

Effects of patient characteristics on the efficacy of complete revascularization for treatment of ST-segment elevation myocardial infarction with multivessel disease

A meta-analysis

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Abstract

Background: Several randomized controlled trials (RCTs) have evaluated the efficacy of complete vs culprit-only revascularization for treatment of ST-segment elevation myocardial infarction (STEMI) with multivessel disease. However, the efficacy of complete revascularization vs culprit-only revascularization in some STEMI patient subgroups remains unclear.

Methods: We searched PubMed and Embase for related RCTs from the start date of databases to January 3, 2020. The endpoint assessed in this meta-analysis was major adverse cardiac events (MACE). Random-effects meta-analysis was conducted stratified by each of the 5 factors of interest (i.e., sex, age, history of diabetes, ECG infarct location, and the number of arteries with stenosis) to estimate pooled hazard ratio and 95% confidence interval. Random-effects meta-regression was conducted to assess subgroup differences. We examined publication bias by drawing funnel plots and performing Egger test. This meta-analysis is reported according to the PRISMA statement.

Results: Six RCTs were included for pooled analysis. Compared with culprit-only revascularization, complete revascularization significantly reduced the risk of MACE (hazard ratio 0.48, 95% confidence interval 0.42–0.55; $I^2=0\%$; P for relative effect $<.001$). This significant reduction in the risk of MACE exhibited by complete revascularization was observed in most of the subgroups of interest. All of the subgroup effects based on the 5 factors of interest were not statistically significant (P_{subgroup} ranged from 0.198 to 0.556). Publication bias was not suggested by funnel plots and Egger test.

Conclusions: Compared with culprit-only revascularization, complete revascularization significantly reduces the MACE risk in patients with STEMI and multivessel disease, which is independent of sex, age, history of diabetes, ECG infarct location, and the number of arteries with stenosis.

Abbreviations: CI = confidence interval, HR = hazard ratio, MACE = major adverse cardiac events, RCTs = randomized controlled trials, STEMI = ST-segment elevation myocardial infarction.

Keywords: complete revascularization, culprit-only revascularization, MACE, multivessel disease, STEMI

1. Introduction

Patients with ST-segment elevation myocardial infarction (STEMI) often have multivessel coronary artery disease.^[1] It is a common dilemma whether to only deal with these culprit

lesions conservatively with guideline-based medical therapy or to routinely revascularize both the culprit and non-culprit lesions.^[2–4] To revascularize non-culprit lesions with stable coronary artery plaques may not offer additional benefit,^[5]

Editor: Ajay Yadlapati.

This work is supported by the Shenzhen Key Medical Discipline Construction Fund (SZXK063).

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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How to cite this article: Li LF, Qiu M, Liu SY, Zhou HR. Effects of patient characteristics on the efficacy of complete revascularization for treatment of ST-segment elevation myocardial infarction with multivessel disease: A meta-analysis. *Medicine* 2021;100:25(e26251).

Received: 15 November 2020 / Received in final form: 17 May 2021 / Accepted: 19 May 2021

<http://dx.doi.org/10.1097/MD.00000000000026251>

whereas to revascularize non-culprit lesions with unstable plaques may lead to more benefits in reducing cardiovascular events.^[6,7]

Several randomized trials have been reported to evaluate the efficacy of complete vs culprit-only revascularization for treatment of STEMI with multivessel disease. However, the relative efficacy of complete revascularization compared with culprit-only revascularization in some subgroups among STEMI patients with multivessel disease remains unclear. The 2 key reasons for this are that inconsistent results for specific subgroups were reported in different trials and that individual trials were not powered to assess the efficacy of complete revascularization in specific subgroups.

For example, in 3 trials^[8–10] complete revascularization vs culprit-only revascularization showed a significant reduction in the risk of major adverse cardiac events (MACE) in the subgroup of STEMI patients with age ≥ 65 years, whereas in 1 other trial^[11] complete revascularization did not show that. For another example, in 1 trial^[9] compared with culprit-only revascularization complete revascularization showed a significant reduction in the risk of MACE in female STEMI patients, whereas in 3 other trials^[8,10,11] complete revascularization did not show that. Besides, 2 trials^[9,11] were not powered to assess the efficacy of complete revascularization in the subgroup of STEMI patients with history of diabetes and 1 trial^[11] was not powered to assess that in the subgroup of STEMI patients with non-anterior infarct, in which complete revascularization was not observed to significantly reduce the MACE risk.

