# Electrophysiology, Arrhythmias

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**Beat-to-Beat Variations of Ejection Fraction in Atrial Fibrillation. A Model To Assess Its Preload-Dependency**

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Ejection fraction (EF) is routinely used to guide many forms of cardiac therapy. Although its preload dependency is known, correction methods are infrequently used. In view of the beat-to-beat changes of cycle length (CL), and consequently changes of left ventricular (LV) preload in patients with atrial fibrillation (AF), it was hypothesized that this arrhythmia could serve as an ideal model to study preload dependence of EF at a constant inotropic state. This might allow a more precise assessment of cardiac performance at different heart rates (HR) and load conditions. **Methods:** Forty patients (Pts) (52% males), with chronic AF and a variety of cardiovascular pathologies and minimal or no mitral regurgitation, referred for echocardiography (echo), were included in the study. With the Pts in relaxed expiratory apnea, 3 to 7 consecutive beats were recorded by M-Mode echo, selected because of better resolution. Measurements of LV end-diastolic (EDD) and end-systolic dimension (ESD) were made at the level of the edge of opened mitral valve leaflets in the long-axis view. End-diastolic (EDV) and end-systolic volumes (ESV) were calculated as $7*d^3 / (2.4+d)$, where d is the linear LV dimension, and ejection fraction (EF), as (EDV-ESV)/EDV*100). Correlation coefficients and regressions were calculated between changes of EF vs. EDV and vs. HR. Beat-to-beat plots of stroke volume (SV) vs. EDV (Starling regression) were made for every Pt. **Results:** 1. EF was strongly influenced by changes of EDV ($R = 0.88$, $P < 0.001$) and HR ($R = 0.73$ $P < 0.001$). 2. All patients showed a positive relationship between SV and EDV, following Starling's model (mean slope = 1.03 ± 0.19, $P < 0.001$). 3. ESV remained constant with CL from 400 to 2,600 ms in all Pts ($R^2 = 0.043$, P = NS) (Example, Fig. 1). **Conclusions:** 1. EF is strongly preload and HR-dependent. 2. ESV is preload and HR-independent. 3. Findings suggest that ESV is a better parameter to assess changes of cardiac function in patients with AF.

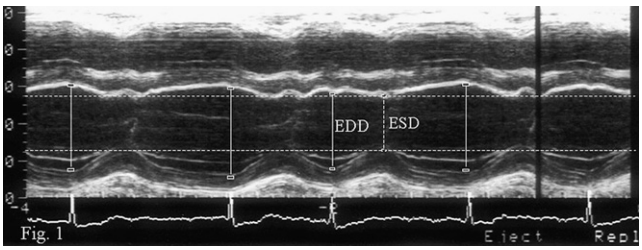

Fig. 1

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**KChIP2 Attenuates Cardiac Hypertrophy through Regulation of Ito**

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**Background:** Recent evidence shows that the auxiliary subunit KChIP2 represents a new potential regulator of Ito density. KChIP2 expression has been found to be significantly decreased in hypertrophy and heart failure. Our aim was to examine the role of KChIP2 in the regulation of hypertrophic pathways and induction of cardiac hypertrophy and failure. **Methods/results:** We studied cultured cardiomyocytes and rat hearts subjected to aortic banding (AB) infected with an adenovirus carrying either the KChIP2 gene (Ad.KChIP2) or the β-galactosidase gene (Ad.β-gal). KChIP2 overexpression in neonatal cardiomyocytes resulted in a significant increase in Kv4.2 and Kv4.3 proteins, suggesting that KChIP2 may facilitate the trafficking of these proteins to the cell surface. Echocardiography, performed 8−10 days post banding and viral infection, showed that banded hearts transduced with Ad.KChIP2 demonstrated significant decreases in interventricular septal (IVS) thicknesses (IVSd 0.26 ± 0.03 cm; IVSs 0.37 ± 0.05 cm, n = 10) as well as left ventricular posterior wall (LVPW) thicknesses (LVPWd 0.27 ± 0.02 cm; LVPWs 0.34 ± 0.03 cm, n = 10) compared to Ad.β-gal (IVSd 0.31 ± 0.03 cm; IVSs 0.44 ± 0.03 cm, n = 6; $P < 0.04$ and LVPWd 0.37 ± 0.01 cm; LVPWs 0.38 ± 0.04 cm, n = 6, respectively). Ito density was decreased in myocytes isolated from banded hearts infected with Ad.β-gal (10.9 ± 1.0 pA/pF n = 11) compared to myocytes derived from sham hearts (25.6 ± 0.40 pA/pF n = 14, $P < 0.05$ at +60 mV). Overexpression of KChIP2 significantly increased Ito densities (32.3 ± 0.9 pA/pF, n = 12) and remarkably shortened the APD at 90% (10.2 ± 2.4 ms, n = 10) compared to AB myocytes infected with Ad.β-gal (58.9 ± 4.2 ms, n = 20 $P < 0.05$). These data demonstrate that KChIP2 gene transfer can specifically shorten APD and increase the expression of Kv4.2/3-based Ito which mirrors the increase in Ito density. Mechanical properties of myocytes isolated from aortic banded hearts infected with Ad.β-gal were associated with increased peak calcium and cell shortening when compared with Sham. However, overexpression of KChIP2 attenuated the enhanced contractile function seen in Ad.β-gal hearts. These electrical and hypertrophic changes produced by KChIP2 were also paralleled by blockade of protein synthesis and MAP kinases activation following angiotensin II-induced hypertrophy response in cultured neonatal myocytes. **Conclusion:** Taken together, these data suggest that overexpression of KChIP2 can attenuate the development of cardiac hypertrophy possibly through restoration of Ito densities and modulation of MAPK pathway.

