Clinical Outcomes Following Simple or Complex Stenting for Coronary Bifurcation Lesions: A Meta-Analysis

Qun Zhang1,2,3*, Hengshan Huan1,4*, Yu Han1,2,3*, Shukun Sun1,2,3, Bailu Wang5 and Shujian Wei1,2,3*

1Department of Emergency and Chest Pain Center, Qilu Hospital, Cheelo College of Medicine, Shandong University, Jinan, Shandong, China. 2Clinical Research Center for Emergency and Critical Care Medicine of Shandong Province, Qilu Hospital, Cheelo College of Medicine, Shandong University, Jinan, Shandong, China. 3Key Laboratory of Emergency and Critical Care Medicine of Shandong Province, Key Laboratory of Cardiopulmonary-Cerebral Resuscitation Research of Shandong Province, Qilu Hospital, Cheelo College of Medicine, Shandong University, Jinan, Shandong, China. 4The Forth People’s Hospital of Linyi, Linyi, Shandong, China. 5Clinical Trial Center, Qilu Hospital, Cheelo College of Medicine, Shandong University, Jinan, Shandong, China.

ABSTRACT

BACKGROUND: Stent placement remains a challenge for coronary bifurcation lesions. While both simple and complex stenting strategies are available, it is unclear which one results in better clinical outcomes. This meta-analysis aims to explore the long-term prognosis following treatment with the 2 stenting strategies.

METHOD: Randomized controlled trials found from searches of the PubMed, EMBASE, and Cochrane Central Register of Controlled Trials were included in this meta-analysis. The complex stent placement strategy was identified as the control group, and the simple stent placement strategy was identified as the experimental group. Data were synthesized with a random effects model. The quality of the randomized controlled trials was assessed by Jadad scale scores. The clinical endpoints at 6 months, 1 year, and 5 years were analyzed.

RESULTS: A total of 11 randomized controlled trials met the inclusion criteria. A total of 2494 patients were included in this meta-analysis. The odds ratio [OR] of the major adverse cardiac events (MACEs) at 6 months was 0.85 (95% confidence interval [CI] 0.53-1.35; P = .49, P = 0%). The OR of the MACEs at 1 year was 0.61 (95% CI 0.36-1.05; P = .08, P = 0%). The OR of the MACEs at 5 years was 0.69 (95% CI 0.51-0.92; P < .01, P = 0%). Compared with the complex strategy, the simple strategy was associated with a lower incidence of MACEs at 5 years.

CONCLUSION: Compared to the complex stenting strategy, the simple stenting strategy can better reduce the occurrence of long-term MACEs for coronary bifurcation lesions.

KEYWORDS: Coronary bifurcation lesions, stent strategy, major adverse cardiac events, long-term prognosis

Introduction

A coronary bifurcation lesion is a coronary artery stenosis adjacent to and/or including the origin of a significant side branch (SB). It is often arbitrarily diagnosed according to the subjective judgment of an interventionalist, a factor leading to possible underdiagnosis of the condition. While coronary bifurcation lesions occur in approximately 15% of percutaneous coronary interventions (PCIs),1 treatment remains challenging due to technological limitations and the occurrence of restenosis. Various stent strategies are clinically used for coronary bifurcation lesions.2 The simple stent placement strategy involves implanting stents only into the main vessel (MV), with optional stenting of the SB. If SB stenting is required, the techniques include provisional T- and T-and-protrusion (TAP) stenting. In contrast, the complex stent implantation strategy involves definite, planned stenting of both the MV and the SB using various techniques, including the crush, culotte, and T-stenting techniques.

While the simple stent placement strategy has better short- and long-term prognoses than the complex strategy,3 stent placement is associated with restenosis. For bare metal stents, the incidence of restenosis ranges from 16% to 44%;4 for the first-generation drug-eluting stents (DES), the incidence of restenosis is 5% to 15%; and for the second-generation DES, the incidence of restenosis is lower.5 The incidence of restenosis is increased by the implantation of multiple stents,1 such as

*These two authors contributed equally to this work.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: Shujian Wei, Department of Emergency, Qilu Hospital, Cheelo College of Medicine, Shandong University, No. 107 Wenhua Xi Road, Jinan 250012, China. Email: weishujian@sdu.edu.cn
in the complex strategy for the treatment of coronary bifurcation lesions. With the development of DES, the incidence of restenosis is further reduced.\(^6\) For the complex stenting strategy, clinical trials have shown that DES can reduce the incidence of restenosis.\(^7\) Furthermore, some studies indicated the complex stent strategy may have better clinical results. Thus, the best stent placement method for coronary artery bifurcation lesions remains unclear.\(^8\)

The present study aims to clarify the best technique to treat coronary bifurcation lesions. We compare the cardiovascular outcomes after interventional treatment with the simple versus the complex stenting strategy for bifurcation lesions. In this meta-analysis, the clinical outcomes—the major adverse cardiovascular events (MACEs), including myocardial infarction (MI), cardiac death, stent thrombosis (ST), target lesion revascularization (TLR), and target vessel revascularization (TVR) were compared between the 2 groups. We combined the follow-up time of all eligible studies to explore the long-term prognosis of simple and complex stent placement strategies.

