Prognostic Value of Programmed Electrical Stimulation Among Implantable Cardioverter-Defibrillator Recipients
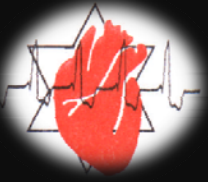## Real-World Data from the Israeli National ICD Registry

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On Behalf of the Israeli Working Group on Pacing and Electrophysiology
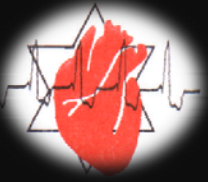
National ICD Registry

Disclosure

No Conflicts of Interest

Background

- Inducibility of ventricular arrhythmias with programmed electrical stimulation (PES) suggests an increased risk for sudden arrhythmic death
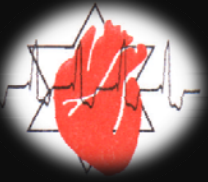
MADIT I, MUSTT, MADIT II, DEFINITE

Background

- While earlier trials used PES for risk stratification of SCD, mainly in patients with coronary artery disease, recent data from RCTs, support a benefit of ICDs in patients with reduced LVEF without performing PES
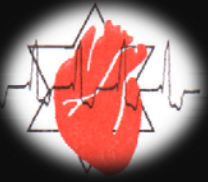
MADIT II, SCDHeFT

Purpose

- To evaluate the clinical characteristics and outcomes of patients enrolled in the Israeli National ICD Registry who underwent PES prior to device implantation
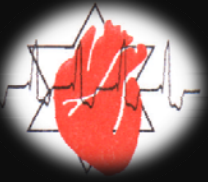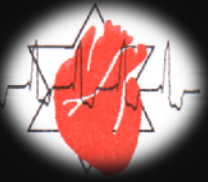
Study Population

- Non inducible patients who did not receive a device, were not included in the registry

- 1188 registry patients (age 66.2±10.9, 89% male) who underwent device implantation were prospectively followed for a median period of 323 days
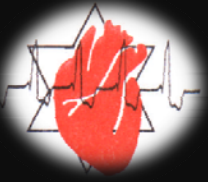
Programmed Electrical Stimulation

- No particular PES protocol was adopted

- Inducibility was reported by the implanting physician if monomorphic/polymorphic VT or VF was obtained at PES
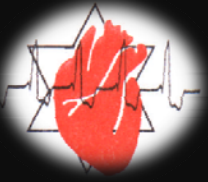
Outcomes

➢ First occurrence of appropriate ICD therapy for VT/VF and/or death

Arrhythmic Events

- Arrhythmic events were defined as ICD shocks or anti-tachycardia pacing for ventricular tachycardia or fibrillation (VT/VF)

Results

- Of 2971 patients undergoing ICD implantation, 504 (17%) patients had PES prior to ICD implantation

- 413/504 (82%) patients belong to the primary prevention group

- Among patients who underwent PES, 460 (91%) were inducible for VT/VF

Baseline Clinical Characteristics

	No PES n=2467	PES n=504	p value
Mean age ±SD (years)	63.8 ± 13.2	66.2 ±10.9	<0.01
Gender- Female	19%	11%	<0.01
CRTD	41%	29%	<0.01
Ischemic heart disease	71%	87%	<0.001
Prior MI	88%	89%	0.32
Prior CABG	41%	40%	0.62
Prior PCI	75%	75%	0.96
Atrial fibrillation	22%	16%	<0.01
LVEF≥30%	40%	65%	<0.01
Creatinine (mg/dl)	1.34±0.3	1.41±0.4	0.37
Hemoglobin (g/dl)	13	13	0.92
QRS (ms)	119±13	113±15	<0.01
LBBB	73%	74%	0.23
Hypertension	62%	61%	0.84
Diabetes mellitus	36%	36%	0.98
NYHA class ≥III	35%	23%	<0.01
Medications			
ACEI	74%	73%	0.68
Diuretics	72%	59%	<0.01
Beta Blockers	81%	82%	0.68
Antiarrhythmic drugs	19%	12%	<0.01
Aspirin	70%	72%	0.62
Clopidogrel	28%	23%	0.11
Oral anticoagulants	23%	13%	<0.01

