Drug-Coated Balloon vs. Drug-Eluting Stent in Acute Myocardial Infarction: A Systematic Review and Updated Meta-Analysis

ABSTRACT

Background: This study aimed to systematically review the evidence of drug-coated balloon used in the treatment of acute myocardial infarction and compared with using drug-eluting stent in terms of clinical and angiographic outcomes for a relatively long follow-up period.

Methods: Electronic databases including PubMed, Embase, and the Cochrane Library were used to search for the information of each study. A total of 8 studies involving 1310 patients were included in this meta-analysis.

Results: During a median follow-up duration of 12 months (range 3-24 months), there were no statistical differences between the drug-coated balloon and drug-eluting stent group in terms of a major adverse cardiovascular event (odds ratio = 1.07; \( P = .75; 95\%\) CI: 0.72-1.57), all-cause death (odds ratio = 1.01; \( P = .98; 95\%\) CI = 0.56-1.82), cardiac death (odds ratio = 0.85, \( P = .65; 95\%\) CI = 0.42-1.72), target lesion revascularization (odds ratio = 1.72; \( P = .09; 95\%\) CI: 0.93-3.19), recurrent myocardial infarction (odds ratio = 0.89, \( P = .65; 95\%\) CI = 0.42-1.72), and thrombotic event (odds ratio = 1.10; \( P = .90; 95\%\) CI: 0.24-5.02). Drug-coated balloon was not linked with risk of late lumen loss compared with drug-eluting stent (mean difference = −0.06 mm; \( P = .42; 95\%\) CI: −0.22-0.09 mm). However, there was a higher incidence of target vessel revascularization noted in the drug-coated balloon group compared with the drug-eluting stent group (odds ratio = 1.88; \( P = .02; 95\%\) CI: 1.10-3.22). The subgroup analysis stratified by different study types and ethnicities showed there were no significant differences between the 2 groups.

Conclusions: Using drug-coated balloon might serve as a potential alternative strategy for patients with acute myocardial infarction because of the similar clinical and angiographic outcomes compared with using drug-eluting stent; nevertheless, the issue of target vessel revascularization should be more focused on. Larger and more representative studies are needed in the future.

Keywords: Drug-coated balloon, drug-eluting stent, acute myocardial infarction, major adverse cardiovascular event