**Materials and Methods**

*Inclusion criteria*

The studies analyzed met the following inclusion criteria: (1) contained randomized controlled trials (RCTs), (2) used a complex stent placement strategy as the control group and a simple stent placement strategy as the experimental group, (3) had study populations consisting of patients with coronary bifurcation lesions, and (4) had follow-up periods of 6 months, 1 year, and 5 years. Reviews and non-English articles were excluded from our analysis.

*Retrieval strategy*

Literature retrieval was carried out by searching the PubMed, EMBASE, and Cochrane Central Register of Controlled Trials databases for the following search terms: "simple or complex," "stenting," and "coronary bifurcation lesions." Two researchers screened the literature by reading titles, abstracts, and full texts. If necessary, additional study details were used to determine whether studies met the inclusion criteria. Disagreements were submitted to a third reviewer for consensus. In addition, we reviewed the references from meta-analyses of simple and complex stenting strategies for the treatment of coronary bifurcation lesions to find other relevant published and unpublished studies.

*Data extraction and clinical outcomes*

Paired reviewers independently extracted data from the original trials and assessed the qualifications of all identified citations. The name of the project or the first author's last name, the time of publication, the study design, the disease population, the main end point of the study, and the follow-up time, patient's characteristics, comorbidities, procedural characteristics, as well as binary variable data, were extracted. The primary outcome was any MACE, including cardiac death, ST, MI, and all-cause death. The secondary outcomes were TLR and TVR. We analyzed the primary and secondary clinical outcomes at 6 months, 1 year, and 5 years.

**Statistical analysis and quality assessment**

All data were binary variables. We combined the medical treatment effects (odds ratios [ORs] and risk ratios [RRs]) with the corresponding 95% confidence intervals (CIs) to evaluate the impact of simple and complex stent placement strategies on adverse clinical events. Data were analyzed using a random effects model. The \(Q\) and \(P\) tests were used for heterogeneity analysis. A \(P\)-value < .1 or an \(I^2\)-value > 50% indicated greater heterogeneity. To visualize the heterogeneity, prediction intervals were used in forest plots for the primary outcomes. A sensitivity analysis was performed by omitting each study in order to evaluate the reliability and stability of all studies. When \(P\) was >50%, we performed a sensitivity and subgroup analysis.

The methodological quality of the RCTs was assessed by the Cochrane Collaboration risk-of-bias tool. Inclusion of any studies that caused heterogeneity was determined after reading the full text. Egger's test and funnel plots were used to assess potential bias. The quality of the RCTs was assessed using the Jadad scale. The statistical analyses in this meta-analysis were performed using a combination of STATA statistical software (version 16; Stata Corp, College Station, Texas, USA) and Review Manager software (version 5.3; Copenhagen; The Nordic Cochrane Center, The Cochrane Collaboration, 2014). Lastly, the GRADE system was used to evaluate the quality of the evidence for all results.

**Results**

*Included studies*

A total of 1602 articles were retrieved from online databases. Of these, 62 articles were eliminated because of duplication. Four articles meeting the inclusion criteria were manually retrieved from the references of previous meta-analyses. Based on the title and abstract, 1529 articles were excluded, and 15 articles were identified. Finally, 4 articles were excluded based upon the full text contents. The flowchart of the literature retrieval and exclusion rationale is shown in Figure 1.

Of the 11 studies meeting the inclusion criteria, a total of 2494 patients were included in this meta-analysis. Five had a follow-up of 6 months,\(^3,9-12\) 4 had a follow-up of 1 year,\(^9,13-15\) and 3 had a follow-up of 5 years.\(^3,16,17\) The characteristics of all studies meeting the inclusion criteria are summarized in Table 1. The risk of bias assessment of all eligible studies is shown in Figure 2.
The primary outcomes

The OR of MI at 6 months was 0.76 (95% CI 0.45-1.29; \(P = .31, I^2 = 0\%\)). The OR of all-cause death at 6 months was 1.13 (95% CI 0.32-4.06; \(P = .85, I^2 = 0\%\)). The OR of cardiac death at 6 months was 1.32 (95% CI 0.29-5.96; \(P = .72, I^2 = 0\%\)). The OR of MACEs at 6 months was 0.85 (95% CI 0.53-1.35; \(P = .49, I^2 = 0\%\)). There was no significant difference between the 2 stenting strategies for MACEs at 6 months (Figure 3).

The OR of MI at 1 year was 0.54 (95% CI 0.25-1.15; \(P = .11, I^2 = 0\%\)). The OR of MACEs at 1 year was 0.61 (95% CI 0.36-1.05; \(P = .08, I^2 = 0\%\)). The OR of all-cause death at 1 year was 1.57 (95% CI 0.52-4.77; \(P = .43, I^2 = 0\%\)). There was no significant difference between the 2 stenting strategies for MACEs at 1 year (Figure 4).

