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Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute myocardial infarction

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KEYWORDS
Acute myocardial infarction;
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Aims To compare the efficacy and safety of drug-eluting stents vs. bare-metal stents in patients with acute ST-segment elevation myocardial infarction.

Methods and results We performed a meta-analysis of eight randomized trials comparing drug-eluting stents (sirolimus-eluting or paclitaxel-eluting stents) with bare-metal stents in 2786 patients with acute ST-segment elevation myocardial infarction. All patients were followed up for a mean of 12.0–24.2 months. Individual data were available for seven trials with 2476 patients. The primary efficacy endpoint was the need for reintervention (target lesion revascularization). The primary safety endpoint was stent thrombosis. Other outcomes of interest were death and recurrent myocardial infarction. Drug-eluting stents significantly reduced the risk of reintervention, hazard ratio of 0.38 (95% CI, 0.29–0.50), $P < 0.001$. The overall risk of stent thrombosis: hazard ratio of 0.80 (95% CI, 0.46–1.39), $P = 0.43$; death: hazard ratio of 0.76 (95% CI, 0.53–1.10), $P = 0.14$; and recurrent myocardial infarction: hazard ratio of 0.72 (95% CI, 0.48–1.08, $P = 0.11$) was not significantly different for patients receiving drug-eluting stents vs. bare-metal stents.

Conclusion The use of drug-eluting stents in patients with acute ST-segment elevation myocardial infarction is safe and improves clinical outcomes by reducing the risk of reintervention compared with bare-metal stents.

Introduction

Primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy for patients presenting with acute myocardial infarction with ST-segment elevation.[1,2] Compared with balloon angioplasty, routine implantation of bare-metal stents has been associated with improved clinical outcome mainly because of the decreased risk for reintervention.[3,4] Nevertheless, restenosis remains an important limitation of the use of bare-metal stents in patients with acute myocardial infarction.[4–7]

Drug-eluting stents effectively reduce restenosis while maintaining a good safety profile in many lesion and patients groups.[8,9] However, concerns have been raised with regard to the safety of drug-eluting stents in patients with acute myocardial infarction.[10] Data from registry studies have suggested that implantation of drug-eluting stents during primary PCI could be associated with an increased risk for stent thrombosis, which is associated with high-morbidity and -mortality rates.[11,12] Recently, the results of several randomized trials of drug-eluting stents in patients undergoing primary PCI for acute ST-segment elevation myocardial infarction have been reported. These studies had, however, insufficient power to assess the risk of rare adverse events. Furthermore, they did not consistently show the superior effectiveness of drug-eluting stents in that particular setting.[13–15] Meta-analyses of randomized trials have the potential to increase the power and improve the precision of treatment effects.[16] A meta-

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analysis has recently been published including seven randomized trials with a total number of 2357 patients.[17] However, this meta-analysis was based on summary data extracted from meeting abstracts in four of the seven trials.[17] Toma *et al.*[18] suggest caution in the use of these data because of common discrepancies in results between meeting abstracts and subsequent full-length publications. A meta-analysis on the basis of individual patient data yields much more accurate results and is the 'gold standard' to perform time-to-event analyses.[19]

We performed a meta-analysis predominantly based on individual patient data from randomized trials comparing drug-eluting stents with bare-metal stents to evaluate the efficacy and safety of drug-eluting stents in patients with acute ST-segment elevation myocardial infarction.

Methods

Literature search

We performed an electronic search of the United States National Library of Medicine (PubMed, at http://www.pubmed.gov), the United States National Institutes of Health clinical trials registry (http://www.clinicaltrials.gov), and the Cochrane Central Register of Controlled Trials (http://www.mrw.interscience.wiley.com/cochrane/cochrane_clcentral_articles_fs.html). The key words used included 'myocardial infarctio', 'primar', 'angioplast', 'PC', 'ST-segment elevatio', 'drug-eluting sten', sirolimus-'eluting sten', 'paclitaxel-eluting sten', 'clinical tria', and 'randomize'. Internet-based sources of information on the results of clinical trials in cardiology (http://www.cardiosource.com/clinicaltrials, http://www.theheart.org, and http://www.clinicaltrialresults.com, and http://www.tctmd.com) were also searched. Additional data sources included conference proceedings from the American College of Cardiology, American Heart Association, and European Society of Cardiology meetings. We also identified relevant reviews and editorials from major medical journals published within the last year and assessed for possible information on trials of interest. The search period was between January 2002 and February 2007.

