Inappropriate ICD shocks. How big is the problem and how to prevent them

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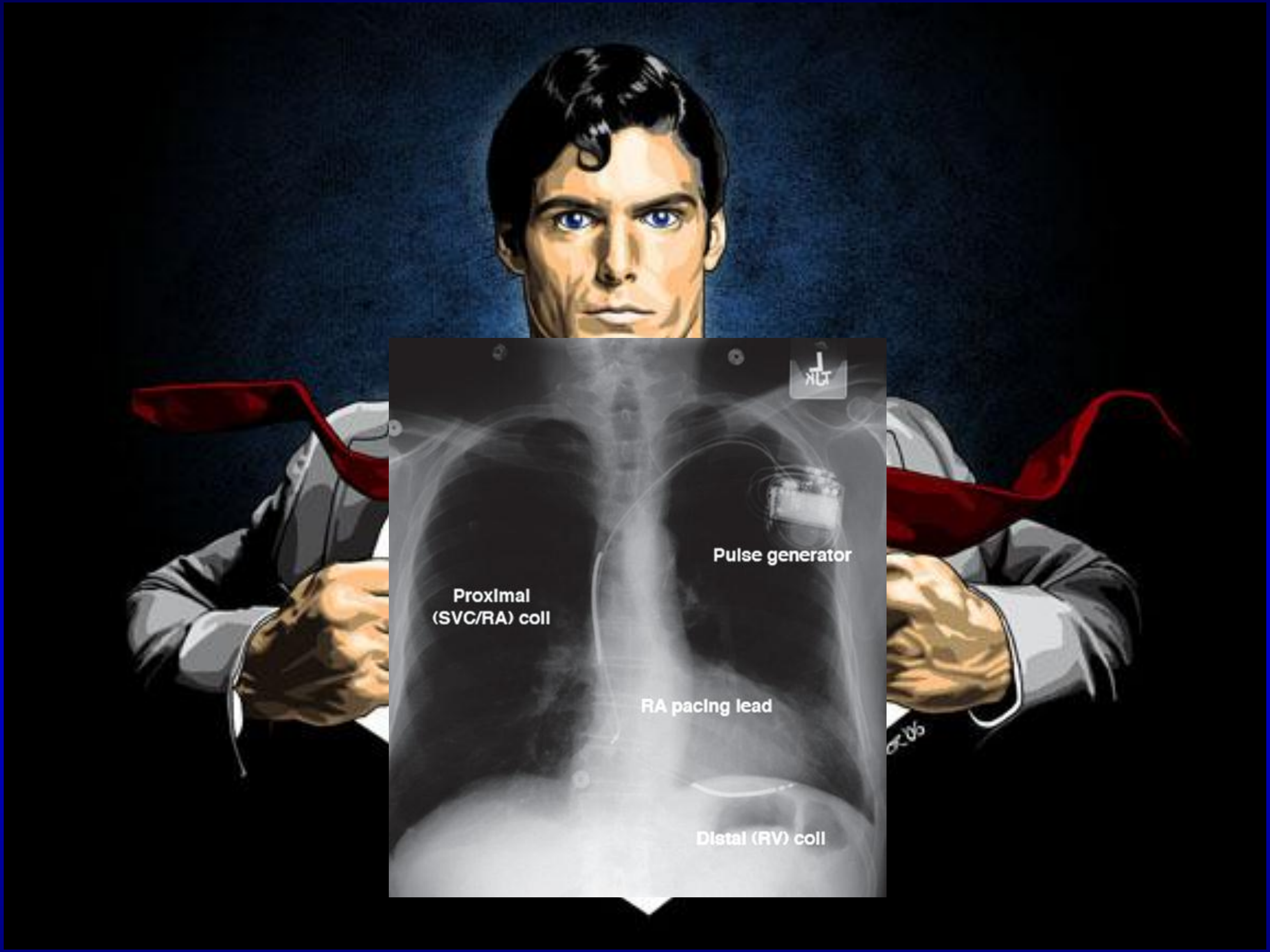
Advances in cardiac arrhytmias and great innovations in cardiology

Torino, September 27, 2013



ICD and shocks: only joys (or also sorrows?)

Introduction

- Despite a 3 decades of advancement in ICD therapy, inappropriate shocks remain a major clinical problem
- In the primary prevention era inappropriate shocks are even more important: shocks are being delivered to patients with no history of symptomatic arrhythmias
- Therefore, effectiveness and appropriateness of ICD therapy is mandatory

Tecnical and clinical reasons for inappropriate ICD therapy

Tecnical reasons
Lead failure/artifacts
Lead dislocation
Adaptor or connector malfunction
Integrated bipolare sensing
Electromagnetic interference
– Minimum electrical current leakage
– Spinal cord stimulation
– External muscle stimulation
– External magnetic fields
– Electro-acupunture
– MRI
– External electrical (short) circuits

Clinical reasons
T wave oversensing
Double counting due to wide QRS
Double counting in biventricular pacing
Far-field sensing
Oversensing of diaphragmatic potentials
Acceleration after antitachycardia pacing
Inappropriate discrimination of supraventricular arrhythmias (proper sensing, but algorithms ineffective)
Atrial tachicardia vith 1:1 AV conduction
Atrial fibrillation/flutter with rapid ventricular response

Res, JCJ. Clin Res Cardiol 2006; 95:Suppl 3, III/17–III/21

PREVALENCE OF INAPPROPRIATE SHOCKS

INAPPROPRIATE SHOCKS IN CLINICAL TRIALS

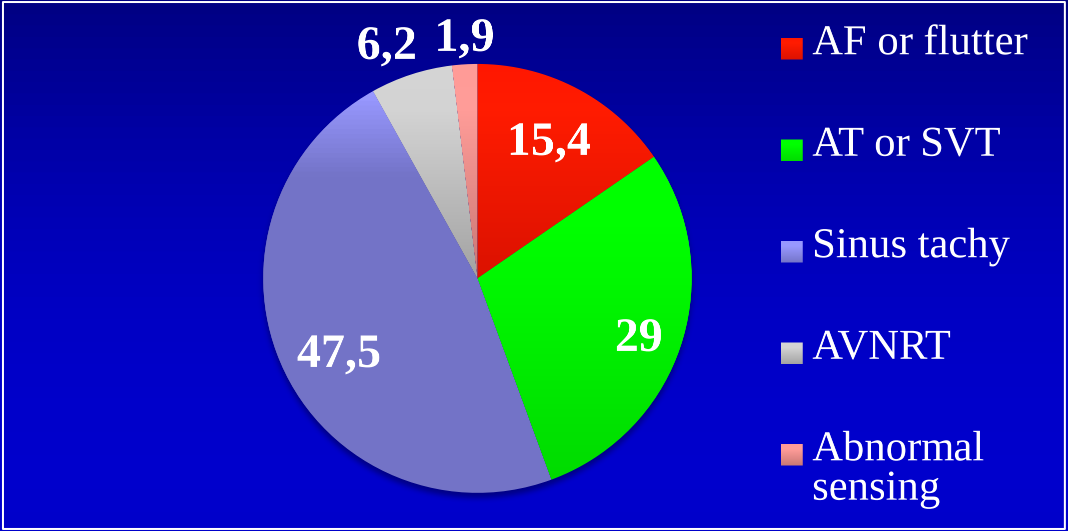
QUARTERLY FOCUS ISSUE: HEART RHYTHM DISORDERS   State-of-the-Art Paper

Appropriate Evaluation and

	AVID 1997	MADIT-II 2002	DEFINITE 2004	SCD-HeFT 2005
Patient #	492	719	227	811
Indication	Secondary prevention	Primary prevention	Primary prevention	Primary prevention
Follow up (months)	12	22	29	45
Appropriate shocks	39%	14.1%	18.1%	16%
Inappropriate shocks	**20%**	**11.5%**	**21%**	**11%**

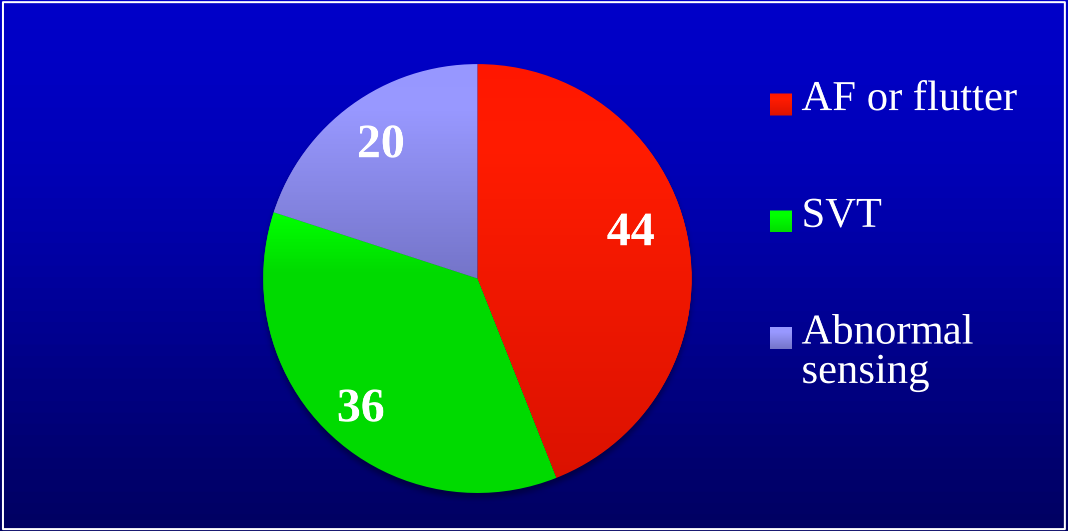
Mishkin, JD. J Am Coll Cardiol 2009;54:1993–2000

Reasons for inappropriate ICD shocks



SCD-HeFT

Poole JE. *N Eng J Med* 2008; 359:1009-17.



MADIT II

Daubert JB. *J Am Coll Cardiol* 2008; 51:1357-65.

OBSERVATIONAL STUDIES

Prevalence of shocks in Observational/Follow-Up Studies - Registries

	# Pts	years	Mean F-U	Total shocks %	Inapprop shocks %	Prevailing mechanism
Saxon, ALTITUDE, 2010[(1)]	69556	2001-2008	33±16 mos	14% @ 1 yr 39% @ 5 yrs	32% of total shocks	45% FA/flutter
ECOST, control, 2010[(2)]	212	2007-2008	24,2±7,3 mos	26,4	10,4	NA
Van Rees, Leiden Univ, 2011[(7)]	1544	1996-2006	41±18 mos	NA	13% total 7% @ 1 yr 13% @ 3 yrs 18% @ 5 yrs	75% SVT 45% AF 12% abnormal sensing 11% sinus tachy
Kleemann, Ludwigshafen, 2012[(3)]	1411	1992-2008	3 yrs	NA	21	60% FA 24% lead defects/T wave overs 14% sinus tachy
Deyell, British Columbia, 2013[(4)]	1608	1998-2008	30 mos	27,4	10% @ 1 yr 14 @ 2 yrs	45% Sinus/SVT tachy 43% FA/flutter 8.5% Lead failure 8,2% P/T overs
DANISH, 2013[(5)]	1609	2007-2011	1,9±1,3 yrs	9,4	2,6	NA
Shah, Pittsburgh, 2013[(6)]	2050	2009-2011	Study period	3,6	1,6	53% SVT with 1:1 AV association

Heart 2013; 99: 1250-5. [5] Weeke, P. *Europace* 2013;15:1150-7. [6] Shah, H. *PACE* 2013;36:547-52. [7] Van Rees, JB. *J Am Coll Cardiol* 2011;57:556–62

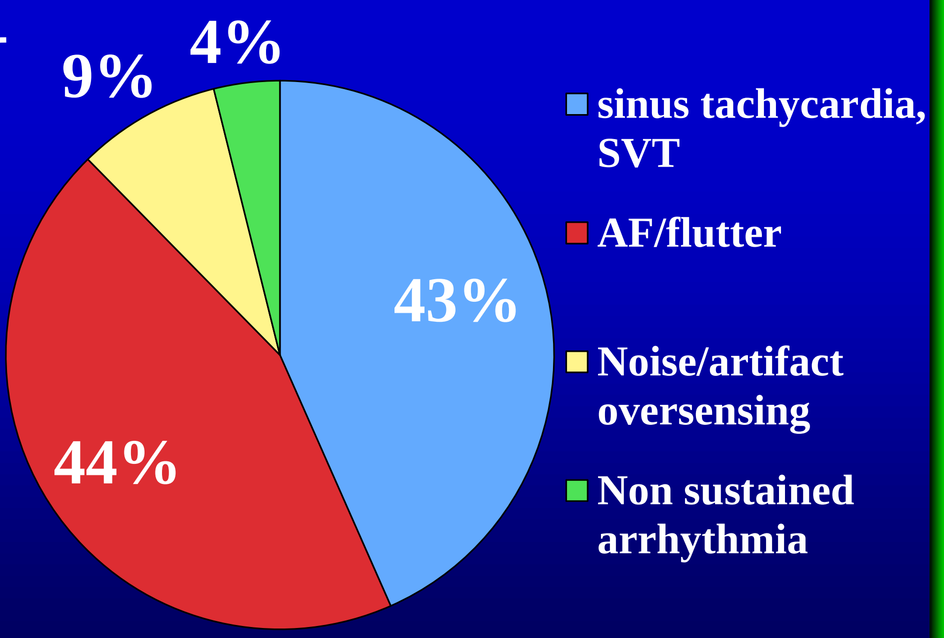
ALTITUDE

69556 Pts networked, June 14, 2001- October 21,2008

Boston LATITUDE-compatible ICD and CRTD devices, 2096 US Centres

87% M, mean age 69±10 yrs, F-U 33±16 mos

	Years of F-U	1	5
Prevalence of shocks (% of Pts, at least one shock)	Total	14	39
	Appropriate	8	23
	Inappropriate	6	16



Saxon, LA. Circulation 2010; 122: 2359-67.