Thus, we conducted the present meta-analysis to evaluate the efficacy of complete vs culprit-only revascularization on MACE in several STEMI patient subgroups defined according to 5 key factors relevant with the clinical characteristics of patients.

2. Methods

This meta-analysis was carried out based on the PRISMA statement.^[12] The PRISMA checklist for this article is shown in Table S1 (Supplemental Content, which presents the PRISMA checklist, <http://links.lww.com/MD2/A247>).

2.1. Inclusion and exclusion criteria

To obtain related randomized trials we searched PubMed and Embase from the start date of databases to January 3, 2020. The search strategies used in this study derived from those used in a prior meta-analysis.^[13]

Studies included in the study were randomized controlled trials (RCTs) which evaluated the efficacy of complete vs culprit-only revascularization on MACE in STEMI patient subgroups of interest. MACE was defined as a composite of all-cause mortality, myocardial infarction, heart failure, and ischemic-driven revascularization.^[10] Subgroups of interest were the subgroups of patients with STEMI and multivessel disease stratified by sex (male vs female), age (< 65 years vs ≥ 65 years), history of diabetes (no vs yes), ECG infarct location (non-anterior vs anterior), and the number of arteries with stenosis (2 vs 3).

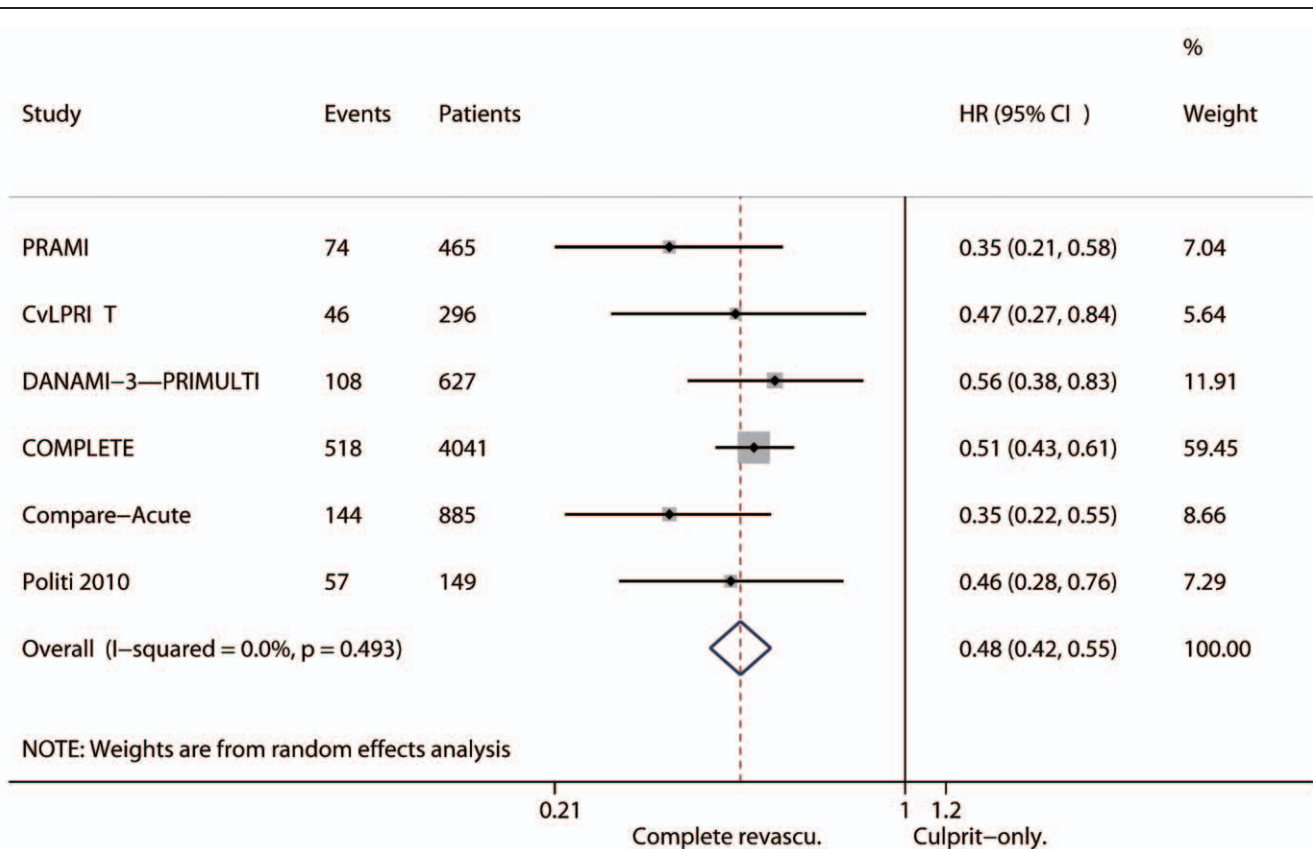


Figure 1. Forest plot of complete vs culprit-only revascularization on MACE, from meta-analysis based on the overall patients. MACE, major adverse cardiac events.

2.2. Study selection and risk of bias assessment

