 Jaguszewski M, Gilis-Malinowska N, Gutierrez-Chico JL, Chmielecki M, Skarzynski P, Burakowski S, *et al*. Periprocedural myocardial injury after recanalization of single chronic coronary occlusion: a propensity score analysis comparing long-term clinical outcomes. *J Invasive Cardiol* 2017; **29**:63–67.

16 Jang WJ, Yang JH, Choi SH, Song YB, Hahn JY, Kim WS, *et al*. Association of periprocedural myocardial infarction with long-term survival in patients treated with coronary revascularization therapy of chronic total occlusion. *Catheter Cardiovasc Interv* 2016; **87**:1042–1049.

17 Kim JH, Kim BK, Kim S, Ahn CM, Kim JS, Ko YG, *et al*. Incidence, predicting factors, and clinical outcomes of periprocedural myocardial infarction after percutaneous coronary intervention for chronic total occlusion in the era of new-generation drug-eluting stents. *Catheter Cardiovasc Interv* 2018; **92**:477–485.

18 Toma A, Stähli BE, Gebhard C, Gick M, Minners J, Mashayekhi K, *et al*. Clinical implications of periprocedural myocardial injury in patients undergoing percutaneous coronary intervention for chronic total occlusion: role of antegrade and retrograde crossing techniques. *Eurointervention* 2018; **13**:2051–2059.

19 Zhang Q, Hu J, Yang ZK, Ding FH, Zhang JS, Du R, *et al*. Correlates and outcomes related to periprocedural myocardial injury during percutaneous coronary intervention for chronic total occlusion: results from a prospective, single center PCI registry. *Catheter Cardiovasc Interv* 2016; **87** (Suppl 1):616–623.

20 Zhong X, Li H, Yang H, Yao K, Liu X, Hu K, *et al*. Clinical outcomes and risk factors of periprocedural myocardial injury after successful percutaneous

coronary intervention for chronic total occlusions. *Eur Heart J* 2015; **17**:B57–B64.
21 Park DW, Kim YH, Yun SC, Ahn JM, Lee JY, Kim WJ, *et al*. Frequency, causes, predictors, and clinical significance of peri-procedural myocardial infarction following percutaneous coronary intervention. *Eur Heart J* 2013; **34**:1662–1669.
22 Prasad A, Singh M, Lerman A, Lennon RJ, Holmes DR Jr, Rihal CS. Isolated elevation in troponin T after percutaneous coronary intervention is associated with higher long-term mortality. *J Am Coll Cardiol* 2006; **48**:1765–1770.
23 Feldman DN, Kim L, Rene AG, Minutello RM, Bergman G, Wong SC. Prognostic value of cardiac troponin-I or troponin-T elevation following nonemergent percutaneous coronary intervention: a meta-analysis. *Catheter Cardiovasc Interv* 2011; **77**:1020–1030.
24 Lee SW, Lee PH, Kang SH, Choi H, Chang M, Roh JH, *et al*. Determinants and prognostic significance of periprocedural myocardial injury in patients with successful percutaneous chronic total occlusion interventions. *JACC Cardiovasc Interv* 2016; **9**:2220–2228.
25 Lo N, Michael TT, Moin D, Patel VG, Alomar M, Papayannis A, *et al*. Periprocedural myocardial injury in chronic total occlusion percutaneous interventions: a systematic cardiac biomarker evaluation study. *JACC Cardiovasc Interv* 2014; **7**:47–54.
26 Stone GW, Mehran R, Dangas G, Lansky AJ, Kornowski R, Leon MB. Differential impact on survival of electrocardiographic Q-wave versus enzymatic myocardial infarction after percutaneous intervention: a device-specific analysis of 7147 patients. *Circulation* 2001; **104**:642–647.
27 Porto I, Selvanayagam JB, Van Gaal WJ, Prati F, Cheng A, Channon K, *et al*. Plaque volume and occurrence and location of periprocedural myocardial necrosis after percutaneous coronary intervention: insights from delayed-enhancement magnetic resonance imaging, thrombolysis in myocardial infarction myocardial perfusion grade analysis, and intravascular ultrasound. *Circulation* 2006; **114**:662–669.
28 Proudfit WJ, Bruschke AV, MacMillan JP, Williams GW, Sones FM Jr. Fifteen year survival study of patients with obstructive coronary artery disease. *Circulation* 1983; **68**:986–997.
29 Kanaparti PK, Brown DL. Relation between coronary atherosclerotic plaque burden and cardiac enzyme elevation following percutaneous coronary intervention. *Am J Cardiol* 2000; **86**:619–622.
30 Mehran R, Dangas G, Mintz GS, Lansky AJ, Pichard AD, Satler LF, *et al*. Atherosclerotic plaque burden and CK-MB enzyme elevation after coronary interventions: intravascular ultrasound study of 2256 patients. *Circulation* 2000; **101**:604–610.
31 Saadeddin SM, Habbab MA, Sobki SH, Ferns GA. Association of systemic inflammatory state with troponin I elevation after elective uncomplicated percutaneous coronary intervention. *Am J Cardiol* 2002; **89**:981–983.
32 Pasceri V, Patti G, Nusca A, Pristipino C, Richichi G, Di Sciascio G; ARMYDA Investigators. Randomized trial of atorvastatin for reduction of myocardial damage during coronary intervention: results from the ARMYDA (atorvastatin for reduction of myocardial damage during angioplasty) study. *Circulation* 2004; **110**:674–678.
33 EPISTENT Investigators. Randomised placebo-controlled and balloon-angioplasty-controlled trial to assess safety of coronary stenting with use of platelet glycoprotein-IIb/IIIa blockade. *Lancet* 1998; **352**:87–92.
34 Chen WH, Lee PY, Ng W, Tse HF, Lau CP. Aspirin resistance is associated with a high incidence of myonecrosis after non-urgent percutaneous coronary intervention despite clopidogrel pretreatment. *J Am Coll Cardiol* 2004; **43**:1122–1126.