Study selection

To be selected for this meta-analysis, studies comparing drug-eluting stents with bare-metal stents in patients undergoing primary PCI of ST-segment elevation acute myocardial infarction had been randomized and had their results reported or made available by the trial investigators for a mean follow-up period of at least 12 months. Articles were searched and reviewed independently by two of the authors (A.D. and J.M.); those meeting the inclusion criteria were selected for further analysis. A total of nine trials were identified. The trial of Pasceri *et al.*[20] was excluded because it reported only preliminary data of the first 34 patients over a follow-up of 4 ± 2 months. Finally, eight trials were included in this meta-analysis (*Figure 1*).[13–15,21–25]

Study outcomes and data collection

The primary efficacy endpoint of this meta-analysis was the need of reintervention (target lesion revascularization). The primary safety endpoint of this meta-analysis was stent thrombosis. Secondary endpoints were death and recurrent myocardial infarction. The composite of death, recurrent myocardial infarction, or reintervention was also assessed. The event definitions used in individual trials are given in *Table 1*. The adjudication of events in each trial was performed by the same event committee over the entire follow-up period. Survival was calculated from the date of randomization to the date of death. Data for surviving patients were censored on the date of last follow-up.

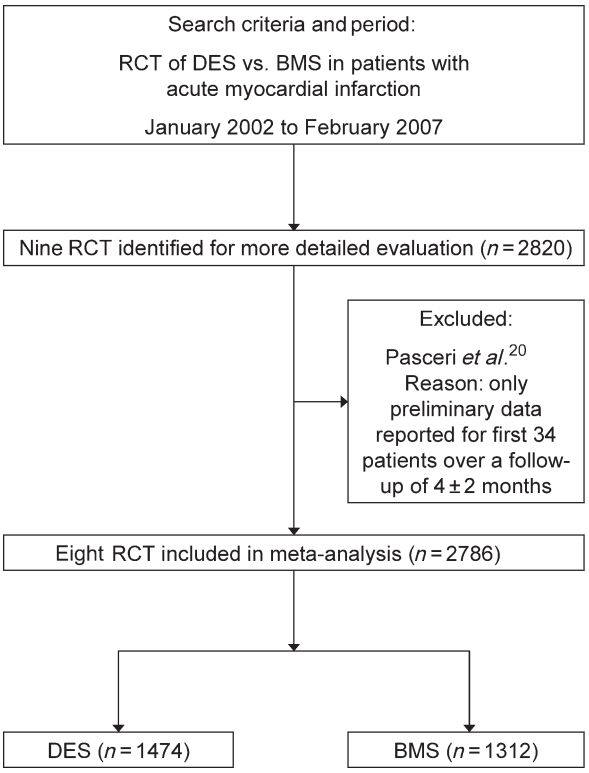

Figure 1 Flowchart of selected studies. BMS, bare-metal stent; DES, drug-eluting stent; RCT, randomized control trial.

An electronic form containing the data fields to be completed for individual patients was sent to all principal investigators of the trials. Individual patient data could be obtained for seven trials.[13–15,21–24]

The data requested for each enrolled patient included the date of randomization, allocated treatment, diabetes status, event status [including death, myocardial infarction, coronary reintervention (percutaneous or surgical), stent thrombosis, and their respective dates of occurrence], and date of last follow-up. All data were thoroughly checked for consistency (logical checking and checking against the original publications). Any queries were resolved and the final database entries were verified by the responsible trial investigator.

Each trial was evaluated for the adequacy of allocation concealment, performance of the analysis according to the intention-to-treat principle, and blind assessment of the outcomes of interest. We used the criteria recommended by Altman *et al.*[26] and Jüni *et al.*[27] to assess the adequacy of allocation concealment. In two trials, a modified intention-to-treat principle, i.e. exclusion of patients who did not receive the study stent, was used.[14,25]

Statistical methods

We performed survival analyses using the Mantel–Cox method stratified by trial. The log-rank test was used to calculate hazard ratios and their 95% CIs.