Factors Independently Associated with the Performance of PES

Variable	Odds Ratio	95% Confidence Interval	P-value
Procedure year (per 1-year increment)	0.48	0.39 – 0.55	<0.001
Ischemic heart disease	2.98	2.00 – 4.46	<0.001
NYHA class ≥ III	0.71	0.54 – 0.93	0.02
LVEF < 30%	0.45	0.38 - 0.56	<0.001
Treatment with diuretics	0.65	0.49 - 0.87	<0.001
Age (per 1-year increment)	1.01	1.002 – 1.03	0.02
Sinus rhythm at the time of implant	1.63	1.03 – 2.58	<0.001

Clinical Outcomes by Performance of PES

- Among 1188 registry patients with available follow-up, the rate of appropriate ICD therapy for VT/VF was similar between patients with a positive PES (15%) and those who underwent device implantation on the basis of LVEF alone (76%)

Clinical Outcomes by Performance of PES

- The cumulative probability of VT/VF was 7% among patients with a positive PES prior to ICD implantation and 8% among patients in whom PES was not performed prior to device implantation, log-rank p-value=0.92

- Consistently, multivariate analysis showed similar VT/VF risk between the 2 groups (HR=0.95 [95%CI 0.71 – 1.28]; p=0.49) after adjustment for age, gender, type of prevention, NYHA, and LVEF
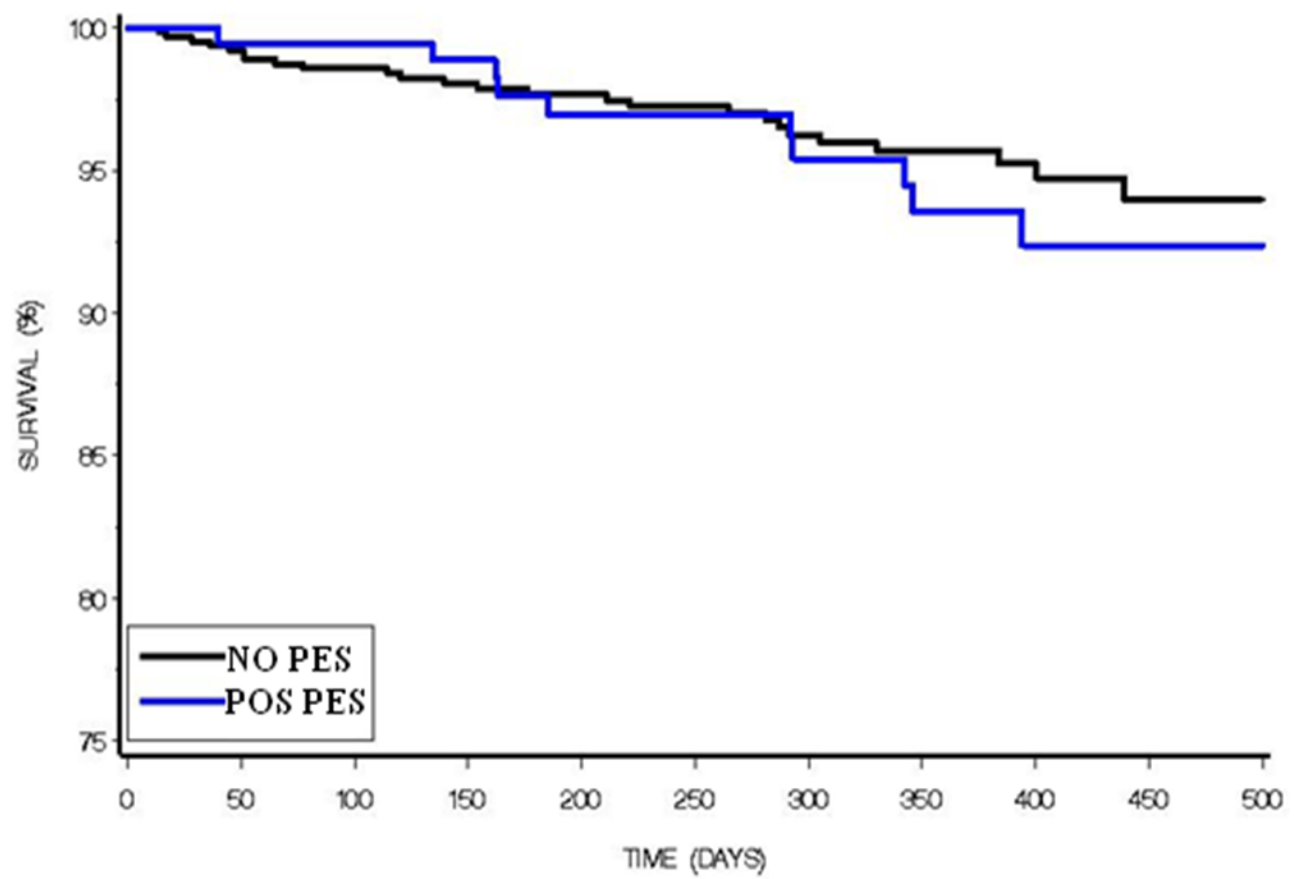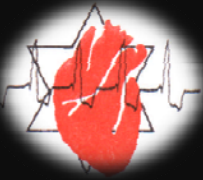
What About Primary Prevention?
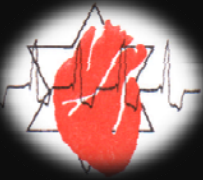
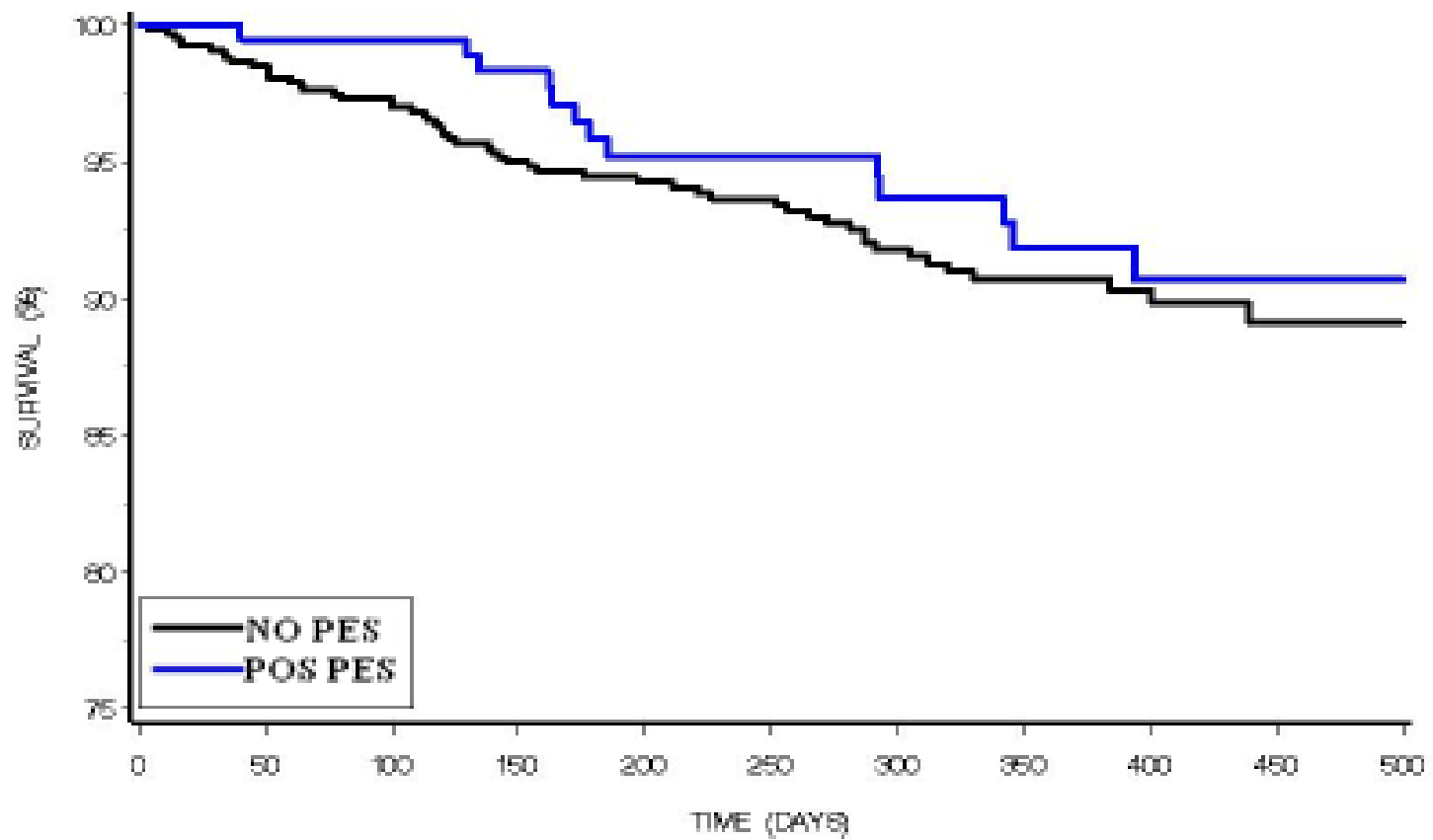Event Free Survival-First Appropriate Therapy (Primary Prevention)

