Letter to the Editor

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Drug-eluting stents: meta-analysis in diabetic patients

Dear Editor,

We read with interest the systematic review on drug-eluting stents (DES) by Hill et al.[1] The early data available indicate that DES reduce in-stent restenosis and major adverse cardiac events (MACE), mainly revascularizations. Although diabetes mellitus represents a major risk factor for coronary heart disease, no specific attention has been devoted to this particular population in this remarkable review. In the ARTS study, diabetic patients undergoing coronary stenting had a poorer prognosis than non-diabetic patients and diabetic patients treated with bypass surgery.[2] A recent meta-analysis of six trials in patients receiving coronary angioplasty with bare-metal stents (BMS) reported that the odds ratio (OR) of restenosis associated with diabetes was 1.61 (95% CI 1.21–2.14, $p = 0.004$).[3] As DES significantly reduce restenosis rates,[4] especially in small vessels, it would be interesting to specifically analyse the potential impact of DES in diabetic patients. We performed a meta-analysis of the results from six recent trials comparing DES and BMS, using sirolimus (RAVEL, SIRIUS and E-SIRIUS) or paclitaxel (TAXUS II, TAXUS IV and TAXUS VI). These trials provided adequate figures which allowed us to recalculate the rate of in-stent restenosis (defined as a stenosis $\geqslant$ 50%) after a follow-up of 6–12 months in both diabetic (around 20% of the population) and non-diabetic patients (Fig. 1). OR of restenosis was markedly lower when comparing DES with BMS and similar in both non-diabetic (OR: 0.16; 0.12–0.20; $p < 0.00001$) and diabetic (OR: 0.16; 0.11–0.24; $p < 0.00001$) patients. However, as compared to non-diabetic individuals, the OR of in-stent restenosis associated with diabetes still averaged 1.96 (1.28–3.01) in the groups receiving DES ($p = 0.002$), a figure quite similar (although less consistent between studies) to that observed with BMS (OR = 1.90; 1.49–2.43; $p < 0.00001$). Interestingly, in the SIRIUS substudy specifically devoted to diabetes,[5] in-lesion restenosis was significantly reduced with DES compared to BMS in the non-insulin-requiring patients (7.7% vs. 49.3%, $p < 0.001$), but not in the insulin-requiring patients (35% vs. 50%, $p = 0.38$). MACE incidence after 9 months was reduced from 25% with BMS to 9.2% with DES ($p < 0.001$) in diabetic patients and from 16.5% to 6.5% ($p < 0.001$) in non-diabetic patients, respectively. Finally, in the RESEARCH registry of DES use in the real world,[6] diabetes was a significant predictor of MACE (OR = 1.62; 1.09–2.43; $p = 0.02$), especially clinically driven target vessel revascularization (OR = 1.81; 1.10–2.99; $p = 0.02$).

In conclusion, DES are associated with a 80% remarkable relative risk reduction of restenosis during the first year of follow-up in diabetic patients as compared to BMS, similar to that observed in non-diabetic subjects. However, despite the use of DES, diabetes mellitus still remains an independent risk factor of restenosis, need for revascularization and MACE. Further specific prospective studies with highly effective DES should be performed in this high risk diabetic population.

References

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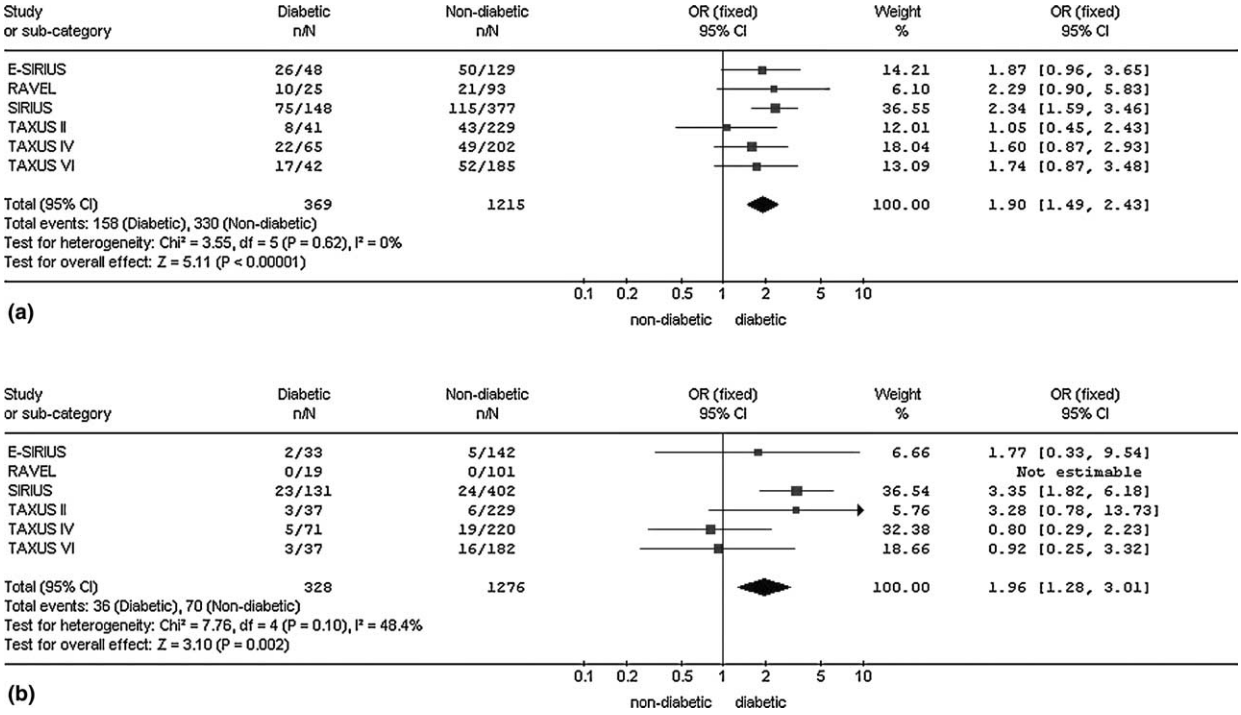
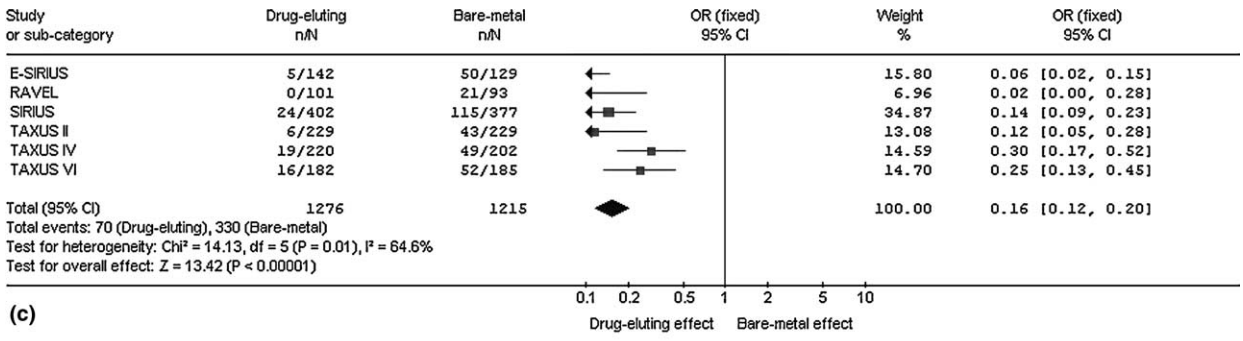


