Preoperative Diagnosis of Diabetes Affects Long-Term Outcome in Patients After Heart Transplantation

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Background. To compare long-term outcome in patients with and without diabetes at the time of heart transplantation.

Methods. A retrospective analysis of 773 consecutive adult patients who underwent primary heart transplantation from 1986 through 2000 was conducted. The total population consisted of 633 patients without diabetes (male n=552; 84%) and 140 patients with diabetes (male n=156; 6%).

Results. Long-term survival rates of patients with diabetes mellitus were lower as compared with patients without diabetes mellitus (survival at 10 years with diabetes: 40% vs. w/o diabetes: 58%; log-rank=0.025). Both patient groups showed the same incidence of angiographically documented transplant coronary artery disease-TxCAD (TxCAD at 10 years with diabetes: 28% vs. w/o diabetes: 22%; n.s.). Patients with diabetes were older as compared with patients w/o diabetes (with diabetes: 49.7±5.8 vs. w/o diabetes: 46.9±9.5, p=0.001) and showed a higher incidence of coronary artery disease as indication for transplantation as compared with patients w/o diabetes (with diabetes: 52% vs. w/o diabetes: 30%; p=0.001). In multivariate analysis regression, the presence of diabetes at the time of transplantation (HR 1.69; 95%CI 1.09-2.51; p=0.045) was as well as the use of thymoglobulin induction therapy (HR 0.47; 95%CI 0.31-0.71; p=0.003) were independent predictors affecting long-term survival. Female gender (HR 0.75; 95%CI 0.10-0.53; p=0.012) as well as thymoglobulin antibody induction therapy (HR 0.58; 95%CI 0.39-0.96; p=0.033) were independent predictors affecting the development of TxCAD. Interestingly, diabetes did not exhibit any influence on the occurrence of TxCAD.

Conclusion. The diagnosis of diabetes at the time of transplantation adversely affects long-term survival but not the occurrence of transplant coronary artery disease. The major limitation for patients with diabetes seems to be advanced age and a higher incidence of coronary artery disease resulting in an impairment of overall function and consequently, in a diminished physiologic reserve.

FEATURED ORAL PRESENTATION

838FO Featured Oral Session...Ventricular Hypertrophy/Remodeling

Monday, March 18, 2002, 4:00 p.m.-5:30 p.m.
Georgia World Congress Center, Room 267W

Temporal Evolution of Molecular, Functional, and Structural Phenotypes in a Transgenic Rabbit Model of Human Hypertrophic Cardiomyopathy


Hypertrophic cardiomyopathy (HCM) is a genetic disease with protean clinical and pathologic phenotypes including left ventricular hypertrophy (LVH), myocyte disarray (MD), interstitial fibrosis (IF), heart failure, and sudden death. Slow evolution of phenotypes in transgenic rabbits has hampered determination of their temporal sequence in humans. We developed transgenic rabbits with cardiac-specific expression of fmyosin heavy chain-glutamine (MyHC-Q403), known to cause HCM in humans. Transgenic rabbits exhibit LVH, MD, IF, and myocardial dysfunction. We determined temporal evolution of molecular, functional, and structural phenotypes in the MYH6C-Q403 rabbits by performing serial M-mode, 2-D, Doppler echocardiography and tissue biopsy. Doppler imaging, histological staining of myocardial sections, and immunoblotting for hypertrophic signaling kinases in 36 B-MyHC-Q 403 and 35 non-transgenic rabbits (>6 months of age) compared to control rabbits. LV wall thickness increased progressively in the B-MyHC-Q403 rabbits (septal thickness: 2.4±0.2, 2.8±0.5, and 3.1±0.4, respectively, p0.001). End diastolic and end systolic diameters were increased and fractional shortening reduced progressively (p<0.001). Doppler indices of LV filling pressure and left atrial size were also increased progressively (<0.05). Myocardial contraction and relaxation velocities were decreased in B-MyHC-Q403, compared to controls, in all three age groups. IF increased progressively with aging (2.7±0.2, 7.6±0.7, and 9.0±1.7%, p<0.005). Myocardial disarray was present early and did not change with aging (90±4.2, 11.9±3.8, 10.6±4.0%). Myocardial velocities were reduced even in the absence of IF and MD. Expression of active but not ERK1/2 was increased in 62-64 month old rabbits. Expression levels of active and total p38, JNKs, and GTP bound Ras, Rac1 and Rho1 were unchanged. Thus, myocardial dysfunction occurs early and in the absence IF and MD. Disarray precedes LVH and IF, which are progressive. Preserved global systolic function evolves into progressive systolic dysfunction with LV and left atrial enlargement and increased filling pressures.