Trials in which the event of interest was not observed in either treatment group were discarded from the analysis of that event. In case, only one of the groups of an individual trial had no event of interest, the treatment effect estimate and its standard error were calculated after adding 0.5 to each cell of the 2×2 table for that trial.[28]

We used the Cochran's test to assess the heterogeneity across trials. We also calculated the I^2 statistic to measure the consistency among trials with values of 25, 50, and 75% showing, respectively, low, moderate, and high heterogeneity.[29] Hazard ratios from

Table 1 Endpoint definitions in each trial

Study	Death	Recurrent myocardial infarction	Reintervention	Stent thrombosis
BASKET-AMI[22]	Cardiac, if clearly due to a cardiac event, otherwise non-cardiac	Typical chest pain with either typical rise (and fall) of cardiac enzymes or new pathologic Q-waves/ST-T wave changes on ECG	Intervention (PCI or CABG) driven by a lesion in the same epicardial vessel as initially treated	Angiographic evidence in the presence of an ischaemic clinical event
Di Lorenzo[21]	Cardiac unless a non-cardiac cause could be identified	Recurrence of anginal symptoms with typical ECG changes and increase of CK-MB or troponin	Any CABG or PCI of the target vessel in the presence of symptoms or signs of ischemia	Angiographically documented thrombus within the stent associated to typical chest pain and ST-segment modification in the territory of the infarct related vessel with or without a significant rise of enzymes
HAAMU-STENT[23]	Cardiac if sudden unexpected death or witnessed fatal arrhythmia or cardiac failure	Clinical picture of myocardial infarction with ST-segment changes and elevated cardiac markers or angiographic stent thrombosis	Any CABG of the target vessel or a PCI because of angiographic restenosis in the presence of symptoms or signs of ischaemia	Acute ST-segment elevation myocardial infarction plus angiographic thrombus
MISSION[a25]	Cardiac unless a non-cardiac cause could be identified	Development of new Q-waves on ECG or a troponin-T rise above normal ($>$25% above previous value) with symptoms or need for reintervention	Any CABG or PCI of the target vessel	Angiographically documented thrombus within the stent and/or typical chest pain with recurrent ST-segment elevation in the territory of the infarct-related vessel in combination with a significant rise of troponin levels and/or the presence of new Q-waves in the territory of the infarct-related vessel
PASSION[13]	Cardiac unless a noncardiac cause could be identified	Either pathological Q-waves on ECG or an increase in the creatine kinase level $\geq$2 times the upper normal level or $>$50% the previous value (if they were still elevated) with symptoms or need for reintervention	Any CABG of the target vessel or a PCI because of angiographic restenosis in the presence of symptoms or signs of ischaemia	Angiographic documentation of either vessel occlusion or thrombus formation within, or adjacent to, the stented segment
SESAMI[24]	Cardiac unless an unequivocal non-cardiac cause could be established	Recurrent ischaemic symptoms or ECG changes accompanied by an increase in cardiac enzymes $\geq$2 times the upper normal level (if values were previously normalized) or $>$50% the previous value (if they were still elevated)	Any CABG of the target vessel or a PCI due to angiographic restenosis in the presence of symptoms or signs of ischemia	Angiographic evidence in the presence of an acute coronary syndrome
STRATEGY[15]	Cardiac unless an unequivocal non-cardiac cause could be established	Recurrent ischaemic symptoms or ECG changes accompanied by an increase in cardiac enzymes above the normal limit (if values were previously normalized) or $>$50% the previous value (if they were still elevated)	Any CABG or PCI of the target vessel in the presence of symptoms or signs of ischaemia	Angiographic evidence in the presence of clinical symptoms or ECG changes suggestive of acute ischaemia

Continued

Table 1 *Continued*

Study	Death	Recurrent myocardial infarction	Reintervention	Stent thrombosis
TYPHOON[a14]	Cardiac if a cardiac cause cannot be excluded	Recurrence of clinical symptoms or the occurrence of electrocardiographic changes accompanied by a new elevation of cardiac enzymes (1.5 times the previous value or three times the upper limit of normal)	Any CABG of the target vessel or a PCI because of angiographic restenosis in the presence of symptoms or signs of ischaemia, or only because of severe restenosis (≥70% diameter stenosis)	Acute and subacute stent thromboses were defined as angiographic proof of vessel occlusion, any recurrent Q-wave myocardial infarction in the territory of the stented vessel, or any death from cardiac causes. Late stent thrombosis was defined as any recurrent myocardial infarction with angiographic proof of vessel occlusion[b]

CABG, aorto-coronary bypass surgery; PCI, percutaneous coronary intervention; HAAMU-STENT, The Helsinki area acute myocardial infarction-treatment re-evaluation—should the patient get a drug-eluting or a normal stent trial; MISSION, a prospective randomized controlled trial to evaluate the efficacy of drug-eluting stents vs. bare-metal stents for the treatment of acute myocardial infarction; PASSION, the paclitaxel-eluting stent vs. conventional stent in myocardial infarction with ST-segment elevation trial; SESAMI, the randomized trial of sirolimus stent vs. bare stent in acute myocardial infarction trial; STRATEGY, the single high-dose bolus Tirofiban and sirolimus eluting stent vs. Abciximab and bare-metal stent in myocardial infarction trial; TYPHOON, the trial to assess the use of the Cypher stent in acute myocardial infarction treated with balloon angioplasty.