The OR of cardiac death at 5 years was 0.92 (95% CI 0.42-2.02; \(P = .84, I^2 = 0\%\)). The OR of MI at 5 years was 0.65 (95% CI 0.35-1.24; \(P = .19, I^2 = 0\%\)). The OR of ST at 5 years was 1.33 (95% CI 0.56-3.14; \(P = .52, I^2 = 29\%\)). The OR of all-cause death at 5 years was 0.58 (95% CI 0.34-1.00; \(P = .05, I^2 = 0\%\)). The OR of MACEs at 5 years was 0.69 (95% CI 0.51-0.92; \(P = .01, I^2 = 0\%\)). Compared with the complex strategy, the simple strategy was associated with a lower incidence of MACEs at 5 years. The simple strategy was associated with the lower incidence of all-cause death at 5 years (Figure 5).

The secondary outcomes

The OR of TLR at 6 months was 1.05 (95% CI 0.58-1.90; \(P = .88, I^2 = 0\%\)). The OR of TVR at 6 months was 1.36 (95% CI 0.61-3.03; \(P = .45, I^2 = 0\%\)). The OR of MV restenosis at 6 months was 0.64 (95% CI 0.13-3.23; \(P = .59, I^2 = 0\%\)). The OR of SB restenosis at 6 months was 0.59 (95% CI 0.23-1.52; \(P = .27, I^2 = 0\%\)). There was no significant difference between the 2 groups for the occurrence of restenosis of the MV and the SB (Figure 3).

The OR of TLR at 1 year was 1.98 (95% CI 1.20-3.27; \(P = .007, I^2 = 17\%\)). The OR of TVR at 1 year was 2.29 (95% CI 1.23-4.27; \(P = .009, I^2 = 0\%\)). Compared with the simple strategy, the complex strategy was associated with a lower incidence of TVR and TLR at 1 year (Figure 4).

The OR of TLR at 5 years was 1.17 (95% CI 0.47-2.90; \(P = .74, I^2 = 82\%\)). The OR of TVR at 5 years was 1.07 (95% CI 0.54-2.12; \(P = .85, I^2 = 77\%\)). There was no significant difference between the 2 groups for TLR and TVR at 5 years.

Discussion

In our meta-analysis of 11 RCTs, we compared the advantages and disadvantages of simple and complex stent strategies for treating coronary bifurcation lesions. We found that the simple strategy improved the long-term prognosis of MACEs better than the complex stenting strategy.
| STUDY REFERENCE | YEAR | SUBJECTS INCLUDED | STUDY DESIGN | AGE, Y MEAN ± SD | MALE, N (%) | HYPERTENSION, N (%) | HYPERLIPIDEMIA, N (%) | DIABETES MELLITUS, N (%) | CLINICAL OUTCOMES | POPULATION | FOLLOW-UP TIME | QUALITY ASSESSMENT |
|-----------------|------|-------------------|---------------|-----------------|-------------|---------------------|----------------------|------------------------|-----------------|-------------|----------------|-------------------|
| Culotte stenting VS TAP stenting | BBK 2016 | 150/150 | RCT | 66.3 ± 10.6 | 62.9 ± 10.8 | 76 (78) | 66 (88) | 70 (70) | Cardiac death, TLR, TVR, MI | Bifurcation Lesions | 1 y | 5 |
| Culotte stenting VS PRO | Hildick-Smith 2016 | 103/97 | RCT | 68.3 ± 10.8 | 66 (88) | 70 (70) | 26 (25) | All-cause death, MI, target vessel failure | Bifurcation Lesions | 1 y | 5 |
| DK VS PRO | DKCRUSH-II 2011 | 185/185 | RCT | 63.9 ± 11.1 | 145 (75.8) | 62 (33.7) | 42 (23.1) | Cardiac death, MACEs, MI, TVR | Bifurcation Lesions | 6mo.1y | 4 |
| | DKCRUSH-II 2017 | 183/183 | RCT | 63.9 ± 10.7 | 145 (78.6) | 62 (33.7) | 42 (23.1) | Cardiac death, MACEs, MI, TVR, ML | Bifurcation Lesions | 5y | 3 |
| | CACTUS 2009 | 173/177 | RCT | 66 ± 10 | 142 (80.2) | 113 (63.8) | 38 (22.0) | All-cause death, MI, TVR | Bifurcation Lesions | 30d, 6mo | 4 |
| Routine T-stenting VS PRO | Ferenc 2008 | 101/101 | RCT | 66.9 ± 10.5 | 79 (78.2) | 90 (89.1) | 19 (18.8) | Cardiac death, MI, TVR | Bifurcation Lesions | 1 y | 5 |
| Simple (PRO or other techniques) vs Complex (Crush or other techniques) Stenting | Nordic 2006 | 207/206 | RCT | 62 ± 10 | 162 (79) | 149 (7.3) | 24 (12) | All-cause death, MI, TVR, ST, MI | Bifurcation Lesions | 6mo | 6 |
| | Pan 2004 | 47/44 | RCT | 58 ± 11 | 38 (86) | 25 (57) | 18 (41) | 20 (42) | Restenosis | Bifurcation Lesions | 6mo | 6 |
| | Colombo 2004 | 22/63 | RCT | 62 ± 9 | 48 (76) | 13 (21) | 6 (26) | Restenosis | Bifurcation Lesions | 6mo | 4 |
| | Nordic 2013 | 207/206 | RCT | 63 ± 10 | 78 (38.6) | 52 (28.7) | 72 (35.6) | Cardiac death, All-cause death, MI, TVR, MI | Bifurcation Lesions | 5y | 6 |
| Crush or Culotte VS PRO | BBC one 2010 | 245/238 | RCT | 64 ± 11 | 193 (77) | 142 (57) | 189 (76) | 31 (13) | All-cause death | Bifurcation Lesions | 5y | 5 |