ALTITUDE-NOISE

2000 Pts, random sample, June 14, 2001- October 21,2008

Boston LATITUDE-compatible ICD and CRTD devices, 2096 US Centres

Retrospective analysis of ICD EMGs stored

Mechanism of Noise, Artifact, Oversensing that resulted in ICD shocks

	Episodes	**Patients**	**% of all episodes**	**% of NAO episoodes**
External noise	76	56	1,4	56,7
Lead/connector	37	30	0,7	27,6
Muscle noise	11	11	0,2	8,2
Ventricular far-field of the atrium	7	3	0,1	5,2
T-wave oversensing	2	2	0,1	1,5
Other noise, oversensing	1	1	0,1	0,7
Total	134	101	2,6	100

Powell, BD. PACE 2012; 35:863-9.

ALTITUDE-NOISE

2000 Pts, random sample, June 14, 2001- October 21,2008

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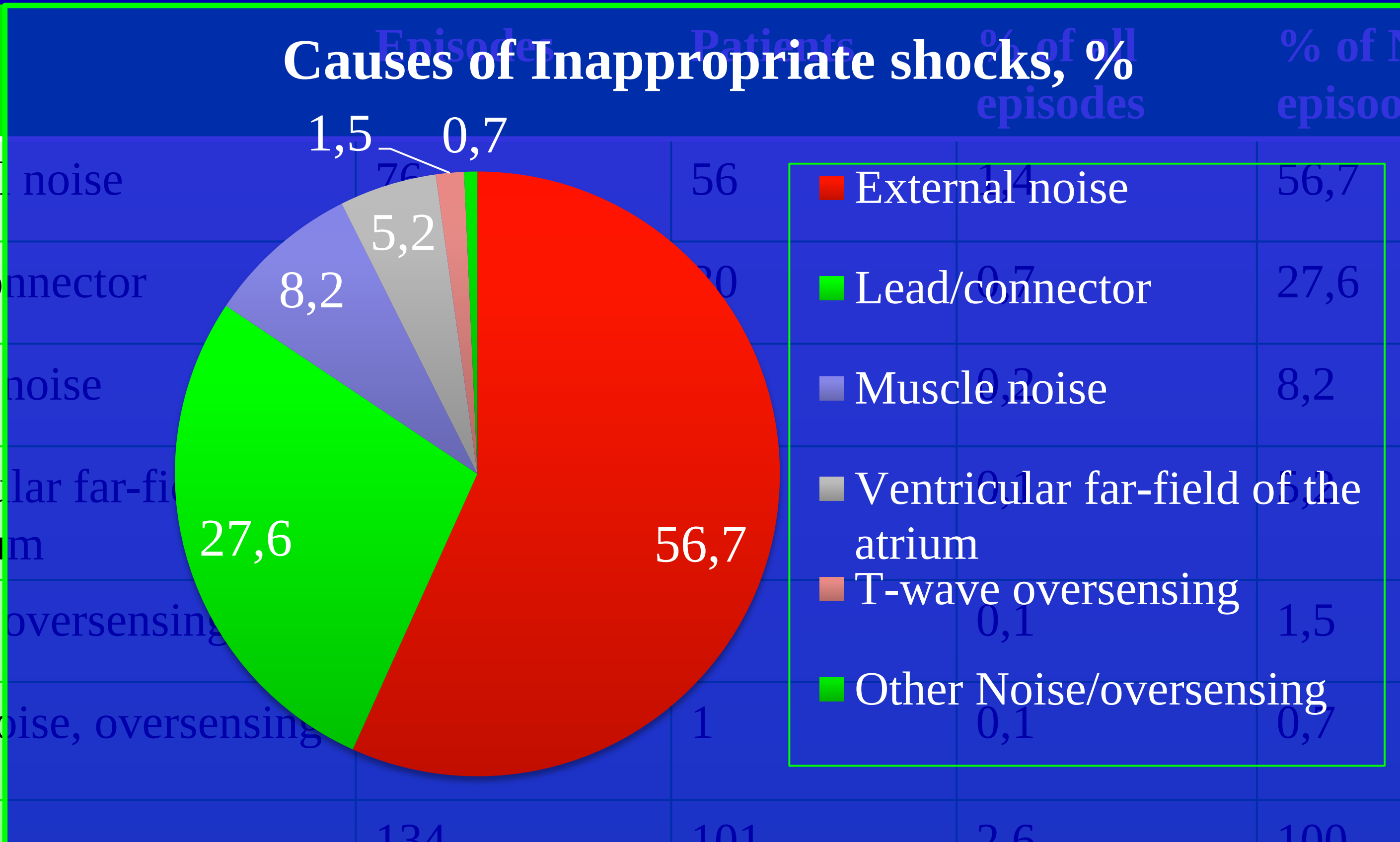
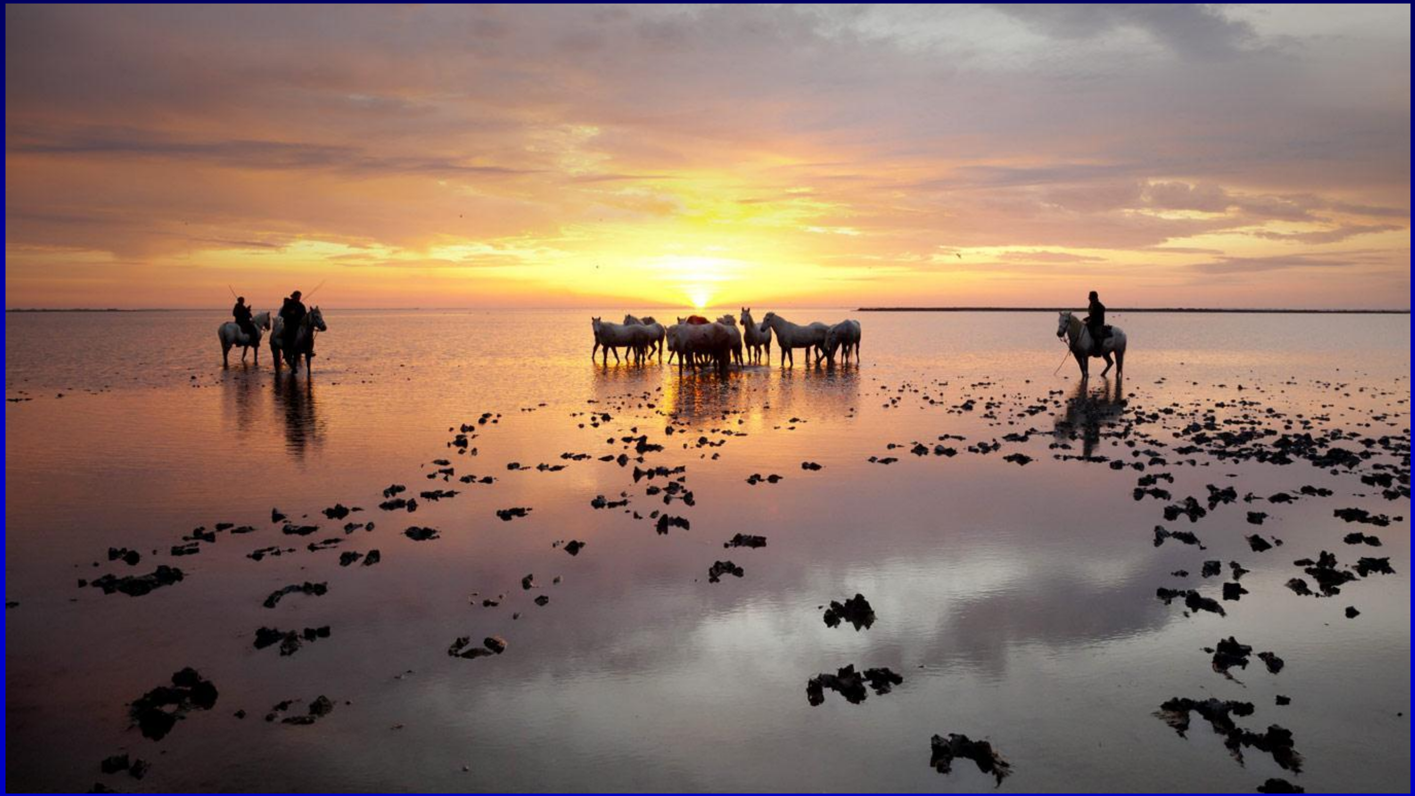
Lead/connector	[illegible]	[illegible]	0,7	27,6
Muscle noise	[illegible]	[illegible]	0,2	8,2
Ventricular far-field of the atrium	[illegible]	[illegible]	0,1	[illegible]
T-wave oversensing	[illegible]	[illegible]	0,1	1,5
Other noise, oversensing	[illegible]	1	0,1	0,7
Total	134	101	2,6	100



Powell, BD. PACE 2012; 35:863-9.



PROGNOSIS RELATED TO ICD SHOCKS

Prognosis related to ICD shocks

First trials: negative impact on prognosis

Author, (Reference) Publication Year	**Clinical Trial**	**Shock and/or ATP-related findings**
Poole, [1] 2008	SCD-HeFT	HR 5,68: for mortality for appropriate shocks HR 1,98 for mortality for an inappropriate shock
Daubert, [2] 2008	MADIT II	HR 2,29 for mortality associated with an inappropriate shock
Moss, [3] 2004	MADIT II	HR >3,3 for mortality associated with VT or VF
Pacifico, [4] 1999	ICD shocks as predictors of survival	Survival differences demonstrated for for Pts with no shocks compared with any type of shock *(P=0.05)*
Van Rees, [5] 2011	Leiden University	Single inappropriate shock increased risk of all-cause mortality (HR: 1.6, *P= 0.01*). Risk increased with every subsequent shock, up to an HR of 3.7 after 5 inappropriate shocks.
Larsen, [6] 2011 Correction for SHF, yrs 1994-2008	Portland and Stanford	1-5 shock days: HR for death NS vs no shock 6-10: HR 2,2 (P<0.01) <10: HR 3,66 (P<0,01)

(1) Poole, JE. *N Eng J Med* 2008; 359:1009-17
(2) Daubert, JP. *J Am Coll Cardiol* 2008; 51:1357-65
(3) Moss, AJ. *Circulation* 2004; 110:3760-65.
(1) Pacifico, A. *J Am Coll Cardiol* 1999; 34:204-10
(2) Van Rees, JB. *J Am Coll Cardiol* 2011;57:556–62
(3) Larsen, GK. Heart Rhythm 2011;8:1881–1886

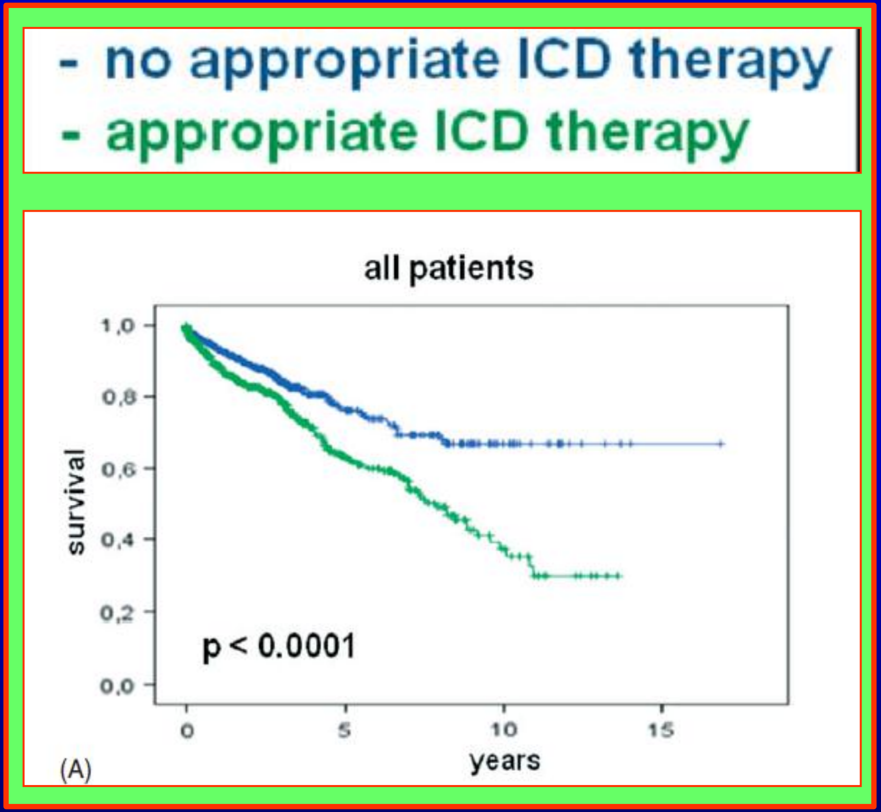
Recent trials, "adjusted models": inappropriate shocks do not affect survival