INTRODUCTION

The second-generation drug-eluting stent (DES) has been the safest and most effective standard management during the percutaneous coronary intervention (PCI) transition process over 40 years, superior to the plain old balloon angioplasty (POBA) and bare metal stent (BMS) implantation in the long term.1-4 Despite this, DES implanting seems to still arise a number of adverse events in practical procedures, for instance, in-stent restenosis (ISR) and late-stent thrombosis as well as bleeding caused by the long-term duration of dual antiplatelet therapy (DAPT).5,6 The drug-coated balloon (DCB) currently demonstrated its effect in the treatment of ISR,7,8 which is recommended by the 2018 European Society of Cardiology guidelines for myocardial revascularization as the evidence of class I.9 In addition to ISR, DCB has been used in other circumstances, such as small vessel lesions,10,11 bifurcation lesion,12 high bleeding risk,13 and acute myocardial infarction (AMI).14 Recently, Megaly et al15 performed a meta-analysis of short-term clinical and angiographic outcomes of patients with DCB vs. DES in AMI.
indicating that there was no statistical difference between the 2 groups. However, larger sized, wider representative analyses guidelines (PRISMA). The present meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Search Strategy We performed a systematic computerized search via PubMed, Embase, and the Cochrane Library from April 2002 to October 2022 using the following keywords “drug-eluting balloon,” “DEB,” “drug-coated balloon,” “DCB,” “paclitaxel-coated balloon,” and “acute myocardial infarction.” We screened the eligible studies by browsing titles, abstracts, and full texts. We deleted reviews, case reports, letters, comments, and others. The specific references were also screened to avoid missing any research. Study Selection and Data Collection We enrolled in randomized controlled trials (RCTs) or observational cohort studies comparing DCB with DES in the treatment of AMI. In the DCB arm, we excluded those cases with preferred choice of DCB followed by a bailout strategy, defined as stent application to remedy residual stenosis or dissection. The hybrid strategy defined as a combination utilizes of DCB and DES was not allowed in the DCB group. The eligible data were selected independently by 2 researchers (F.Z. and X.B.), and any disagreement was determined by a third one (J.J.) finally. The ethics approval and patient consent were not required for this analysis. The baseline characteristics of the included studies involved age, sex, and history of diabetes, hypertension, dyslipidemia, and smoking. The quality of included studies was assessed using the Cochrane risk assessment tool for RCTs and The Newcastle Ottawa Scale for observational studies. METHODS The present meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA). Search Strategy We performed a systematic computerized search via PubMed, Embase, and the Cochrane Library from April 2002 to October 2022 using the following keywords “drug-eluting balloon,” “DEB,” “drug-coated balloon,” “DCB,” “paclitaxel-coated balloon,” and “acute myocardial infarction.” We screened the eligible studies by browsing titles, abstracts, and full texts. We deleted reviews, case reports, letters, comments, and others. The specific references were also screened to avoid missing any research. Study Selection and Data Collection We enrolled in randomized controlled trials (RCTs) or observational cohort studies comparing DCB with DES in the treatment of AMI. In the DCB arm, we excluded those cases with preferred choice of DCB followed by a bailout strategy, defined as stent application to remedy residual stenosis or dissection. The hybrid strategy defined as a combination utilizes of DCB and DES was not allowed in the DCB group. The eligible data were selected independently by 2 researchers (F.Z. and X.B.), and any disagreement was determined by a third one (J.J.) finally. The ethics approval and patient consent were not required for this analysis. The baseline characteristics of the included studies involved age, sex, and history of diabetes, hypertension, dyslipidemia, and smoking. The quality of included studies was assessed using the Cochrane risk assessment tool for RCTs and The Newcastle Ottawa Scale for observational studies. RESULTS A total of 8 studies (1310 patients; DCB group, n = 568; DES group, n = 742) were included in this meta-analysis (Figure 1). The characteristics of these 8 studies are described in Table 1, and the baseline information of those is described in Table 2. Only 4 studies are RCTs and another 4 studies are observational trials. Most of the studies are single-centered except EPCAD study which includes 5 centers of German. The population of this meta-analysis is derived from European and Asian countries. The median follow-up time was 12 months ranging from 3 months to 24 months. We compared the outcomes of DCB with the second-generation DES. Bailout stenting procedures in the DCB group ranged from 1.1% to 18%, with 6 studies whose bailout stenting data are available. Risk of Bias and Quality Assessment The funnel plot for MACE of this meta-analysis was assessed as symmetrical visually with an approximately equal number of studies on both sides of the vertical axis (Supplementary Figure 1 in the Data Supplement). The results of Cochrane risk assessment for RCTs and Newcastle Ottawa Scale for observational studies were illustrated by Supplementary Figure 2 and Supplementary Table 1 in the Data Supplement. Clinical and Angiographic Outcomes A total of 8 studies reported data on MACE, cardiac death, and recurrent MI. All-cause death was assessed in all the 8