Abbreviations: DK, PRO, Provisional Stenting; MACEs, major adverse cardiovascular events; MI, myocardial infarction; ST, stent thrombosis; TLR, target lesion revascularization; TVR, target vessel revascularization.

Values are mean ± SD or n (%).
The disadvantages of the conventional crush technique were associated with crushed stent struts. In addition, this technique could lead to uncovered nonapposed stent struts occurring at or near the bifurcations, which might be related to the delayed coverage of the neointima. In comparison, the conventional culotte technique was associated with a higher incidence of restenosis and ST. In addition, both techniques were related to a higher incidence of SB occlusion. Fortunately, the crush and culotte techniques have undergone improvements. One modification of the crush technique was the optimization of the stent placement procedure, where a separate step was used to crush the SB stent, followed by inserting a stent into the MV. Intermediate balloon-kiss expansion was performed before positioning a stent in the MV. The overlap of the 2 stents was shorter than in the conventional culotte technique. Intermediate balloon-kiss expansion was then performed before positioning a stent in the MV. For simple stent placement strategies, the accepted criteria for the SB stent placement is based on angiographic results: a vessel severity greater than 75% diameter stenosis, and stenosis length greater than 5 mm. The clinical results from the DKCRUSH studies were of great significance; the double kissing crush replaced the traditional crush in the treatment of coronary bifurcation lesions, had lower angiographic restenosis rates, and was the preferred strategy for PCI. In addition, for complex coronary bifurcation lesions, the double kissing crush was better than provisional stenting.

In the DKCRUSH-II study, researchers compared the MACEs between the double kissing double crush technique and the provisional stenting strategy. The clinical endpoints were followed up at 1, 6, 8, and 12 months. Although the aim of this study was to demonstrate the best strategy for coronary bifurcation lesions, the 2 techniques demonstrated no significant difference in MACEs. The 5-year follow-up results of Chen et al showed that the double kissing crushing stenting strategy had a lower incidence of TLR; however, the 5-year MACEs was not statistically significant, which may indicate the need for a larger sample size to illustrate the best strategy. The Nordic study was also a long-term follow-up study, comparing the clinical outcomes of the simple and complex stenting strategies at 5 years. Even though the simple strategy had a better trend, there was no significant difference in the clinical endpoint for the 2 strategies. In the CACTUS study, similar conclusions were drawn, and the complex stent placement strategy did not show any superiority. Therefore, the simple, optional SB stenting implantation strategy was still recommended for the treatment of coronary bifurcation lesions. However, the long-term follow-up data from the 2 studies illustrated differences in the patients’ illnesses, such as the severity of the SB stenosis, leading to significant differences in the TLR, which could explain the heterogeneity of the 5-year TLR in our meta-analysis. In addition, the functional assessment of bifurcation lesion is very significant. According to the latest research results, fractional flow reserve (FFR) has a certain degree of potential for assessing the functional assessment of bifurcation lesion. The evaluation results of FFR for coronary bifurcation lesions may provide a certain degree of reference for whether to adopt simple or complex strategies.

In a previous meta-analysis, the simple stenting strategy played a beneficial role in reducing the incidence of early acute MI compared to the complex stenting strategy. Niccoli et al also showed that the simple strategy reduced the risk of early MI; however, for MACEs, there was no significant difference between the 2 strategies. In contrast to the previous meta-analyses, we combined the follow-up times to demonstrate which strategy had a better long-term prognosis. In our meta-analysis, we discussed whether the simple stent placement strategy was better than the complex strategy at 6 months, 1 year, and 5 years, and our results showed that the simple stent strategy can reduce the occurrence of MACEs at 5 years.