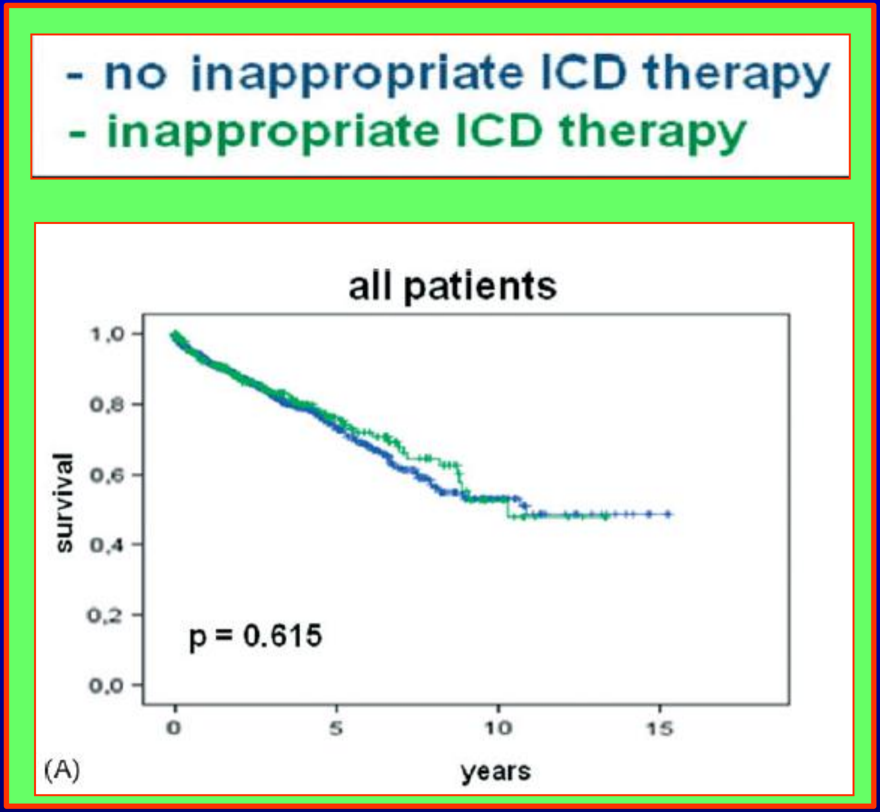
Author, [Ref] Year	Clinical Trial	Shock and/or ATP-related findings
Kleemann, [1] 2012	Ludwigs-hafen	Inappropriate single shock due to AF not associated with worse prognosis. Multiple shocks due to AF associated. Shocks caused by lead failure (single or multiple) not associated with increased mortality (HR 0.99)
Deyell, [2] 2013	British Columbia	In the adjusted model, inappropriate shocks not associated with death or transplantation (HR=0.97, 95% CI 0.70 to 1.36, *P=0.873*). In contrast, appropriate shocks associated with adverse outcomes (HR=3.11, 95% CI 2.41 to 4.02, *P<0.001*).
Streitner, [3] 2013	Manheim	Appropriate shocks: trend to higher mortality in the overall patient population, significant in Ischemic CM, within 4 years from implantation. Inappropriate shocks: no impact on survival.
Dichtl, [4] 2011	Zurich and Basel	Appropriate ICD therapy strong impact on survival, for I and II prevention. Inappropriate therapy does not affect survival

(1) Kleeman, T. *J Cardiovasc Electrophysiol*, 2012; 23:735-740.
(2) Deyell, MW. *Heart* 2013; 99:1250–1255
(3) Streitner, F. *PLoS ONE* 2013; 8(5): e63911.
(4) Dichtl, W. *Clin cardiol* 2011; 34:433-6.

Prognostic Impact of ICD Shocks

inappropriate shocks do not affect survival

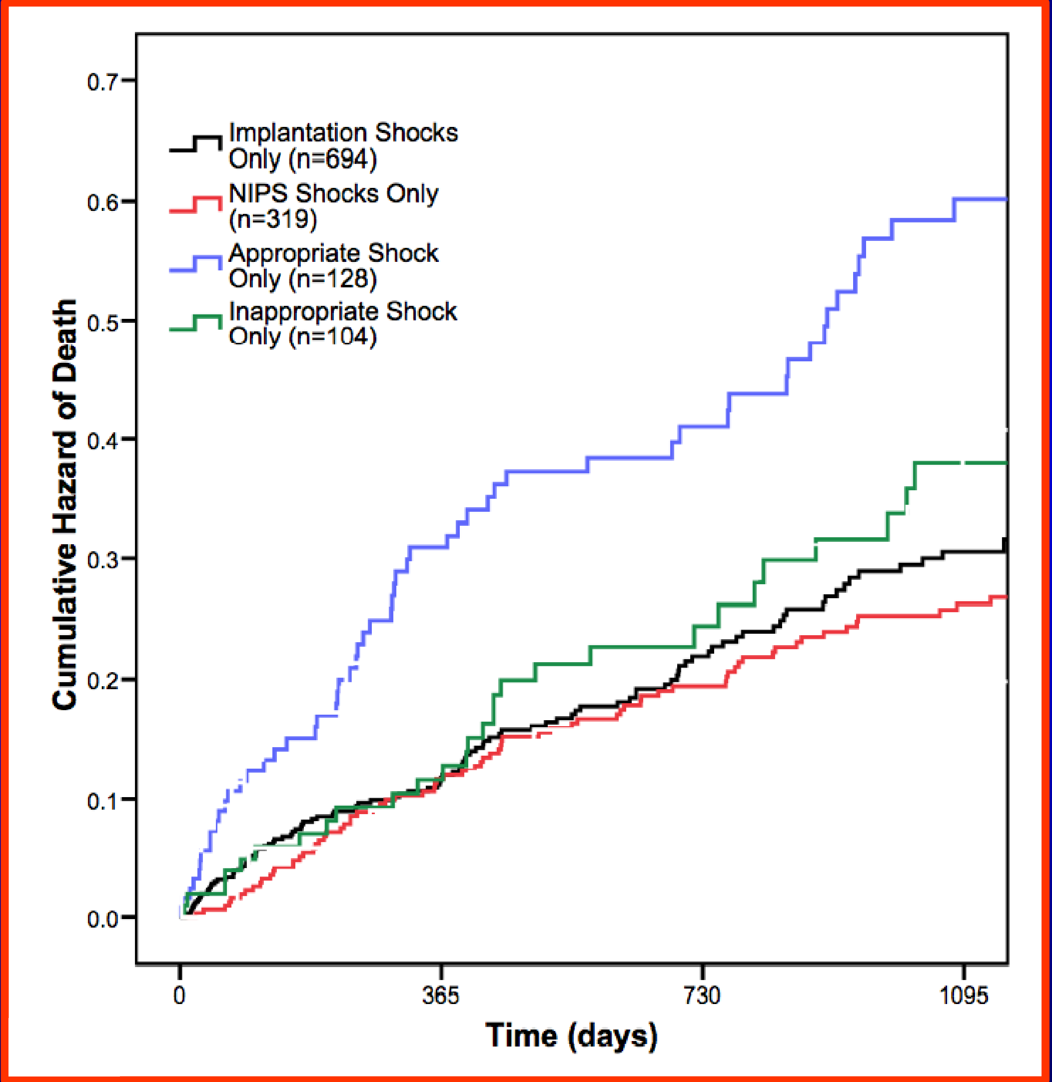




Dichtl, W. *Clin Cardiol* 2011; 34:433-6.

Prognostic Impact of ICD Shocks

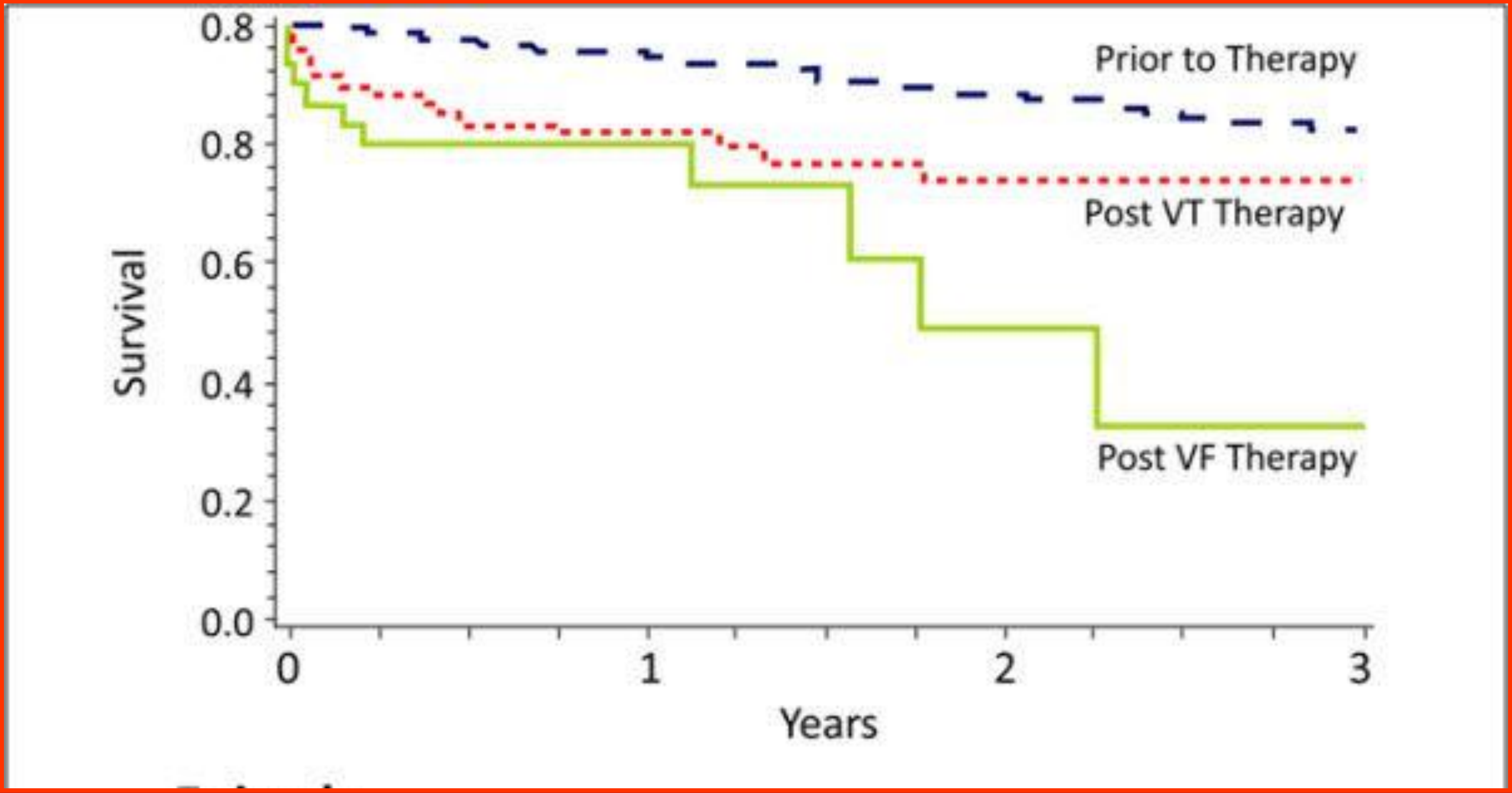
shocks “per se” do not influence



Bhavnani et al Heart Rhythm 2010;7:755–760

Prognostic Impact of Shocks

shocked arrhythmia counts:VF is worse than VT



Sweeney MO, www.medscape.org/viewarticle/733873

ALTITUDE Survival by Rhythm Study

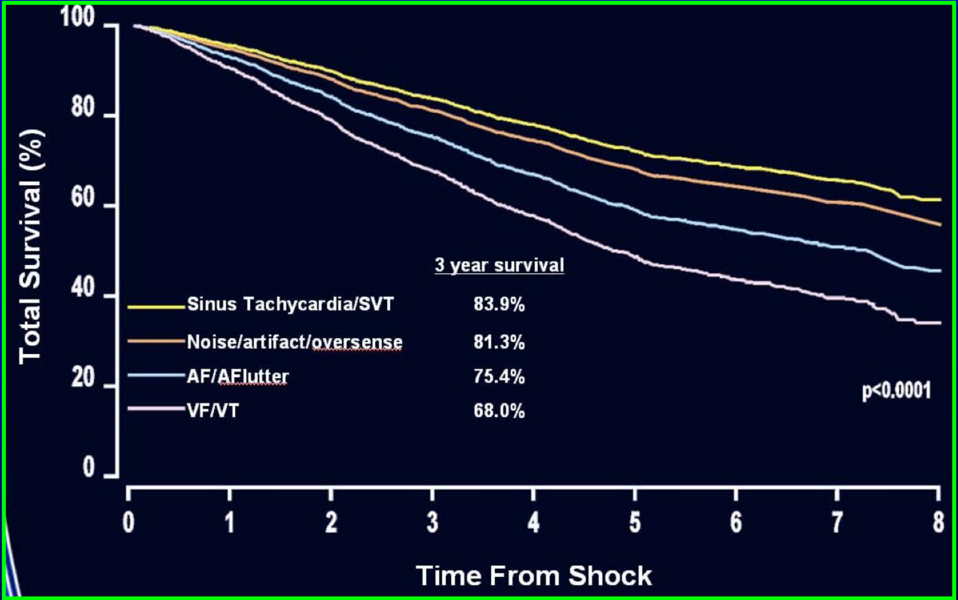
Powell, BD. *J Am Coll Cardiol* Accepted manuscript

DOI: 10.1016/j.jacc.2013.04.083

127.134 ICD and CRT-D patients with remote monitoring capability (Boston LATITUDE® System)
1550 USA Centres
Random sample of 3809 patients (M 78%, mean age 64±13 years), case-control matching with 3630 patients with no shock.
Followed for an average of 3,1±1,7 years from implant,
Analysis of intracardiac electrograms (iEGMs) at time of therapy