Study selection, data extraction, and risk of bias assessment were independently completed by 2 reviewers. Risk of bias assessment was performed on the basis of the Cochrane risk of bias tool, according to which the following 5 types of risks were assessed: risk of selection bias (concerning random sequence generation), risk of selection bias (concerning allocation concealment), risk of reporting bias (concerning selective reporting), risk of attrition bias (concerning incomplete outcome data), and risk of detection bias (concerning blinding of outcome assessment). Any disagreements were resolved by a third reviewer being involved into the discussion. We quantified the consensus using kappa (*k*) measure, and *k* ≥ 0.85 is considered as reaching a consensus.

2.3. Statistical analysis

We conducted meta-analysis with a random-effects model using hazard ratios (HRs) and 95% confidence intervals (CIs) from included original studies, and performed subgroup analysis stratified by each of the 5 factors of interest (i.e., sex, age, history of diabetes, ECG infarct location, and the number of arteries with stenosis). *I*² statistic was calculated to measure statistical

heterogeneity,^[14] and *I*² more than 50% represents substantial heterogeneity. Random-effects meta-regression was conducted to assess subgroup differences, and *P*_{subgroup} less than 0.05 denotes statistically significant difference. We conducted sensitivity analyses by serially excluding each study to assess the robustness of meta-analysis results. We drew funnel plots and performed Egger test^[15] to evaluate publication bias. *P* for relative effect < .05 means statistical significance. All statistical analyses were completed in the Stata/SE software (version 15.1).

2.4. Ethical statement

The data analyzed in this study were extracted from previously published studies, and therefore ethical approval was not necessary.

3. Results

3.1. Characteristics of included studies

We finally included 6 RCTs^[8-11,16,17] for synthesis analysis after study selection. The study selection process is shown in Figure S1 (Supplemental Content, which presents the process of study