In the treatment of coronary bifurcation lesions, ST is a common problem. Even though the technique of the complex stent implantation strategy has improved, it still faces challenges. The crush and the culotte techniques have different characteristics; however, they are both associated with a higher risk of ST. For the simple stent placement strategy, techniques include provisional T- and TAP stenting. Compared with TAP stenting, the culotte technique was associated with a lower incidence of angiographic restenosis. However, the temporary stent placement strategy is currently recommended for the treatment of coronary bifurcation lesions. In our meta-analysis, there was no significant difference between the 2 strategies for MV and SB restenosis in 1 year. With the wide clinical application of drug-eluting balloons and DES, the incidence of restenosis and ST may be further reduced. Further clinical trials are required for confirmation.

Although the studies included in this meta-analysis are RCTs, we cannot deny the limitations of this meta-analysis, of this, the longer follow-up period will increase the accuracy of the conclusion of meta-analysis.

Conclusions
In conclusion, the simple stent placement strategy is superior to other strategies in improving the long-term prognosis of patients with coronary bifurcation disease; nonetheless, both stenting strategies have their own advantages. This study compared the MACEs of simple stent strategy and complex stent strategy of different follow-up time in detail, which provided a certain degree of reference value for clinicians in the treatment of coronary bifurcation lesions.

Author Contributions
Qun Zhang and Hengshan Huan wrote the draft. Bailu Wang provided methodology and software. Yu Han, Han Liu, and
Figure 2. Risk of bias assessment of included studies.
Figure 3. The forest plots of MI, all-cause death, TLR, TVR, MV restenosis, SB restenosis, cardiac death, and MACEs in 6 months. Abbreviations: MACEs, major adverse cardiovascular events; MI, myocardial infarction; MV, main vessel; SB, side branch; TLR, target lesion revascularization; TVR, target vessel revascularization.
### Figure 4

The forest plots of all-cause death, TLR, TVR, MI, ST, and MACEs in 1 year.

**Abbreviations:** MACEs, major adverse cardiovascular events; MI, myocardial infarction; ST, stent thrombosis; TLR, target lesion revascularization; TVR, target vessel revascularization.

| Study or Subgroup | Simple Stenting | Complex Stenting | Risk Ratio | Risk Ratio |
|-------------------|-----------------|------------------|------------|------------|
|                   | Events | Total | Events | Total | Weight | M-H. | Random. | 95% CI | M-H. | Random. | 95% CI |
| DKCRUSH-II2011    | 6      | 185   | 12     | 185   | 32.1%   | 0.50  | [0.19, 1.30] |
| Ferenc2008        | 6      | 101   | 6      | 101   | 24.5%   | 1.00  | [0.33, 3.00] |
| Hillick-Smith2016 | 8      | 103   | 14     | 97    | 43.5%   | 0.54  | [0.24, 1.23] |
| Total (95% CI)    | 389    | 383   | 100.0% |       |         | 0.61  | [0.36, 1.05] |
| Total events      | 20     | 32    |         |       |         |       |         |
|                   |        |       |         |       |         |       |         |
| MACEs             |        |       |         |       |         |       |         |
| BBK2016           | 18     | 150   | 9      | 150   | 35.1%   | 2.00  | [0.93, 4.31] |
| DKCRUSH-II2011    | 24     | 185   | 8      | 185   | 34.6%   | 3.00  | [1.38, 6.50] |
| Ferenc2008        | 11     | 101   | 9      | 101   | 30.3%   | 1.22  | [0.53, 2.82] |
| Total (95% CI)    | 436    | 436   | 100.0% |       |         | 1.98  | [1.20, 3.27] |
| Total events      | 53     | 26    |         |       |         |       |         |
|                   |        |       |         |       |         |       |         |
| TLR               |        |       |         |       |         |       |         |
| DKCRUSH-II2011    | 27     | 185   | 12     | 185   | 92.3%   | 2.25  | [1.18, 4.30] |
| Hillick-Smith2016 | 3      | 103   | 1      | 97    | 7.7%    | 2.83  | [0.30, 26.70] |
| Total (95% CI)    | 288    | 282   | 100.0% |       |         | 2.29  | [1.23, 4.27] |
| Total events      | 30     | 13    |         |       |         |       |         |
|                   |        |       |         |       |         |       |         |
| TVR               |        |       |         |       |         |       |         |
| BBK2016           | 4      | 150   | 3      | 150   | 56.5%   | 1.33  | [0.30, 5.66] |
| Ferenc2008        | 2      | 101   | 1      | 101   | 21.8%   | 2.00  | [0.18, 21.71] |
| Hillick-Smith2016 | 2      | 103   | 1      | 97    | 21.8%   | 1.88  | [0.17, 20.44] |
| Total (95% CI)    | 354    | 348   | 100.0% |       |         | 1.57  | [0.52, 4.77] |
| Total events      | 8      | 5     |         |       |         |       |         |
|                   |        |       |         |       |         |       |         |
| All-cause death   |        |       |         |       |         |       |         |
| DKCRUSH-II2011    | 4      | 185   | 6      | 185   | 36.7%   | 0.67  | [0.19, 2.32] |
| Ferenc2008        | 1      | 101   | 2      | 101   | 10.1%   | 0.50  | [0.05, 5.43] |
| Hillick-Smith2016 | 5      | 103   | 10     | 97    | 53.2%   | 0.47  | [0.17, 1.33] |
| Total (95% CI)    | 389    | 383   | 100.0% |       |         | 0.54  | [0.25, 1.15] |
| Total events      | 10     | 18    |         |       |         |       |         |
|                   |        |       |         |       |         |       |         |
| MI                |        |       |         |       |         |       |         |
| DKCRUSH-II2011    | 2      | 185   | 5      | 185   | 38.6%   | 0.40  | [0.08, 2.04] |
| Ferenc2008        | 3      | 101   | 3      | 101   | 41.1%   | 1.00  | [0.21, 4.84] |
| Hillick-Smith2016 | 1      | 103   | 3      | 97    | 20.3%   | 0.31  | [0.03, 2.97] |
| Total (95% CI)    | 389    | 383   | 100.0% |       |         | 0.56  | [0.20, 1.53] |
| Total events      | 6      | 11    |         |       |         |       |         |
|                   |        |       |         |       |         |       |         |