Mantel-Haenszel Odds Ratio for death following first shock compared with no-shock match

Type of first shock	OR	95% CI	P
VF/polymorphic VT	2,1	1,54 – 2,86	0,0001
Monomorphic VT	1,65	1,36 – 2,01	0,0001
AF/Flutter	1,61	1,17 – 2,21	0,003
Sinus tachycardia/SVT	0,97	0,68 – 1,37	0,86
Noise/Artifacts/Oversensing	0,91	0,50 – 1,67	0,76

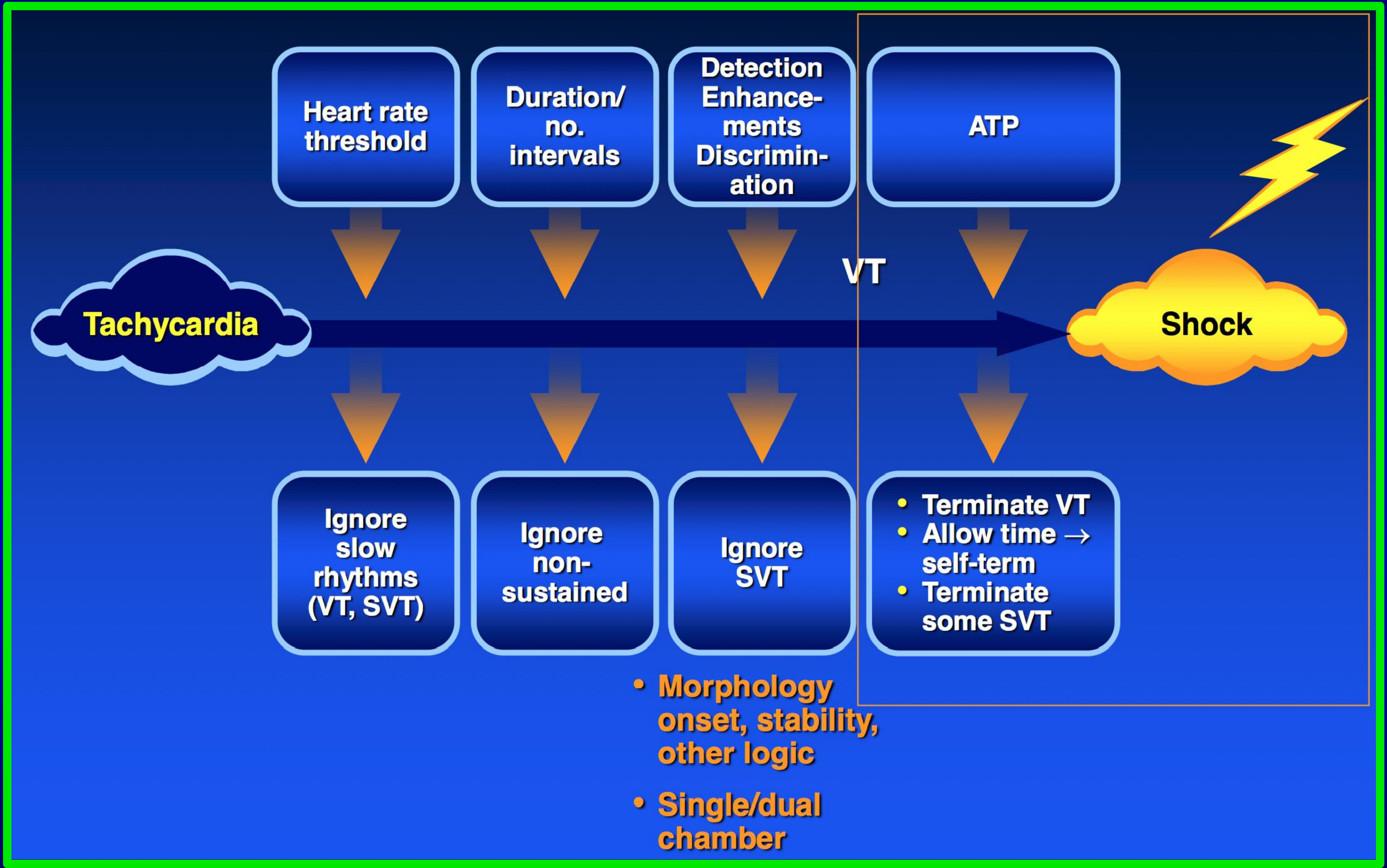


PREVENTION OPTIONS

METHODS TO REDUCE INCIDENCE OF ICD SHOCKS

- ICD programming
- Pharmacological therapy
- Catheter ablation
- More options?

Cascade of events leading to ICD shock

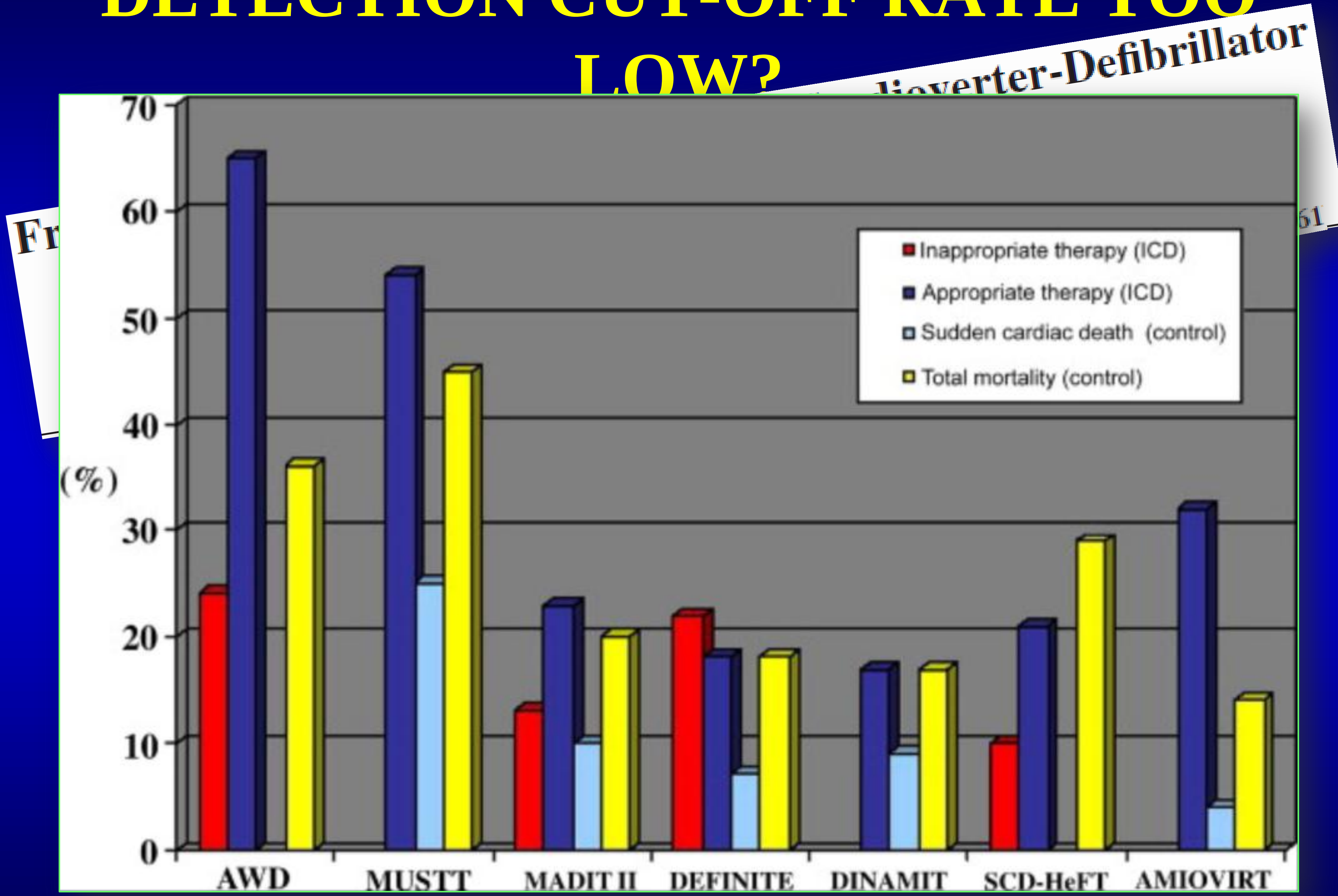


Mahdavan, M. *Circulation* 2013;128:659-672

PROGRAMMABLE DISCRIMINATION OPTIONS

- Rate Cutoff
- Detection Interval (Duration)
- RR Interval Features
  - SUDDEN ONSET
  - STABILITY
  - TIME OUT
- Morphology Discrimination
- Dual Chamber Timing algorithms

DETECTION CUT-OFF RATE TOO LOW?



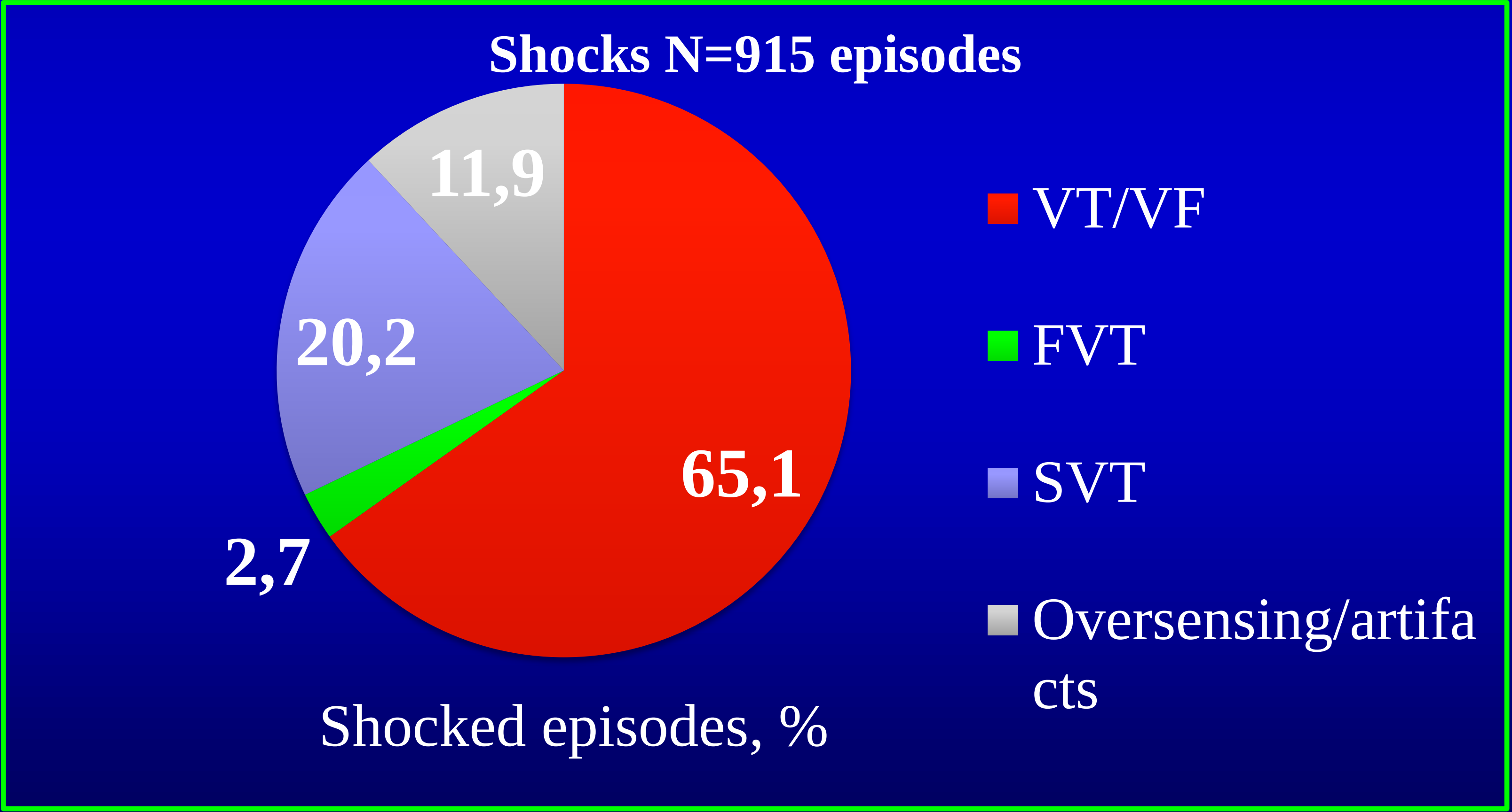
High-rate VF cut-off studies

RATE ONLY DISCRIMINATORS

- In SCD HeFT, single chamber devices programmed to single zone (VF) at 188 bpm with no discriminators
- VF detection set at 18/24 beats
- Inappropriate shocks for supraventricular arrhythmias only 12% at 5 years!
- This is the standard by which other programming options should be assessed

SCD-HeFT: approx 32% of shocks were inappropriate!

