JACC Vol. 47, No. 9, 2006
May 2, 2006:1904–17

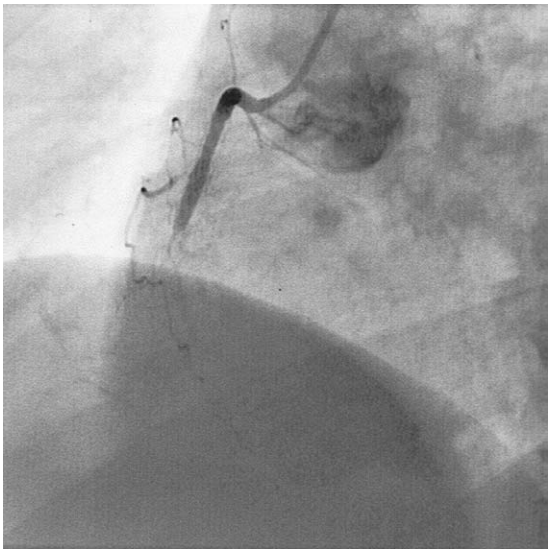

Figure 2. Development of occlusive coronary artery spasm.

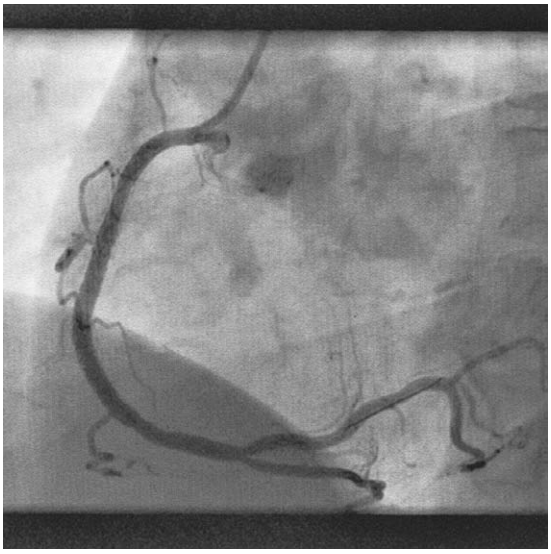

Figure 4. Final angiographic result following Taxus stent deployment.

of the right coronary artery distal to the SES (Fig. 2). This improved following intracoronary nitrate administration (Fig. 3). As we believed the severe spasm in this region to be the cause of the earlier ventricular fibrillation, we elected to deploy a paclitaxel-eluting stent (Taxus Express, Boston Scientific, Marlborough, Massachusetts) to cover the vasospastic arterial segment (Fig. 4). An excellent angiographic result was achieved, and the patient has remained asymptomatic at follow-up.

This case illustrates that occlusive coronary spasm may develop after drug-eluting stent deployment with potentially life-threatening consequences. We can only speculate whether the abnormal vasomotion in the arterial segment distal to the SES was attributable to a local effect of sirolimus on endothelial function (3), or to late endothelial dysfunction following brachytherapy (4). The history of prior treatment of the vessel with paclitaxel may also be relevant. Nonetheless, the potential for drug-eluting stents to unfavorably alter coronary vasomotion is worthy of further study.

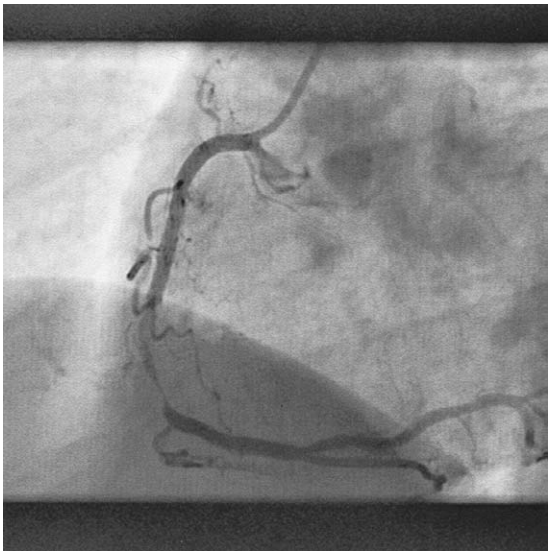

Figure 3. Improved appearances following intracoronary nitrate.