HIGHLIGHTS
- The high-quality evidence of drug-coated balloon utilized in patients with acute myocardial infarction is still lacking.
- The present meta-analysis was performed to determine the effectiveness and safety of drug-coated balloon used in the treatment of acute myocardial infarction in terms of clinical and angiographic outcomes for a relatively long follow-up period.
- Using drug-coated balloon would be an alternative strategy for using drug-eluting stent in patients with acute myocardial infarction since no significant differences in clinical and angiographic outcomes were noted in our meta-analysis.
<table>
<thead>
<tr>
<th>Study (First Author, Year)</th>
<th>Study Type</th>
<th>Numbers of DCB/DES Group</th>
<th>Balloon/Stent Type</th>
<th>Region (Number of Centers)</th>
<th>Follow-up Time (Months)</th>
<th>Enrolment Dates</th>
<th>STEMI/ NSTEMI</th>
<th>Bailout Stenting (%)</th>
<th>Angiographic Outcomes</th>
<th>MACE Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nijhoff, 2015</td>
<td>Observational</td>
<td>40/45</td>
<td>DIOR II (Eurocor GmbH, Bonn, Germany)/Paclitaxel (Taxus Liberté, Boston Scientific, Natick, Mass, USA)</td>
<td>The Netherlands (2)</td>
<td>12</td>
<td>NA</td>
<td>STEMI</td>
<td>10</td>
<td>LLL, binary restenosis, MLD, diameter stenosis</td>
<td>Death, any MI and TVR</td>
</tr>
<tr>
<td>Gobić, 2017</td>
<td>RCT</td>
<td>38/37</td>
<td>Sequent Please (B. Braun, Melsungen, Germany)/Sirolimus (Biomime, Meril Life Sciences, Vapi, India)</td>
<td>Croatia (1)</td>
<td>6</td>
<td>March 2014-January 2015</td>
<td>STEMI</td>
<td>7.3</td>
<td>LLL, MLD</td>
<td>Cardiovascular death, reinfarction, TLR, and stent thrombosis</td>
</tr>
<tr>
<td>Fang, 2018</td>
<td>Observational</td>
<td>75/42</td>
<td>NA</td>
<td>Taiwan (1)</td>
<td>12</td>
<td>November 2011-December 2015</td>
<td>STEMI/NSTEMI</td>
<td>NA</td>
<td>NA</td>
<td>TLR, TVR, recurrent MI, stroke, and cardiovascular mortality</td>
</tr>
<tr>
<td>Scheller, 2019</td>
<td>RCT</td>
<td>85/111</td>
<td>Sequent Please (B. Braun, Melsungen, Germany)/56% with BMS, 44% with DES</td>
<td>Germany (5)</td>
<td>9</td>
<td>December 2012-January 2017</td>
<td>NSTEMI</td>
<td>15</td>
<td>NA</td>
<td>All-cause mortality, myocardial infarction, target lesion revascularization, stroke, or PCI at other vessels</td>
</tr>
<tr>
<td>Zhang, 2020</td>
<td>Observational</td>
<td>180/200</td>
<td>NA</td>
<td>China (1)</td>
<td>3</td>
<td>January 2016-May 2019</td>
<td>STEMI/NSTEMI</td>
<td>1.1</td>
<td>NA</td>
<td>Cardiac death, non-fatal MI, TVR, and in-stent thrombosis</td>
</tr>
<tr>
<td>Tan, 2020</td>
<td>Observational</td>
<td>56/212</td>
<td>Sequent Please (B. Braun, Melsungen, Germany)/(Endeavor Resolute, Metronic company) or (Firebird2, Microport company)</td>
<td>China (1)</td>
<td>24</td>
<td>March 2016-March 2018</td>
<td>STEMI/NSTEMI of SVD</td>
<td>NA</td>
<td>MLD, diameter stenosis, LLL</td>
<td>all-cause death, non-fatal MI, TLR, or TVR</td>
</tr>
<tr>
<td>Hao, 2021</td>
<td>RCT</td>
<td>38/42</td>
<td>Yinyi Biotech BingoDrug Coated Balloon (Liaoning, China)</td>
<td>China (1)</td>
<td>12</td>
<td>January 2018-December 2019</td>
<td>STEMI</td>
<td>9.5</td>
<td>LLL, restenosis</td>
<td>NA</td>
</tr>
<tr>
<td>Niehe, 2022</td>
<td>RCT</td>
<td>56/53</td>
<td>Pantera Lux paclitaxel-coated balloon (Biotronik)/sirolimus-elutingstent (Biotronik)</td>
<td>The Netherlands (1)</td>
<td>24</td>
<td>October 2014-November 2017</td>
<td>STEMI</td>
<td>18</td>
<td>NA</td>
<td>Cardiac death, recurrent MI, and ischemia-driven TLR</td>
</tr>
</tbody>
</table>

