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INFLUENCE OF DONOR TRANSMITTED ATHEROSCLEROSIS ON THE DEVELOPMENT OF CARDIAC ALLOGRAFT VASCULOPATHY

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Background: Following orthotopic heart transplantation (OHT), coronary artery disease is a combination of donor transmitted atherosclerosis (donor lesions) and new lesions that develop to produce cardiac allograft vasculopathy (CAV). This study evaluated the influence of pre-existing donor lesions on the development of CAV.
Methods: IVUS imaging was performed in 301 recipients at 1.3±0.6 months and again at 12.2±0.8 months after OHT. 1103 segments were matched from 333 coronary arteries between studies 1 year apart. In each segment, maximum intimal thickness (MIT), lumen area (LA), external elastic membrane area (EEM area) and intimal area (IA) were measured. Segments with MIT >= 0.5mm at baseline were defined as donor lesions (DL). New lesions (NL) were defined as lesions withμMIT >= 0.5mm at 1 year and baseline MIT <0.5mm.

Comparison of Parameters in Segments With and Without DL at 1 Year

	Donor lesions (n = 196 segments)	No donor lesions (n = 907 segments)	p Value
ΔMIT(mm)	0.06 ± 0.3**	0.1 ± 0.2*	0.03
ΔIA(mm2)	0.5 ± 2.1*	0.8 ± 1.5*	0.1
ΔLA(mm2)	−0.9 ± 3.0*	−0.7 ± 2.7*	0.5
ΔEEM Area (%)	−0.9 ± 14.7	1.9 ± 17.9	0.04

*p < 0.0001; **p < 0.01, compare baseline with 1 year.

Results: The mean donor age was 29.6±12.7 years. 197 segments from 89 (30%) hearts had DL. The mean increase in MIT at DL was 55% less than in segments without DL (Table 1). At 1 year, 16% of hearts with DL exhibited progression of DL (μMIT >= 0.5mm), 6% had a decrease >= 0.5mm in MIT and 8% developed NL. The incidence of NL was similar in the arteries with and without DL (9.4% vs 12.2%, p=0.5). In the arteries with DL, the development of NL was similar in those arteries with and without progression of DL (14.3% vs 8.5%, p=0.6).
Conclusion: At 1 year after OHT, DL do not act as a nidus for further intimal growth. The presence of a DL does not accelerate the development of NL elsewhere in the same artery. DL may impede compensatory positive remodeling as intimal thickening progresses.

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Conclusion: At 1 year after OHT, DL do not act as a nidus for further intimal growth. The presence of a DL does not accelerate the development of NL elsewhere in the same artery. DL may impede compensatory positive remodeling as intimal thickening progresses.

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THE RISK OF CARDIAC DEATH IN HEART TRANSPLANT RECIPIENTS WITH AND WITHOUT ANGIOGRAPHICALLY DETECTED CORONARY VASCULOPATHY

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Due to the diffuse nature of coronary allograft vasculopathy (CAV) surveillance angiograms often underestimate the severity of coronary lesions in heart transplant (HT) recipients. We sought to investigate the risk of cardiac death in HT recipients with and without angiographically detected CAV.
Methods: The results of annual angiograms performed in 26,706 HT recipients between 1990 and 2004 in United States were obtained from the Scientific Registry of Transplant Recipients. Competitive hazards model was used to estimate the relative risk of death due to cardiac versus non-cardiac causes.
Results: Cardiovascular complications were the most common causes of mortality after HT, accounting for 25% of deaths. The evidence of CAV at the first annual angiogram increased risk of both cardiac and non-cardiac death (RR=2.9 vs. 2.1, p<0.001). Despite the correlation between CAV and cardiac death, 38% of patients who died of cardiovascular complications, had repetitively negative angiograms. In HT recipients who either did not have angiograms performed or had no apparent angiographic progression to CAV, left ventricular (LV) ejection fraction <35% defined the group at highest risk of cardiac death. LV dysfunction was associated with the presence of CAV and portended 3.6-fold higher risk of cardiac death, p<0.001. Other risk factors equally contributed to cardiac and non-cardiac mortality, including: retransplantation, recipient African American ethnicity, non-ischemic cardiomyopathy, HLA-DR mismatch, peak PRA>10%, ischemic time>4h, donor age>40 years, donor cerebrovascular cause of death, late rejection and posttransplant renal failure.
Conclusions: The assessment of myocardial function may be a useful tool complementing coronary angiography in prognostic evaluation of patients at high risk of cardiac death. Routine use of more sensitive indicators of CAV, including intravascular ultrasound, may allow better understanding of mechanisms of cardiac death after HT.

