Review: Drug-eluting stents are more effective than bare-metal stents for reducing acute MI at 6 to 12 months after implantation

Moreno R, Fernandez C, Calvo L, et al. **Meta-analysis comparing the effect of drug-eluting versus bare metal stents on risk of acute myocardial infarction during follow-up.** Am J Cardiol. 2007;99:621-5.

Clinical impact ratings: Cardiology ★★★★★☆☆

QUESTION

In patients undergoing stent implantation, are drug-eluting stents (DESs) more effective than bare-metal stents (BMSs) for reducing risk for acute myocardial infarction (MI)?

METHODS

Data sources: MEDLINE and lists of conference abstracts from the European Society of Cardiology, American College of Cardiology, American Heart Association, and Transcatheter Cardiovascular Therapeutics (to January 2006).

Study selection and assessment: Randomized controlled trials (RCTs) that compared DESs with BMSs. 25 RCTs (n = 9791, mean age range 59 to 67 y) met the selection criteria. The DESs evaluated contained sirolimus (11 RCTs), paclitaxel (7 RCTs), tacrolimus (2 RCTs), zotarolimus (1 RCT), everolimus (3 RCTs), and biolimus (1 RCT).

Outcomes: Acute MI (new increase in serum creatine kinase level ≥ 2 times the upper limit of normal reference range, concomitant increase in MB fraction of enzyme, and periprocedural infarction), Q-wave MI, and non–Q-wave MI.

MAIN RESULT

Meta-analysis showed that DESs reduced risk for acute MI more than did BMSs (Table). DESs and BMSs did not differ for Q-wave or non–Q-wave MI (Table).

CONCLUSION

Drug-eluting stents are more effective than bare-metal stents for reducing risk for acute myocardial infarction at 6 to 12 months after implantation.

Source of funding: Not stated.

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Drug-eluting stents vs bare-metal stents at 6 to 12 months after implantation*

Outcomes	Number of trials (n)	Weighted event rates	RRR (95% CI)	NNT (CI)
Acute MI	25 (9703)	3.3% vs 4.2%	20% (2.9 to 35)	118 (69 to 829)
Non–Q-wave MI	19 (6452)	2.7% vs 3.4%	20% (–5.8 to 39)	Not significant
			RRI (CI)	NNH
Q-wave MI	19 (6452)	0.71% vs 0.59%	20% (–34 to 118)	Not significant

*MI = myocardial infarction; other abbreviations defined in Glossary. Weighted event rates, RRR, RRI, NNT, NNH, and CI calculated from odds ratios and control event rates in article using a fixed-effects model.

COMMENTARY

Intracoronary stents are widely regarded as a major therapeutic advance in cardiology because they reduce the rate of angiographic restenosis and subsequent need for repeated percutaneous coronary intervention (PCI). However, compared with balloon angioplasty (BA) and restricted stenting, routine coronary stenting is not associated with reductions in mortality, MI, or coronary artery bypass surgery (1). The higher upfront cost of stenting is outweighed by the benefit of reducing risk for restenosis and associated costs of repeated PCI. However, it is not clear if a similar magnitude of benefit is seen in the "real world," where routine angiographic assessment of restenosis is not performed.

In theory, DESs should have taken this benefit to higher levels as the mechanical scaffolding effect was coupled with drugs to reduce risk for restenosis. Indeed, in the meta-analysis by Kastrati and colleagues, risk for restenosis was further reduced but risk for MI or death was not reduced with DESs compared with BMSs during long-term follow up. The lack of benefit is not unexpected given that "hard" clinical endpoints did not differ between BMSs and BA; however, while the study reduces overall concerns of increased events with DESs, the increase in late stent thrombosis and the apparent lack of benefit in patients with diabetes remain issues of concern.

The meta-analysis by Moreno and colleagues suggested reduced risk for MI using a very conservative creatine-kinase–based definition. Lesser degrees of myocardial necrosis, which may be prognostically important, would have been missed. It is also not clear from the data whether there is a temporal association between avoidance of MI and restenosis. Finally, Moreno and colleagues selectively looked at MI in isolation, whereas patients are likely to be more interested in survival free of MI, as reported by Kastrati and colleagues (2). In addition, the recently published results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation trial may call into question the overall value of PCI (predominantly BMSs) in stable populations with CAD (3).