0.01 0.1 1 10 100 Simple Stenting Complex Stenting
### Figure 5. The forest plots of all-cause death, TLR, TVR, cardiac death, MI, ST, and MACEs in 5 years.

**Abbreviations:** MACEs, major adverse cardiovascular events; MI, myocardial infarction; ST, stent thrombosis; TLR, target lesion revascularization; TVR, target vessel revascularization.

| Study or Subgroup | Simple Stenting | Complex Stenting | Risk Ratio | Risk Ratio |
|-------------------|-----------------|------------------|------------|------------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% CI |
| BBC ONE2010        | 7       | 243   | 14    | 238   | 10.5%   | 0.49 [0.20, 1.18] |                  |
| DKCRUSH-II2017     | 24      | 183   | 30    | 183   | 33.9%   | 0.60 [0.49, 1.31] |                  |
| Nordic2013         | 34      | 202   | 51    | 202   | 55.5%   | 0.67 [0.45, 0.98] |                  |
| **Total (95% CI)** | 630    | 623   | 100.0% | 65    | 95      | 0.69 [0.51, 0.92] |                  |
| **Total events**   | 53      | 47    |       |       |         |                      |                  |

**Heterogeneity:** Tau² = 0.00; Chi² = 0.97, df = 2 (P = 0.62); I² = 0%
Test for overall effect: Z = 2.56 (P = 0.01)

**MACEs**

| Study or Subgroup | Simple Stenting | Complex Stenting | Risk Ratio | Risk Ratio |
|-------------------|-----------------|------------------|------------|------------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% CI |
| DKCRUSH-II2017     | 30      | 183   | 16    | 183   | 48.9%   | 1.86 [1.06, 3.32] |                  |
| Nordic2013         | 23      | 202   | 31    | 202   | 51.1%   | 0.74 [0.45, 1.23] |                  |
| **Total (95% CI)** | 385    | 385   | 100.0% | 53    | 47      | 1.17 [0.47, 2.90] |                  |
| **Total events**   | 63      | 60    |       |       |         |                      |                  |

**Heterogeneity:** Tau² = 0.35; Chi² = 5.71, df = 1 (P = 0.02); I² = 82%
Test for overall effect: Z = 0.33 (P = 0.74)

**TLR**

| Study or Subgroup | Simple Stenting | Complex Stenting | Risk Ratio | Risk Ratio |
|-------------------|-----------------|------------------|------------|------------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% CI |
| DKCRUSH-II2017     | 35      | 183   | 23    | 183   | 49.2%   | 1.52 [0.94, 2.47] |                  |
| Nordic2013         | 28      | 202   | 37    | 202   | 50.8%   | 0.76 [0.48, 1.19] |                  |
| **Total (95% CI)** | 385    | 385   | 100.0% | 63    | 60      | 1.07 [0.54, 2.12] |                  |
| **Total events**   | 19      | 36    |       |       |         |                      |                  |

**Heterogeneity:** Tau² = 0.19; Chi² = 4.28, df = 1 (P = 0.04); I² = 77%
Test for overall effect: Z = 0.19 (P = 0.85)

**TVR**

| Study or Subgroup | Simple Stenting | Complex Stenting | Risk Ratio | Risk Ratio |
|-------------------|-----------------|------------------|------------|------------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% CI |
| DKCRUSH-II2017     | 7       | 183   | 14    | 238   | 36.7%   | 0.65 [0.27, 1.58] |                  |
| Nordic2013         | 12      | 202   | 22    | 202   | 63.3%   | 0.56 [0.28, 1.07] |                  |
| **Total (95% CI)** | 385    | 440   | 100.0% | 19    | 36      | 0.58 [0.34, 1.00] |                  |
| **Total events**   | 12      | 13    |       |       |         |                      |                  |

