# Long-term prognosis of culotte versus different crush strategies in management of unprotected left main bifurcation coronary lesions: A meta-analysis

Huaming Mou, Li Yin, Feng Zhu, Shasha Li, Jianming Zhang, Xiaohua Pang, Jianjun Yang, Shimei Yu, Yangjun Mou, Doudou Wang, Hailong Wang

## Abstract

**Objective:** To assess the long-term clinical effects of Culotte and different Crush techniques in the treatment of unprotected left main bifurcation coronary lesions to determine the best percutaneous coronary intervention strategy.

**Method:** The systematic review and meta-analysis comprised search on PubMed, Embase, Cochrane Library, WanFang Data and the China National Knowledge Infrastructure literature databases to locate randomised controlled trials and cohort studies published in Chinese and/or English language till June 2021 and comprised application of Culotte and Crush stenting techniques for percutaneous coronary intervention in patients with unprotected left main bifurcation coronary lesions. The selected studies were analysed for quality, publication bias and heterogeneity.

**Results:** Of the 197 studies located, 8(4.06%) were subjected to meta-analysis. The incidence of major adverse cardiac events in the Mixed-Crush group was higher than the Culotte group (p=0.02), which, in turn, was higher than the Double Kiss Crush group (p<0.0001), The incidence of target lesion revascularisation in the Culotte group was significantly higher than Double Kiss Crush group (p<0.001). The incidence of myocardial infarction in the Culotte group was higher than the Double Kiss Crush group (p=0.04). The incidence of cardiogenic death in the Double Kiss Crush group was similar to that in the Culotte group (p=0.32).

**Conclusion:** Patients in the Double Kiss Crush group had the most long-term benefits, while those receiving Mixed Crush had the least long-term benefits.

**Keywords:** Culotte, Crush, Unprotected left main bifurcation coronary lesion, Meta-analysis, Systemic review.
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## Introduction

The most serious coronary artery disease is the stenosis or occlusion of the left main coronary artery.[1] At present, a large number of studies support coronary artery bypass graft (CABG) as the main treatment method for unprotected left main bifurcation coronary lesions (UPLMBCLs), but this treatment plan can increase the incidence of target lesion revascularisation (TLR), raising the mortality rate.[2] With the development of percutaneous coronary intervention (PCI), especially the widespread application of drug-eluting stents, the left main coronary artery disease is no longer in an area unmanageable by PCI.[3-5] However, controversy remains about single stenting or provisional stenting for left main bifurcation lesions because the incidence of cardiogenic death (CD) with single or provisional stenting is higher. Therefore, a double-stent technique has emerged for UPLMBCLs.[6,7]

Double-stent technology has many options, including T-stents, Y-stents, Crush stents, and Culotte stents.[7,8] Among these, the Crush and Culotte stents are the most common methods for managing UPLMBCLs, and many studies have confirmed that their use is safe and effective.[9] Current Crush stents include the step-Crush, mini-Crush, nano-Crush and the Double Kiss Crush (DK-Crush) options.[10,11] At present, the effect of PCI is influenced by a variety of factors, such as plaque load, arterial anatomical structure, branching artery, and the surgeon's level of experience. It is still unclear which existing technology is suitable for the treatment of UPLMBCLs.[12,13] Thus, the current systematic review and meta-analysis was planned to study the long-term clinical effects of Culotte and different Crush techniques in the treatment of UPLMBCLs to determine the best PCI strategy.

## Materials and Methods

The systematic review and meta-analysis comprised search on PubMed, Embase, Cochrane Library, WanFang Data and the China National Knowledge Infrastructure literature databases to locate randomised controlled trials (RCTs) and cohort studies published in Chinese and/or English language till June 2021 and comprised

Department of Cardiology, Heart Center, Chongqing University Three Gorges Hospital, China.
**Correspondence:** Hailong Wang. Email: wangjinlong2007666@163.com

application of Culotte and Crush stenting techniques for PCI in patients with UPLMBCLs. The medical subject heading (MeSH) terms and key words included "left main", "LM," "Crush" and "Culotte."