DESs have a role in the management of patients with stable CAD, but this role should not be overemphasized. The recent increase in the United States and Canada of DES utilization rates from 75% to 90% is not justified based on present RCT evidence.

A more rational use of DESs involves the incorporation of clinical and angiographic data to select patients at high risk for restenosis or, if restenosis develops, those at high risk for having more severe consequences. Clinical criteria would include the presence of diabetes or renal insufficiency or a history of bypass surgery. Angiographic criteria include small-vessel diameter and longer lesions, unprotected left main lesions, or disease of the ostial or proximal left anterior descending artery.

(continued on page 14)

Review: Sirolimus-eluting stents do not differ from bare-metal stents for long-term survival in CAD

Kastrati A, Mehilli J, Pache J, et al. **Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents.** N Engl J Med. 2007;356:1030-9.

Clinical impact ratings: Cardiology ★★★★★☆☆

QUESTION

In patients with coronary artery disease (CAD), how do sirolimus-eluting stents (SESs) compare with bare-metal stents (BMSs) for long-term survival?

METHODS

Data sources: MEDLINE; National Institutes of Health clinical trials registry; Cochrane Central Register of controlled trials; lists of conference abstracts from American College of Cardiology, American Heart Association, and European Society of Cardiology; and hand searches of clinical trials in cardiology and relevant studies from major medical journals (January 2002 to September 2006).

Study selection and assessment: Randomized controlled trials (RCTs) that compared SESs with BMSs in patients with CAD and had mean follow up ≥ 1 year. 14 RCTs (n = 4958, mean age range 59 to 67 y, mean follow-up range 12 to 59 mo) met the selection criteria. Quality assessment of individual studies was based on allocation concealment, blinded outcome assessment, and intention-to-treat analysis.

Outcomes: All-cause death. Secondary outcomes were stent thrombosis and the composite outcomes of death or myocardial infarction (MI); and death, MI, or reintervention (major adverse cardiac events).

MAIN RESULTS

Meta-analysis showed that groups did not differ for all-cause death, stent thrombosis (overall), or the composite endpoint of death or MI (Table). SESs led to a lower incidence of the composite endpoint of death, MI, or reintervention than did BMSs (Table). After 1 year, SESs increased risk for stent thrombosis more than did BMSs (0.6% vs 0.05%, P = 0.02).

CONCLUSION

Sirolimus-eluting stents do not differ from bare-metal stents for long-term survival in patients with coronary artery disease.

Source of funding: No external funding.

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Sirolimus-eluting stents vs bare-metal stents in coronary artery disease at 12 to 59 months*

Outcomes	Number of trials (n)	Weighted event rates	RRI (95% CI)	NNH
All-cause death	14 (4958)	6.1% vs 6.0%	2.9% (–20 to 29)	Not significant
Stent thrombosis (overall)		0.3% vs 0.3%	9.0% (–36 to 86)	Not significant
			RRR (CI)	NNT (CI)
Death or MI		9.9% vs 10%	2.8% (–15 to 18)	Not significant
Death, MI, or reintervention†		12% vs 26%	53% (42 to 63)	8 (7 to 10)

*MI = myocardial infarction; other abbreviations defined in Glossary. Weighted event rates, RRR, RRI, NNT, NNH, and CI calculated from hazard ratios and control event rates in article using a random-effects model.
†Reintervention = major adverse cardiac events.

COMMENTARY

(continued from page 13)

Repeated revascularization is not entirely a result of clinical or angiographic within-stent restenosis, particularly after the first year. While the stented segment may remain stable, disease progression in other segments is 4 times more likely to be responsible for adverse clinical outcomes than is stent restenosis (4). As such, aggressive risk factor modification and vascular protection are mandatory.

Finally, all new advances seem to come at a cost: The cost for DESs is a higher risk for late stent thrombosis. However, although the evidence base shows that risk exists, the magnitude is small—around 4 to 6 per 1000 patients stented. While the risk could possibly be mitigated by concomitant and prolonged use of aspirin and clopidogrel, the combination is probably associated with increased risk for bleeding; the magnitude of serious bleeding may be similar to the stent thromboses avoided. Unfortunately, data outlining the optimal duration of dual therapy are not forthcoming. At least 1 year of dual antiplatelet therapy is required for all DES implants. Therapy extending beyond 1 year may be indicated for patients at high risk for late stent thrombosis or severe consequences from thrombosis—for example, unprotected left mainstem stenosis or multiple stents.

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