**Heterogeneity:** Tau² = 0.00; Chi² = 0.10, df = 1 (P = 0.76); I² = 0%
Test for overall effect: Z = 1.97 (P = 0.05)

**All-cause death**

| Study or Subgroup | Simple Stenting | Complex Stenting | Risk Ratio | Risk Ratio |
|-------------------|-----------------|------------------|------------|------------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% CI |
| DKCRUSH-II2017     | 6       | 183   | 4     | 183   | 39.8%   | 1.50 [0.43, 5.23] |                  |
| Nordic2013         | 6       | 202   | 9     | 202   | 60.2%   | 0.67 [0.24, 1.64] |                  |
| **Total (95% CI)** | 385    | 385   | 100.0% | 12    | 13      | 0.92 [0.42, 2.02] |                  |
| **Total events**   | 15      | 23    |       |       |         |                      |                  |

**Heterogeneity:** Tau² = 0.00; Chi² = 0.98, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 0.21 (P = 0.84)

**Cardiac death**

| Study or Subgroup | Simple Stenting | Complex Stenting | Risk Ratio | Risk Ratio |
|-------------------|-----------------|------------------|------------|------------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% CI |
| DKCRUSH-II2017     | 6       | 183   | 7     | 183   | 35.4%   | 0.86 [0.29, 2.50] |                  |
| Nordic2013         | 9       | 202   | 16    | 202   | 64.6%   | 0.56 [0.25, 1.24] |                  |
| **Total (95% CI)** | 385    | 385   | 100.0% | 15    | 23      | 0.65 [0.35, 1.24] |                  |
| **Total events**   | 15      | 23    |       |       |         |                      |                  |

**Heterogeneity:** Tau² = 0.00; Chi² = 0.38, df = 1 (P = 0.54); I² = 0%
Test for overall effect: Z = 1.31 (P = 0.19)

**MI**

| Study or Subgroup | Simple Stenting | Complex Stenting | Risk Ratio | Risk Ratio |
|-------------------|-----------------|------------------|------------|------------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% CI |
| DKCRUSH-II2017     | 5       | 183   | 5     | 183   | 49.6%   | 1.00 [0.29, 3.40] |                  |
| Nordic2013         | 7       | 202   | 4     | 202   | 50.4%   | 1.75 [0.52, 5.89] |                  |
| **Total (95% CI)** | 385    | 385   | 100.0% | 12    | 9       | 1.33 [0.56, 3.14] |                  |
| **Total events**   | 12      | 9     |       |       |         |                      |                  |

**Heterogeneity:** Tau² = 0.00; Chi² = 0.41, df = 1 (P = 0.52); I² = 0%
Test for overall effect: Z = 0.64 (P = 0.52)

**ST**

---
Shukun Sun contributed to data curation. Shujian Wei and Bailu Wang contributed to conception, design of this study and revised the article. All authors read and approved the publication of the article.

Research Involving Human Participants and/or Animals

The present study is a meta-analysis of published articles, and neither a human nor animal study that should be approved by the appropriate ethics committee and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed Consent

The present study is a meta-analysis of published articles, and there are no persons who gave their informed consent prior to their inclusion in the study.