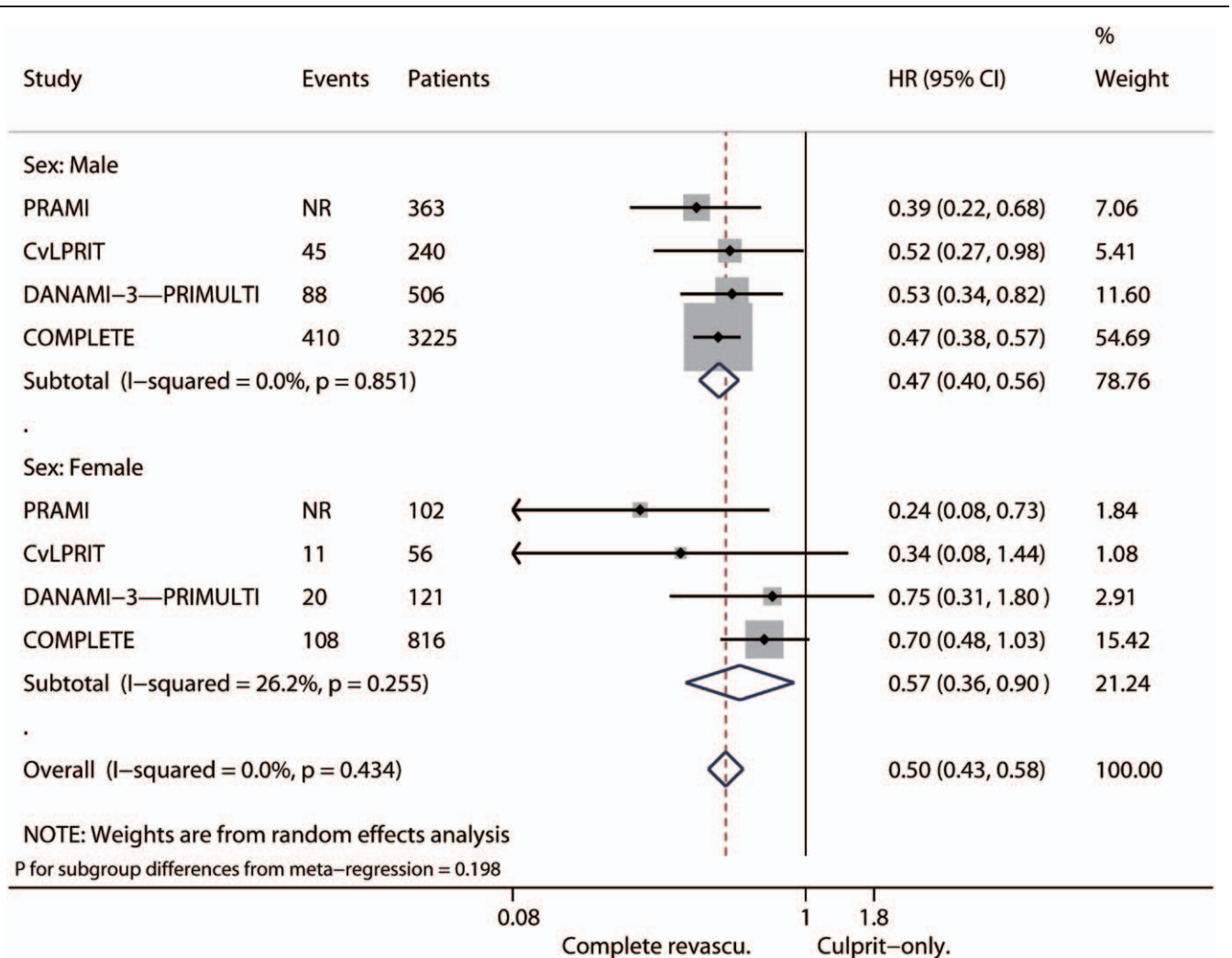


Figure 2. Forest plot of complete vs culprit-only revascularization on MACE, from meta-analysis stratified by sex. MACE, major adverse cardiac events.

selection, <http://links.lww.com/MD2/A243>). As is presented in Figure S2 (Supplemental Content, which summarizes the risk of bias of included studies, <http://links.lww.com/MD2/A244>), the overall quality of included trials was to be considered high. Six studies^[8–11,16,17] were included in overall meta-analysis, whereas only 4^[8–11] of them reported the subgroup analyses of interest and were accordingly included in subgroup meta-analysis. All the original data analyzed in the study are provided in Table S2 (Supplemental Content, which presents the original data analyzed in the present meta-analysis, <http://links.lww.com/MD2/A248>).

3.2. Meta-analyses

The forest plot (Fig. 1) of meta-analysis based on the overall participants shows that complete revascularization vs culprit-only revascularization significantly reduced the risk of MACE (HR 0.48, 95% CI 0.42–0.55; $I^2=0\%$; P for relative effect $<.001$).

As is shown in Figure 2, compared with culprit-only revascularization, complete revascularization significantly reduced the MACE risk in the subgroups of male patients (HR

0.47, 95% CI 0.40–0.56; $I^2=0\%$; P for relative effect $<.001$) and female patients (HR 0.57, 95% CI 0.36–0.90; $I^2=26.2\%$; P for relative effect = .017). The subgroup effect based on sex was not statistically significant ($P_{\text{subgroup}}=0.198$).

As is shown in Figure 3, compared with culprit-only revascularization, complete revascularization significantly reduced the MACE risk in the subgroups of patients with age <65 years (HR 0.46, 95% CI 0.37–0.57; $I^2=0\%$; P for relative effect $<.001$) and patients with age ≥ 65 years (HR 0.51, 95% CI 0.33–0.79; $I^2=61.3\%$; P for relative effect = .003). The subgroup effect based on age was not statistically significant ($P_{\text{subgroup}}=0.556$).

