Factors influencing mortality in a long-term follow-up after heart transplantation; role of immunomonitoring

Authors:
E. Alyaydin¹, H. Welp², C. Pogoda¹, R. Pistulli¹, H. Reinecke¹, I. Tuleta¹, ¹Department of Cardiology I, University of Muenster - Muenster - Germany, ²Department of Cardiothoracic Surgery, University of Muenster - Muenster - Germany.

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Background: Despite relevant improvements in the last years, increased mortality limits the success of heart transplantation therapy. Although many factors influencing mortality have been identified, the most studies analyzed relatively short follow-up time following heart transplantation.

Purpose: Therefore, the aim of our present study was to evaluate risk factors for enhanced mortality with emphasis on quantitative changes in immunological blood cells late after heart transplantation.

Methods: 174 patients with a mean time after heart transplantation of 13.1±6.5 years were retrospectively analyzed using data collected during follow-up visits in our center. Clinical examinations, results of laboratory tests, including immunomonitoring of CD4+, CD8+, CD19+ cells and natural killer cells, ultrasound vessel visualization and coronary angiography were evaluated with respect to the all-cause mortality.

Results: In patients who were still alive at the time of data analysis (group 1, n=134), glomerular filtration rate, erythrocyte count, hemoglobin and mean corpuscular hemoglobin concentration were significantly increased compared to the group encompassing patients who died before this time point (group 2, n=40) (p<0.05 for all). In contrast, c-reactive protein (CRP), leukocyte count, triglycerides and N-terminal pro-brain natriuretic peptide were significantly decreased in group 1 versus group 2 (p<0.05 for all). In the first group the patients were relevantly less frequently on dialysis, presented lower NYHA classes, later onset of cardiac allograft vasculopathy and received hearts from donors with lower body mass (p<0.05 for all). Additionally, patients from the first group were characterized by significantly higher CD4 and lower CD8 percentages as well as a tendency towards higher CD19 cell count. In a multivariate cox regression analysis CD4 percentage (hazard ratio (HR): 0.454, confidence interval (CI): 0.236–0.871; p=0.018), onset of cardiac allograft vasculopathy (HR: 0.422, CI: 0.190–0.941; p=0.035) and CRP (HR: 0.325, CI: 0.170–0.621; p=0.018) were independent risk factors for increased mortality.

Conclusions: Increased inflammation, anemia, renal and heart insufficiency, early onset of cardiac allograft vasculopathy, worse functional status and donor associated factors such as higher body mass correlated significantly with enhanced mortality among patients after heart transplantation. In contrast to the early phase following heart transplantation, where the suppression of CD4+ cell number contributes to the decrease in the frequency of acute rejections, aggressive reduction of CD4+ cells by high doses of immunosuppressive agents late after cardiac transplantation may augment risk of mortality. It may be explained due to the creation of a subclinical chronic immunosuppressive condition and potentiation of side effects of immunosuppressive drugs.