Stephen Wheatcroft, PhD, MRCP
Jonathan Byrne, PhD, MRCP
Martyn Thomas, MD, FRCP
***Philip MacCarthy, PhD, MRCP**

*King's College Hospital
Cardiology
Bessemer Road
Denmark Hill
London, SE6 9RS
United Kingdom
E-mail: philip.maccarthy@kingsch.nhs.uk

doi:10.1016/j.jacc.2006.02.017

REFERENCES

1. Togni M, Windecker S, Cocchia R, et al. Sirolimus-eluting stents associated with paradoxic coronary vasoconstriction. J Am Coll Cardiol 2005;46:231–6.
2. Serry R, Penny WF. Endothelial dysfunction after sirolimus-eluting stent placement. J Am Coll Cardiol 2005;46:237–8.
3. Jeanmart H, Malo O, Carrier M, Nickner C, Desjardins N, Perrault LP. Comparative study of cyclosporine and tacrolimus vs newer immunosuppressants mycophenolate mofetil and rapamycin on coronary endothelial function. J Heart Lung Transplant 2002;21:990–8.
4. Togni M, Windecker S, Cocchia R, et al. Deleterious effect of coronary brachytherapy on vasomotor response to exercise. Circulation 2004;110:135–40.

REPLY

Regarding our recent study in *JACC* (1), we would like to thank Drs. Kipshidze and Leon for the clarifying arguments on the effects of sirolimus and paclitaxel on endothelial cells. We agree that endothelial dysfunction and incomplete vascular healing may play a key role in the development of peristent lesions and late stent thrombosis after drug-eluting stent (DES) implantation, although this link has not been established so far. We can only support the need for inclusion of functional studies before introduction of new DESs in order to identify potential negative effects on endothelial recovery and vascular healing.

The observation by Dr. Wheatcroft and colleagues of life-threatening coronary artery spasm following sirolimus-eluting stent deployment is impressive and underscores the important role of vasomotor function after stent implantation. A recent report demonstrated severe multivessel spasms and aborted sudden cardiac death 10 h after paclitaxel-eluting stent implantation (2). A similar phenomenon has been described after high-dose intracoronary beta-radiation by Scheinert et al. (3), who concluded that vasoconstriction is a frequent finding a few minutes after beta-radiation and may be due to acute radiation-induced endothelial dysfunction.

These two letters underline the key role of re-endothelialization for maintaining a normal vascular function after stent implantation or intracoronary radiotherapy.

Mario Togni, MD
***Otto M. Hess, MD**

*University Hospital
CH-3010 Bern
Switzerland
E-mail: Otto.Hess@insel.ch

doi:10.1016/j.jacc.2006.02.016

REFERENCES

1. Togni M, Windecker S, Cocchia R, et al. Sirolimus-eluting stents associated with paradoxic coronary vasoconstriction. J Am Coll Cardiol 2005;46:231–6.
2. Kim JW, Park CG, Seo HS, Oh DJ. Delayed severe multivessel spasm and aborted sudden death afer Taxus stent implantation. Heart 2005; 91:e15.
3. Scheinert D, Strnad V, Müller R, et al. High-dose intravascular β-radiation after de novo stent implantation induces coronary artery spasm. Circulation 2002;105:1420–3.

Preventing Type 2 Diabetes Mellitus With Angiotensin Blockade: Is it Clinically Relevant?

Diabetes mellitus is a serious, costly, and increasingly common disease. In light of the dramatic epidemic of type 2 diabetes and its adverse prognostic implications, strategies to prevent or delay this major health problem are of paramount importance.

