Impact of Insulin Resistance on Clinical Outcomes After Implantation of Drug-Eluting Stents

Masaaki Miyata, MD, PhD

Percutaneous coronary intervention (PCI) using drug-eluting stents (DES) is a widespread and efficacious treatment for coronary artery disease, and has dramatically reduced the incidence of restenosis after PCI compared with bare-metal stents or balloon angioplasty. However, stent thrombosis and the late catch-up phenomenon are major problems of DES implantation. In this issue of the Journal, Komatsu et al analyze 109 patients who underwent elective PCI and implantation of 1st-generation DES and demonstrated that insulin resistance (IR) was associated with the late catch-up phenomenon after DES implantation. These findings are clinically interesting and evaluation of IR may provide useful information for predicting clinical outcomes after DES implantation.

IR is a key pathological factor of the metabolic syndrome, and associated with the risk of diabetes mellitus, microalbuminuria, and cardiovascular events. IR refers to an impaired or failed cellular response to insulin receptor-activated signaling in insulin-sensitive tissues such as the liver, skeletal muscle, adipose, and brain, which results in reduced glucose uptake by these tissues and concomitant increase in hepatic glucose output, both leading to elevated plasma glucose concentrations. The subsequent change in glucose homeostasis places an increased burden on pancreatic β-cells to produce and secrete more insulin in order to restore normal blood carbohydrate levels. The hyperinsulinemia upregulates glucose transport, glycogen synthesis, gluconeogenesis, lipolysis, protein synthesis, proliferation, differentiation, and inflammation.

Uetani et al have reported the effect of IR on post-procedural myocardial injury and clinical outcomes after elective PCI with DES deployment. The incidence of late and very late stent thrombosis increases after implantation of 1st-generation DES, in which delayed arterial healing and poor re-endothelialization may play a major role. In addition, late incomplete stent apposition was observed in 8.7% of patients after implantation of a sirolimus-eluting stent (SES), a 1st-generation DES. An autopsy case...
IR and Clinical Outcomes of DES

Circulation Journal Vol.80, March 2016

593

demonstrated medial necrosis at the implantation site of the SES, which suggests cytotoxic effects of sirolimus can induce medial necrosis and late incomplete stent apposition. The possible interaction of potent antiproliferative agents and the permanent non-biodegradable synthetic polymer has raised concerns regarding these phenomena via toxic effects and inflammation. IR progresses the inflammation at the site of DES implantation and thus increases the incidence of the late catch-up phenomenon (Figure).

The DES have been improving year by year. Biodegradable polymer DES aim to reduce polymer-induced late inflammation by utilizing biodegradable polymers that finally convert to water and carbon dioxide after their carrier vehicle function has been accomplished. The Nobori biolimus-eluting stent is a stainless steel platform loaded with polylactic acid as a polymer eluting biolimus A9, a highly lipophilic analog of sirolimus, and there is a bioabsorbable polymer only on the abluminal side. Meta-analysis has demonstrated that the use of the Nobori biolimus-eluting stent is associated with a similar safety and efficacy as permanent polymer DES at 1-year follow-up, albeit it is superior to paclitaxel-eluting stents in terms of target lesion revascularization rates. In addition, of the next generation DES, the Nobori biolimus-eluting stent demonstrated a lower inflammatory response in the stented segment compared with the SES in a porcine coronary artery model.

Therefore, it is unknown whether IR will be a predictor of the late catch-up phenomenon after implantation of next-generation DES, and further prospective studies using these DES are needed.

Interestingly Komatsu et al. mention that evaluation of the homeostasis model assessment of IR (HOMA-IR) level at 8-month follow-up and the degree of change in HOMA-IR from baseline to the 8-month follow-up is important in addition to the baseline levels. They analyzed the HOMA-IR data at 8-month follow-up, and found no significant difference from the HOMA-IR baseline data. Therefore, treatment of IR by exercise and/or medication may be important after PCI with DES implantation. Pioglitazone is a peroxisome proliferator-activated receptor-gamma agonist, and used clinically as an antidiabetic agent for improving insulin sensitivity in patients with diabetes mellitus. Metformin also improves IR. Therefore, I am interested in whether or not these drugs can reduce the late catch-up phenomenon after DES implantation, and it is worth investigating the preventive effect of these drugs on the late catch-up phenomenon.

The evaluation of IR is important in clinical practice. HOMA-IR is widely used to evaluate IR but cannot be used in patients being administered pioglitazone or insulin, and/or with a fasting glucose level >200mg/dl. Therefore, a novel index of IR needs to be developed, so it can be evaluated even in these patients.

Disclosures

There is no conflict of interest for the author.

References