[a]A 'modified intention-to-treat' principle was adopted in the trial, i.e. a randomized patient was included in the analysis only if he received stent(s).

[b]According to protocol, patients undergoing reintervention had to be censored from further assessment of stent thrombosis.

individual trials were pooled using the DerSimonian and Laird method for random effects.[30]

We performed sensitivity analyses by comparing the treatment effects obtained with each trial removed consecutively from the analysis with the overall treatment effects. Results were considered statistically significant at two-sided $P < 0.05$. Statistical analysis was performed using the Stata software, version 9.2 (Stata Corp, College Station, TX, USA). Survival curves are presented as simple, non-stratified Kaplan–Meier curves across all trials and constructed with the use of S-Plus software version 4.5. (Insightful Corporation, Seattle, WA, USA).

Results

Eight trials with 2786 patients were included in this meta-analysis. The main characteristics of these trials are summarized in *Table 2*. The mean age of participants in individual trials varied from 59.2 to 64.0 years. Drug-eluting stents consisted of paclitaxel-eluting stents in two of the trials and sirolimus-eluting stents in four other trials; in the remaining two trials, a three-arm design was used including both paclitaxel-eluting and sirolimus-eluting stents.[21,22] The recommended length of post-procedural thienopyridine therapy was 3[15], 6[13,14,21,22] or 12 months.[23–25] The mean length of follow-up ranged from 12.0 to 24.2 months. Patient-level data were available for seven trials with 2476 patients.[13–15,21–24]

Figure 2A shows the number of patients who experienced the primary efficacy endpoint of reintervention according to the treatment group, with the hazard ratio for each of the trials. Overall, the use of drug-eluting stents was associated with a hazard ratio of 0.38 for reintervention (95% CI, 0.29–0.50), $P < 0.001$, compared with the use of the bare-metal stent. There was no heterogeneity across trials ($I^2 = 0\%$) and no significant interaction ($P = 0.07$) between the effect of treatment and the type of drug-eluting stent (sirolimus-eluting stent or paclitaxel-eluting stent) used. Sequential exclusion of each individual trial from the analysis of the primary endpoint yielded hazard ratios ranging from 0.33 (95% CI, 0.24–0.45) to 0.42 (95% CI, 0.30–0.57), which were not significantly different from the overall hazard ratio. Specifically, the hazard ratio for reintervention associated with the use of drug-eluting stents was 0.39 (95% CI, 0.29–0.53) when the trial for which no individual patient data were available was excluded.[25] *Figure 2B* shows 1-year probability curves for reintervention in the two treatment arms. An early and continuous separation of the curves is readily visible. The probability of reintervention was 5.0% in the drug-eluting stent group and 13.3% in the bare-metal stent group.

Figure 3A shows the number of patients who suffered the primary safety endpoint of stent thrombosis according to the treatment group, with the hazard ratio for each of the trials. The hazard ratio for stent thrombosis was 0.80 (95% CI, 0.46–1.39), $P = 0.43$. There was no heterogeneity across trials ($I^2 = 0\%$) and no significant interaction ($P = 0.89$) between the effect of treatment and the type of drug-eluting stent used (sirolimus-eluting stent or paclitaxel-eluting stent). In addition, the hazard ratio for stent thrombosis associated with the use of drug-eluting stents was 0.82 (95% CI, 0.46–1.47) when the trial for which no individual patient data were available was excluded.[25] *Figure 3B* shows 1-year curves of stent thrombosis probability for the two treatment groups. The probability of stent thrombosis was 1.6% in the drug-eluting stent group and 2.2% in the bare-metal stent group. Three stent thromboses occurred after 1 year: two in the drug-eluting stent group and one in the bare-metal stent group.

Figure 4A shows the number of patients who died according to the treatment group, with the hazard ratio for each of the trials. There was no heterogeneity across the trials ($I^2 = 1\%$) and no significant interaction ($P = 0.48$) between the effect of treatment and the type of drug-eluting stent used. Overall, the use of the drug-eluting stent was associated with a hazard ratio of 0.76 for death (95% CI, 0.53–1.10), $P = 0.14$, compared with the use of the bare-metal stent.