Abuissa et al. (1), in a meta-analysis of 12 recent randomized controlled clinical trials that enrolled patients with hypertension, chronic heart failure, or coronary heart disease, showed that angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) produced a highly significant 25% reduction (95% confidence interval [CI], 18% to 31%) in the incidence of new-onset diabetes when compared to placebo, diuretics, beta-blockers, or calcium channel antagonists. Apart from some limitations (e.g., new-onset diabetes as secondary end point or as post hoc analysis; open-blinded end point design in some trials; higher proportion of patients receiving drugs that increase insulin resistance such as diuretics and beta-blockers in the comparator groups; and absence of standardization for serial testing of blood glucose levels), the investigators concluded that the use of an ACE inhibitor or ARB should be considered in patients with prediabetic conditions such as metabolic syndrome, hypertension, impaired fasting glucose, family history of diabetes, obesity, congestive heart failure, or coronary heart disease.

However, focusing solely on the relative risk (RR) reduction and utilizing a surrogate marker (prevention of a fasting plasma glucose ≥126 mg/dl at two different visits in patients with no diabetes at the time of presentation) make it difficult to estimate the real benefit of the proposed intervention.

On the basis of the Abuissa et al. (1) meta-analysis, despite a significant RR reduction of 25%, the absolute risk difference between an ACE inhibitor or an ARB and the other agents was only 3.1 cases per 1,000 patient-years (decreasing from 17.4 to 14.3 per 1,000 patient-years), which means that 323 patients (1/0.0031) must be treated for one year to prevent the new onset of one case of diabetes mellitus. Moreover, it is important to mention that the final goal of the inhibition of the renin-angiotensin-aldosterone system in this particular situation is to prevent the diabetes-related morbidity and mortality rather than merely the diagnosis of diabetes. If one assumes that the risk of any diabetes-related macrovascular or microvascular complication is about 46 per 1,000 patient-years for newly diagnosed patients with type 2 diabetes (2), the number needed to treat (NNT) per year in order to prevent not only the development of type 2 diabetes mellitus but also any one of its subsequent complications increases to 7,013 [(1/0.0031) × (1/0.046)]. Even with a longer-term follow-up, let us say 10 years, given the time frame from onset of diabetes to diabetes-related complications, the NNT to prevent a clinical event would be extraordinarily high.

Needless to say, this type of analysis does not contemplate the already proved beneficial effects of ACE inhibitors and ARBs (by other mechanisms) on the reduction of major vascular events in certain conditions such as heart failure or after myocardial infarction. Of note, in another recent meta-analysis (3), ACE inhibitors or ARBs decreased patients' odds of developing new-onset type 2 diabetes but did not reduce the odds of mortality, cardiovascular, or cerebrovascular outcomes among patients with hypertension. Therefore, instead of searching for pharmacological therapies that are statistically attractive but will never be clinically relevant or cost-effective, prevention of diabetes mellitus should be fundamentally approached by reducing the patient's weight and increasing his or her physical activity (4,5).

***Anis Rassi, Jr., MD, PhD, FACC**

*Department of Cardiology
Anis Rassi Hospital
Avenida Jose Alves, 453
Setor Oeste
Goiânia, GO 74110-020
Brazil
E-mail: arassijr@terra.com.br

doi:10.1016/j.jacc.2006.02.015

REFERENCES

1. Abuissa H, Jones PG, Marso SP, O'Keefe JH Jr. Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers for prevention of type 2 diabetes. A meta-analysis of randomized clinical trials. J Am Coll Cardiol 2005;46:821–6.
2. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352:837–53.
3. Gillespie EL, White CM, Kardas M, Lindberg M, Coleman CI. The impact of ACE inhibitors or angiotensin II type 1 receptor blockers on the development of new-onset type 2 diabetes. Diabetes Care 2005;28: 2261–6.