The studies included were prospective or retrospective RCTs using Crush stenting options, such as mixed-Crush, mini-Crush, nano-Crush, and DK-Crush, and/or Culotte stenting, with a follow-up time of >2 years and having specific follow-up results, such as major adverse cardiac events (MACEs), target lesion revascularisation (TLR), CD, myocardial infarction (MI), stent thrombosis (ST), and target vascular revascularisation (TVR). Those excluded were controlled studies without Crush or Culotte stenting, those from which follow-up results could not be extracted, those published in languages other than English or Chinese, and reviews or comments.

Two researchers systematically retrieved studies based on pre-designation strategies; screened and evaluated them in accordance with the inclusion/exclusion criteria; and extracted full-text internal data, including the first author's name, basic study characteristics, study period, PCI strategy, and follow-up period and other data. The endpoints of interest were MACEs, CD, MI, ST, TVR and TLR. In case of a conflict of opinion, the matter was decided by two other reviewers.

The Newcastle-Ottawa scale (NOS) was used to assess the quality of the cohort study,[13] the Cochrane bias tool (CBT) was used to assess the bias of RCTs, and the RevMan software (version 5.3; Cochrane, London, England) was used for meta-analysis.[14] Values <25% indicated low heterogeneity, and 75% indicated high heterogeneity, while those in the middle indicated medium heterogeneity. The Mantel-Haenszel method was used to calculate the aggregate estimate of odd ratios (ORs) with 95% confidence intervals (CIs). All p-values were two-tailed, and $p<0.05$ was indicative of a significant statistical difference. The included studies used funnel plotting for bias analyses, including the analysis of publication bias.[15]

## Results

Of the 197 studies located, 8(4.06%) were subjected to meta-analysis (Figure-1); 5(62.5%) cohort studies and 3(37.5%) RCTs.

Of the 1,283 patients who underwent PCI, 710(55.3%)

**Table-1:** Characteristic of the included studies.

| First author/year | Type | PCI strategy | Patients (n) | Follow-up | Primary endpoint event(s) | Secondary endpoint event(s) | CBT/NOS |
|---|---|---|---|---|---|---|---|
| Kervinen 2013[11] | RCT | Crush vs. Culotte | 41 | 3 years | MACEs | TLR, MI, CD | High |
| Chen 2015[6] | RCT | DK-Crush vs. Culotte | 419 | 3 years | MACEs | TLR, MI, CD | High |
| Maximkin 2017[19] | RCT | Crush vs. Culotte | 140 | 5 years | MACEs | NA | Medium |
| Takagi[17] 2014 | Cohort study | Mini-Crush vs. Culotte | 182 | 3 years | MACEs | CD | 7 |
| Kawamoto 2017[16] | Cohort study | Mini-Crush vs. Culotte | 225 | 5 years | MACEs | TLR, MI, CD | 8 |
| Pavani 2018[18] | Cohort study | Mini-Crush vs. Culotte | 172 | 2.27 years | MACEs | TLR, MI | 8 |
| Rigatelli 2018[19] | Cohort study | Nano-Crush vs. Culotte | 39 | 3 years | MACEs | TLR, MI | 8 |
| Rigatelli 2019[20] | Cohort study | Nano-Crush vs. Culotte | 65 | 27.4 ± 10.8 months | MACEs | TLR, CD | 8 |

RCT: Randomised controlled trial, MACE: Major adverse cardiovascular event, TLR: Target lesion revascularisation, MI: Myocardial infarction, CD: Cardiac death, CBT: Cochrane bias tool, NOS: Newcastle-Ottawa scale, NA: No available data.