DCB, drug-coating balloon; DES, drug-eluting stent; LLL, late lumen loss; MACE, major adverse cardiovascular event; MLD, minimal lumen diameter; NA, not available; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; SVD, small vessel coronary artery disease; TLR, target lesion revascularization; TVR, target vessel revascularization.
studies, although a few studies did not report non-cardiac death. Target vessel revascularization (including TLR) was assessed in 7 out of 8 studies. Target vessel revascularization was assessed in 6 out of 7 studies. During a median follow-up duration of 12 months (range 3-24 months), no statistically different effects were found between the applications of DCB and DES in terms of MACE (OR = 1.07; P = .75; 95% CI: 0.72-1.57; Figure 2), all-cause death (OR = 1.01; P = .98; 95% CI: 0.56-1.82; Figure 3), cardiac death (OR = 0.85; P = .65; 95% CI: 0.42-1.72; Figure 3), TLR (OR = 1.72; P = .09; 95% CI: 0.93-3.19; Figure 4), recurrent MI (OR = 0.89; P = .76; 95% CI: 0.44-1.83; Figure 5), and thrombotic event (OR = 1.10; P = .90; 95% CI: 0.24-5.02; Figure 5). However, there was a higher incidence of TVR noted in the application of DCB compared with DES (OR = 1.88; P = .02; 95% CI: 1.10-3.22; Figure 4). The heterogeneity among the 8 studies (I^2 = 35%) was displayed when we pooled ORs of each study concerned with MACE. The sensitivity analysis showed deleting any one of the studies did not change the tendency in terms of all-cause death, cardiac death, TLR, and recurrent MI, except for TRV. When either Nijhoff’s study or Zhang’s study was deleted, no statistically significant difference was noted between DCB and DES groups.

During the median follow-up duration of 12 months, DCB strategy was not associated with LLL compared with DES implanting (MD = −0.06 mm, 95% CI = −0.22-0.09 mm, Figure 2).

### Subgroup Analysis

Subgroup analysis of outcomes (MACE, all-cause death, cardiac death, TVR, TLR, and recurrent MI) was stratified by the type of RCT or observational study and by the population of European or Asian. The results showed that there were still no significant differences between 2 groups with either RCTs or observational studies as well as either Europeans or Asians (Figure 6).

### DISCUSSION

In this meta-analysis of 8 clinical trials including 1310 patients with AMI undergoing PCI, we compared the clinical outcomes of DCB versus DES used in the operation. The principal

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**Table 2. Baseline Characteristics of the Patients in Each Study Included.**

