Abstract:

In a recent study, analysis of gene expression in atherectomy specimens derived from restenotic coronary lesions revealed 223 differentially expressed genes. Thirty-seven of these genes indicated activation of interferon- (IFN-) gamma signaling in neointimal smooth muscle cells. Moreover, genetic disruption of IFN-gamma signaling in a mouse model of restenosis significantly reduced the vascular proliferative response. Thus, IFN-gamma is assumed to play an important role in the control of tissue proliferation during neointima formation. We hypothesized that genetic variants of IFN-gamma and its receptor subunits are involved in upregulation of IFN-gamma related genes in neointimal tissue of patients that develop in-stent restenosis. Polymorphisms in the genes encoding for IFN-gamma (IFNG T874A) and its receptors 1 (IFNGR1 C-56T) and 2 (IFNGR2 A839G) were tested for their association with restenosis. IFNG T874A, IFNGR1 C-56T and IFNGR2 A839G genotypes were determined in a consecutive series of patients (n=2591) that had been treated with coronary stents. Follow-up angiography 6 months after stent implantation was performed in 76.8% of the patients. Genotyping was performed with PCR-based methods. IFNG T874A, IFNGR1 C-56T and IFNGR2 A839G genotypes were not associated with the incidence of
angiographic and clinical restenosis (P>0.23). Moreover, there was no association between IFNG, IFNGR1 and IFNGR2 genotypes and the combined incidence of death from any cause and non-fatal myocardial infarction during the first 12 months following the intervention (P>0.61). Thus, this study does not support a clinically relevant role of the studied polymorphisms in the processes leading to in-stent restenosis.