**Table-2:** Clinical baseline characteristics of the included studies (Crush versus Culotte).

| First author/ year | Age (years) | Female, % | Smoking, % | Diabetic, % | Hypertension, % | Hypercholesterolemia, % | LVEF, % | Tri-vessel disease | SNYTAX score (points) |
|---|---|---|---|---|---|---|---|---|---|
| Kervinen 2013[11] | 65 ± 10/65 ± 11 | 71/71 | 20/27 | 13/15 | 62/60 | 84/74 | 57 ± 11/57 ± 12 | NA | NA |
| Chen 2015[6] | 64.3 ± 10.3/63.3 ± 9.2 | 22.9/20.1 | 45.2/43.5 | 31.9/30.1 | 70.5/61.2 | 41.4/42.1 | NA | 71.3/69.5 | NA |
| Maximkin 2017[19] | NA | NA | NA | NA | NA | NA | NA | NA | < 32 |
| Takagi 2014[17] | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| Kawamoto 2017[16] | 69.9 ± 9.6/67.4 ± 11.2 | 21.2/17.8 | 28.6/16.7 | 39.1/29.4 | 84.4/76.1 | 84.4/76.1 | 56.9 ± 9.1/57.3 ± 8.1 | 57.0/67.8 | 30.4 ± 10.5/27.5 ± 9.4 |
| Pavani 2018[18] | 71 ± 10/71 ± 9.2 | 17.5/22 | 39/40 | 39.7/30 | 81/73.5 | 64.0/64.0 | 54 ± 10/55 ± 9.5 | NA | 30 ± 10.4/28 ± 9.4 |
| Rigatelli 2018[19] | 61.4 ± 13.6/64.1 ± 10.5 | 45/38.1 | NA | 30/19 | NA | 30/18.6 | 47.2 ± 8.6/50.1 ± 3.3 | 56.2/42.2 | 36.8 ± 6.3/35.6 ± 7.7 |
| Rigatelli 2019[20] | 77.1 ± 5.8/78.1 ± 6.8 | 42.8/39.3 | 37.5/27.2 | 25/27.2 | 68.5/60.6 | 75/63.6 | 48.1 ± 6.6/46.3 ± 7.1 | NA | 26.3 ± 7.2/21.4 ± 4.8 |

LVEF: Left ventricular ejection fraction, NA: No available data.