As is shown in Figure 4, compared with culprit-only revascularization, complete revascularization significantly reduced the MACE risk in the subgroups of patients with no history of diabetes (HR 0.48, 95% CI 0.40–0.57; $I^2=0\%$; P for relative effect $<.001$) and patients with history of diabetes (HR 0.58, 95% CI 0.42–0.81; $I^2=0\%$; P for relative effect = 0.001). The subgroup effect based on history of diabetes was not statistically significant ($P_{\text{subgroup}}=0.349$).

As is shown in Figure 5, compared with culprit-only revascularization, complete revascularization significantly re-

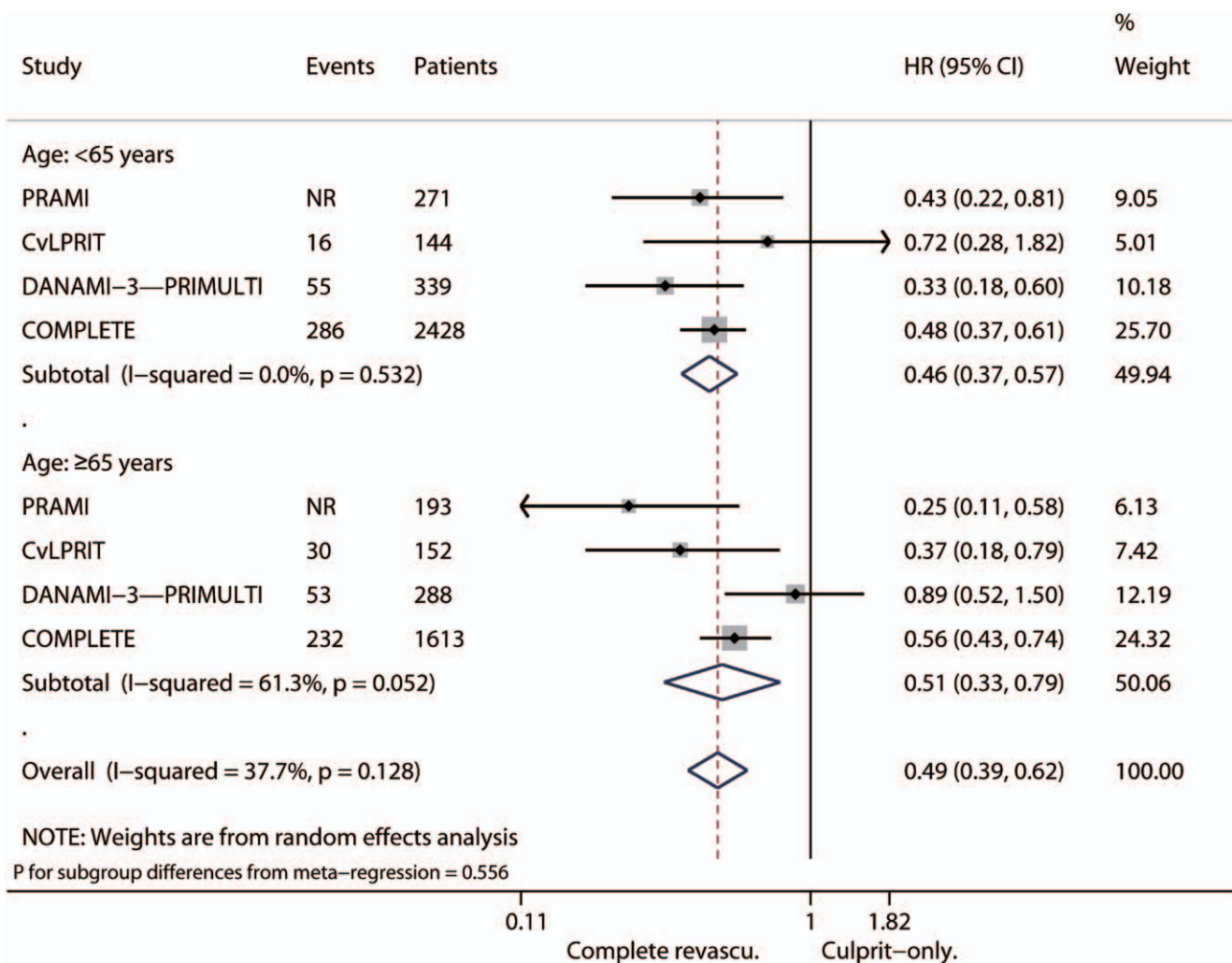


Figure 3. Forest plot of complete vs culprit-only revascularization on MACE, from meta-analysis stratified by age. MACE, major adverse cardiac events.