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**Acute Change in Dyssynchrony Indices before and after CRT in Heart Failure Patients with Narrow QRS from a Multi-Center Study: ESTEEM-CRT**

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**Introduction:** Recent findings suggest that echocardiographic indices of mechanical dyssynchrony (MD) may be difficult to collect and inconsistent among multiple centers. The aim of this report is to compare changes in dyssynchrony indices immediately after turning on and off CRT pacing. **Methods:** ESTEEM-CRT was a multicenter feasibility study that evaluated the effects of CRT in patients with a narrow QRS and MD. Enrollment criteria were: EF ≤ 35%, NYHA Class III, optimal drug therapy, QRS < 120ms, and MD as defined by the standard deviation of time to peak velocity of 12 segments (Ts-SD) > 28.7 ms. Centers underwent 2 days of Ts-SD training from a prominent expert. An echo core lab assessed patient exams. Acute changes between CRT off vs. on were recorded at baseline and after 6 months of pacing. Multiple previously published echo indices of MD were evaluated post-hoc. ''Improved'' and ''worsened'' were defined as any change in the calculated index. **Results:** Baseline: n = 61; NYHA Class III (100%); EF = 25 ± 7 %; QRS = 103 ± 10 ms; LVEDV = 172 ± 62 ml; LVESV = 115 ± 52 ml; QOL = 60 ± 22, and peak $VO_2$ = 14 ± 4 ml/kg/min. Overall, indices did not improve when CRT was turned on at baseline, nor worsen when CRT was turned off at 6-months. The table shows the % of patients that exhibited acute changes for each index. Across all indices, 51% improved with CRT on, and 47% worsened with CRT off. **Conclusions:** In the multi-center ESTEEM-CRT study, indices of MD failed to demonstrate acute changes between CRT on versus off. This may be due to a lack of correctable dyssynchrony to begin with, or substantial variability or noise in the calculation of the indices making them unreliable to assess dyssynchrony. Further study of echo indices for CRT is needed.

| | Acute changes for indices # 1−8 | | | Acute changes for indices # 9−16 | |
|---|---|---|---|---|---|
| | Baseline | +6 months | | Baseline | +6 months |
| Dyssynchrony indices | % improved with CRT on | % worsened with CRT off | Dyssynchrony indices | % improved with CRT on | % worsened with CRT off |
| SPWMD (PSAX) | 42% | 29% | Ts-maxdiff−12 | 53% | 52% |
| IVMD | 42% | 63% | Ts-maxdiff−8 | 68% | 52% |
| LVEMD | 30% | 33% | Ts-maxdiff−6 basal | 50% | 45% |
| LLW delay | 56% | 59% | Ts-maxdiff−6 midwall | 53% | 52% |
| DLC | 37% | 39% | Ts-maxdiff−4 | 59% | 45% |
| Ts-SD−12 | 56% | 47% | PVD | 53% | 48% |
| Ts-SD−8 | 62% | 47% | Sep-Lat Delay basal | 39% | 55% |
| Ts-SD−6 basal | 57% | 43% | Sep-Lat Delay midwall | 43% | 55% |

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**Recorded Heart Sounds for Identification of Ventricular Tachycardia**

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**Introduction:** The ECG discrimination of ventricular tachycardia (VT) vs. wide-complex supraventricular tachycardia (SVT) is often difficult, particularly in non-electrophysiology lab settings such as in the ER or out-patient clinics. **Hypothesis:** In this study, we tested the hypothesis that recorded digital cardiac acoustic data reflect hemodynamic changes that can be used for VT detection. **Methods:** We studied 57 subjects (42 males, mean age 57, range 24 to 83 years) who had undergone electrophysiological testing for known and suspected cardiac arrhythmias. Acoustic cardiography (Audicor®, Inovise Medical, Inc.) was performed during each subject's electrophysiological study. We evaluated the ability of S1 variability (S1 intensity standard deviation/S1 intensity mean) to discriminate between VT and SVT. **Results:** The 57 subjects had 17 episodes of VT and 70 episodes of supraventricular rhythm - including 22 episodes of SVT. VT had a higher S1 variability than supraventricular rhythm (0.45 ± 0.28 vs. 0.21 ±011, T = 5.46, $P < 0.0001$, see figure 1 below). The sensitivity of S1 variability for detecting VT was 50% at 100% specificity and 67% at 90% sensitivity.