P(log_rank)= 0.25

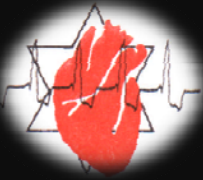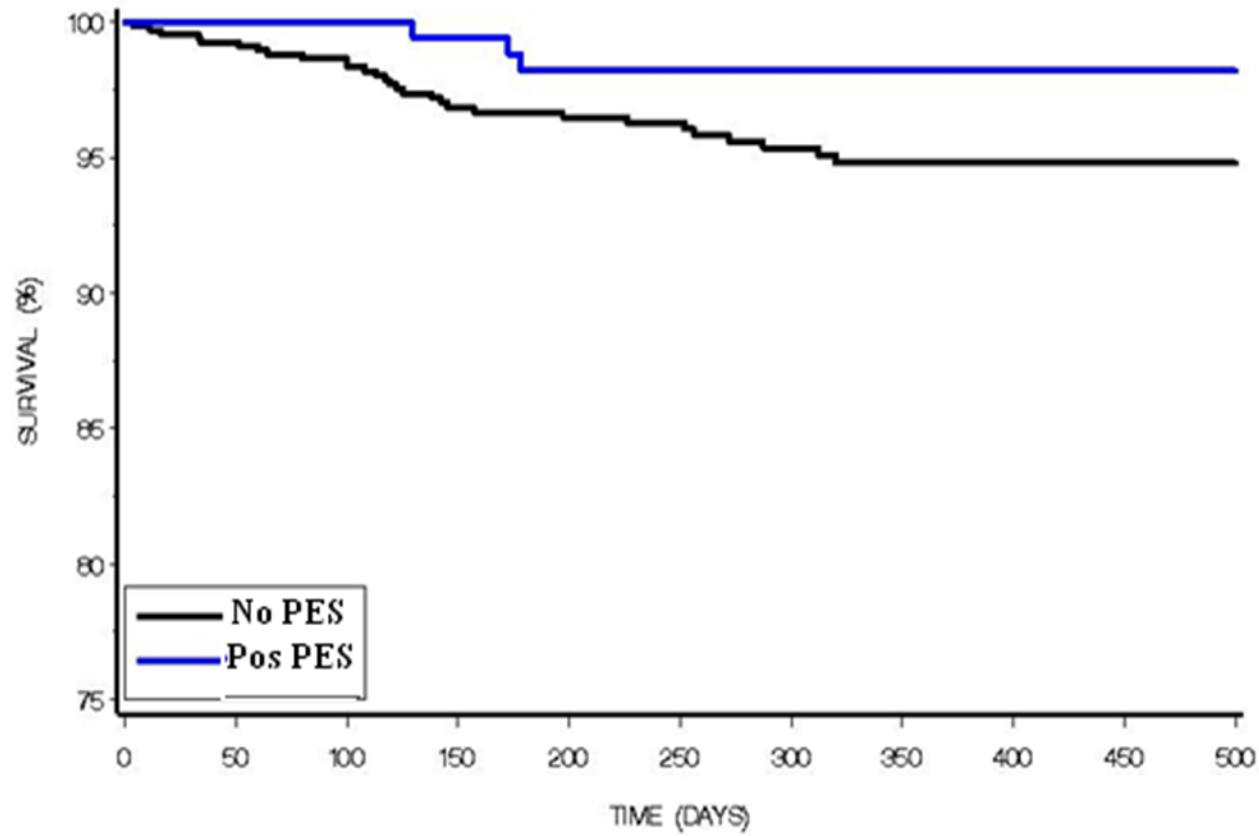VTVF OR DEATH (COMBINED) AMONG PRIMARY PREVENTION PATIENTS

