



ORAL ABSTRACT SESSION: NOVEL NON-INVASIVE RISK MARKER

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Predictors for arrhythmic and major adverse cardiovascular events in patients with hypertrophic cardiomyopathy

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Introduction: Late gadolinium enhancement cardiac magnetic resonance (LGE-CMR) is useful for in vivo assessment of myocardial fibrosis, perfusion defect, volumetric factors. However, the clinical implication of these parameters of LGE-CMR in hypertrophic cardiomyopathy (HCM) remains unclear.

Methods: Relation between LGE-CMR parameters and Major adverse events (MAEs) was evaluated in 310 consecutive patients with HCM (57.5 ± 13.4 years old, male: female =241:69). The extent of left ventricular (LV) LGE was scored. MAEs included sustained ventricular tachyarrhythmia (VTA), atrial fibrillation (AF), ischemic stroke, hospitalization for heart failure (HF) and cardiac death.

Results: During the 49 ± 45 month follow-up, MAEs were noted in 73 (23.5%) of 310 patients with HCM. Arrhythmic events were observed in 46 patients (14.8%); AF in 35 and defibrillator implantation due to sustained VTA in 11 patients, respectively. Twenty two patients (7.1%) developed ischemic stroke and 15 patients (4.8%) were hospitalized for HF treatment. Patients with supramedian LGE score were more frequently associated with MAEs (29% versus 19%, P=0.033) or with arrhythmic events (18% versus 12%, P=0.09). LGE extent (odds ratio 1.14, 95% CI 1.01 to 1.30, P=0.043) and hypertension (odds ratio 2.22, 95% CI 1.13 to 4.35, P=0.021) were independent predictors for MAEs in multivariate analysis adjusted by LV maximal thickness, LV dimensions, and LV ejection fraction. Hypertension was also independently associated with total arrhythmic events (P < 0.003).

Conclusions: LGE extent and hypertension were related with adverse clinical outcomes including arrhythmic events in patients with hypertrophic cardiomyopathy.

Association of plasma proinflammatory biomarkers and circulating endothelial progenitor cells to risk of cardiac arrhythmia among diabetes mellitus patients

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Background: Some epidemiological studies have been shown a positive association between biomarkers representing inflammation, such as C-reactive protein, osteoprotegerin, osteopontin, and cardiovascular morbidity and mortality. Circulating endothelial progenitor cells (EPCs) might have a pivotal role in the presence of atherosclerosis, chronically diseased vessels or following acute vascular injury. Mobilization of EPCs can be related with proinflammatory activity.

The aim: To evaluate the association of plasma proinflammatory biomarkers and EPCs to risk of cardiac arrhythmia among diabetes mellitus patients.

Methods: 72 subjects (92 male) aged 46-62 years with diabetes mellitus and 25 healthy volunteers were enrolled to the study. C-reactive protein, osteoprotegerin, osteopontin were measured by ELISA. Immunostaining and flow cytometric technique (FCT) were used for identification of cEPCs. Circulating EPCs are defined as CD34 / VEGFR2 positive cells in absent CD45 expression. 10,000 events were analyzed from each tube. Mononuclear cells were cultured for functional analysis (CFUs) after FCT. Multivariable logistic regression tested each biomarker and cEPCs in association with incident of both supraventricular and ventricular arrhythmia at a follow-up examination during 1 year.

Results: All biomarkers were associated with the outcome with adjustment for age, sex, and cohort. A three-fold increase in plasma osteoprotegerin (OPG) was a significant predictor of the incident of cardiac arrhythmia (odds ratio [OR] = 1.98, 95% confidence interval [CI] 1.34 - 3.02; p=0.004). Total CFU count and also circulating CD34+ CD45- VEGFR2+, and CD34+ CD45- Tei-2+ VEGFR2+ cells were significantly (All P < 0.01) lower in diabetes patients when compared with healthy volunteers. However, decrease of cEPCs count and elevation of plasma concentration of other proinflammatory biomarkers did not associated with cardiac arrhythmia during 1 year observation period. Both high OPG and low CD34+ CD45- Tei-2+ VEGFR2+ cells subset (OR = 3.16, 95% CI 2.20 - 5.40, p=0.002) conferred increased risk of the cardiac arrhythmia but did not remain statistically significant after adjustment for fatal cases as covariates in diabetes population.

Conclusions: Osteoprotegerin can be associate with incidents of the cardiac arrhythmia in diabetes patients. Two biomarkers high OPG and low CD34+ CD45- Tei-2+ VEGFR2+ might be an effective resource to predict of cardiac arrhythmias in subjects with type 2 diabetes mellitus.