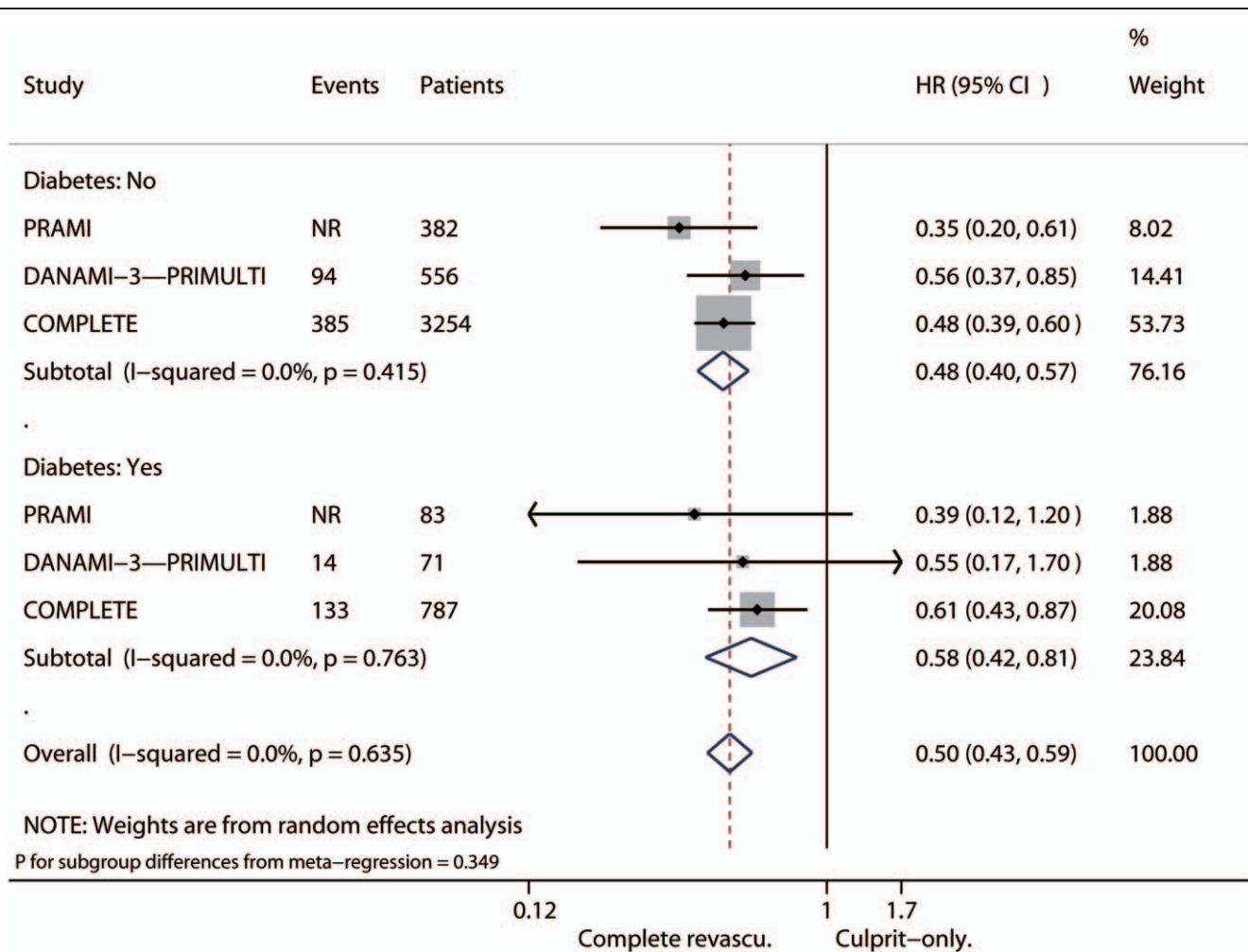


Figure 4. Forest plot of complete vs culprit-only revascularization on MACE, from meta-analysis stratified by history of diabetes. MACE, major adverse cardiac events.

duced the MACE risk in the subgroups of patients with non-anterior infarct (HR 0.56, 95% CI 0.37–0.86; $I^2 = 15.9\%$; P for relative effect = .008) and patients with anterior infarct (HR 0.34, 95% CI 0.19–0.62; $I^2 = 0\%$; P for relative effect < .001). The subgroup effect based on ECG infarct location was not statistically significant ($P_{\text{subgroup}} = .295$).