VT zone only, > 188 bpm, no discriminators



High-Rate cut-off studies

Author, [Ref] Year	Clinical Trial	Programming	Shock and/or ATP-related findings
Wilkoff, [1] 2006	**EMPIRIC** -Randomized -445 + 455 pts, 20% Ischemic -Primary and secondary prevention	***"EMPIRIC" programming*** **VF**: 250 bpm, 18/24 beats, shocks **FVT via VF**: 200 bpm, 18/24 beats, burst + shocks **VT**: 150 bpm, 16 beats, burst + ramp + shocks ***"TAILORED" programming*** decided by treating physician	Noninferiority demonstrated for all-cause shock with EMPIRIC vs TAILORED ICD programming (HR 0.95; CI 0,74-1,23) with *(P=0.0016)*
Clementy, [2] 2013	**"Tours Study"** -Follow-up -365 pts, 63% Ischemic -Primary prevention only	***"shock-only zone"*** over 220 bpm *and a* ***"monitoring zone"*** between 170 and 220 bpm	FU 40 mos. 11, 2% appropriate, 6,6 inappropriate shks 43 episodes in monitoring zone, 7 symptomatic, none lethal

(1) Wilkoff, BL. *J Am Coll Cardiol* 2006;48:330 (2) Clementy, N. *Europace* 2012; 14:968–974

Long detection VF studies

"Long detection" studies

Author, [Ref] Year	Clinical Trial	Programming	Shock and/or ATP-related findings
Gasparini, [1] 2009	**RELEVANT** FU, controlled, non-randomized 324 primary prevention non-ischaemic HF patients CRT-D devices	VF: < 240 ms, shock only FVT: 330-240 ms, 1 ATP during charge, -> shocks VT: monitor only ***"PROTECT"*** NID 30/40 beats, RNID 12/16, shocks ***"CONTROL"*** NID 12/16 beats, RNID 9/12, shocks	FU 14±10.4 mos **Protect group:** 331 therapy episodes, 20 inappropriate, 311 appropriate. **Control group:** 552 therapy episodes, 242 inappropriate, 310 appropriate
Gasparini, [2] 2013	**ADVANCE III** -Randomized 1:1 -1902 pts, 94 Centres -Ischemic and non ischemic -75% primary prevention	VF: < 200 ms, shock only FVT: 320-200 ms, 1 ATP during charge, -> shocks VT: monitor only **"*LONG DETECTION*":** NID 30/40 **"*STANDARD DETECTION*"**: NID 18/24	FU 12 mos. In Long Detection Group reduction of shocks (19 vs 30/100 persons/yr) and of inappropriate shocks (5,1 vs 11,6/100 persons/yr)

(1) Gasparini, M. European Heart Journal 2009; 30: 2758–2767 (2) Gasparini, M, N. *JAMA* 2013; 309:1903-11.

Long detection, high-rate cut-off

PREPARE: Programming Strategies to Reduce Shocks in Primary Prevention Pts

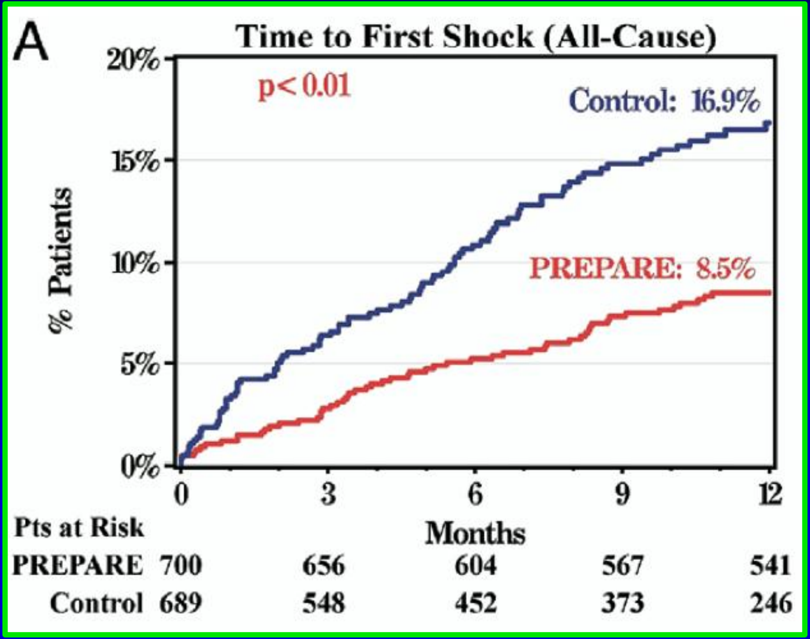
700 pts, 12 mo.; shock morbidity endpoints

PREPARE VT/VF Programming Parameters

- Longer detection durations (NID 30/40 vs 18/24)
  - ➡ *>25% of ICD detected VF is non-sustained*
- 330 ms slowest treated cut-off
  - ➡ *excludes most rapid SVTs*
- VT monitor zone to 360 ms
- SVT discriminators ON to 300 ms
- ATP for VT 240-330 ms

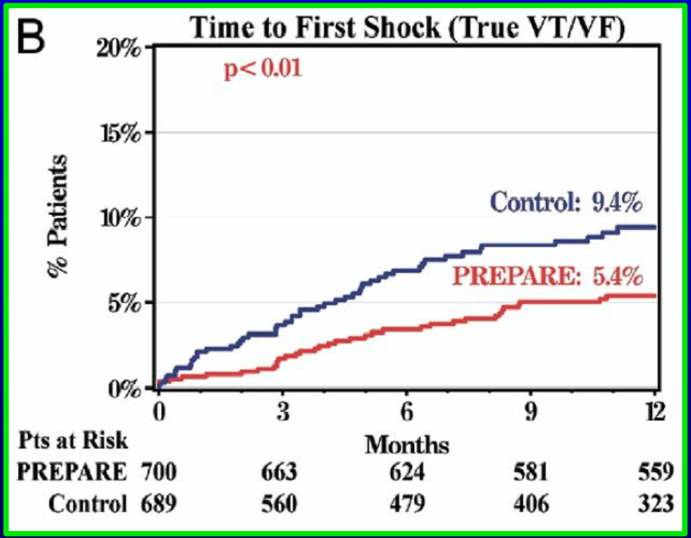
Wilkoff, BL. *J Am Coll Cardiol* 2008; 52:541-50.

PREPARE TRIAL

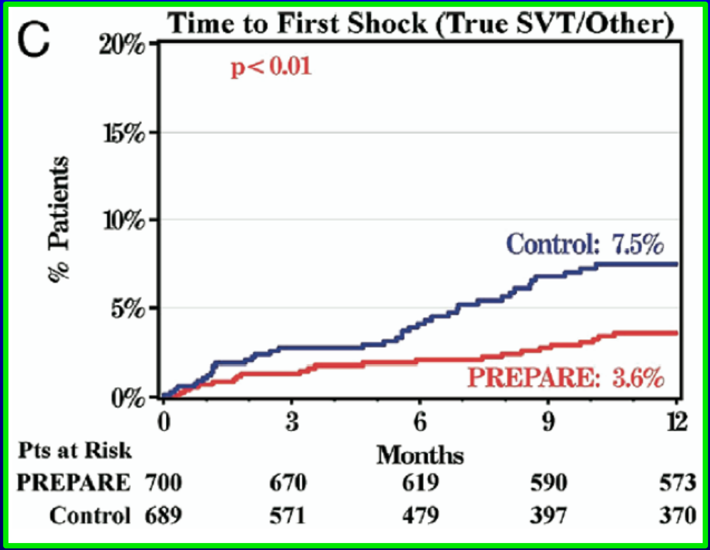


Wilkoff, BL. *J Am Coll Cardiol* 2008; 52:541-50.

Strategically chosen VT/VF detection and therapy can safely reduce shocks in primary prevention ICD patients.

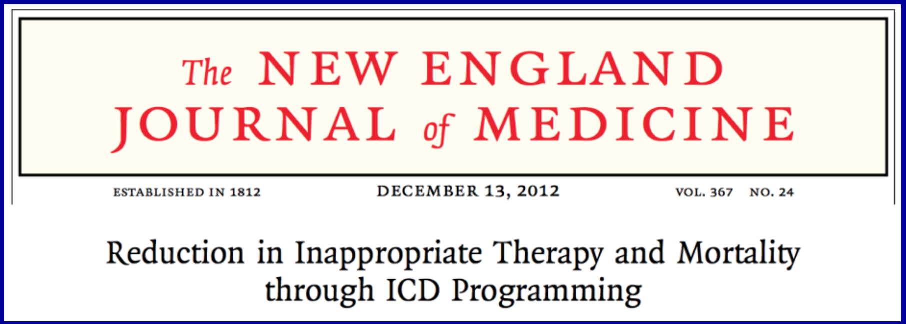


Kaplan-Meier curves and percentage of patients (Pts) in each study cohort receiving a first shock during the first 12 months of F-U



MADIT-RIT

Moss, AJ. *N Engl J Med* 2012;367:2275-83.


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 13, 2012 VOL. 367 NO. 24

Reduction in Inappropriate Therapy and Mortality through ICD Programming

OBJECTIVE

Determine if dual-chamber ICD or CRT-D devices with high rate cutoff and/or long delay

are associated with **fewer inappropriate therapies**

than standard programming during post-implant follow-up of patients with indication for primary prevention device therapy

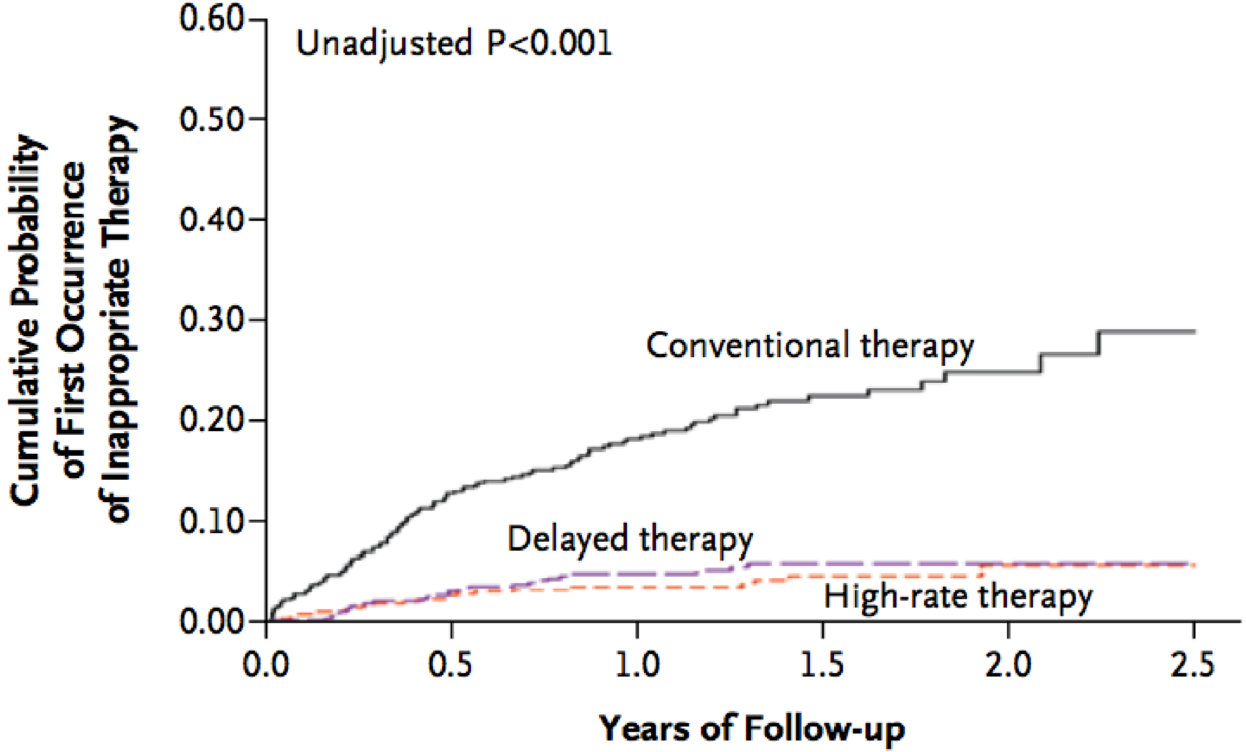
Randomization arms

MADIT-RIT A (Standard programming)	MADIT-RIT B (High rate cutoff)	MADIT-RIT C (Long delay)
Zone 1 (VT):	**Zone 1 (VT):**	**Zone 1 (VT-1):**
• 170 bpm, 2.5s delay	• 170 bpm	• 170 bpm, 60s delay
• Onset/Stability Detection Enhancements ON	• Monitor only	• “Rhythm ID Detection” Enhancements ON
• ATP + Shock		• ATP + Shock
Zone 2 (VF):	**Zone 2 (VF):**	**Zone 2 (VT):**
• 200 bpm, 1s delay	• 200 bpm, 2.5s delay	• 200 bpm, 12s delay
• “Quick Convert ATP” • Shock	• “Quick Convert ATP” • Shock	• “Rhythm ID Detection” Enhancements ON
		• ATP + Shock
		Zone 3 (VF):
		• 250 bpm, 2.5s delay • “Quick Convert ATP”
		• Shock

All programming is within approved labeling

Moss, AJ. *N Engl J Med* 2012;367:2275-83.