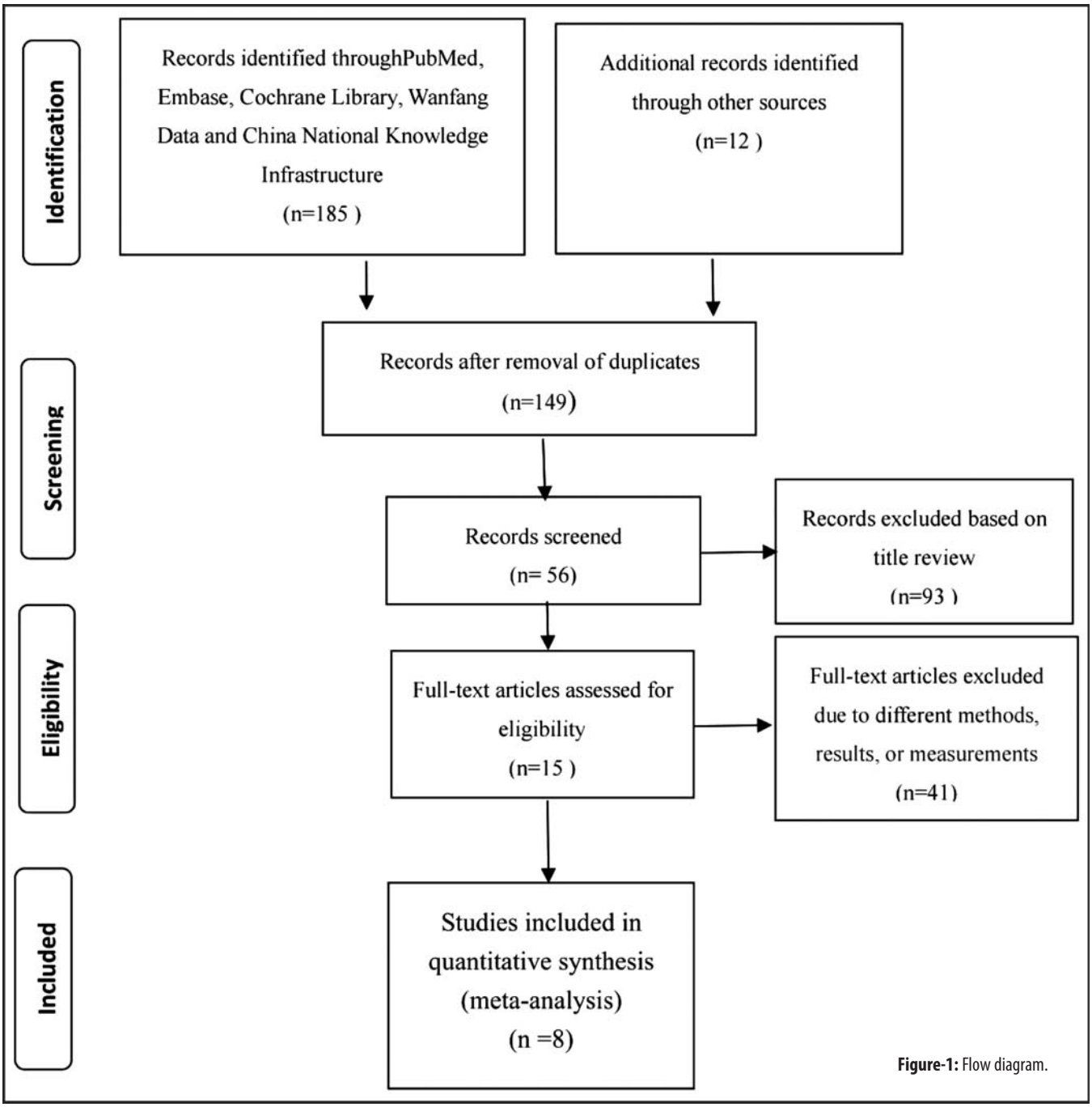


**Figure-1:** Flow diagram.

were treated using the 4 different Crush stenting strategies, and 573(44.6%) were treated using Culotte. The characteristics of the included studies were compared (Table-1), while the clinical baseline characteristics of the study participants were also compared (Table-2).

The heterogeneity of the included studies was low, and a fixed-effects model was chosen for analysis. The incidence of MACEs in the Mixed-Crush group was higher than the Culotte group (p=0.02), which, in turn, was higher than the DK-Crush group (p<0.0001) (Figure-2).

The incidence of TLR in the Culotte group was significantly higher than DK-Crush group (p<0.001) (Figure-3).

The incidence of MI in the Culotte group was higher than the DK-Crush group (p=0.04) (Figure-4).

The incidence of CD in the DK-Crush group was similar to that in the Culotte group (p=0.32) (Figure-5).