Table 2 Main characteristics of the trials

Study	No. of patients	Mean age (years)	Type of DES	Availability of individual patient data	Primary endpoint	Length of thienopyridine therapy (months)	Mean length of follow-up (months)
BASKET-AMI[22]	216	62.2	PES SES	Yes	Cardiac death, myocardial infarction, or reintervention	6	18.0
Di Lorenzo[21]	270	64.0	PES SES	Yes	Death, myocardial infarction, or reintervention	6	12.0
HAAMU-STENT[23]	164	63.0	PES	Yes	Angiographic late lumen loss	12	16.7
MISSION[25]	310	59.2	SES	No	Angiographic late lumen loss	12	12.0
PASSION[13]	619	60.8	PES	Yes	Cardiac death, myocardial infarction, or reintervention	6	12.0
SESAMI[24]	320	61.6	SES	Yes	Angiographic binary restenosis	12	12.3
STRATEGY[15]	175	62.6	SES	Yes	Death, myocardial infarction, stroke, or angiographic binary restenosis	3	24.2
TYPHOON[14]	712	59.3	SES	Yes	Cardiac death, myocardial infarction, or reintervention	6	12.1

DES, drug-eluting stent; PES, paclitaxel-eluting stent; SES, sirolimus-eluting stent; BASKET-AMI, Basel Stent Kosten Effektivitäts in Acute Myocardial Infarction trial; HAAMU-STENT, The Helsinki area acute myocardial infarction-treatment re-evaluation—should the patient get a drug-eluting or a normal stent trial; MISSION, A prospective randomized controlled trial to evaluate the efficacy of drug-eluting stents vs. bare-metal stents for the treatment of acute myocardial infarction; PASSION, the Paclitaxel-eluting stent vs. conventional stent in myocardial infarction with ST-segment elevation trial; SESAMI, the randomized trial of sirolimus stent vs. bare stent in acute myocardial infarction trial; STRATEGY, the single high-dose bolus tirofiban and sirolimus eluting stent vs. Abciximab and bare-metal stent in myocardial infarction trial; TYPHOON, the trial to assess the use of the Cypher stent in acute myocardial infarction treated with balloon angioplasty.

Ninety-eight of the 121 death cases (81.0%) observed in seven trials for which patient-level data were available were of cardiac origin, without any significant difference between the drug-eluting stent group (45 of 58 cases) and bare-metal stent group (53 of 63 cases), $P = 0.36$. *Figure 4B* shows the 1-year mortality curves for the two treatment groups. The probability of death was 4.0% in the drug-eluting stent group and 5.0% in the bare-metal stent group. Twelve patients died after 1 year: six in the drug-eluting stent group and six in the bare-metal stent group.

Figure 5A shows the absolute numbers of patients who suffered a recurrent myocardial infarction according to the treatment group, with the hazard ratio for each of these trials. No evidence of heterogeneity was observed across the trials ($I^2 = 0\%$). Overall, the use of the drug-eluting stent was associated with a hazard ratio of 0.72 for the recurrent myocardial infarction (95% CI, 0.48–1.08), $P = 0.11$, compared with the use of the bare-metal stent. *Figure 5B* shows 1-year probability curves for recurrent myocardial infarction for the two treatment arms. The probability of recurrent myocardial infarction was 2.5% in the drug-eluting stent group and 3.3% in the bare-metal stent group.

The composite of death, recurrent myocardial infarction, or reintervention was observed in 158 of the 1474 patients in the drug-eluting stent group and 252 of the 1312 patients in the bare-metal stent group. The use of the drug-eluting stent was associated with a hazard ratio of 0.53 for this composite endpoint (95% CI, 0.42–0.67), $P < 0.001$, compared with the use of the bare-metal stent. The probability of the composite of death, recurrent myocardial infarction, or reintervention was 9.5% in the drug-eluting stent group and 17.8% in the bare-metal stent group.

Discussion

In this study, we performed a meta-analysis of eight randomized trials comparing drug-eluting stents with bare-metal stents in patients with acute ST-segment elevation myocardial infarction. We found no significant differences in the risk of stent thrombosis, death, or recurrent myocardial infarction between patients treated with drug-eluting stents vs. bare-metal stents. On the other hand, we found that treatment with drug-eluting stents was associated with a 62% reduction in the hazard of reintervention compared with bare-metal stents. The advantage of drug-eluting stents was notable within the first month after stent implantation procedure and continued to increase thereafter.