Cumulative Probability of First Occurrence of Inappropriate Therapy According to Treatment Group



No. at Risk

Conventional therapy	514	420 (0.13)	305 (0.18)	149 (0.22)	56 (0.25)	8 (0.29)
High-rate therapy	500	454 (0.03)	339 (0.04)	191 (0.05)	70 (0.06)	17 (0.06)
Delayed therapy	486	445 (0.03)	342 (0.05)	177 (0.06)	82 (0.06)	13 (0.06)

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Milan Gupta, M
[a] Dep
[b] C
[c] Dep

Key Clinical Trials of 2012

Study Primary Author	Reference	Patients, N	Intervention Tested
FAME-2 De Bruyne B, et al	N Engl J Med 2012;367:991-1001	447	FFR guided PCI and OMT vs OMT alone in stable CAD
FREEDOM Farkouh ME, et al	N Engl J Med 2012;367:2375-2384	1900	Multivessel revascularization strategy in diabetics
C-PORT Aversano T, et al	N Engl J Med 2012;367:1792-1802	18,867	Stand alone elective PCI
MADIT-RIT Moss AJ, et al	N Engl J Med 2012;367:2275-2283	1500	ICD programming strategy for inappropriate shocks
TRILOGY ACS Roe MT, et al	N Engl J Med 2012;367:1297-1309	7243	Prasugrel vs clopidogrel in medically managed ACS
dal-Outoomes Schwartz GG, et al	N Engl J Med 2012;367:2089-2099	15,871	Dalcetrapib in ACS
WOEST Dewilde W, et al	Lancet 2013;381:1107-15	573	DAPT in OAC requiring patients undergoing PCI
Einstein-PE investigators	N Engl J Med 2012;366:1287-1297	4833	Rivaroxaban in symptomatic pulmonary embolism
ALTITUDE Parving HH, et al	N Engl J Med 2012;367:2204-2213	8561	Dual RAAS blockade with aliskiren in diabetics
PHS II Sesso HD, et al	JAMA 2012;308:1751-1760	14,641	Vitamin C and Vitamin E for primary prevention
The ORIGIN Investigators	N Engl J Med 2012;367:309-318	12,536	n-3 fatty acids in high cardiovascular risk patients
Giugliano RP, et al	Lancet 2012;380:2007-17	629	PCSK9 inhibitors in combination with statins
Roth EM, et al	N Engl J Med 2012;367:1891-1900	92	PCSK9 inhibitors with atorvastatin in primary hypercholesterolemia

Tre braccia di randomizzazione: controlli – delayed therapy – High rate terapy

DETECTION ENHANCEMENTS: STABILITY, ONSET, MORPHOLOGY

RR Interval Enhanced features

Stability and Onset: ASTRID Study

(Atrial Sensing To Reduce Inappropriate Defibrillation study)

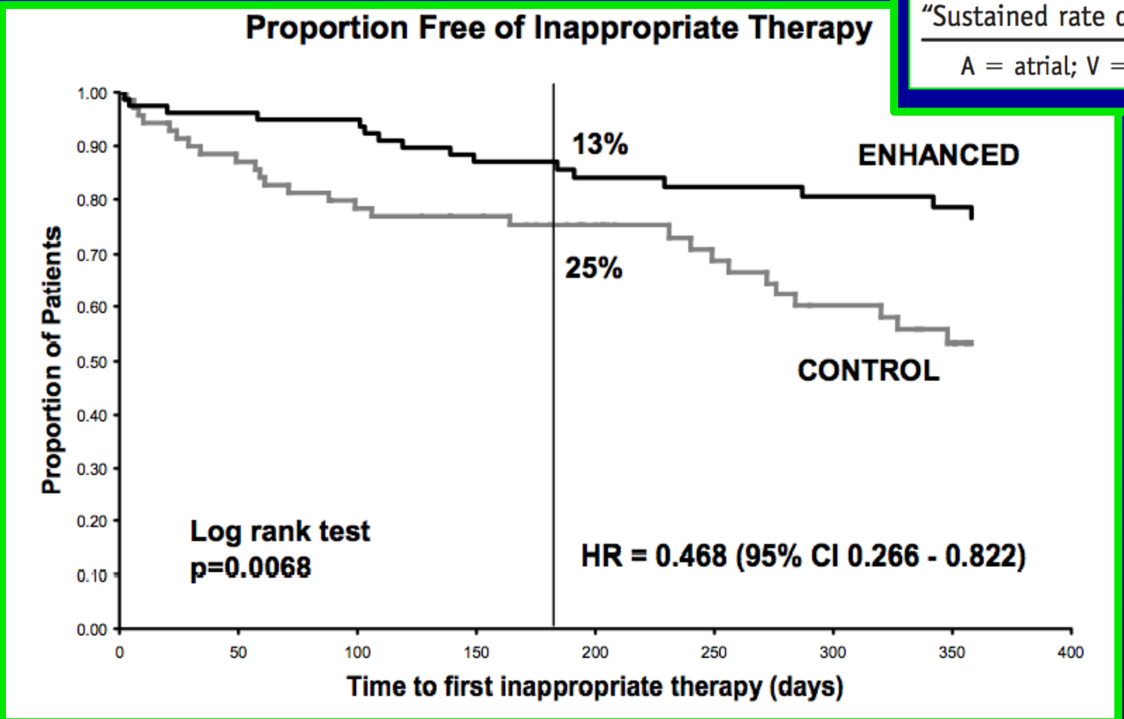
- 141 Pts with sustained VT or VF
- Mean age 60±13 yrs, M 83%, FE 35±15
- Randomization 1:1 at ICD implant:
  - **Enhanced** (N=73) and **Control** (N=70)

Dorian, P. *Heart Rhythm* 2004;1:540–547

Rate detect and discriminator programming

Parameter	Enhanced	Control
Onset	9%	Off
Inhibit if unstable	10 ms	Off
Atrial fibrillation		
(atrial) rate threshold	250 beats/min	Off
V rate > A rate	On	—
"Sustained rate duration"	3 min	3 min

A = atrial; V = ventricular.



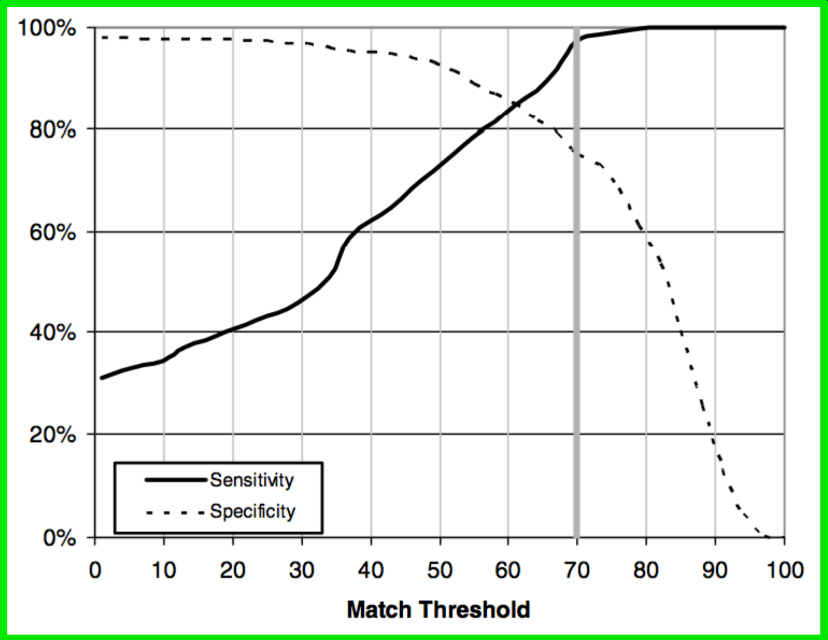
High-energy shocks were reduced from 0.58 ± 4.23 shocks/patient/month in the control group to 0.04 ± 0.15 shocks/patient/ month in the enhanced group (P = .0425).

Morphology

Worldwide Wave Study: Wavelet

Klein, GJ. *J Cardiovasc Electrophysiol* 2006; 17:1310-1319

- 1222 Pts
- Non-randomized prospective study
- Wavelet operating at minimal algorithm setting (RV coil-can electrogram, match threshold of 70%)
- Wavelet **ON**, other SVT discriminators **OFF** within SVT rate range (usually >320 ms)
- SVT rate limit and rate timeout left to clinician's decision



Wavelet VT/SVT discrimination performance as a function of match threshold.

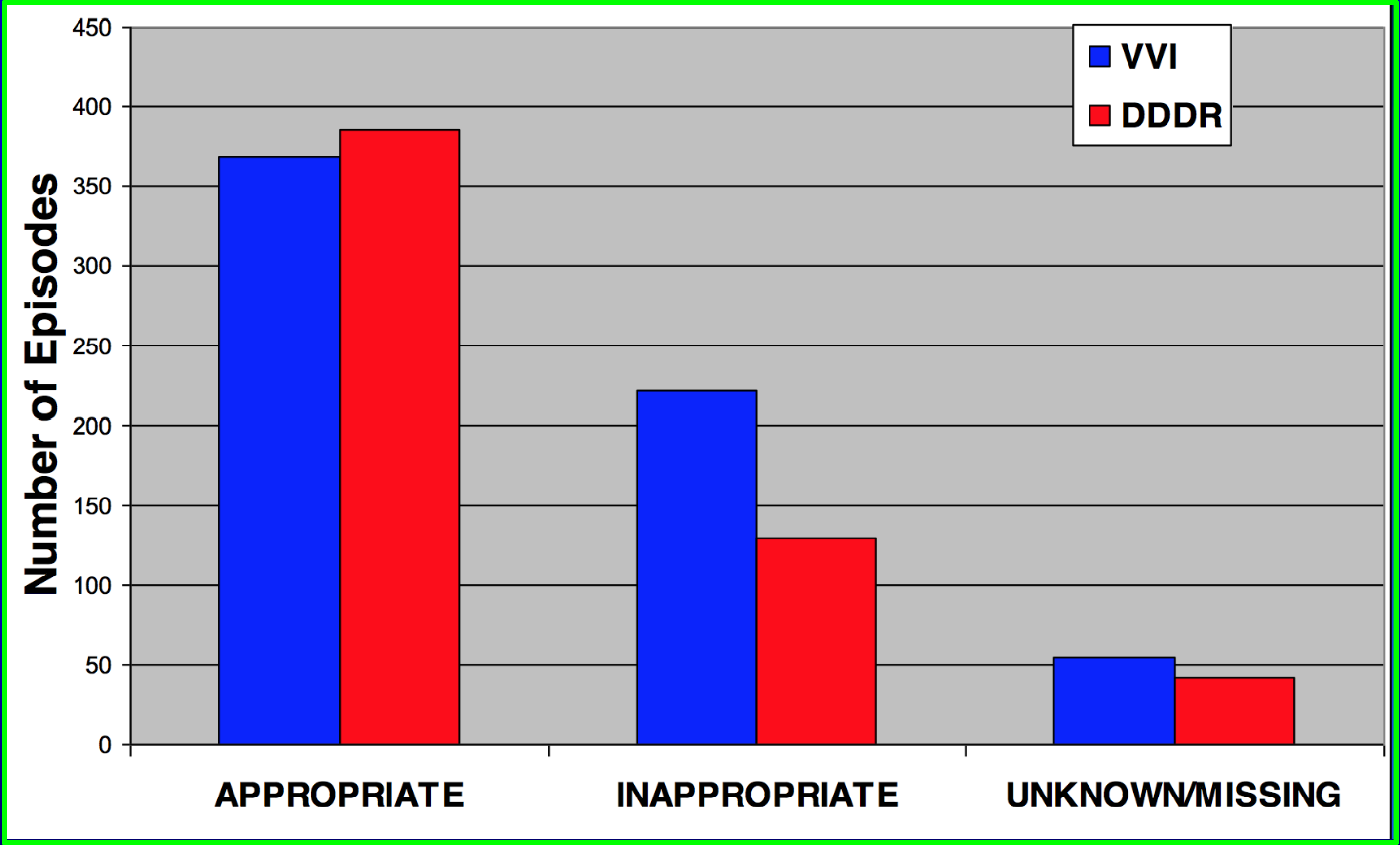
Inappropriate therapies for SVT reduced by 78% (90% CI: 72.8–82.9%) for episodes within the range of rates where Wavelet was programmed to discriminate.

Sensitivity for sustained ventricular tachycardia 98.6% (90% CI: 97–99.3%) without the use of high-rate time out.