As is shown in Figure 6, compared with culprit-only revascularization, complete revascularization significantly reduced the MACE risk in the subgroup of patients with 2 stenosis arteries (HR 0.33, 95% CI 0.20–0.56; $I^2 = 0\%$; P for relative effect < .001), while complete revascularization showed the trend of a reduction in the risk of MACE in the subgroup of patients with 3 stenosis arteries (HR 0.54, 95% CI 0.23–1.27; $I^2 = 55.0\%$; P for relative effect = 0.160). The subgroup effect based on the number of arteries with stenosis was not statistically significant ($P_{\text{subgroup}} = 0.388$).

Substantial heterogeneity was found only in 2 STEMI patient subgroups, which were the subgroups of patients with age ≥ 65 years ($I^2 = 61.3\%$) and the subgroups of patients with 3 stenosis arteries ($I^2 = 55.0\%$). Figure S3 (Supplemental Content, which presents the results of sensitivity analyses, <http://links.lww.com/MD2/A245>) shows that the minimum low limit of HR was 0.36 and the maximum upper limit of HR was 0.57, which was similar

with the overall pooled effect size (complete vs culprit-only revascularization: HR 0.48, 95% CI 0.42–0.55). This suggested the robustness of meta-analysis results. Publication bias was not observed in the overall meta-analysis and any of the subgroup meta-analyses, as is suggested by funnel plots and Egger test (Figs. S4–S14, Supplemental Content, which show the results of publication bias detection, <http://links.lww.com/MD2/A246>).

4. Discussion

Compared with prior meta-analysis studies^[13,18–21] in the same field, for the first time our study evaluated the effects of important factors relevant with patient characteristics on the efficacy of complete revascularization vs culprit-only revascularization for treatment of STEMI with multivessel disease by conducting subgroup meta-analysis stratified by 5 factors of interest (i.e., sex, age, history of diabetes, ECG infarct location, and the number of arteries with stenosis) and conducting meta-regression analysis with the 5 factors as independent variables. Accordingly, 3 main findings were produced as follows.

First, compared with culprit-only revascularization, complete revascularization significantly reduced the risk of MACE (HR 0.48, 95% CI 0.42–0.55) in the overall STEMI patients with