A large number of studies have shown that the use of drug-eluting stents is associated with favourable outcomes in patients with various clinical and angiographic characteristics.[9,31] However, data on the outcome of patients undergoing primary PCI with implantation of drug-eluting stents have been limited, and whether the favourable results obtained with drug-eluting stents in other settings also

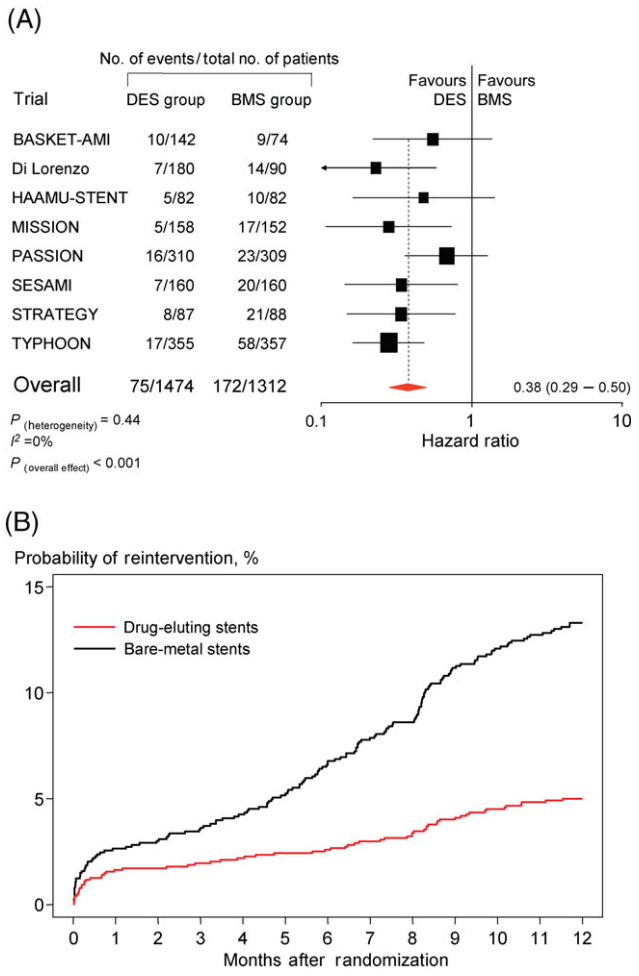

Figure 2 (**A**) Absolute numbers of patients requiring reintervention and hazard ratios for this endpoint with drug-eluting stents vs. bare-metal stents for individual trials and the pooled population. Hazard ratios are shown on a logarithmic scale. The size of the square is proportional to the weight of the individual studies, measured as the inverse of the estimated variance of the log hazard ratio. DES, drug-eluting stent; BMS, bare-metal stent. (**B**) Kaplan–Meier curves of reintervention in each of the stent groups for the pooled population.

