1086-174 Effects of Heart Transplantation on Plasma Levels of TNF-α in Patients with Congestive Heart Failure

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The citokine tumor necrosis factor-α (TNF-α) has been implicated in the pathogenesis of chronic heart failure (CHF) as well as in acute and chronic heart transplant rejection. The time course of plasma levels of TNF-α was assessed in 19 patients with CHF (age 54 ± 7 years) before heart transplantation (b-HTx) and 3, 6 and 12 months after surgery (HTx-3, -6, -12). Blood was withdrawn from the antecubital vein and a myocardial biopsy was performed within 12 hours. TNF-α plasma levels were assessed also in 10 age-matched control subjects. Analysis was performed by a sandwitch ELISA method. Statistics were performed by ANOVA. The TNF-α plasma levels (pg/ml) were as follows:

Controls	b-HTx	HTx-3	HTx-6	HTx-12
6.7 ± 3.3	28.1 ± 10.7*	23.1 ± 10.6*	23.2 ± 12.4*	23 ± 11.5*

ANOVA: $p < 0.0001$. *$p < 0.05$ vs Controls.

In 5 myocardial biopsies of 5 different patients a multifocal moderate rejection (grade 3A or B of Billingham Scale) was detected. The TNF-α plasma levels in case of grade 3 rejection were increased when compared to the levels observed in case of mild (grade 1A or B) and no rejection (40 ± 10.8 vs 20.7 ± 8.9 pg/ml, $p < 0.05$) and when compared to the b-HTx values ($p < 0.05$). No differences were observed between TNF-α plasma levels in case of no rejection compared to grade 1A or B acute rejection (21.7 ± 8.6 vs 19.5 ± 9.5 pg/ml, ns).

Conclusions: 1) the elevated plasma levels of TNF-α of patients with CHF tend to decrease after HTx in absence of multifocal moderate rejection (grade 3A or B) but they remain elevated compared to the plasma levels of control subjects; 2) TNF-α plasma levels increase markedly in case of grade 3A or B acute rejection also in comparison to the b-HTx levels.

1086-175 Reappraisal of the Practice of Performing Surveillance Endomyocardial Biopsies After Heart Transplantation: Decreased Utility for Clinical Decision Making Over Time

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Endomyocardial biopsies (EMBs) in heart transplant recipients are routinely performed in an attempt to detect subclinical episodes of rejection. Because episodes of rejection occur more frequently early after transplantation and then decrease with time, it is unclear whether performing surveillance EMBs > 1 year post transplantation alters therapy. To investigate the effect of surveillance EMBs on changes in immunosuppression therapy, we reviewed the results of 1949 EMBs performed in 134 consecutive heart transplant patients between 1989–1996. We performed 1357 EMBs < 1 year post transplant and 592 in all subsequent years. Histological scores of rejection that resulted in changes in therapy occurred in 210 of 1357 (15.5%) EMBs performed < 1 year, whereas only in 16 of 592 EMBs (2.7%) performed > 1 year, $p < 0.001$. Furthermore, in the group of EMBs performed > 1 year, clinically driven EMBs resulted in higher diagnostic yield and consequently more changes in therapy compared to EMBs obtained for surveillance (8/146 vs 8/446 respectively, $p < 0.001$). We conclude that surveillance EMBs performed < 1 year but not thereafter result in frequent recognition of rejection episodes and consequently changes in immunosuppressive therapy. Our data demonstrate that the utility of obtaining surveillance EMBs for clinical decision making decreases over time and suggest that > 1 year post transplant only clinically driven EMBs should be performed.

1086-176 Identification of Patients not Requiring Endomyocardial Biopsies Late after Cardiac Transplantation

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The risk for cardiac allograft rejection is highest early after transplantation (tx) but graft rejection requiring intensified immunosuppression (Rej) may occur late after tx. Yet, many patients (pts) are absolutely free of Rej. Therefore, we tried to identify pts late after tx who may not need further surveillance endomyocardial biopsies (EMB). In 112 pts (age 45 ± 12 years) with a follow-up of ≥ 3 years, a total of 4194 EMB were performed. Of these, 1364 were performed after the 2nd post-tx year. EMB were divided into 3 groups according to the severity of graft rejection: Rejection score (Rs) = 0: ISHT 0 or 1A or Texas 0–2; Rs = 1: ISHT 1B or 2 or Texas 3–4; Rs = 2: ISHT ≥ 3A or Texas ≥ 5. When considering all EMB ≥ 2 years after tx, sum of Rs (OR = 1.05 per score point), mean cyclosporine level in the first 2 years (cyclo; OR = 1.05 per percent of upper therapeutic range), age (OR = 0.96 per year), time after tx (OR = 0.75 per year), cyclosporine level below therapeutic range (OR = 1.75), and reduction of prednisone (OR = 1.97) were independent predictors of Rej (all $p < 0.05$). 31 of 112 (28%) pts had at least one further Rej (mean 1.7) after the 2nd post-tx year. Independent predictors identifying pts with Rej were the sum of Rs (OR = 1.07), cycle (OR = 1.07), as well as recipient age (OR = 0.96; all $p < 0.05$). Rs ≤ 17, age ≥ 25 years, and cyclo ≤ 90th percentile identified 52% of pts who would not have needed EMB after the 2nd post-tx year whereas the other 48% had a risk of 54% to develop further Rej. *Conclusion:* Risk of Rej remains considerably high in some pts even late after tx justifying further EMB. However Rs, cyclo after tx, and age accurately identify 52% pts in whom EMB are no longer necessary as long as immunosuppressive therapy remains unchanged.

1086-177 Accuracy of Serum Troponin T For Predicting Acute Cellular Rejection in Orthotopic Heart Transplant Recipients

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Allograft rejection is a leading cause of morbidity and mortality following orthotopic heart transplantion. Right ventricular endomyocardial biopsy is the gold standard for diagnosis of acute cellular rejection. Noninvasive testing and serum markers have been of limited utility in predicting rejection. The presence of Troponin-T in the serum is an accurate marker of myocyte damage in patients with ischemic syndromes, but has unknown clinical utility for detecting rejection. This study sought to determine the accuracy of Troponin-T to predict high-grade biopsy proven cellular rejection in transplant recipients. 65 consecutive patients underwent 127 biopsies 1 week to 8 years after transplant. Blood was obtained from the sheath prior to the biopsy. A monoclonal antibody assay was used for measuring serum cardiac Troponin-T levels. Values ≥ 0.1 ng/mL were considered abnormal. Standard ISHLT histologic criteria were used to grade the biopsy samples. Rejection episodes were defined as: low-grade (≤ grade 2); high-grade (≥ 3A).

	All Patients (n = 127 biopsies)	> 6 Months post transplant (n = 85 biopsies)
Sensitivity	50%	50%
Specificity	80%	86%
Positive predictive value	32%	27%
Negative predictive value	90%	94%

Despite a low sensitivity, serum Troponin-T values < 0.1 ng/dL provide an accurate non-invasive marker for identifying patients without high-grade rejection.

1086-178 Pharmacokinetic, Blood Pressure, and Renal Effects of Cyclosporine Sandimmune Vs Neoral Formulation in Heart Transplant Recipients

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Sandimmune Neoral (C-Neo) is a new formulation of cyclosporine A (cyclo)