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Magnetic field imaging fails to predict sudden cardiac death or ventricular tachyarrhythmias in ICD carriers

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Purpose: Magnetic field imaging (MFI) is a novel non-invasive method to evaluate cardiac electromagnetic activity. Early reports have demonstrated a positive predictive value of the electromagnetic QRS fragmentation index (eQFI) for the occurrence of ventricular arrhythmias and death. Aim of this study was to investigate, whether an elevated eQFI could predict the occurrence of death or ventricular arrhythmias in ICD carriers.

Methods: Between 12/2009 and 06/2012, 135 consecutive patients underwent an MFI investigation prior to receiving an ICD. The Apollo CXS MFI system developed by BMDSys, Magdeburg, Germany was used for data acquisition. An eQFI ≥ 1.2 was considered pathologic. Median follow-up time was 473 days (223-733). Study endpoints were death and ventricular arrhythmias requiring ICD intervention.

Results: Eighty patients (59%) had an elevated eQFI. Independent predictors of elevated eQFI were atrial fibrillation and QRS width over 110 msec. Clinical characteristics of patients with elevated and normal eQFI are shown in the table. The occurrence of ventricular arrhythmias requiring ICD therapy and/or death was 17.5% among patients with elevated vs 9.1% among patients with low eQFI (p=0.17). In a multivariate analysis with adjustment for 9 clinical parameters, elevated eQFI was not associated with an increased total mortality or occurrence of ventricular arrhythmias (HR 2.03, 95% CI 0.65-6.35).

Conclusion: Nearly two thirds of patients undergoing ICD implantation have an elevated eQFI. After a median follow up time of about 15 months, mortality and/or ventricular arrhythmias requiring ICD therapy were not significantly different between patients with low versus elevated eQFI. Further investigations with longer follow-up periods and larger cohorts are needed to determine the usefulness of MFI in risk stratification of patients in clinical practice.

	eQFI ≥ 1.2 n=80	eQFI < 1.2 n=55	p-Value
Age (years, median)	65 (55-73)	69 (53-73)	0.87
Female	82.5%	83.6%	0.86
Underlying heart disease			
Ischemic cardiomyopathy	50%	53%	0.76
Non ischemic cardiomyopathy	41%	42%	0.95
EF < 40%	76%	73%	0.64

Novel non invasive detection of arrhythmia substrate using supervised learning support vector machine

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Purpose: Myocardial scar burden, quantified by MRI, predicts ventricular arrhythmogenesis. MRI use is resource and cost limited whereas conventional 12 lead ECG is readily available. Manual assessment of ECG time domain features lacks specificity for scar. We hypothesise that frequency and phase domain ECG analysis could yield data indicative of myocardial scar burden, although considering multiple features simultaneously is beyond human calculation. A supervised learning method (support vector machine, SVM) was used to "train" a novel computerised algorithm capable of screening ECGs for the presence of myocardial scar, so allowing large data volumes to be processed.

Methods: 153 consecutive adult patients (age 63 ± 12, male 65%), attending for cardiac MRI with scar analysis for clinical reasons were recruited, and underwent digital ECG acquisition (500Hz, 18bit) at the time of scanning. Semi automated quantification of late gadolinium contrast enhancement was used to identify myocardial scar. The ECGs from those with no scar were used to construct a median template beat for each of the standard 12 leads. ECGs from 35 patients with scar and 35 with no scar were used to train the SVM by feature comparison with the median beat. The algorithm was then tested on the remaining 83 ECGs.

Results: 16 comparative parameters were included: cross correlation, covariance, magnitude and phase of wavelet coherence, mean value, median value, variance, standard deviation, inter-quartile range, skewness, kurtosis, mobility and complexity of the power spectrum, Hurst exponent slope, detrended fluctuation factor, and differential entropy. Clinical and ECG characteristics in those with scar (age 64 ± 11, LVEF 56 ± 17%, QRS width 115 ± 22ms) and no scar (age 61 ± 13, LVEF 60 ± 19, QRS width 110 ± 18ms) were similar (p value=NS). The test set consisted of ECGs from 72 patients with scar and 11 patients with no scar. SVM was able to classify the test ECGs with 80.6% sensitivity and 72.7% specificity.

Conclusion: Digital ECG analysis of frequency and phase signals, using a newly developed SVM, characterises features which classify myocardial scar. Our observations require confirmation in larger prospective studies. The sensitivity and specificity of this approach could make it valuable in population screening for more costly complex investigations such as MRI scanning.