A Dominant Role of the Generated Force in Modulating the Cardiac Action Potential in Rat Trabeculae

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Mechanical inhomogeneities can elicit arrhythmias by triggering after-depolarization or generating spatial electrical disparity. However, the cellular mechanisms remain elusive. The prevalent hypothesis relates the phenomenon to stretch-activated channels. An alternate hypothesis postulates that mechanical perturbations affect calcium dissociation from troponin, and the ensuing changes in the intracellular free calcium concentration ($[Ca^{2+}]_i$) alter the action potential duration (APD). These stretch- and calcium-mediated hypotheses were investigated in trabeculae (n=7) isolated from rat right ventricle, by separately controlling sarcomere length (SL) and $[Ca^{2+}]_i$. SL was controlled by a rapid servomotor. $[Ca^{2+}]_i$ was clamped by utilizing tetanic contractions at different extracellular calcium concentrations ($[Ca^{2+}]_0$s). Tetanus was achieved by 8 Hz stimulation in the presence of cyclopiazonic acid. APD was evaluated by the voltage-sensitive dye Di-4-ANEPPS. SL was measured by laser diffraction and force by strain gauge. Sarcomere lengthening from 1.85 to 2.2μm at constant $[Ca^{2+}]_0$ =3 mM decreased the APD_{90} from 90.7±4.1 to 62±1.5 msec. However, an increase in $[Ca^{2+}]_0$ from 1.5 to 4.5 mM, at the same SL (2 μm) decreased the APD_{90} from 84.6±3.8 to 69.2±1.6 msec. Interestingly, a consistent identical inverse relationship between APD_{90} and force was obtained, and identical APD_{90} was observed at similar force with different pairs of SL and $[Ca^{2+}]_0$. The APD_{90} decreased from 89.8±2.1 to 62±1.3 msec as the force increased from 6.5±0.9 to 100.1±10.6 mN/mm^2. These conspicuous observations are readily explained by calcium-dependent reverse excitation–contraction coupling, where the cross-bridges determine the affinity of troponin for calcium and calcium extrusion via the Na^+-Ca^{2+}-exchanger affects the APD.

Effect of the Second Lebanon War on the Incidence of Appropriate Implanted Cardioverter-Defibrillator Discharge Among Israeli Patients – Final Results

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Background: Previous data have suggested that emotional stress may trigger malignant ventricular arrhythmias and hence Implanted Cardioverter-Defibrillator (ICD) Activations (Rx.). However, no data exist about the influence of a war on ICD Rx. Therefore, we retrospectively analyzed ICD interrogations of our entire ICD patients (pts.) (No= 233) and compared between the incidence of appropriate (app.) ICD Rx. (Anti-Tachycardia Pacing and shocks) during the Second Lebanon war period and three control periods.

Results: Mean age was 65.8 (22-90 yrs); 202 (86.7 %) were males; 166 (71.2 %) had ischemic heart disease; mean LVEF was 31.3 % (15-70 %); the indication for the implantation was aborted sudden cardiac death or sustained ventricular arrhythmia (i.e. secondary prevention) in 104 pts. (44.6 %), and 211 pts. (90.6 %) were exposed to alarms and/or rockets falls. The incidence of ICD App. Rx. was not significantly different during the war in comparison to the control periods.

Incidence of App. ICD Rx.

Patients N (%)	War period 13/07-14/08/2006	Control periods 12/06-12/07/2006	Control periods 15/08-15/09/2006	Control periods 13/07-14/08/2005
Exposed 211	10 (4.7 %)	9 (4.3 %)	9 (4.3 %)	5 (2.4%)

Conclusions:

1. The exposure of our ICD pts. to a huge emotional stress, such as the second lebanon war, did not cause a significant increase in ventricular tachyarrhythmias and appropriate ICD activations compared to the control periods.
2. As our findings are in contrast to previous studies, we suggest that the prolonged exposure of the Israeli pts. to emotional stress, precondition them to adapt stress during the war.

Admission for Syncope: Evaluation, Cost and Prognosis, According to Etiology

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Background: Syncope is a common clinical problem which often remains undiagnosed despite extensive and expensive diagnostic evaluation.

