EVEROLIMUS PREVENTS MICROVASCULAR DAMAGE IN HEART TRANSPLANT PATIENTS: EVIDENCE FROM MONITORING ENDOMYOCARDIAL BIOPSIES

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Objective: Everolimus, an m-TOR inhibitor, has been shown to prevent IVUS based diagnosed epicardial allograft vasculopathy in cardiac transplant. Aim of our study was to evaluate the effect of everolimus on microvascular remodelling in monitoring endomyocardial biopsies (EMB).

Methods: Two groups of patients were compared: Group A, 8 pts treated with cyclosporine, everolimus and steroids; Group B, 8 pts treated with cyclosporine, azathyaprine or mycophenolate and steroids. At 1st year EMB, External or outer area, excluding adventitia, internal, or lumen area and wall thickness area (external area-lumen area) were measured in all small intramyocardial coronary arteries (SIMCA) from each EMB by quantitative morphometry, using a computer-integrated digital microscope system (Image-Pro Plus, Silver Spring, MD). Diameters of each parameter were then obtained by mathematical formula. According to the size of the outer diameter SIMCA were identified as microvascular arteries (<300 μm in diameter). Total Rejection Score (TRS) and Total Severe Rejection Score (TSRS) (according to a modification of ISHLT grading system) were calculated for all patients.

Results: Age at heart transplant was not different between everolimus treated pts and standard immunosuppresed pts (52±12 yrs vs 56±9 yrs, p=0.4 respectively). No differences between the two groups in terms of pre-transplant diagnosis, gender and TRS (0.8±0.5 vs 1.2±0.6 p=0.2) and STRS (0.6±0.6 vs 0.7±0.5 p=0.7) were present as well.
Quantitative morphometry showed microvascular remodeling as follows:

	EVEROLIMUS (n=8)	No EVEROLIMUS (n=8)	P
External diameter (μm)	35.4 ± 13.9	73.4 ± 47.1	0.05
Lumen diameter (μm)	17.8 ± 7.3	37.6 ± 29.5	0.1
Wall thickness (μm)	8.8 ± 3.6	17.9 ± 9.3	0.02

At linear regression analysis everolimus was a determinant of wall thickness also when adjusted for TRS or STRS (β =-0.533, p=0.04; β=-0.564, p=0.02 respectively).

Conclusions: Everolimus prevents microvascular damage in heart transplant allograft as assessed at EMB. Our results suggest that assessment of microvascular remodelling on EMB could be helpful in the clinical setting to evaluate graft outcome.