ORCID iD

Shujian Wei https://orcid.org/0000-0002-0896-6032

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

1. Steigen TK, Maeng M, Wise B, et al. Randomized study on simple versus complex stenting of coronary artery bifurcation lesions: the Nordic bifurcation study. Circulation. 2006;114:1955-1961.
2. Arokiaraj MC, De Santis G, De Beule M, Palacios IF. A novel tram stent method in the treatment of coronary bifurcation lesions - finite element study. PLoS One. 2016;11:e0149838.
3. Colombo A, Jabbour RJ. Bifurcation lesions: no need to implant two stents when one is sufficient! Eur Heart J. 2016;37:1929-1931.
4. Farooq V, Gogas BD, Serruys PW. Restenosis: delineating the numerous causes of drug-eluting stent restenosis. Circ Cardiovasc Interv. 2011;4:195-205.
5. Gao L, Wang YB, Jing J, Zhang M, Chen YD. Drug-eluting balloons versus new generation drug-eluting stents for the management of in-stent restenosis: an updated meta-analysis of randomized studies. J Geriatr Cardiol. 2019;16:448-457.
6. Lee DH, Park TK, Song YB, et al. Clinical outcomes of biodegradable polymer biolimus-eluting BioMatrix stents versus durable polymer everolimus-eluting Xience stents. PLoS One. 2017;12:e0183079.
7. Zhang L, Zhong W, Luo Y, Chen L. A pilot study on culottes versus crossover single stenting for true coronary bifurcation lesions. Acta Cardiol Sin. 2016;32:450-459.
8. Hildick-Smith D, de Belder AJ, Cooter N, et al. Randomized trial of simple versus complex drug-eluting stenting for bifurcation lesions: the British bifurcation coronary study: old, new, and evolving strategies. Circulation. 2010;121:1235-1243.
9. Chen SL, Santsoso T, Zhang JJ, et al. A randomized clinical study comparing double kissing crush with provisional stenting for treatment of coronary bifurcation lesions: results from the DKCRUSH-II (Double kissing crush versus provisional stenting technique for treatment of coronary bifurcation lesions) trial. J Am Coll Cardiol. 2011;57:914-920.
10. Colombo A, Bramucci E, Sacca S, et al. Randomized study of the crush technique versus provisional side-branch stenting in true coronary bifurcations: the CACTUS (Coronary bifurcations: Application of the crushing technique using Moltenus-eluting stents) study. Circulation. 2004;109:1244-1249.
11. Pan M, de Lezo JS, Medina A, et al. Rapamycin-eluting stents for the treatment of bifurcated coronary lesions: a randomized comparison of a simple versus complex strategy. Am Heart J. 2004;148:857-864.
12. Ferenc M, Gick M, Comberg T, et al. Culotte stenting vs. TAP stenting for treatment of de-novo coronary bifurcation lesions with the need for side-branch stenting: the Bifurcations Bad Krozingen (BBK) II angiographic trial. Eur Heart J. 2016;37:3399-3405.
13. Ferenc M, Gick M, Kienzl RP, et al. Randomized trial on routine vs. Provisional T-stenting in the treatment of de novo coronary bifurcation lesions. Eur Heart J. 2008;29:2859-2867.
14. Hildick-Smith D, Belsen MW, Lassen JF, et al. The EBC TWO Study (European Bifurcation Coronary TWO): a randomized comparison of provisional T-Stenting versus a systemic 2 stent culotte strategy in large caliber true bifurcations. Circ Cardiovasc Interv. 2016;9:e003643.
15. Chen SL, Santsoso T, Zhang JJ, et al. Clinical outcome of double kissing crush versus provisional stenting of coronary artery bifurcation lesions: the 5-year follow-up results from a randomized and multicenter DKCRUSH-II study (Randomized study on double kissing crush technique versus provisional stenting technique for coronary artery bifurcation lesions). Circ Cardiovasc Interv. 2017;10:e004497.
16. Moses JW, Holm NR, Erglis A, et al.; Nordic-Baltic Percutaneous Coronary Intervention Study Group. Long-term results after simple versus complex stenting of coronary artery bifurcation lesions: Nordic bifurcation study 5-year follow-up results. J Am Coll Cardiol. 2013;62:30-34.
17. Costa RA, Mintz GS, Catlett SG, et al. Bifurcation coronary lesions treated with the "crush" technique: an intravascular ultrasound analysis. J Am Coll Cardiol. 2005;46:599-605.
18. Chevalier B, Glatt B, Royer T, Guyon P. Placement of coronary stents in bifurcation lesions by the "culotte" technique. Am J Cardiol. 1998;82:943-949.
19. Le YH, Gao C, Li M, Zhang MB, Wang ZL. Modified double-stent strategy may be an optimal choice for coronary bifurcation lesions: A systematic review and meta-analysis. Medicine. 2018;97:e13377.
20. Chen E, Cai W, Chen LL. Crush versus culotte stenting techniques for coronary bifurcation lesions: A systematic review and meta-analysis of clinical trials with long-term follow-up. Medicine. 2019;98:e14865.
21. Zhang JJ, Chen SL. Classic crush and DK crush stenting techniques. Eur J Cardiovasc Endovasc Ther. 2015;11:V102-V105.
22. Fan L, Chen L, Luo Y, et al. DK mini-culotte stenting in the treatment of true coronary bifurcation lesions: a propensity score matching comparison with T-provisional stenting. Heart Vessels. 2016;31:308-321.
23. Lassen JF, Burzotta F, Banning AP, et al. Percutaneous coronary intervention for the left main stem and other bifurcation lesions: 12th consensus document from the European Bifurcation Club. EuroIntervention. 2018;13:1540-1553.
24. Chen SL, Zhang JJ, Ye F, et al. Study comparing the double kissing (DK) crush with classical crush for the treatment of coronary bifurcation lesions: the DKCRUSH-I bifurcation study with drug-eluting stents. Eur J Clin Invest. 2008;38:361-371.
25. Vassilier D, Mileva N, Coller C, et al. Determinants of functional significance of coronary bifurcation lesions and clinical outcomes after physiology-guided treatment. Int J Cardiol Heart Vasc. 2022;38:100929.
26. Zhang F, Dong L, Ge J. Simple versus complex stenting strategy for coronary artery bifurcation lesions in the drug-eluting stent era: a meta-analysis of randomised trials. Heart. 2009;95:1676-1681.
27. Nicolosi G, Ferrante G, Porti I, et al. Coronary bifurcation lesions: stent one branch or both? A meta-analysis of patients treated with drug eluting stents. Int J Cardiol. 2010;139:80-91.