Objectives: to assess the diagnostic evaluation, costs and prognosis of patients hospitalized for syncope in a tertiary referral center (TRC) according to discharge etiology (DE).

Methods: We retrospectively reviewed medical records of patients admitted for syncope in a TRC throughout 1999. Mortality data were obtained, a year post-discharge, for each patient. Evaluation costs were calculated based on prices from the Ministry of Health basket services in 2002.

Results: 376 patients qualified for this study. DE's distributed as following: Vasovagal-26.6%, cardiac-17.3%, neurological-4.3%, metabolic-0.5%, unexplained-47.3%, and other-4%.

Cardiac and neurological tests were used more often, with higher yield in patients with cardiac and neurological DE respectively.

Mean evaluation cost was 11,210+8,133 NIS, higher in ICCU than in Internal Medicine (IM) wards (19,210+11855 vs.10443+7314 NIS, p=0.0015). Mean in-hospital stay was 4.9+4.2 days, longer in ICCU than in IM wards (7.2+5.6 vs. 4.6+3.5 days, p=0.024).

Short term mortality- 30 days and long term mortality (LTM) - 1 year rates were 1.9% and 8.8% respectively, and differed according to DE. LTM rates were significantly higher in patients with Cardiac, Neurological and Unknown DE (not vasovagal), compared with age adjusted general population of Israel (LTM = 2.2%) and higher in patients with cardiac compared with non-cardiac DE (15.4% vs. 7.4%, p=0.04).

Higher mortality rates were associated with higher evaluation costs.

Conclusions: hospitalization in a TRC for syncope is associated with increased mortality for most etiologies (except vasovagal), cardiac>non-cardiac. Despite high costs of in-patient evaluation, associated with more diagnostic tests, longer in-hospital stay and higher mortality rates, nearly half of the patients were discharged undiagnosed. Out-patient evaluation should be considered when medically possible.

Left Ventricular Lead Placement and Impact on Outcome of Cardiac Resynchronization Therapy

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Background: The response to cardiac resynchronization therapy (CRT) has been shown to be related to the location of the left ventricular (LV) lead in the posterior and lateral areas of LV. However, information is scarce about the difference between the two.
Objectives: To compare the clinical outcome between LV lead placement in the lateral and posterior cardiac segments for CRT.
Methods: We studied 102 patients with advanced heart failure, LV ejection fraction ≤35% and QRS duration >120 ms who underwent CRT device implantation. Clinical and echocardiographic variables before and after 3-month follow-up were compared between patients with lateral LV lead (lateral group) and posterior LV lead location (posterior group).
Results: The lateral group included 80 patients (71% with ischemic etiology) and the posterior group 22 patients (81% with ischemic etiology). There were no significant differences in baseline clinical and echocardiograpic characteristics of patients between the two groups. In a pre-defined positive clinical response (including 3 clinical criteria) there was no significant difference between the posterior group compared with lateral group (73% vs. 60% response respectively, p=.274). There was an improvement in 6-min walk distance (mean±SE 63±25 vs. 17±11 meters, p=.027) in the posterior group compared with the lateral group. We found no significant differences in improvement in LVEF, LV volumes, or intraventricular systolic dissynchrony between groups.
Conclusions: This study shows no different outcomes between LV lead placement in the lateral and the posterior cardiac segments. The best location of LV lead for CRT may depend on other measures such as scar tissue localization.

Clinical and Echocardiographic Predictors of Response to Cardiac Resynchronization Therapy in Patients Upgraded from Conventional Pacemakers

Roy Beinart [1,2], Eyal Nof [1,2], Osnat Gurevitz [1,2], David Bar Lev [1,2], David Luria [1,2], Hava Granit [1], Sharona Bachar [1], Micha Feinberg [1,2], Rafael Kuperstein [1,2], Shemy Carasso [3], Michael Eldar [1,2], Michael Glikson [1,2]

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Background: Most randomized controlled trials of CRT did not include patients with previous pacemakers therefore selection criteria for CRT in this population are poorly defined. We sought to evaluate potential predictors for response to CRT in patients upgraded from conventional pacemakers.