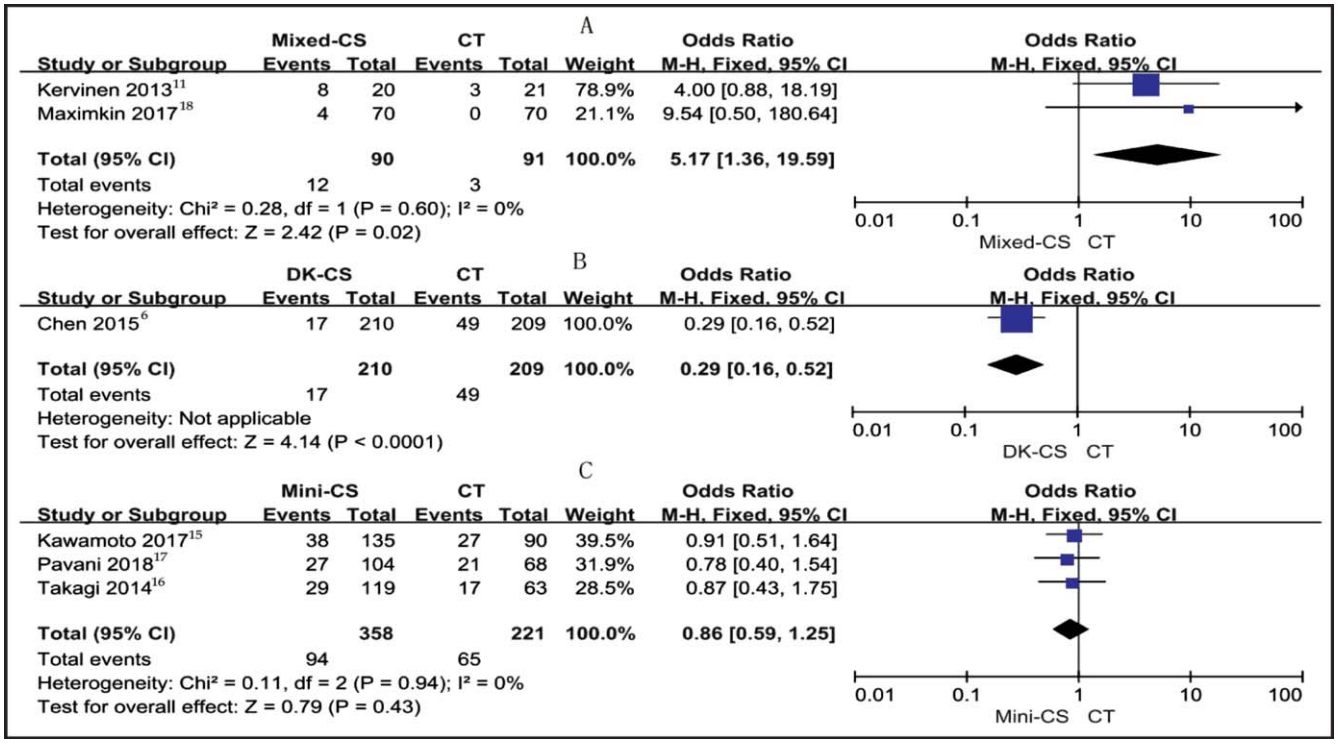


**Figure-2:** (A) Fixed-effects meta-analysis for major adverse cardiovascular events (MACEs). The figure presents the number of events, the number of patients in the Culotte and mixed-Crush groups, the odds ratio (OR) and 95% confidence interval (CI) values for each trial, the overall OR estimate with 95% CI and the p-value for the association test, the p-value for the heterogeneity test, and between-trial inconsistency (I2) measures. (B) Fixed-effects meta-analysis for MACEs in the Culotte and Double Kiss Crush (DK-Crush) groups. (C) Fixed-effects meta-analysis for MACEs in the Culotte and mini-Crush groups.