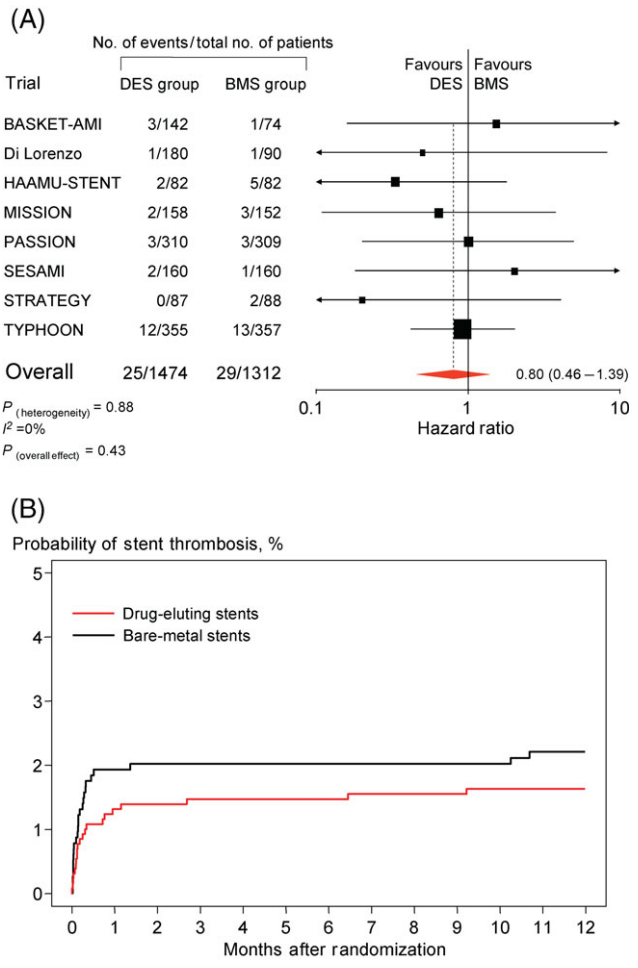

Figure 3 (**A**) Absolute numbers of patients with stent thrombosis and hazard ratios for stent thrombosis associated with drug-eluting stents vs. bare-metal stents for individual trials and the pooled population. Hazard ratios are shown on a logarithmic scale. The size of the square is proportional to the weight of the individual studies, measured as the inverse of the estimated variance of the log hazard ratio. DES, drug-eluting stent; BMS, bare-metal stent. (**B**) Kaplan–Meier curves of stent thrombosis in the pooled population according to stent type.

extend to patients with acute ST-segment elevation myocardial infarction has not been firmly established. A major concern with drug-eluting stents in this group of patients has been an increased risk for stent thrombosis, especially acute (within 24 h of stent implantation) and subacute (within 30 days of stent implantation).[10] There is an increased platelet activation in acute coronary syndromes, especially in acute myocardial infarction,[32] and coronary stenting is associated with a more intense platelet activation than balloon angioplasty alone.[33] A greater platelet activation coupled to delayed healing, lack of endothelialization, and exposure of proinflammatory and prothrombogenic environment of the necrotic core could provide the rationale for an increased risk of drug-eluting stent thrombosis in patients with acute myocardial infarction.[10] Recently, Park *et al.*[12] found that primary stenting with implantation of sirolimus-eluting or paclitaxel-eluting stents in patients with acute myocardial infarction was a major predictor for acute and subacute stent thrombosis. However, registry studies of patients with acute ST-segment elevation myocardial infarction have not shown an increased risk of stent thrombosis with drug-eluting stents compared with bare-metal stents.[34–36]

In our meta-analysis, the incidence of stent thrombosis was similar among patients treated with drug-eluting stents vs. bare-metal stents, as was the incidence of death or recurrent myocardial infarction. These findings support the safety of use of these types of stents. However, they should be interpreted with caution. Despite the advantage conferred by meta-analysis that has the potential to increase the statistical power, the rare occurrence of the previously discussed adverse events might limit the capacity of this meta-analysis to detect a possible difference between the two treatment arms with regard to the safety outcomes. Larger studies with a longer follow-up period will be needed to definitely answer the question of whether primary stenting with drug-eluting stents is safe.[37,38]

In conclusion, the results of this meta-analysis show that the use of drug-eluting stents in patients undergoing PCI for acute ST-segment elevation myocardial infarction is safe and improves clinical outcomes by reducing the risk of reintervention compared with bare-metal stents.