Methods: 48 consecutive patients who underwent successful upgrading from conventional pacemaker to CRT, and had complete follow-up within the first year were included in the study. Response was defined by a score combined of NYHA class, MLHF quality-of-life score and 6-minute walk. Each component was classified as improved (+1), unchanged (0) or worsened (-1) and responders were defined as patients who had a combined score of ≥1. We compared the occurrence of various parameters among responders versus non-responders.

Results:

	Responders (n=29, 60%)	Non-responders (n=19, 40%)	P value
Age	68±12	71±11	0.4
Male (%)	79%	74%	0.7
Ischemic cardiomyopathy	69%	83%	0.2
NYHA I-II, III, IV	7%,76%,17%	11%,84%,5%	0.5
6-min walk, m	254±127	324±146	0.1
Quality-of-life	65±23	55±24	0.2
QRS mean ± SD	183±35	179±29	0.9
Chronic atrial fibrillation	17%	16%	0.6
LVESV (average), ml	139±67	149±78	0.7
LVEF (average), %	24±8	24±6	0.8
Septal to lateral delay (>60 msec)	59%	53%	0.5
Yu standard deviation(>32)	79%	63%	0.2
Interventricular delay(>40 msec)	72%	63%	0.4

Conclusion: A positive response to upgrading to CRT in patients with previous pacemakers was observed in 60%. None of the parameters tested here was a significant predictor of response. Further studies are needed to define predictors of success in this population

Clinical Spectrum of Dual Atrioventricular Nodal Physiology

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Introduction

Dual atrio-ventricular nodal physiology (DAVNP) is longitudinal dissociation of AV conduction. It is the anatomic substrate of reentrant circuit responsible for the initiation and perpetuation of AVN reentrant tachycardia (AVNRT), which is the most common clinical presentation of DAVNP. Other forms of DAVNP may present as single nodal echo beats, or in rare occasions 2 for 1 ventricular response.

In this presentation we will discuss other forms of atypical clinical presentations of DAVNP. These include: AV conduction delay due to spontaneous conduction of sinus beats over the slow pathway, 2:1 ventricular responses or non reentrant AVN tachycardia, and the drug modulation of conduction over the slow pathway (see table below)

Patients Data

Age	Gender	Past History	Symptoms	ECG findings
24	Female	None	Asymptomatic	Long PR interval
36	Female	None	Asymptomatic	Long PR interval
74	Female	CAD S/P PCI	Angina Palpitations	Long PR interval & AVNRT
64	Male	CAD	Angina Palpitations	Irregular wide and narrow QRS tachycardia
67	Male	IDCMP ICD	9 ICD Shocks	2:1 ventricular responses

Discussion

DAVNP may present in different clinical forms. Non reentrant AVN tachycardia due to 2:1 responses via DAVNP, is an uncommon but an important form of irregular tachycardia. It may present as incessant form associated with tachycardia induced cardiomyopathy. It is usually misdiagnosed as atrial fibrillation. Treatment with antiarrhythmic agents may perpetuate tachycardia and convert it from paroxysmal to incessant form. Patients with prolonged PR interval are asymptomatic, and electrocardiographic finding could be interpreted as AV conduction delay. Pharmacologic agents or autonomic maneuvers may help in making the diagnosis.

Radiofrequency ablation of slow pathway terminates tachycardia and may restore LV function.

Echocardiographic Predictors of Response to Cardiac Resynchronization Therapy

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Background: A significant number of patients currently selected for CRT by traditional clinical and electrocardiographic criteria do not respond to this therapy. We investigated the potential role of echocardiographic, Doppler and tissue Doppler imaging parameters as predictors of response to CRT.

Methods: 137 consecutive patients who were successfully implanted with CRT/CRTD system according to guidelines-based indications and had complete follow-up within the first year were included in the study. Response was defined by a score combined of NYHA class, MLHF quality-of-life score and 6-minute walk (6MW). Each component was classified as improved (+1), unchanged (0) or worsened (-1) and responders were defined as patients who had a combined score of ≥1. We compared the frequency of the various parameters among responders versus non-responders.