<table>
<thead>
<tr>
<th>Study</th>
<th>DCB Age (Mean ± SD)</th>
<th>DCB Male (%)</th>
<th>DCB Diabetes (%)</th>
<th>DCB Dyslipidemia (%)</th>
<th>DCB Hypertension (%)</th>
<th>DCB Smoking (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nijhoff, 2015</td>
<td>57.9 ± 10.0</td>
<td>55.9 ± 9.7</td>
<td>26 (65)</td>
<td>41 (83.7)</td>
<td>5 (12.5)</td>
<td>2 (4.1)</td>
</tr>
<tr>
<td>Gobić, 2017</td>
<td>56.6 ± 13.2</td>
<td>54.3 ± 10.6</td>
<td>27 (71.1)</td>
<td>27 (73)</td>
<td>2 (5.3)</td>
<td>4 (10.8)</td>
</tr>
<tr>
<td>Fang, 2018</td>
<td>67.5 ± 11.6</td>
<td>69.9 ± 11.0</td>
<td>46 (61.3)</td>
<td>46 (61.3)</td>
<td>58 (77.3)</td>
<td>26 (61.9)</td>
</tr>
<tr>
<td>Scheller, 2019</td>
<td>66.0 ± 11.4</td>
<td>67.0 ± 13.1</td>
<td>69 (66.3)</td>
<td>72 (67.9)</td>
<td>28 (26.9)</td>
<td>38 (35.8)</td>
</tr>
<tr>
<td>Zhang, 2020</td>
<td>66.4 ± 12.3</td>
<td>63.1 ± 18.2</td>
<td>152 (76.0)</td>
<td>122 (67.8)</td>
<td>25 (13.9)</td>
<td>40 (20.0)</td>
</tr>
<tr>
<td>Tan, 2020</td>
<td>64.96 ± 8.82</td>
<td>62.39 ± 991</td>
<td>34 (60.7)</td>
<td>139 (65.6)</td>
<td>18 (32.14)</td>
<td>58 (26.85)</td>
</tr>
<tr>
<td>Hao, 2021</td>
<td>59 ± 11</td>
<td>56 ± 11</td>
<td>30 (75)</td>
<td>35 (82)</td>
<td>10 (28)</td>
<td>15 (35)</td>
</tr>
<tr>
<td>Niehe, 2022</td>
<td>57.4 ± 9.2</td>
<td>57.3 ± 8.3</td>
<td>52 (87)</td>
<td>52 (87)</td>
<td>8 (13)</td>
<td>4 (7)</td>
</tr>
</tbody>
</table>

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findings were as followed: In terms of clinical and angiographic outcomes, performing PCI with DCB only strategy had no significant difference associated with doing that with DES strategy. Furthermore, our subgroup analysis demonstrated different study types and populations did not alter the stability of results.

Role of Drug-Eluting Stent in Percutaneous Coronary Intervention

The new generation DES rather than BMS or POBA has become the cornerstone management during PCI for its advantages in reducing elastic recoil, flow-limiting dissections, and restenosis caused by cellular proliferation.17,18
Despite this, the patients treated with DES are still at risk for late-stent thrombosis, ISR, and a prolonged DAPT post-operative. Moreover, PCI with DES strategy is also limited in tackling complex lesions such as long, bifurcated, calcified, or chronic total occlusions (CTO) lesions.

Role of Drug-Coated Balloon in Percutaneous Coronary Intervention

Drug-coated balloon, an attractive alternative therapy of DES, has played a vital role in the treatment of ISR and obtained a recommendation of class IA. However, using DCB...
in de novo lesions such as bifurcation lesions, and small vessel disease (SVD) has been getting increasing evidences with regard to recent multiple trials and meta-analyses. In recent years, DCB strategy also has been tried to be applied in the treatment of ACS, even AMI. Ho et al in Singapore first reported a case of STEMI treated with DCB. Their subsequent study found that patients with AMI treated with DCB only had a low rate of ischemic events within 30 days, which demonstrated that DCB was safe and feasible. In 2015, Nijhoff et al reported the therapeutic effect of the DEB-only strategy compared with DES strategy in primary PCI, indicating that DEB might increase risks of LLL, restenosis, and MACE compared to DES. DEB-only strategy was still recommended as a valid alternative for DES strategy since no acute or late thrombotic events occurred in the trial. In 2017, Gobić et al published their results of the first RCT for DCB vs. DES in the primary PCI setting, providing evidence for the positive efficiency of DCB-only strategy in further reduction of MACE and LLL. In 2018, Fang et al claimed that DCB is an alternative strategy to AMI with ISR due to its acceptable low clinical outcomes similar to DES. A recent meta-analysis performed by Megaly et al included
4 studies that drew a conclusion that DCB was associated with significant short-time outcomes (MACE, all-cause mortality, cardiac death, myocardial infarction (MI), TLR) compared with DES. Nevertheless, its findings were limited to a small sample, short follow-up duration, and European only. REVELATION trial, a prospective randomized control trial planning for 5-year follow-up, displayed no significant differences between the DCB and DES groups in terms of fractional flow reserve in a 9-month follow-up.26 Then they recently brought out that DCB angioplasty was inferior to a 2-year follow-up.27 Tan et al28 reported there were no differences in 24-month MACE and LLL noted between the DCB group and DES group in a retrospective research enrolling 268 patients of AMI with de novo small coronary artery disease.28 Besides, Zhang et al29 and Hao et al30 found that the incidences of MACE rate were no significant differences between the DCB and the stent group during 3 months and 1 year respectively in the Chinese population.

