Diabetes Is Still a Risk Factor for Restenosis After Drug-Eluting Stent in Coronary Arteries

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We read with interest the metaanalysis of the effect of diabetes on restenosis rates among patients receiving coronary angioplasty stenting (1). This meta-analysis of six clinical trials showed that the odds ratio (OR) of coronary artery restenosis associated with diabetes was 1.61 (95% CI 1.21-2.14, P = 0.004) in univariate logistic regression models, but it decreased to 1.30 (0.99-1.70, P = 0.055) after age was controlled in multivariate models. All trials selected in this meta-analysis used classical bare-metal stents. However, drug-eluting stents (DESs) have been shown to improve outcomes among patients undergoing percutaneous coronary intervention by significantly reducing restenosis rates (2).

We performed a meta-analysis of the results from four recently published trials comparing bare-metal stents with DESs, two using sirolimus (RAVEL and SIRIUS) (3, 4) and two using paclitaxel (TAXUS II and TAXUS IV) (5,6) (Fig. 1). These four trials comprised a significant proportion of diabetic patients (\sim 20%) and provided figures that allowed us to recalculate the rate of restenosis after a follow-up of at least 6 months in both the diabetic and nondiabetic populations. The OR of in-stent restenosis in diabetic patients compared with control subjects averaged 1.94 (95% CI 1.46-2.58) in the groups receiving bare-metal stents (P < 0.00001). Unfortunately, none of the studies gave details about the respective ages of the diabetic and nondiabetic patients, so corrections for possible differences in age were not feasible (1). A similar OR was found when DESs were considered (OR 2.24 [1.39-3.61], P = 0.0009), suggesting that the use of new DESs does not allow to suppress differences between diabetic and nondiabetic patients. In both groups of patients, the rate of restenosis was markedly and significantly (P < 0.00001) higher with bare-metal stents compared with DESs, with an OR of 6.33 (4.57-8.76) in the nondiabetic population and 5.27 (3.36-8.28) in the diabetic population.

These results demonstrated the potential interest of DESs in patients at high risk of restenosis. Nevertheless, even when using DESs, the diabetes status remains a significant risk factor. This was recently confirmed in a large cohort of patients who benefited from unrestricted utilization of sirolimus-eluting stents compared with conventional bare-metal stent implantation in the "real world" (7). This research registry focused on a 1-year cumulative rate of major adverse cardiac events rather than on restenosis. It showed that the benefit of DESs did not reach statistical significance in diabetic patients (OR 0.72 [95% CI 0.30-1.77], P = 0.50). Furthermore, diabetes was a significant predictor of major adverse cardiac events (OR 1.62 [1.09-2.43], P = 0.02) and of clinically driven target vessel revascularization (OR 1.81 [1.10-2.99], P = 0.02) (Fig. 1).

In conclusion, diabetes remains a major risk factor for restenosis after both bare-metal stents and DESs. Considering the high prevalence and burden of coronary heart disease in diabetic patients, specific studies should be performed in this population in order to test the possibility of reducing the risk of restenosis and major cardiac events, including the use of more effective DESs (2).

Figure 1: *Meta-analysis of four trials comparing the effects on restenosis of bare-metal stents and drug-eluting stents in diabetic and nondiabetic patients.*

Bare-metal stent

Study or sub-category	diabetic n/N	non-diabetic n/N		OR (fixed) 95% CI				OR (fixed) 95% Cl		
RAVEL	10/25	21/93							2.29 [0.90, 5	.831
SIRIUS	75/148	115/377				-	_		2.34 [1.59, 3	-
TAXUS II	8/41	43/229				_			1.05 [0.45, 2	
TAXUS IV	22/65	49/202				-			1.60 [0.87, 2	
otal (95% CI)	279	901							1.94 [1.46, 2	. 581
otal events: 115 (diabetic),	228 (non-diabetic)								•	-
est for heterogeneity: Chi ²	= 3.46, df = 3 (P = 0.33), $P = 1$	3.3%								
Fest for overall effect: Z = 4										
			0.1	0.2	0.5	1 2	5	10		
				поп	-diabetic	diabetic				

Drug-eluting stent

Study	diabetic	non-diabetic	OR (fixed)	OR (fixed)
or sub-category	n/N	n/N	95% CI	95% Cl
RAVEL	0/19	0/101		Not estimable
SIRIUS	23/131	24/402		3.35 [1.82, 6.18]
TAXUS II	3/37	6/229		3.28 [0.78, 13.73]
TAXUS IV	5/71	19/220		0.80 [0.29, 2.23]
Total (95% Cl) Total events: 31 (diabetic), 4 Test for heterogeneity: Chi ^a Test for overall effect: Z = 3	= 5.82, df = 2 (\hat{P} = 0.05), \hat{P} = 69	952		2.24 [1.39, 3.61]
			0.1 0.2 0.5 1 2 5 10	T. 100 C.

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