Dual-chamber discrimination

Single and dual chamber discrimination
DAVID Trial

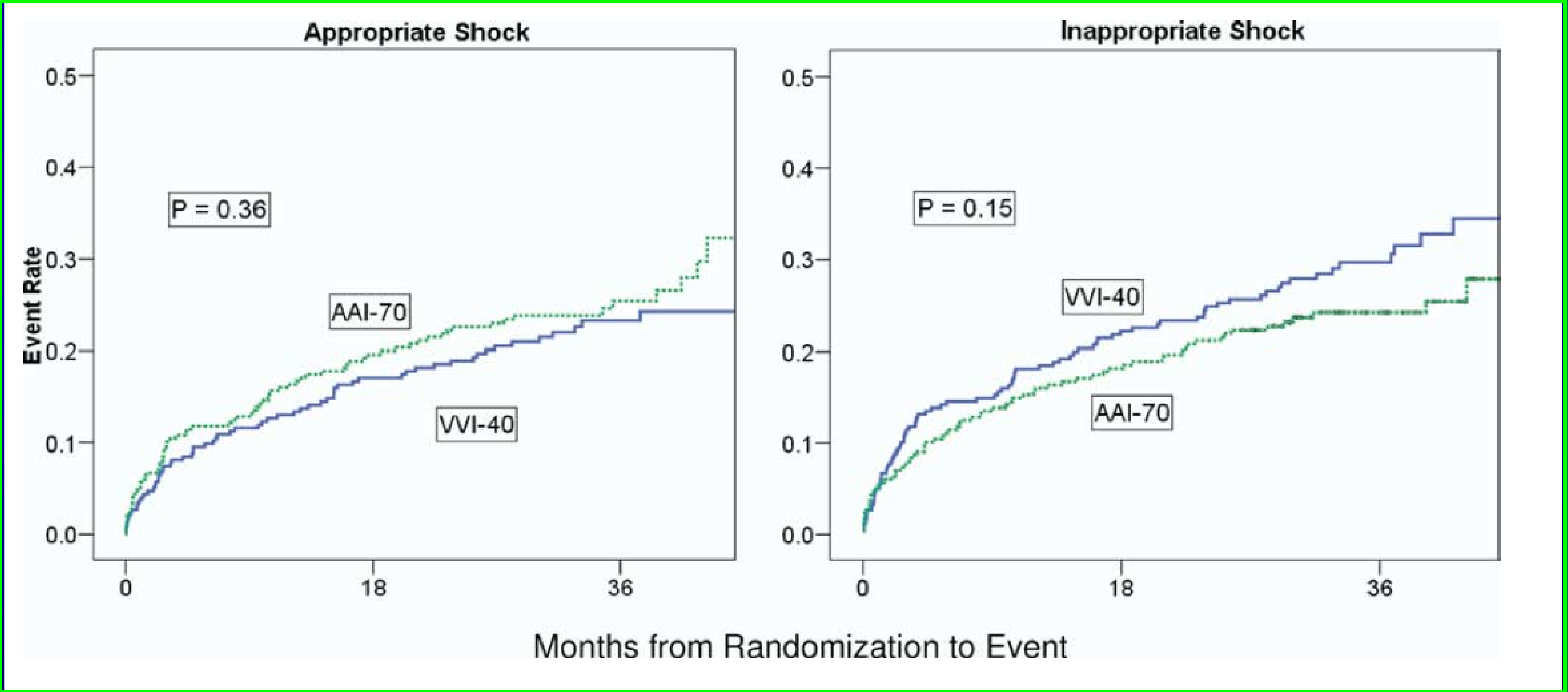
600 Pts, 29 USA Centres, ICD I and II prevention, no need for pacing, Randomly assigned to AAI 70 and VVI 40 bpm, mean F_U 22,7 yrs



Wilkoff, BL. *J Am Coll Cardiol* 2009;53:872–80

Single and dual chamber discrimination
DAVID Trial

600 Pts, 29 USA Centres, ICD I and II prevention, no need for pacing, Randomly assigned to AAI 70 and VVI 40 bpm, mean F_U 22,7 mos



Wilkoff, BL. *J Am Coll Cardiol* 2009;53:872–80

Meta-Analysis of Trials Comparing Single- and Dual-Chamber Discrimination

Study	Kuhlkamp et al	Deisenhofer et al	PINAPPs	1+1 Trial	Detect SVT
Study design	Non-randomized	Parallel randomized	Parallel randomized	Cross-over randomized	Parallel randomized
Blinding	Not	Not	Yes	Yes	Yes
Characteristic					
Pt (no.)	94	92	60	102	400
Mean age (yr)	65	61	59	65	65
Men (%)	NR	90	78	NR	80
CAD (%)	65	68	78	82	81
LVEF (%)	36	NR	30	37	32
Prior Hx of AT (%)	19	11	25	NR	29
Mean F-U (mo)	16	7.5	12	6*	6
No. with DC-ICD	39	47	31	50	201

*First phase of cross-over trial

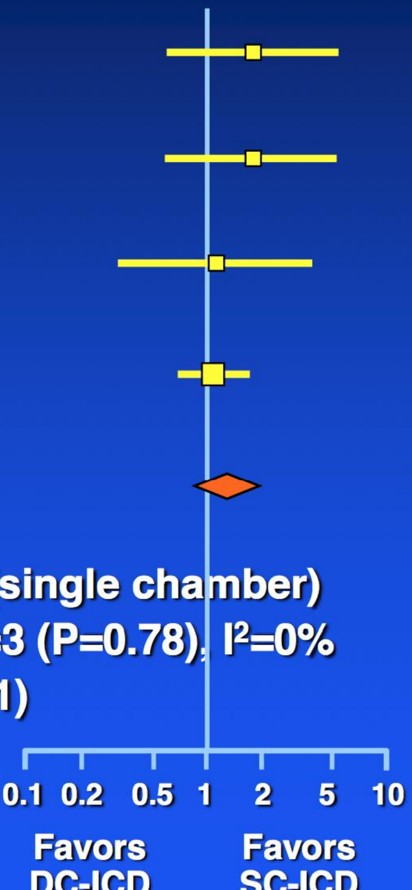
Programmed Arrhythmia Discrimination Parameters

Study	Manufacturer	Single chamber	Dual chamber
Kuhlkamp et al	Guidant	Onset; stability	Onset; stability; V > A; AFib threshold
Deisenhofer et al	Biotronik, ELA, Guidant, Medtronic, St. Jude Medical	Onset, stabilitly	Onset; stability; DC algorithm
1+1 Trial	ELA	Onset; stability	Onset; stability; PARAD
PINAPPs	Biotronik, Guidant	Onset; stability	Onset; stability; V > A; AFib threshold; SMART
Detect SVT	St. Jude Medical	Onset; stability; MD	Stability; MD; rate branch

Theuns, DAMJ. *Int J Cardiol* 2007;125:352-7

Meta-Analysis of Trials Comparing Single- and Dual-Chamber Discrimination

Study or subcatagory	Dual chamber (no.)	Single chamber (no.)	Wt (%)	OR (fixed) 95% CI
Kuhlkamp	8/39	7/55	10.07	1.77 (0.58-5.37)
Deisenhofer	10/47	6/45	10.53	1.76 (0.58-5.32)
PINAPPs	7/31	6/29	10.47	1.12 (0.33-3.83)
Detect SVT	43/201	40/199	68.93	1.08 (0.67-1.75)
Total (95% CI)	318	328	100.00	1.23 (0.83-1.81)



Total events: 68 (dual chamber), 59 (single chamber)

Test for heterogeneity $Chi^2=1.10$, df=3 (P=0.78), $I^2=0\%$

Test for overall effect: Z=1.03 (P=0.31)

Approx. 20% pts Received inappropriate Rx for SVT

Theuns, DAMJ. *Int J Cardiol* 2007;125:352-7

PREVENTION OPTIONS: DRUG THERAPY

Drug therapy
Rationale

- Optimal medical HF therapy
- Betablockers may reduce ventricular rates in Pts with SVT/AF
- May be inadequate to prevent shocks (OPTIC Study)
- Antiarrhythmic drugs (AAD) may be warranted
- AAD potentially proarrhythmic and with extracardiac toxic effects
- AAD addiction needs to be individualizes, carefully weighing risk-to-benefit ratio
- Potential drug/device interaction

Drug therapy

Author, (Reference) Publication Year	Clinical Trial	Type of Study	# Pts	Mean FU, yrs	Drugs evaluated	Main findings
Lee, [1] 2008	Ulsan College	RCT	65	2,6±2,0	1)Amio 2)Sotalol 3)β-Bs	4-yrs inappropriate shocks: Amio 12,5%,Sotalol 41,7%, β-Bs 52,6%; P=0.008 Amio discontinued 16% pulmonary toxicity
Connolly [2] 2006	OPTIC	RCT	414	1 (0,9-1,1)	1)Amio+β-B 2)Sotalol 3)β-Bs alone	1 yrs shock for any reason: 6,6 vs 20,8 vs 33,2, P=0,001 Amio discontinued 18,2%, Sotalol 23,5, β-Bs 5,3
Ruwald, [3] 2013	MADIT CRT	F-U	1790	3,4±1,1	Carvedilol vs metoprolol	Carvedilol 36% reduction of inappropriate ATP and shocks compared to metoprolol. Inappropriate therapy due to AF reduced by 50%
Adler, [4] 2013	Tel-Aviv	Cases series	5	14 mos	Ivabradine 5-10 mg/day	No recurrence of Inappropriate shocks due to Sinus Tachy

(1) Lee, CH. *Circ J* 2008; 72:102-5 (2) Connolly, SJ. *JAMA* 2006; 295:165-71 (3) Ruwald, M. DOI 10.1016/j.jacc.2013.03.087. JACC IN PRESS (4) Adler, A. *Europace* 2013; 15:362–365

Drug therapy

Potential drug/device interaction

- Increase of ventricular tachycardia cicle lenght, leading to VT undersensing
- Increase in ventriculare pacing threshold, especially at fast pacing rates
- Increase in defibrillation threshold (DFT)
- Increase in bradycardia pacing due to changes in sinus rate/AV conduction
- Inrease device therapy due to proarrhythmia and rhythm misclassification

PREVENTION OPTIONS: ABLATION

Ablation to minimize inappropriate shocks

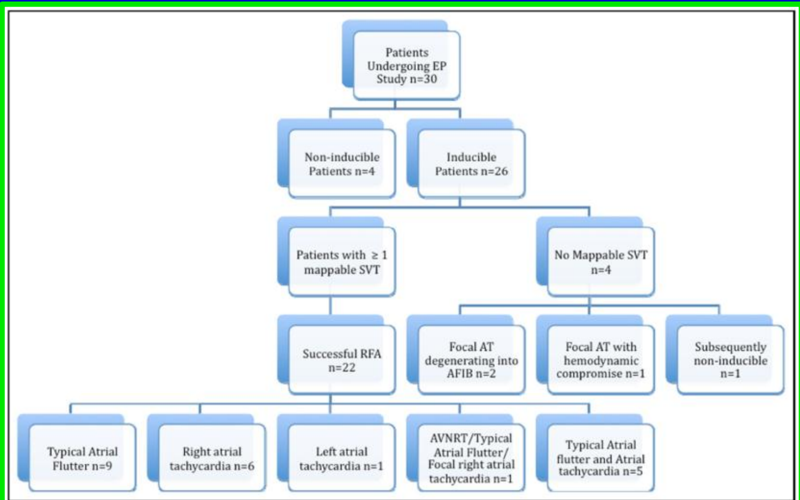
- Ablation: different chances
  - Atrial tachycardia, flutter, AVNRT
  - AF
  - AV node ablation

Ablation

SVT ablation

Usefulness of Radiofrequency Ablation of Supraventricular Tachycardia to Decrease Inappropriate Shocks from Implantable Cardioverter–Defibrillators

Sumeet K. Mainigi, MD*, Khalid Almuti, MD, Vincent M. Figueredo, MD, Nils A. Guttenplan, MD, Asma Aouthmany, MD, Jessica Smukler, MHS, PA-C, Bernadette Sheeron, MSN, CRNP, Bryan Meldrum, RN-BC, BS, Agustina D. Saenz, MD, Gia Tran, DO, and Allan M. Greenspan, MD



Outcome of patients undergoing electrophysiologic (EP) study

Mainigi, SK. *Am J Cardiol* 2012;109:231–237

Albert Einstein Medical Center, Philadelphia, Pensylvania
2005 – 2009, 660 pts ICD/ICD-CRT implanted
84 (13%) with Inappropriate Therapies due to non-AF sustained SVT, despite medications and ICD programming:
122 inappropriate shocks and 130 ATPs
30 EPS
22 successful RFA for AT, af, AVNRT

No furher inappropriate therapy compared to 63% of patients in whom ablation was not performed during a mean follow-up of 20.7 ±11.9 months

Ablation

AF ablation

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Ablation of atrial fibrillation in Brugada syndrome patients with an implantable cardioverter defibrillator to prevent inappropriate shocks resulting from rapid atrial fibrillation☆

Akinori Sairaku [a,b,*,1], Yukihiko Yoshida [a,1], Yukiko Nakano [b,1], Yasuki Kihara [b,1]

[a] Department of Cardiology, Nagoya Daini Red Cross Hospital, Nagoya, Japan
[b] Department of Cardiology, Graduate School of Medicine, Hiroshima University, Hiroshima, Japan

- 104 BS Pts, 97.1% M, mean age 48±14 yrs
- ICD implantation 2009-2011
  Single VF zone > 188 (Nagoya)/200 bpm (Hiroshima)
- 20 Pts (19.2%) paroxismal AF
- 6 Pts (5.8%) Inappropriate shocks from Rapid AF

6 ablation procedure (4 single and 2 re-do procedure)
Electroanatomic mapping (CARTO Biosense Webster). PV isolation by means of circumferential lesion.

After the last procedure, no AF recurrence without AAD during a median FU period of 43.2 [range 19.9-74.4] months

Sairaki, A. *Int J Cardiol* 2013. http://dx.doi.org/10.1016/j.ijcard.2013.08.016 . IN PRESS

CONCLUSIONS

- Inappropriate ICD shocks remain a major problem, particularly in a primary prevention setting
- A wide spectrum of prevention options exists (ICD programming, pharmacological therapy, ablation)
- But the most effective option in avoiding inappropriate shocks is to avoid inappropriate ICD implantations

Back-up Slides

The Fidelis experience: the past

The NEW ENGLAND JOURNAL of MEDICINE

Perspective
MARCH 6, 2008

Maisel WH. N Engl J Med 2008;358:985-7

Semper Fidelis — Consumer Protection for Patients with Implanted Medical Devices

William H. Maisel, M.D., M.P.H.

When the Food and Drug Administration (FDA) approved the Medtronic Sprint Fidelis implantable cardioverter–defibrillator (ICD) lead in 2004 on the basis of bench testing but no human clinical data, there was no public outcry. Physicians rapidly incorporated the new electrode into their practice, welcoming its small diameter and ease of implantation.

During the ensuing 3 years, 90% of Medtronic ICDs were implanted with this lead (see diagram). But in October 2007, after 38 months on the U.S. market and 268,000 implantations worldwide, the Fidelis was voluntarily recalled by Medtronic because of its propensity to fracture.