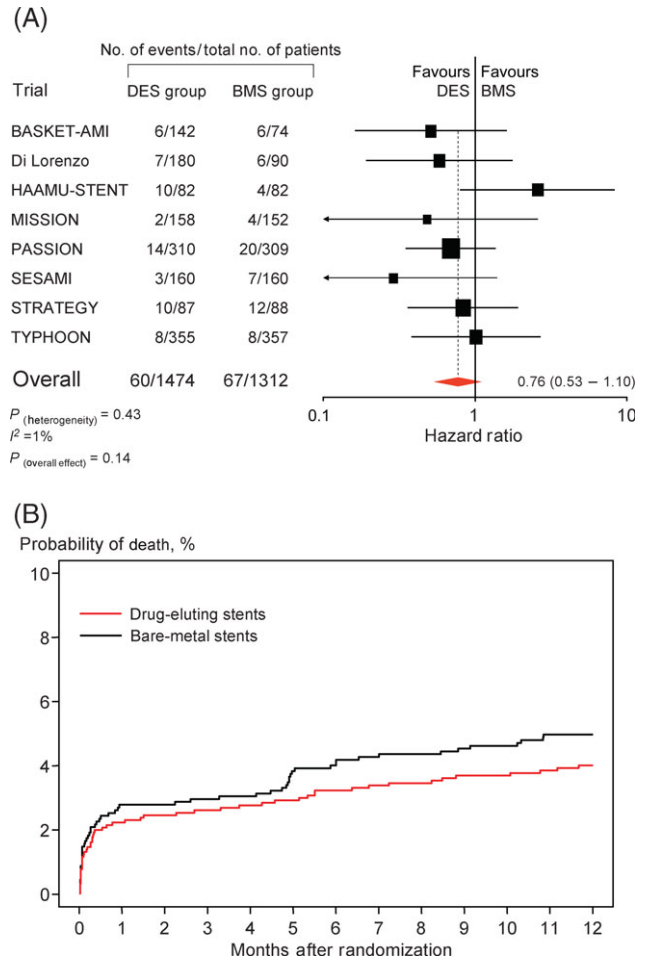

Figure 4 (**A**) Absolute numbers of patients experiencing death and hazard ratios for death associated with drug-eluting stents vs. bare-metal stents for individual trials and the pooled population. Hazard ratios are shown on a logarithmic scale. The size of the square is proportional to the weight of the individual studies, measured as the inverse of the estimated variance of the log hazard ratio. DES, drug-eluting stent; BMS, bare-metal stent. (**B**) Kaplan–Meier curves of mortality in each of the stent groups for the pooled population.

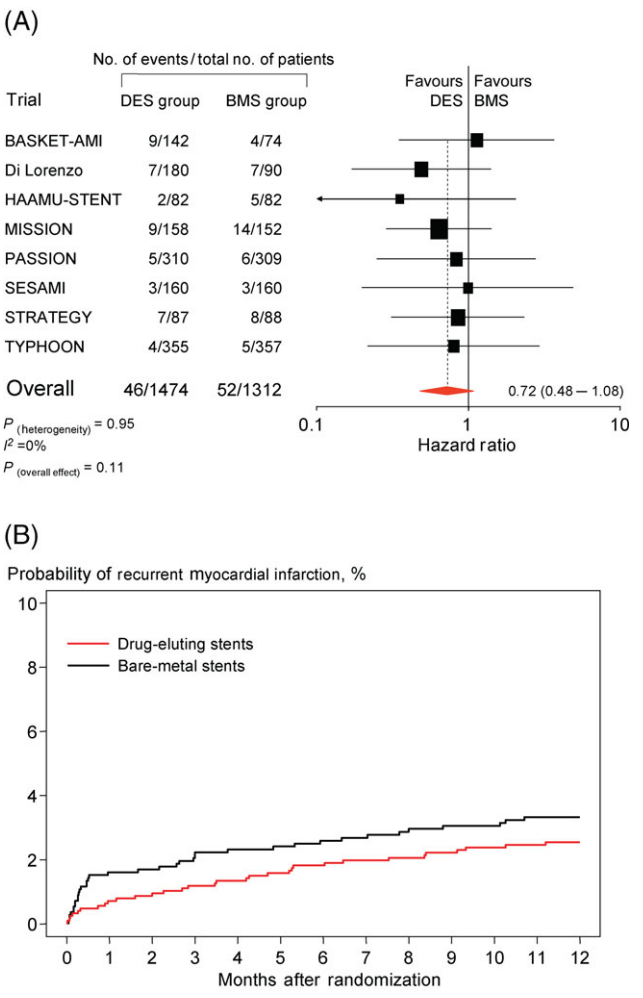

Figure 5 (**A**) Absolute numbers of patients experiencing recurrent myocardial infarction associated with drug-eluting stents vs. bare-metal stents for individual trials and the pooled population. Hazard ratios are shown on a logarithmic scale. The size of the square is proportional to the weight of the individual studies, measured as the inverse of the estimated variance of the log hazard ratio. DES, drug-eluting stent; BMS, bare-metal stent. (**B**) Kaplan–Meier curves of recurrent myocardial infarction in each of the stent groups for the pooled population.

Conflict of interest: Dr Kastrati reports having received lecture fees from Bristol-Meyers, Cordis, Glaxo, Lilly, Medtronic, Novartis, and Sanofi-Aventis. Drs Spaulding and Varenne report having received lecture fees from Abbott, Boston Scientific, Cordis, and Lilly. Dr Laarman reports having served on the advisory board of Boston Scientific and received lecture fees from Cordis and Medtronic. Dr Valgimigli reports having received honoraria for lectures, consultancy and research grants from Merck. Dr Tierala reports having received unrestricted research grants via the Helsinki University Hospital Research Institute from Boston Scientific, Lilly, Roche, and Sanofi-Aventis, as well as lecture fees from Glaxo-Smith-Kline, MSD, Lilly, Sanofi-Aventis, and Bristol-Myers-Squibb. Dr Dirksen reports having received lecture fees from Boston Scientific. Dr Violini reports having received lecture fees from Boehringer Ingelheim and Medtronic. Dr Schömig reports receiving unrestricted grant support for the Department of Cardiology he chairs from Amersham/General Electric, Bayerische Forschungsstiftung, Bristol-Meyers Squibb, Cordis, Cryocath, Guidant, Medtronic, Nycomed, and Schering.

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