Implications for Clinical Practice
Our meta-analysis integrated previous clinical trials, supporting that there were no significant different effects between applications of DCB and DES with respect to MACE as well as LLL either in European or Asian populations. The higher incidence of TVR after DCB angioplasty compared with DES implantation was found, which might be the obstacle to the widespread use of DCB for acute coronary lesions.

Study Limitations
Several limitations in this meta-analysis are as followed. First, the significant heterogeneity between included studies should be taken into account, although we have attempted to tackle this item with sensitive analysis and use a random effective model on occasion. Second, 3 observational studies included may bring selective bias. Third, some other clinical events such as bleeding were not available. Fourth, the inconsistent definitions of MACE must be noted. Last, the new sirolimus-coated balloons were not used in the included studies, even though there is a potential alternative to the paclitaxel-coated balloons.31

CONCLUSION
In patients with AMI, PCI with DCB is not statistically associated with LLL, a high risk of MACE and all-cause death, cardiac death, recurrent MI, TLR, and thrombotic event compared with DES in a median 1-year follow-up. Drug-coated balloon appears as an attractive alternative to DES in patients with AMI, but TVR risk at follow-up time should be concentrated on. Therefore, more long-term and large-sample clinical trials are still warranted.

Ethics Committee Approval: As all data analyzed in this study were from previous published studies, no ethical approval and patient consent are required.

Peer-review: Internally peer-reviewed.

Author Contributions: Z.F.: Conception, Data Collection and/or Processing, Analysis, Writing; J.J.: Supervision, Materials, Data Collection and/or Processing; S.H.: Supervision, Analysis and/or Interpretation, Literature Review; N.L.: Data Collection and/or Processing, Literature Review; B.X.: Design, Supervision, Fundings, Critical Review.

Declaration of Interests: The authors have no conflict of interest to declare.

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REFERENCES


Supplementary Figure 1. The funnel plot for MACE in this meta-analysis.

Supplementary Table 1. The Quality Assessment for Observational Studies in this Meta-Analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection</th>
<th>Comparability</th>
<th>Outcomes</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nijhoff (2015)</td>
<td>Y Y Y Y Y</td>
<td>Y Y Y Y Y Y</td>
<td>Y Y Y Y</td>
<td>9</td>
</tr>
<tr>
<td>Fang (2018)</td>
<td>Y Y Y Y Y</td>
<td>Y Y Y Y Y Y</td>
<td>Y Y Y Y</td>
<td>9</td>
</tr>
<tr>
<td>Zhang (2020)</td>
<td>Y Y Y Y Y</td>
<td>Y Y N Y Y Y</td>
<td>Y Y Y Y</td>
<td>8</td>
</tr>
<tr>
<td>Tan (2020)</td>
<td>Y Y Y Y Y</td>
<td>Y Y Y Y Y Y</td>
<td>Y Y Y Y</td>
<td>9</td>
</tr>
</tbody>
</table>

1, representativeness of the exposed cohort; 2, selection of the nonexposed cohort; 3, ascertainment of exposure; 4, Demonstration that outcome of interest was not present at the start of study; 5A, Comparability of cohorts on the basis of the design; 5B, comparability of cohorts on the basis of the analysis; 6, assessment of outcome; 7, follow-up long enough for outcomes to occur; 8, adequacy of follow-up of cohorts.

Y, yes; N, no.