(I-IV). Progression was defined as an increase of focal stenosis ≥30% or detection of a new coronary lesion after a mean observation period of 2.8±1.0 years. A multivariate analysis (backward logistic regression) was performed including potential risk factors for CAVD (see below). Patients on dialysis were excluded.

Results: Initially plasma homocysteine levels were elevated in the entire cohort (mean 19.3±8.3 μmol/L) and ranged from 6.6 to 56.4 μmol/L. A total number of 106 patients (57,9%) presented with CAVD at first angiography and progression was detected in 51 transplant recipients (28%). Patients with progressive CAVD presented with significantly higher plasma homocysteine levels (21.7±6.3 μmol/L) at baseline investigation as compared to those with a stable course (17.4±7.7μmol/L) ($p< 0.001$). These results were independent of parameters like gender, age, time after transplantation, dyslipoproteinemia, cyclosporine blood levels, initial indication for transplantation and severity of CAVD at baseline examination.

Conclusions: Progress of cardiac allograft vasculopathy is strongly associated with elevated plasma homocysteine levels. The intervals of routine surveillance angiography should be shortened in patients with hyperhomocysteinemia and medical treatment to lower elevated homocysteine is recommended in these patients.

4

EFFECT OF FOLATE ADMINISTRATION ON HEART ALLOGRAFT ATHEROSCLEROSIS ONE YEAR AFTER TRANSPLANT: A PROSPECTIVE RANDOMIZED STUDY

L. Potena,[1] G. Magnani,[1] S. Sorbello,[1] F. Grigioni,[1] S. Sassi,[2] P. Ortolani,[1] F. Coccolo,[1] S. Carigi,[1] A. Marzocchi,[1] C. Magelli,[1] A. Branzi,[1] [1]Institute of Cardiology, University of Bologna, Bologna, Italy; [2]Institute of Angiology, Universty of Bologna, Bologna, Italy

Introduction. Graft atherosclerosis (TxCAD) is a major determinant of mortality in heart transplant (HT) recipients. High homocysteine (tHcy) levels are a possible risk factor for TxCAD. Folate administration decrease tHcy even in HT recipients, but it is unknown whether folate administration may delay or prevent TxCAD. The aim of this prospective randomized trial is to examine the effect of 5-n-methil-tetra-hydrofolate (MTF) administration on TxCAD.

Methods. 32 recipients (75% males, aged 52±12, 35% with ischemic cardiomyopathy) who underwent HT between August 1998 and June 2000 were randomized to receive MTF 15mg. Serum levels of tHcy were determined before HT and 6 and 12 months after HT. Intravascular ultrasound of proximal 30 mm of left anterior descending was performed after one and 12 months from HT.

Results. 16 patients received MTF and 16 did not ($P>0.1$ for all baseline characteristics). Mean plasma tHcy increased after HT only in non-MTF patients, while it decreased in those assuming MTF ($P=0.002$). Mean coronary intimal area increased in patients assuming MTF (+98%;$P<0.01$) and in those not assuming MTF (+102%; $P<0.01$). Among all the study variables, only high LDL levels were associated to the rate of increase in intimal area ($R=0.365$, $P=0.037$). However, the association between LDL and increase in coronary intimal area was stronger in non- MTF recipients ($R=0.56$, $P=0.02$) than in MTF ones ($R=0.1$, $P=0.74$)

Conclusions. The results of this prospective randomized trial show that although MTF significantly decreased tHcy after HT, it does not prevent coronary intimal growth. Although high LDL levels seem to be a major determinant of coronary intimal hyperplasia , our data suggest that MTF may reduce the negative impact of LDL on TxCAD.

5

IMPROVED SURVIVAL AFTER DIAGNOSIS OF CARDIAC ALLOGRAFT VASCULOPATHY (CAV) THROUGH EXTREME REDUCTION OF CHOLESTEROL AND FIBRINOGEN

B.R. Jaeger,[1] P. Braun,[2] D. Nagel,[1] L. Bennett Edwards,[3] M. Oberhoffer,[4] J.W. Park,[5] M.C. Deng,[6] D.B. Gysan,[7] E. Kreuzer,[4] S. Schueler,[8] B. Reichart,[4] D. Seidel,[1] [1]Institute of Clinical Chemistry, Ludwig-Maximilians-University, Munich, Germany; [2]Cardiology, Ev.Kaiser-Wilhelm-KHK, Duisburg, Germany; [3]ISHLT Registry/MCSD Database, ISHLT, Richmond/New York, VA/NY; [4]Abteilung f. Herzchirurgie, Ludwig-Maximilians-University, Munich, Germany; [5]Cardiology, Klinikum Hoyerswerda, Hoyerswerda, Germany; [6]Kardiologie, Roelshover Hof, Koeln, Germany; [7]Cardiac Surgery, Freeman Hospital, Newcastle upon Tyne, United Kingdom

Purpose: we wanted to know whether heart transplant patients with cav benefit from extreme reduction of ldl-cholesterol, crp and fibrinogen by means of heparin-mediated extracorporeal ldl/fibrinogen precipitation (h.e.l.p.) apheresis combined with statins. end points were all cause and specific mortality and adverse events.

Procedures: we analyzed data of all centers (n=11) who had treated patients after diagnosis of cav as described. actuarial survival was calculated by the life table method and compared with data of the ishlt registry. follow-up comprised 1983- 6/2002.

Results: 28 patients enrolled had a severe atherogenic risk profile (4.8 risk factors/pat.) including elevated baseline plasma ldl-cholesterol:185 ±mg/dl, fibrinogen: 4.1±0.9 g/l, and lipoprotein (a) levels: 38 ±45 mg/dl. transplantations were performed 1983-1997. cav was diagnosed angiographically 4 ± 3 y. after transplantation. h.e.l.p. apheresis was done every 11 days, statin medication continued in the highest tolerable dose. the mean observation time was 10.1±3.4 years after transplantation. during this period 5 out of 28 patients died (17.8 %): 1 pat. due to cav, 4 due to non-cav reasons (n=2 cancer, n=1urgency gallbladder operation, n=1 tricuspidal replacement).

The calculated 10-year actuarial survival is 96 %, the general expectancy is merely 46 %. the apheresis did not impede immunosuppression, lowered cholesterol, crp, and fibrinogen by 60 %, and was well tolerated, statins were withdrawn in 3 patients for myalgia.

ConclusioN: After diagnosis of CAV, intensification of treatment by extreme reduction of cholesterol, fibrinogen, CRP through regular application of H.E.L.P. apheresis and statins is capable of improving the outcome: 10 y. after transplantation, 82.2% CAV patients are still alive.

6

PARAOXONASE-1 M55L SINGLE NUCLEOTIDE POLYMORPHISM: A NEW MUTATION ASSOCIATED WITH TRANSPLANT CORONARY ARTERY DISEASE?

S.G. Miriuka, P.C. Chan, E. Keren, B. Wong, D.H. Delgado, D.E. Cole, H.J. Ross, Heart Transplant, Toronto General Hospital - University of Toronto, Toronto, ON, Canada

Objectives: A cohort of cardiac transplant recipients (CTRs) and healthy controls were genotyped to test the hypothesis that single nucleotide polymorphisms (SNPs) in Paraoxonase-1 and -2 (PON1 and PON2) may be significant predictors of transplant coronary artery disease (TxCAD).

Methods: PON1 M55L and Q192R and PON2 A148G and S311C SNP analysis was done by endonuclease digestion after multiplex PCR. TxCAD was screened with routine annual coronary angiography. Plasma total homocysteine levels (tHcy) were measured by HPLC.