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BLOOD GLUTATHIONE AS A MARKER OF CARDIAC ALLOGRAFT VASCULOPATHY IN HEART TRANSPLANT RECIPIENTS

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Background: Cardiac allograft vasculopathy (CAV) limits survival after heart transplantation (HTx). Between immunologic and non immunologic factors, reactive oxygen species generation has been proposed as pathogenetic mechanism. This study was aimed at evaluating redox status in HTx recipients and verifying whether it could be independently associated with CAV.
Methods: Fifty-five consecutive male HTx recipients, median [interquartile range] age 60 [50, 64] years, underwent angiography 67 [21, 97] months after HTx to assess CAV, defined as significant stenosis in >1 epicardial vessel or any distal vessel attenuation. All patients underwent blood sampling 89 [67, 119] months after HTx for biochemical (glucose, creatinine, total and LDL cholesterol, and cyclosporine levels) and redox evaluation [plasma reduced and total homocysteine, cysteine, cysteinylglycine, glutathione, blood reduced glutathione (GSH_{bl}) and vitamin E]. Univariate Odds Ratios (OR) with 95% confidence interval (CI) were estimated on the basis of a logistic regression analysis between clinical, conventional biochemical and redox data. Only the significant variables at univariate entered into multivariate analysis.
Results: CAV was documented in 15 (27%) patients. Univariate analysis showed that time from HTx to angiography (OR 3.97, 95% CI 1.15–14, p=0.03) and GSH_{bl} (OR 0.31, 95% CI 0.14–0.70, p=0.005) were significantly associated with CAV. However, multivariate analysis revealed GSH_{bl} as the only independent predictor of CAV (OR 0.31, 95% CI 0.13–0.74, p=0.008).
Conclusions: In HTx recipients reduced levels of GSH_{bl} are independently associated with CAV. Given its potent intracellular scavenger properties, GSH_{bl} may serve as a marker of antioxidant defence consumption, favouring CAV development.

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HIGH REJECTION SCORE IS ASSOCIATED WITH LOWER CORONARY FLOW RESERVE IN HEART TRANSPLANTATION RECIPIENTS WITH NORMAL CORONARY ANGIOGRAPHY

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To assess correlates of coronary flow reserve (CFR) in heart transplantation (HT) patients (pts) with normal coronary arteries, we studied 36 consecutive pts, 24 male, aged 50±13 years (yrs) at HT, follow up (f-u) 6.3±4.5 yrs. Rejection scores (RS) on endomyocardial biopsy were calculated (ISHLT grades: 0=0; 1A=1; 1B=2; 2=3; 3A=4; 3B=5; 4=6) in the first year (yr) and during whole f-u. RS including only severe grades (≥3A) (sevRS) were also calculated. Coronary blood flow velocity in the left anterior coronary descending artery was noninvasively detected by contrast-enhanced transthoracic echocardiography at rest and during intravenous infusion of adenosine (0.14 mg/kg/min). CFR was obtained as the ratio of hyperaemic diastolic peak velocity (DPV) to resting DPV. All pts had normal coronary angiography, left ventricular systolic function and mass. 7 pts (19%) had a CFR< 2.9 (group A) and 29 (81%) ≥ 2.9 (group B). Systolic and diastolic blood pressure, heart rate and blood haemoglobin were similar in the two groups. Group A had a higher number of treated rejections in the first yr (4.5±2.6 vs 2.3±2, p=0.01) and in whole f-u (5.1±3