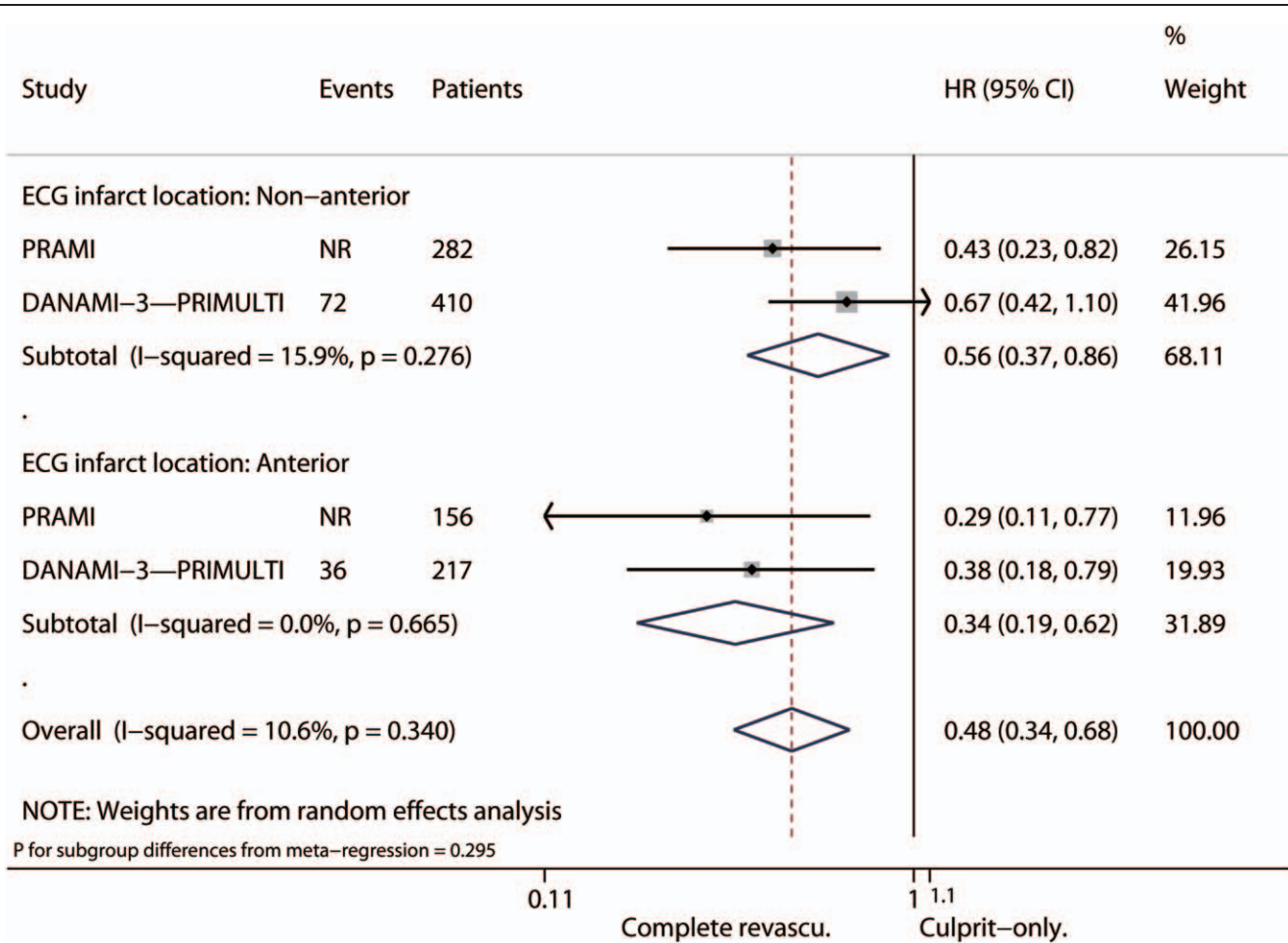


Figure 5. Forest plot of complete vs culprit-only revascularization on MACE, from meta-analysis stratified by ECG infarct location. MACE, major adverse cardiac events.

multivessel disease. Second, this significant reduction in the risk of MACE exhibited by complete revascularization was found in all of the subgroups defined by the 5 factors of interest except the subgroup of patients with 3 stenosis arteries in which complete revascularization showed the trend of a reduction in the MACE risk. Third, this significant reduction in the MACE risk exhibited by complete revascularization was consistent across various subgroups defined by each of the 5 factors of interest.

Two prior meta-analysis studies^[13,21] have demonstrated the superiority of complete revascularization over culprit-only revascularization in reducing cardiovascular death, myocardial infarction, and repeated revascularization among STEMI patients with multivessel disease. Moreover, the study selection process and the result of risk of bias assessment in the present meta-analysis are similar to that in meta-analysis^[13] published in the *European Heart Journal*. However, these meta-analyses^[13,21] failed to explore the effects of patient characteristics on the efficacy of complete revascularization vs culprit-only revascularization. Our present meta-analysis revealed that the superiority of complete revascularization over culprit-only revascularization in reducing MACE did not vary with important clinical characteristics of patients. This finding will further inform clinical decision-making between cardiologists and STEMI patients with multivessel disease.

As strength of this study, publication bias was not observed in the overall meta-analysis and any subgroup meta-analysis. Oppositely, this study has 2 main weaknesses. First, this meta-analysis only evaluated the impact of 5 important factors on the efficacy of complete revascularization, but failed to evaluate that of other important factors, such as type of stent, Killip class, and residual SYNTAX score, since the subgroup data according to these factors were not available. Second, substantial heterogeneity found in few subgroups requires further investigation. Ongoing RCTs (NCT03621501, NCT03135275, and NCT03772743) may help address this issue.

In conclusion, compared with culprit-only revascularization, complete revascularization significantly reduces the MACE risk in patients with STEMI and multivessel disease, which is independent of sex, age, history of diabetes, ECG infarct location, and the number of arteries with stenosis.

Author contributions

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Validation: Hai-Rong Zhou.

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