ABSTRACT

The progression of chronic glomerulopathy and graft rejection is affected by a number of proinflammatory cytokines, whose role in the pathogenesis of damage is poorly understood. The aim of this dissertation was to identify reliable risk markers of renal dysfunction progression and thereby contribute to a more effective patient treatment.

Human native kidney biopsies with histologically confirmed diagnosis of glomerulopathy or kidney graft biopsies were analysed. Intrarenal gene expressions were measured by RT-qPCR. Single nucleotide polymorphisms were detected by methods based on PCR-RFLP. Immunohistochemical staining was used to identify and quantify the mononuclear cell infiltration.

Gene expression of *TGF-β1*, *HGF*, *BMP7*, *MCP-1*, *RANTES* and mononuclear cell infiltration were associated with poor renal function and proteinuria at the time of IgA nephropathy diagnosis. Progression of IgA nephropathy during the 2-year follow-up was shown to be dependent on the degree of chronic vasculopathy and *TGF-β1* expression in the kidney. Patients with graft dysfunction and enhanced intrarenal expression of *TGF-β1*, *MCP-1* had significantly shorter graft survival. Higher mRNA expression of *IL-10, TGF-β 1, IL-6, MCP-1, RANTES* and *TNF-α* was observed in patients with graft dysfunction presented at the time of biopsy. Correlation between the degree of allograft tubulitis and *MCP-1*, *RANTES* and *TGF-β1* gene expression was found. None of the examined functionally relevant gene polymorphisms increased the risk of subclinical rejection, acute rejection or allograft nephropathy in selected patients.

In conclusion, this study helps to find new biomarkers of IgA nephropathy progression and complications after kidney transplantation and thereby identify patients with increased risk.

Key words: IgA nephropathy, graft dysfunction, gene expression, gene polymorphism