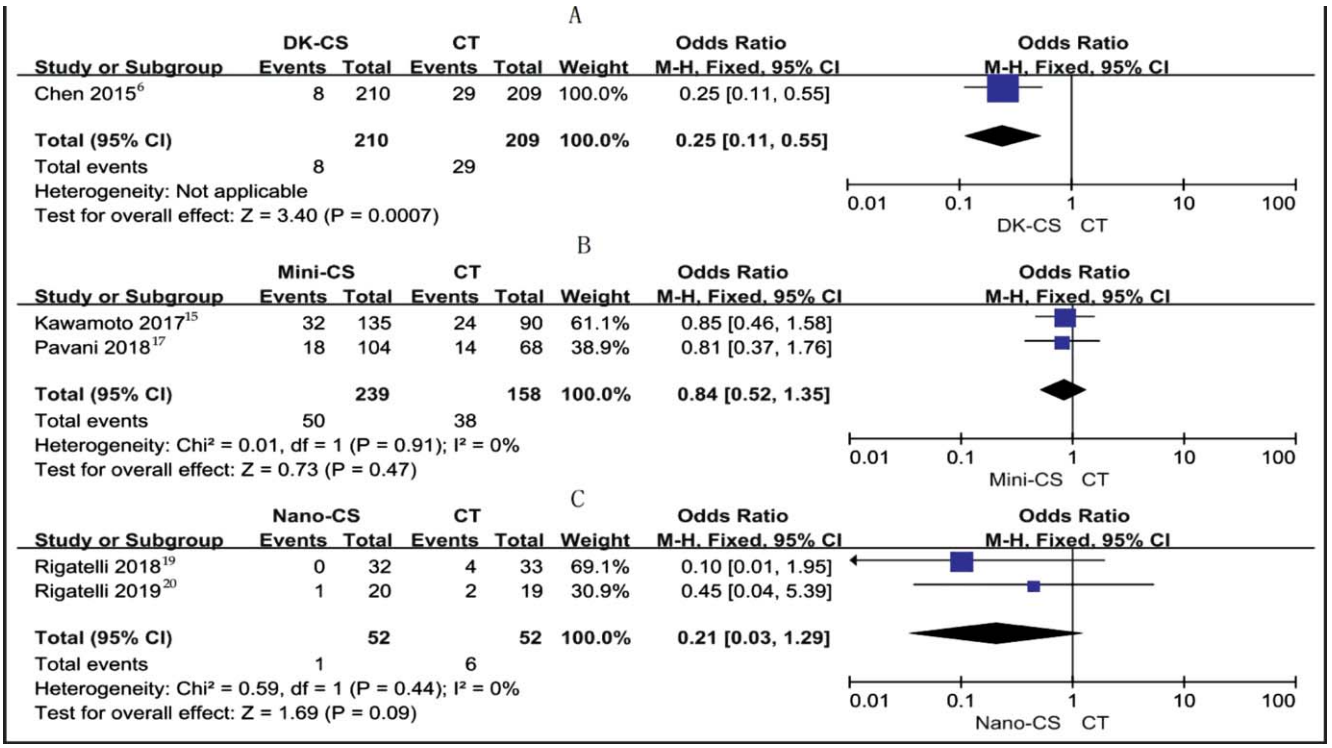


**Figure-3:** (A) Fixed-effects meta-analysis for target lesion revascularisation (TLR) in the Culotte and Double Kiss Crush (DK-Crush) groups. (B) Fixed-effects meta-analysis for TLR in the Culotte and mini-Crush groups. (C) Fixed-effects meta-analysis for TLR in the Culotte and nano-Crush groups.

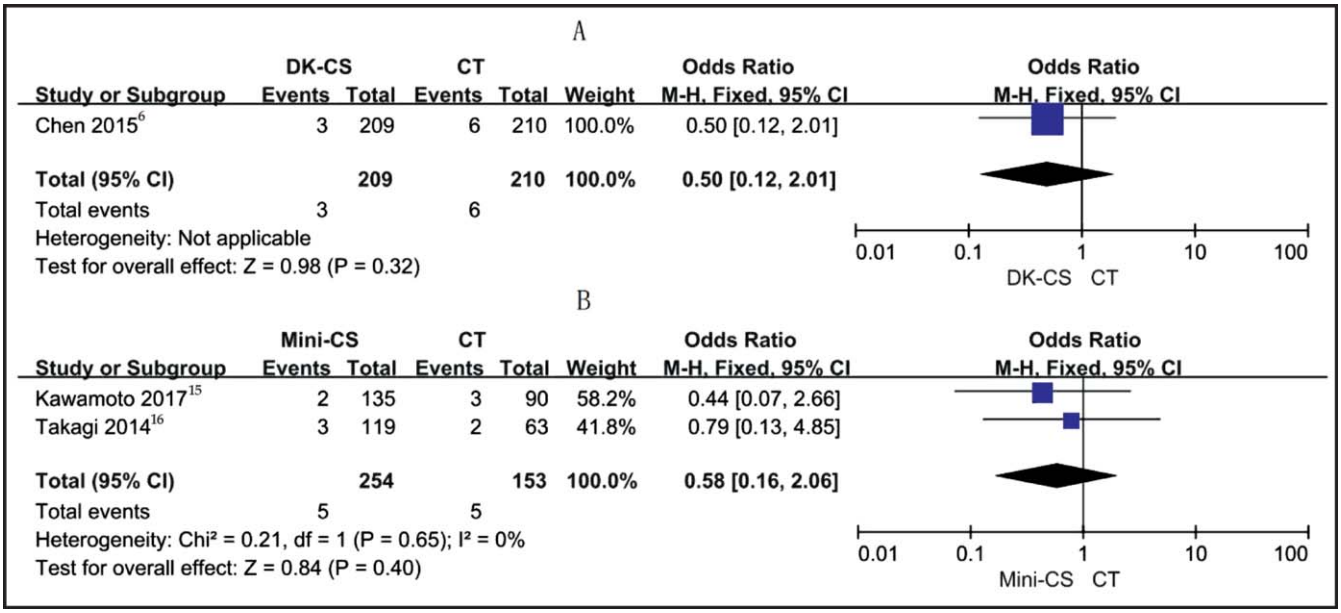


**Figure-4:** (A) Fixed-effects meta-analysis for myocardial infarction (MI) in the Culotte and Double Kiss Crush (DK-Crush) groups. (B) Fixed-effects meta-analysis for MI in the Culotte and mini-Crush.

