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Intravascular Ultrasound-Guided Implantation of Drug-Eluting Stents to Improve Outcome

A Meta-Analysis

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Objectives The aim of this study was to systematically review and perform a meta-analysis of randomized trials and observational studies of intravascular ultrasound (IVUS)-guided versus angiography-guided implantation of drug-eluting stents (DES).

Background Although studies in the bare-metal stents era suggested that there were clinical benefits to IVUS guidance, it is still controversial whether percutaneous coronary intervention (PCI) with DES guided by IVUS leads to better clinical outcomes.

Methods Relevant studies published through March 31, 2013, were searched for and identified in the electronic databases. Summary estimates were obtained using a random-effects model.

Results From 138 initial citations, 3 randomized trials and 12 observational studies with 24,849 patients (11,793 IVUS-guided and 13,056 angiography-guided) were included in this study. Comparison of IVUS- versus angiography-guided PCI disclosed odds ratios (ORs) for major adverse cardiac events of 0.79 (95% confidence interval [CI]: 0.69 to 0.91; $p = 0.001$). IVUS-guided PCI was also associated with significantly lower rates of all-cause mortality (OR: 0.64; 95% CI: 0.51 to 0.81; $p < 0.001$), myocardial infarction (OR: 0.57; 95% CI: 0.42 to 0.78; $p < 0.001$), target vessel revascularization (OR: 0.81; 95% CI: 0.68 to 0.95; $p = 0.01$), and stent thrombosis (OR: 0.59; 95% CI: 0.42 to 0.82; $p = 0.002$). A meta-analysis of propensity-matched studies demonstrated similar results in terms of clinical outcomes, but not repeat revascularization.

Conclusions IVUS-guided DES implantation is associated with significantly lower rates of adverse clinical events compared with angiography guidance. Further study is needed to clarify which subgroups of subjects with IVUS guidance will have greater benefit. (J Am Coll Cardiol Intv 2014; 7:233–43) © 2014 by the American College of Cardiology Foundation

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Intravascular ultrasound (IVUS) plays a substantial role in percutaneous coronary intervention (PCI) using coronary stents not only by providing more accurate information about the coronary artery and implanted stents but also by allowing earlier detection of procedure-related complications and suboptimal stent expansion. Previous studies and meta-analyses have demonstrated that IVUS-guided stent implantation may decrease restenosis and the adverse clinical outcomes after bare-metal stent (BMS) implantation (1–3).

It is still controversial whether implantation of drug-eluting stents (DES) guided by IVUS could reduce adverse clinical outcomes. Zhang et al. (4) recently performed a meta-analysis on this topic. They included 1 randomized trial and 10 observational studies comparing IVUS- and angiography-guided DES implantation in the DES era. However, they included a study (5) in which some of the patients received BMS. There has been the recent presentation (6) and publication of additional randomized trials (7,8) and an observational study (9) comparing IVUS and angiographic-guided DES implantation. This suggests the need for an updated meta-analysis to further support the efficacy of IVUS-guided DES implantation.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
CI = confidence interval
DES = drug-eluting stent(s)
HR = hazard ratio
IVUS = intravascular ultrasound
MACE = major adverse cardiac events
MI = myocardial infarction
OR = odds ratio
PCI = percutaneous coronary intervention
TLR = target lesion revascularization
TVR = target vessel revascularization

Methods

Data sources and searches. We identified relevant studies through electronic searches of MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials from January 2001 through March 2013. Medical subject headings and keyword searches included intravascular ultrasound, coronary angiography, stents, drug-eluting stents, coronary angioplasty, and percutaneous coronary intervention. Reference lists of selected articles were reviewed for other potentially relevant citations. In addition, we manually searched the content pages of issues published from 2011 through 2012 by the American College of Cardiology, the European Society of Cardiology, the Transcatheter Cardiovascular Therapeutics, and the American Heart Association to retrieve further potential publications.

Study selection. Two investigators (J.-S.J. and H.-Y.J.) independently conducted the literature search, data extraction, and quality assessment by using a standardized approach. Selected publications were reviewed by the same investigators to assess whether studies met the inclusion criteria: comparison of IVUS- and angiography-guided PCI with DES implantation in which follow-up angiographic and/or clinical outcome data were reported. Final inclusion of studies was based on the agreement of both reviewers.

Data extraction and quality assessment. Two reviewers (J.-S.J. and T.-H.Y.) extracted relevant information from the papers including study design, follow-up duration, patient characteristics (mean age, sex distribution, risk factors), and angiographic/procedural characteristics. To reduce the effect of treatment-selection bias and potential confounding in nonrandomized observational studies, we also abstracted adjusted risk estimates from observational studies. If additional information was needed, the authors of the studies were contacted.

Endpoints. The endpoints of this study were major adverse cardiac events (MACE), all-cause mortality, myocardial infarction (MI), target vessel revascularization (TVR), target lesion revascularization (TLR), stent thrombosis, and post-intervention minimal lumen diameter. The definition of MACE was slightly different across studies, and we used the trial-specific definitions of MACE. Most of the included studies defined MACE as a composite of all-cause death, MI, and TVR. Four studies (7,8,10,11) included cardiovascular death instead of all-cause death, and the other 2 studies (12,13) included TLR instead of TVR. MI included Q-wave MI and non–Q-wave MI. Stent thrombosis was definite or probable according to the definition of the Academic Research Consortium (14).

Data synthesis and analysis. We used random-effects models to produce across-study summary odds ratios (ORs) with 95% confidence intervals (CIs). A crude OR with 95% CI was used to assess the efficacy of IVUS guidance on adverse clinical events in study populations. Continuous data were expressed as mean (SD) and weighted mean differences. All p values were 2 tailed, with statistical significance set at 0.05. For comparison of registry studies with matched pairs by propensity score analysis, adjusted risk estimates were pooled after logarithmic transformation according to random-effects models with generic inverse variance method.

We assessed statistical heterogeneity between trials with the I^2 statistic, which is derived from Cochran's Q and the degree of freedom [100 × (Q–df)/Q)] (15). I^2 values >25%, 50%, and 75% were considered evidence of low, moderate, and severe statistical heterogeneity, respectively. In case of heterogeneity across the studies, we performed sensitivity analyses, serially excluding studies to determine the source of heterogeneity. Additionally, sensitivity analyses were conducted to examine the heterogeneity on the basis of coronary anatomy (bifurcation vs. nonbifurcation and left main vs. non–left main), the study design (randomized vs. nonrandomized studies), and the publication period (previous vs. new studies). Publication bias was examined by visual inspection of constructed funnel plots for clinical outcomes and mathematically by means of the Egger test (p for significant asymmetry <0.1) (16). All statistical