P(log_rank) = 0.70

Legend:
- NO PES
- POS PES

Y-axis: SURVIVAL (%)
X-axis: TIME (DAYS)

Primary Prevention Group Mortality

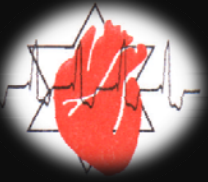P(log_rank)= 0.06

Legend:
- No PES
- Pos PES

Conclusions

Ventricular tachyarrhythmia inducibility at PES in this selected group of patients does not offer any additional information beyond that obtained through LVEF assessment and therefore has limited prognostic implications
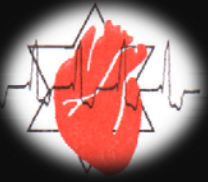
THANK YOU FOR YOUR ATTENTION

Conclusions

However, inducibility may still have a role in decision making regarding the type of device (single vs. dual chamber) and the specific programming of the ICD's detection and therapies zones according to PES findings
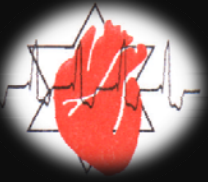
Limitations

- Relatively short follow-up period

- Inducibility has a low positive predictive value and a higher negative predictive value, and in fact, one of the study limitations is that the outcome of an indeterminate number of noninducible patients in whom a device was not implanted and as a consequence not included in the registry, remains unknown, thereby the net benefit of performing an EPS prior to implantation remains unascertained for this cohort and is beyond the scope of this analysis

- Appropriate ICD therapy is much more prevalent than arrhythmic and/or total mortality and therefore, appropriate ICD therapy cannot be used as a surrogate for a live saving episode
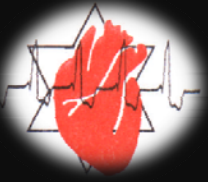
ICD Therapies

- Shocks or anti-tachycardia pacing was determined as appropriate or inappropriate by an experienced clinical electrophysiologist who reviewed the intra-cardiac electrograms

- Arrhythmic events were defined as ICD shocks or anti-tachycardia pacing for ventricular tachycardia or fibrillation (VT/VF)

- Detection and therapy programming was up to the physician's discretion

Why Lower Risk Patients?

- Need to proof pre-implantion inducibility in case of borderline clinical characteristics, as mandated by the main Israeli Health Care Provider (Clalit Health Services)
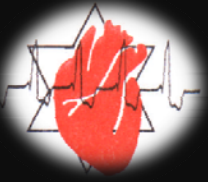
Good News

- No physicians' bias was noted as reflected by a similar arrhythmic event rate between inducible patients and patients implanted according to LVEF alone
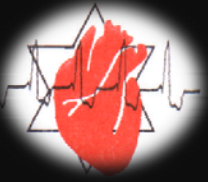
Baseline Clinical Characteristics

- Thus, a lower baseline NYHA class, a higher baseline left ventricular ejection fraction (LVEF), lack of atrial fibrillation, and lack of treatment with diuretics were all independently associated with the performance of PES among registry patients, suggesting that patients selected for this procedure had less advanced heart failure
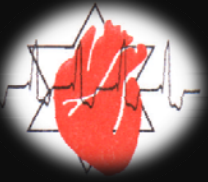
Statistical Analysis

- Baseline characteristics between registry patients who did or did not undergo PES prior to device implantation

I. Kruskal-Wallis and Mann-Whitney U tests for continuous variables

II. Chi-square test for categorical variables

Statistical Analysis

- The cumulative probabilities of the primary and secondary outcomes measures, by the performance of PES

➢ Kaplan- Meier method

➢ Log-rank test

- Independent clinical factors associated with the performance of PES

➢ Multivariate logistic regression modeling

Statistical Analysis

- Multivariate analysis for the endpoints of VT/VF and VT/VF or death

➢ Cox proportional hazards regression modeling