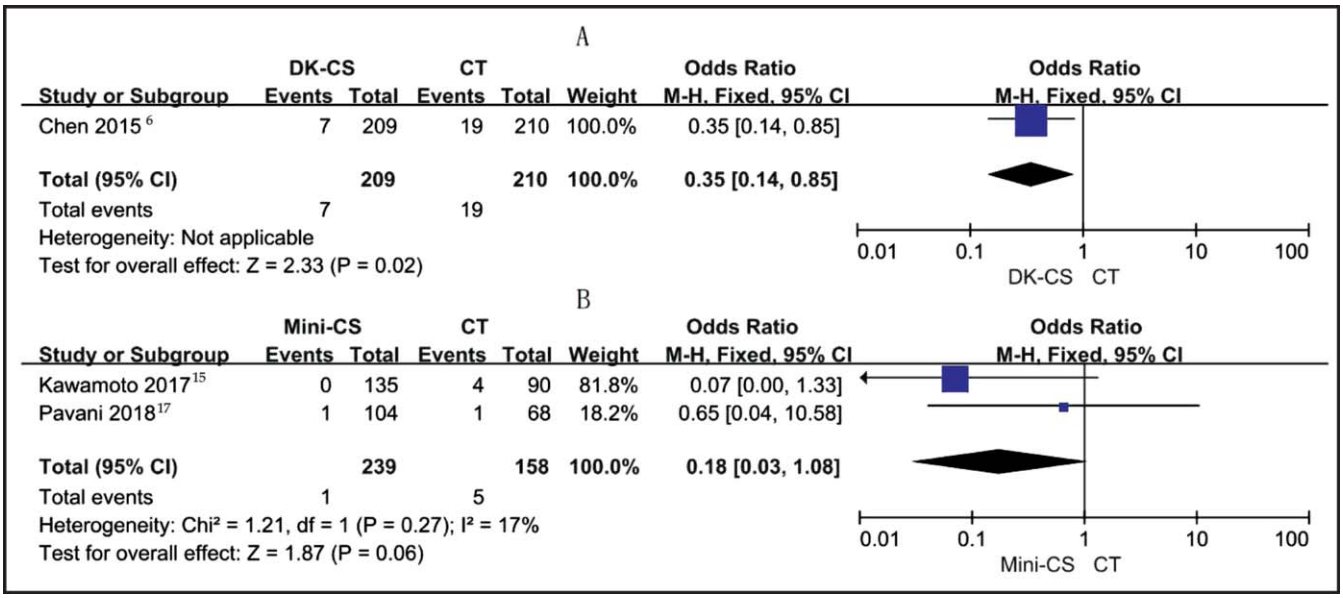


**Figure-5:** (A) Fixed-effects meta-analysis for cardiac death (CD) in the Culotte and Double Kiss Crush (DK-Crush) groups. (B) Fixed-effects meta-analysis for CD in the Culotte and mini-Crush groups.

## Discussion

As also indicated by the studies reviewed,[15-20] left main coronary artery bifurcations are no longer a forbidden area for PCI procedures, and available PCI strategies for patients with UPLMBCLs include Culotte, T-stent, and Crush techniques.[9] The Culotte and Crush techniques are common, with the Culotte operation steps being more complicated than the Crush steps and requiring more operation time, X-ray inspection time, and more contrast agent dosage during the procedure.[20,21] Meanwhile, the Crush technique can be stratified into four types: mini-Crush, nano-Crush, DK-Crush and mixed-Crush.[10,11] To date, a prior meta-analysis on the selection of Culotte and Crush techniques for PCI in patients with UPLMBCLs has been performed,[21] but the analysis method of that previous study was errors because mini-Crush, nano-Crush, DK-Crush and mixed-Crush have very different surgical procedures and effects and cannot be

summarised as a single type of Crush procedure. Such an approach is also the reason for the high heterogeneity in the analysis of the study results and the unreliable conclusions. Thus, the current meta-analysis is the first to evaluate the clinical outcomes of the Culotte and different Crush techniques in the treatment of UPLMBCLs in an effort to suggest the optimal PCI strategy for UPLMBCLs.

