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Fibrosis and apoptosis in different aetiologies of cardiomyopathy and their role in response to cardiac resynchronisation therapy

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Topic(s):
Cardiac Resynchronization Therapy

Citation:
Background:
We investigated the differences of preoperative serum apoptosis markers and histopathological ventricular remodelling between patients with ischaemic cardiomyopathy (ICM) and patients with dilative cardiomyopathy (DCM) who receive cardiac resynchronization therapy (CRT-D). In addition, we examined the prediction of 6-month response to CRT depending on aetiology of CM and preoperative histopathological remodelling.

Methods:
A total of 57 patients with severe heart failure (HF) undergoing CRT-D implantation were enrolled. Serum concentrations of PIIINP (N-terminal pro-peptide of collagen type III) and Fas-L (apoptosis-stimulating fragment ligand) were measured preoperatively at baseline (BL). Right ventricular tissue was obtained at five different areas before procedure. Degree of atrial fibrosis was measured histologically by microscopically quantification using ImageJ software after Elastica-van-Gieson staining and ventricular apoptosis was assessed via TUNEL assay. Transthoracic Echocardiography was performed at BL and 6-months follow-up (6MFU) and response was defined as improvement of left-ventricular end systolic volume (LVESV) higher or equal than 15% after six months.

Results:
ICM was underlying disease in 26 patients and DCM in 32 patients. The average degree of fibrosis at BL was 13,7% ± 5,1% and the average ventricular apoptosis was 26,8% ± 10,5%. Baseline PIIINP was 39,5 ± 24,7 ng/ml and baseline Fas-L was 84,3 ± 33,7 pg/ml. Patients with ICM had a significant higher degree of fibrosis (16,5 ± 6,5 % vs. 11,4 ± 4,3 %; p<0,01) and significant higher ventricular apoptosis (31,8 ± 8,8 vs. 22,8 ± 10,01%; p>0,01) compared to patients with DCM. For concentration of serum apoptosis markers PIIINP and Fas-L there was no significant difference.

Response rate was 59,6% at 6MFU. There was no significant difference between patients with ICM or DCM and response rate (p=0,620). For responders and non-responders there was also no significant difference between pre-implant histopathological measured fibrosis (p=0,349), apoptosis (0,193), PIIINP (0,631) and Fas-L (p=0,263). None was identified as an independent predictor of response.

Conclusion:
Patients with ischaemic cardiomyopathy have a significant higher degree of fibrosis and apoptosis at time of implant but neither aetiology nor degree of remodelling is predictive of response to CRT in this cohort.
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