Results:

	Responders (n=78, 57%)	Non responders (n=59, 43%)	P value
LVEDV (average), ml	186±56	206±83	0.8
LVESV (average), ml	140±50	157±68	0.1
LVEF (average), %	23±7	23±6	0.9
RVFAC, %	37±12	40±11	0.2
LA area, ml	29±7	31±7	0.2
MR grade (1-4)	31%, 31%, 32%, 22%	45%, 30%, 19%, 6%	0.1
SPAP	45±13	44±13	0.8
Septal to lateral delay (>60 msec)	60%	59%	0.5
Yu standard deviation(>32)	85%	78%	0.2
Interventricular delay(>40 msec)	54%	56%	0.5

Conclusion: A positive response to CRT was observed in 57% of the patients. None of the measurements tested, including widely used parameters of mechanical dyssynchrony, was a significant predictor of response to CRT. Further studies are needed to define better predictors.

Clinical Predictors of Response to Cardiac Resynchronization Therapy

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Background: A significant number of patients currently selected for CRT by traditional clinical and electrocardiographic criteria do not respond to this therapy. We investigated the clinical predictors of response to CRT over the first year of follow up.

Methods: 137 consecutive patients who were successfully implanted with CRT/CRTD system for guideline-based indications and had complete follow-up within the first year were included in the study. Response was defined by a score combined of NYHA class, MLHF quality-of-life score and 6-minute walk (6MW). Each component was classified as improved (+1), unchanged (0) or worsened (-1) and responders were defined as patients who had a combined score of ≥1. We compared the frequency of the various predictors among responders vs. non-responders.

Results

	Responders (78, 57%)	Non responders (59, 43%)	P value
Age > 75	25 (32%)	27 (46%)	0.07
Male (%)	67 (83%)	46 (81%)	0.47
Ischemic Cardiomyopathy	57 (74%)	42 (74%)	0.56
NYHA I-II, III, IV	8%, 78%, 14%	17%, 78%. 5%	0.075
6MW	268±122	310±108	0.06
QOL	60±24	58±24	0.60
QRS mean ± SD	164±33	161±32	0.68
Chronic atrial fibrillation	5 (6%)	9 (15%)	0.08
Previous pacemaker implantation	37%	32%	0.34
RBBB	4 (7%)	5 (6%)	0.59

Conclusion: A positive response to CRT was observed in 57% of the patients, all of whom had been selected for CRT by usual criteria. Shorter 6MW distance, higher NYHA class and age < 75 were borderline predictors of response.

The Magnitude of Clinical and Echocardiographic Changes in Response to Cardiac Resynchronization Therapy

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Background: Criteria for significant response of various parameters to CRT vary widely in the literature. We investigated the magnitude of response of clinical and echocardiographic parameters to CRT in our population.

Methods: 137 patients who had been successfully implanted with CRT/CRTD system and had complete follow-up within the first year were included in the study. We recorded clinical and echocardiographic parameters at baseline and up to 12 months post implantation and determined the percentage of responders of each parameter by commonly used criteria.

Results:

	Baseline	Follow-up	P value	Responders (%)*
NYHA (I-II, III, IV)	12%, 78%, 10%	41%, 56%, 3%	**0.0001**	38
Quality-of-life	59±24	41±28	**0.0001**	42
6-min walk	287±117	310±119	**0.02**	34
LVESV ml	147±59	131±60	**0.002**	30
LVEF %	23±7	27±8	**0.0001**	40
RVFAC, %	38±11	37±11	0.85	26
SPAP mmHg	45±13	42±12	**0.006**	18
MR grade (1-4)	30%,25%,22%, 23%	56%,31%,13%, 0%	**0.02**	26
Septal to lateral delay	34±53 (82/137>60msec)	33±56 (66/137>60msec)	0.65	20
Yu standard deviation	38±15 (112/137>32)	37±16 (94/137>32)	0.13	16
Interventricular delay	40±29 (75/137>40msec)	22±20 (50/137>40msec)	**0.0001**	33

* Response: NYHA≥1 class; QOL≥9 point; 6MW≥10%; LVESV≥15%; LVEF/RVFAC≥5%; SPAP≥10 mmHg; MR grade≥1. For dyssynchrony parameters response was defined as change from dyssynchrony to non-dyssynchrony.

Conclusion: Most of the clinical and echocardiographic parameters significantly improved following CRT implantation. However, these improvements were modest and met the commonly used definitions of response in only a minority. No improvement was observed in right ventricular function or in classical measures of intraventricular dyssynchrony in response to CRT.