At present, intracoronary imaging systems, like optical coherence tomography and intravascular ultrasound, are used to evaluate the effects of the dual-stent strategy for the treatment of UPLMBCLs, optimise the PCI strategy, and to obtain better PCI results, thereby reducing short- or long-term incidence rates of cardiovascular events. For the Crush and Culotte technology of PCI strategy, intracoronary imaging systems have also been routinely applied during the dual-stent approach for UPLMBCLs, which reduces the variability of PCI results caused by many factors, including the diameters of the main coronary artery and branch coronary arteries, the angle of the arterial bifurcation, and the experience level of the operator.

The current meta-analysis divided comparative studies of the Culotte and different Crush techniques of PCI into subgroups in detail. Our subgroup analysis showed low heterogeneity, and the included studies were very stable and reliable. In principle, the best solution is to rank PCI strategies through a network meta-analysis. However, all the included studies were RCTs, retrospective studies, or prospective studies, and the primary endpoint events were different, so this meta-analysis could not use the method of network meta-analysis. Instead, a pooled analysis of subgroups of studies was conducted. First, our meta-analysis included controlled studies of mini-Crush and Culotte stenting,[15,17] wherein primary endpoint events, including the incidence rates of MACEs, MI, CD and TLR, were compared, and there was no statistical difference found between the two groups. Therefore, the mini-Crush strategy of PCI for UPLMBCLs showed no advantage over the Culotte strategy in the long-term prognosis, and there was no difference in patient benefit. When comparing the nano-Crush group and the Culotte group,[19,20] the primary endpoint was the long-term TLR results, and there was no significant difference in the follow-up results. Therefore, the long-term TLR benefit of these two groups of patients was not good. However, in comparing the mixed-Crush and Culotte groups,[18] the former group had higher cardiovascular adverse events, and the long-term effect of the Culotte group was better than that of the mixed-Crush group. In the included studies, although there was only one study performed by Chen's team in the DK-Crush and Culotte group comparison, it was an RCT with a large sample size, so the results are considered reliable and stable. However, higher, independent evaluation and analysis should still be conducted. This single study comprehensively analysed the incidence rates of long-term primary endpoint events, including MACEs, MI, CD and TLR, and a significant statistical difference in the incidence of primary endpoint events was determined between the DK-Crush and Culotte groups. Specifically, the DK-Crush group experienced a more significant benefit in reducing the incidence rates of MACEs, MI and TLR than the Culotte group did, but in terms of CD, there was no significant difference between the two groups.[6]

On the basis of the findings, the PCI strategy that had the greatest benefit was DK-Crush, and the one with least benefit was mixed-Crush. During a long-term follow-up comparison of the Culotte and mini-Crush strategies, there was no difference in the primary endpoint, while in the long-term follow-up analysis of Culotte and nano-Crush results, there was also no statistical difference in the primary endpoint. Therefore, it is recommended that the DK-Crush strategy should be selected when patients with UPLMBCLs are being treated, and the mixed-Crush strategy should be abandoned.

The current meta-analysis had several limitations. First of all, because of the lack of large-scale, multicentre, randomised, double-blind, placebo-controlled trials so far, data was only extracted from small-sample or observational studies, and that can lead to inherent biases, such as selection bias, design bias, treatment bias, and publication bias. Further, it also applied the published summary data analysis of various studies, which increased confounding and selection bias and affected the heterogeneity. Finally, it could not determine all study participants' specific medical treatments. However, despite the limitations, the meta-analysis provided a comprehensive comparison of different PCI strategies, which may help surgeons make informed decisions.

## Conclusion

For the treatment of UPLMBCLs, the DK-Crush PCI strategy offered the greatest long-term benefit, while the mixed-Crush strategy had the least long-term benefit for patients. Among the mini-Crush, nano-Crush, and Culotte technologies, the long-term benefits were similar. As such, patients with UPLMBCLs should be treated with the DK-Crush stenting strategy.

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