Fig. 1 Meta-analysis of six trials comparing the effects of bare-metal stents (BMS) (a) vs. drug-eluting stents (DES) (b) on restenosis in diabetic (d) vs. non-diabetic patients. (c) OR: odds ratio.



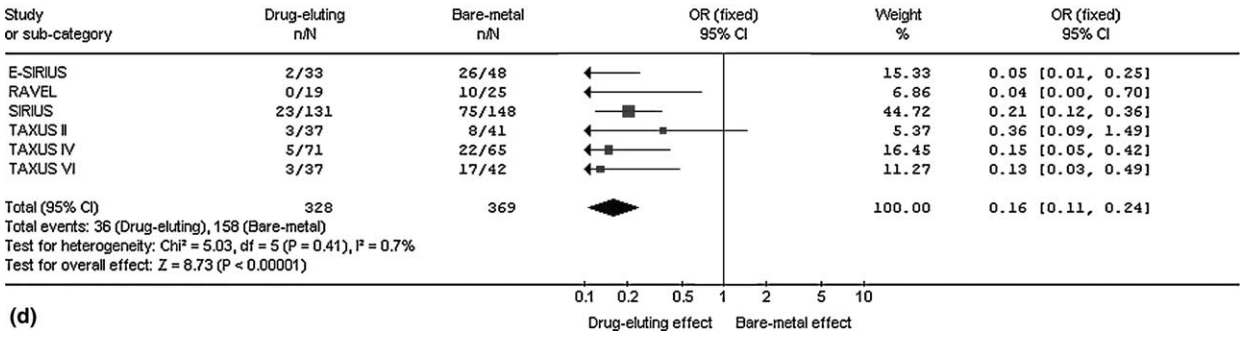


Fig. 1 (*continued*)

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André J. Scheen
Fabian Warzée
Victor M.G. Legrand
Division of Diabetes Nutrition and Metabolic Disorders and the Division of Cardiology Department of Medicine
CHU Sart Tilman (B35)
B-4000 Liège, Belgium
Tel.: +32 4 3667238
Fax: +32 4 3667068
E-mail address:
andre.scheen@chu.ulg.ac.be
(A.J. Scheen)

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Exploring groups at high risk of restenosis

We thank Scheen and colleagues for their interest in our systematic review[1] of drug-eluting coronary artery stents (DES) and congratulate them on their success in obtaining largely unpublished data for diabetic and non-diabetic subgroups for six major trials of DES. We feel it would be useful for the sources of these data to be listed, and the method of interpretation of restenosis rates should be described. Our own analysis of patient subgroups,[2] including diabetes, was conducted for the National Institute for Clinical Excellence early in 2003,[3] but was limited by the data available to us. It is for this reason we did not include these subgroup analyses in our recent publication.[1] We have since utilised further data available from trials and our regional cardiothoracic centre to explore patient subgroups in some detail.

Although Scheen and colleagues provide an interesting analysis, their correspondence does not consider important related, but distinct issues. Our observations on three such topics are as follows:

(1) As Scheen and colleagues' analysis shows, and supported by our own more limited subgroup analysis, there is no convincing evidence that DES act differently in reducing restenosis in patients with diabetes in *relative* terms. It seems that DES benefit all patients with a likely poor outcome to the same degree — absolute differences arise from the underlying propensity to restenose.

(2) In *aggregate* terms, patients with diabetes are more likely to suffer MACE or revascularization than those without. However, in SIRIUS[4] these patients were more likely to have hypertension, triple vessel disease or impaired left ventricular function. It is not clear that after correction for these and other risk factors, as well as anatomical variables, case-mix-adjusted patients with diabetes are at more or less risk of restenosis than non-diabetics. In other words, diabetes may be associated with greater risks, but this is not necessarily causal.