The Fidelis experience

Leads in Registry

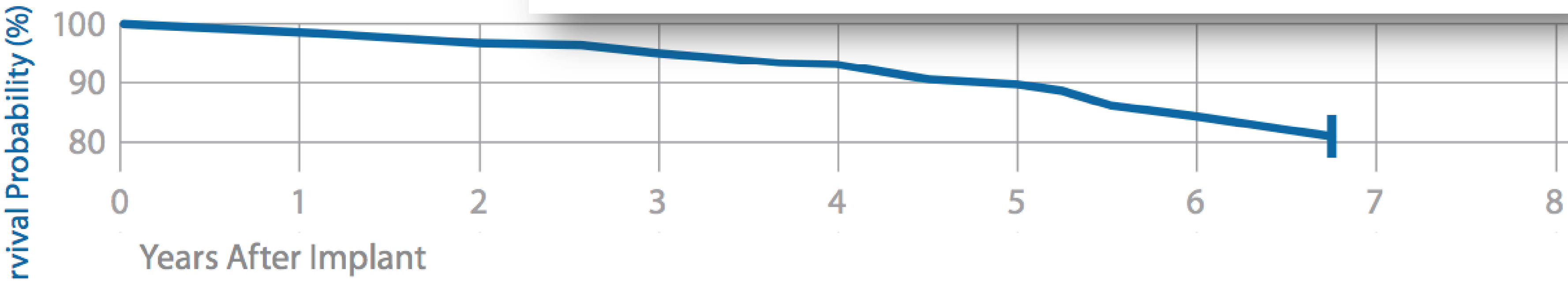
Product Surveillance Registry Results

Number of Leads Enrolled in Study	795
Cumulative Months of Follow-Up	37,326
Number of Leads Active in Study	241

Qualifying complications

Qualifying Complications 75 Total

Conductor Fracture	36	Insulation (not further defined)	2
Failure to Capture	2	Lead Dislodgement	1
Failure to Sense	4	Oversensing	15
Impedance Out of Range	14	Unspecified Clinical Failure	1



	1 yr	2 yr	3 yr	4 yr	5 yr	6 yr	at 81 mo
%	98.7	96.9	94.2	92.4	89.4	84.3	81
# Effective Sample Size	706	612	505	377	263	125	57

Medtronic, Product Performance Report, 1st Issue 2013,March 2013

Lead electrical parameters may not predict integrity of the Sprint Fidelis ICD lead

Melanie Maytin, MD, Laurence M. Epstein, MD

From the Brigham & Women's Hospital, Harvard Medical School, Boston, Massachusetts.

Maytin M et al. Heart Rhythm 2012;9:1446-51

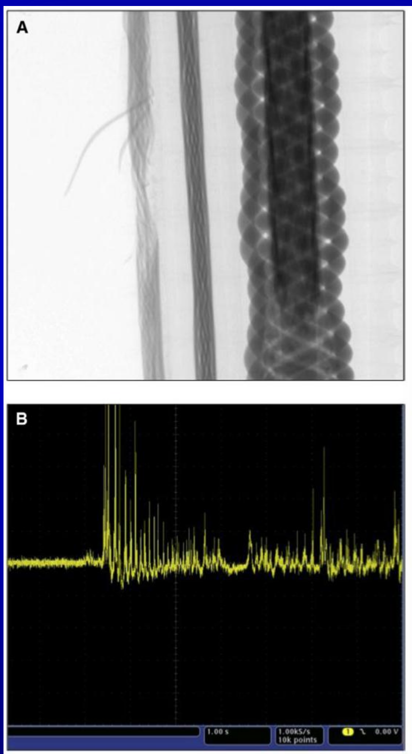


Figure 3 Radiographic and oscilloscope analysis of a Sprint Fidelis 6949 lead with fracture of high-voltage sense cable. **A:** X-ray image showing a chronic wear fracture of the sense cable. **B:** Oscilloscope trace showing indications of fracture as fluctuations are seen in the resistance of the sense cable during lead manipulation.

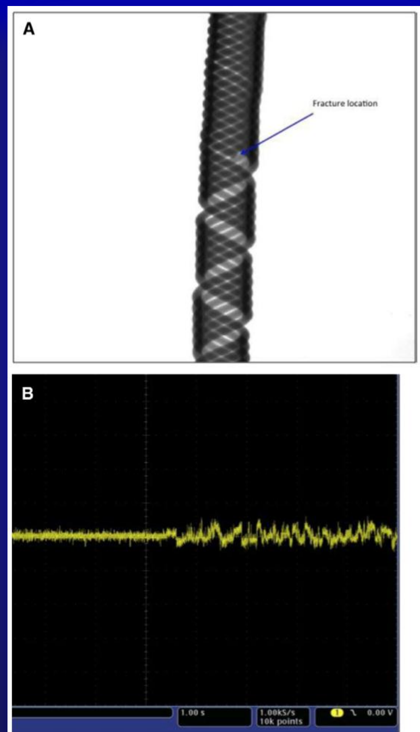


Figure 2 Radiographic and oscilloscope analysis of a Sprint Fidelis 6949 lead with fatigue fracture of pacing coil. **A:** X-ray image showing a pacing coil with a flex fatigue fracture where 1 of the 6 filars is fractured. **B:** Oscilloscope trace showing indications of fracture as fluctuations are seen in the resistance of the pacing coil during lead manipulation.

209 Sprint Fidelis leads
Sept 2005 – Jan 2011
Dwelling time 38.9 mos (0.2-67,2)

<u>Leads extracted:</u>

- Active, normal functioning: 63,1% (84% prophylactically, 9% infections, 7% other indications)
- Clinical evididence of fracture: 36,9%

<u>Extraction</u>:

- Simple traction 39.5%
- Laser assistance 59,9%
- Surgical (CT) 1 case

<u>Analysis</u> of 99 "normal" functioning leads:

- Fractures: 20 leads (20,2%) not related to LE
    - 4/20 (20%) more than 1 fracture
    - 1/20 (5%) 3 separate fracture sites
    - 17 pacing conductor (10 proximal and 7 distal)
    - 6 high-voltage conductor (1 SVC and 5 RV)

Failure of impedance monitoring to prevent adverse clinical events caused by fracture of a recalled high-voltage implantable cardioverter-defibrillator lead

Linda M. Kallinen, BS, Robert G. Hauser, MD, FHRS, Ken W. Lee, MD, Adrian K. Almquist, MD, William T. Katsiyiannis, MD, Chuen Y. Tang, MD, Daniel P. Melby, MD, Charles C. Gornick, MD

From the Minneapolis Heart Institute Foundation, Minneapolis, Minnesota.

Heart Rhythm 2008;5:775-9

Impedance monitoring

December 2004 - February 2008

514 Sprint Fidelis leads at Minneapolis Heart Institute

Lead failure: 17/514 (3.3%) after 23,8±8,0 months (range 11 – 35)

Lead failure n=17 (3,3)	
P/S conductor fractures	15 (88)
HV defects	2 (12)

P/S conductor fractures n=15	
Inappropriate shocks	12
Oversensing	13

Inappropriate shocks n=12	
No impedance rise	4
Shock within 3 hours impedance > 1000 Ω	2
Alarm not heard	2

Data expressed as counts (and percentages), and mean (±SD)

Impedance monitoring did not prevent inappropriate shocks in two-thirds of patients

Lead integrity alert algorithm decreases inappropriate shocks in patients who have Sprint Fidelis pace-sense conductor fractures

Linda M. Kallinen, BS, FHRS, Robert G. Hauser, MD, FHRS, Chuen Tang, MD, Daniel P. Melby, MD, Adrian K. Almquist, MD, William T. Katsiyiannis, MD, Charles C. Gornick, MD

From the Minneapolis Heart Institute Foundation, Minneapolis, Minnesota.

Lead Integrity Alert

Heart Rhythm 2010;7:1048 –1055

October 2004 - January 2010, 461 Sprint Fidelis leads at Minneapolis Heart Institute

Lead failure: 52/461 (11.3%)

	LIA (n=23)	Non LIA (n=26)	p
Inappropriate shocks	4 (17)	18 (69)	0.0004
# of shocks	3.0 ± 2.0	13.2 ±13.6	0.017
Audible alert effective	6 (35)	16 (70)	0.053

Data expressed as counts (and percentages), and mean (±SD)

Overall, 8 (36%) of 22 patients whose audible alerts were triggered did not immediately hear or recognize the tone.

The LIA appears to be an effective method for detecting most Sprint Fidelis lead fractures and for decreasing the incidence and number of inappropriate shocks. However, a better method for alerting patients and caregivers is needed.

Fidelis lead extraction

Data presented as counts (and percentages), or mean (±SD)

Study population	Years	Follow-up (mos)	# of Leads	Failure	Revisions	New shock lead	Pace/sense lead
Canadian HRS, [1] 25 Centres	July 2004-2009	40	6237	310 (4,9)	469 (7,5)	443 (94,5)	25 (5,3)
Da Costa,[2] St Etienne	Jan 2005-Oct 2007	43±15	218	25 (11,5)	NA	NA	NA
Maytin [3] 5 High-Volume Centres	May 2005-Aug 2009	Dwelling time 27,5±14,2	Retrospective study on outcomes of lead extraction				

1. Parkash l et al. Circulation 2010;121:2384-2387
2. Da Costa et al. Arch Cardiovasc Dis 2012;105, 203-10
3. Maytin et al. J Am Coll Cardiol 2010;56:646–50

Fidelis lead extraction

Data presented as counts (and percentages), or mean (±SD)

Study population	Lead extraction	Manual traction	Laser	Non powered	failure	Complications	Major	Minor	Death
Canadian HRS, 25 Centres [1]	310 (4,9)	163 (66)	82 (33)	3 (1)	51 (11)	68 (14,5)	33 (7,0)	35 (7,5)	2 (0,43)
Da Costa, St Etienne [2]	25 (11,5)	1 (4)	23 (92)	1 (4)	0	2 (8)	0	2 (8)	0
Maytin [3] 5 Centres	348	170 (49,9)	142 (41,9)	27 (7,9)	0	2 (0,6)	0	2 (0,6)	0

1. Parkash l et al. Circulation 2010;121:2384-2387
2. Da Costa et al. Arch Cardiovasc Dis 2012;105, 203-10
3. Maytin et al. J Am Coll Cardiol 2010;56:646–50

THE RIATA PARADIGM: THE PRESENT

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

MARCH 8, 2012

Here We Go Again — Another Failure of Postmarketing Device Surveillance

Robert G. Hauser, M.D.

Hauser, RG. N Eng J Med 2012; 366: 873-5.

Dear Doctor Letter, SJM

ST. JUDE MEDICAL
MORE CONTROL. LESS RISK.

St. Jude Medical
Cardiac Rhythm Management Division
15900 Valley View Court
Sylmar, CA 91342-3577 USA
Tel 818 362 6822
800 423 5611
www.sjm.com

IMPORTANT PRODUCT INFORMATION

St. Jude Medical Riata and Riata ST Silicone Endocardial Leads
Models 1560, 1561, 1562, 1570, 1571, 1572, 1580, 1581, 1582, 1590, 1591, 1592,
7000, 7001, 7002, 7010, 7011, 7040, 7041, 7042

December 15, 2010

Attention: Doctors implanting or following patients with Riata® and Riata ST Silicone Endocardial ICD Leads, all serial numbers.

Dear Doctor:

This letter provides important product information regarding the St. Jude Medical Riata and Riata ST family

Recommendations and Mitigations

Based on the above data and demonstrated superior abrasion resistance of defibrillation leads utilizing Optim insulation, St. Jude Medical is completing the planned phase-out of all models of Riata and Riata ST silicone leads by December 31, 2010.

November 28, 2011 ...

Prevalence of lead failure according to SJM

Source	Date	Type of Lead	Patient population	Period	Insulation abrasion rate (%)
Important product information [(1)]	Dec 15, 2010			9 years [(2)]	0,47
Field safety notice update [(1)]	Nov 28, 2011			10 years [(2)]	0,63
Update on clinical performance-PPR [(1)]	Feb 29, 2012			11 years [(2)]	0,30
Riata lead evauation study, Phase I results [(1)]	Jul 10, 2012	8F	459	6,6±1,5 [(3)]	24
		7F	259	4,8±0,9 [(3)]	9,3

1) Available from: http://riatacommunication.com
2) From market release, June 2001, based on returned leads
3) Prospective study, 718 Pts enrolled in 20 sites in North America, evaluation by fluoroscopy

Prevalence of lead failure in "spontaneous" studies

Author	Year	Study	# Pts	F.U. mos	Lead failure	Conductor fractures	Insulation damages	Dislocation	Perforation
Epstein[1]	2009	OPTIMUM, RHYTHM, PAS	7497	22		0,09	0,13	0,88	0,31
Porterfield[2]	2010	23 US, 5 German Centres	15387	18		0,18	0,21	0,93	0,38
Rordorf[3]	2013	Pavia	182	33	6,3				
Parkash[4]	2013	Can HRS	4358	60	4,6				
Valk[5]	2013	Erasmus MC	374	60	7,8				
Sung[6]	2012	Veteran Affairs	1404	2002-2012	3,3				
Liu[7]	2012	Pittsburgh	627	38	6,1				

1. Epstein AE et al. Heart Rhythm 2009; 6:204-9
2. Porterfield JG et al. JCE 2010;21.551-6
3. Rordorf R et al. Heart Rhythm 2013;10:184–190
4. Parkash R et al. Heart Rhythm 2013;10:692–695
5. Valk SDA et al. Neth Heart J 2013; 21:127–134
6. Sung RK et al. Heart Rhythm 2012;9:1954–1961
7. Liu J et al. Circ Arrhyth Electrophysiol 2012;5:809-14

Electrical abnormalities

Failure rate of the Riata lead under advisory: A report from the CHRS Device Committee

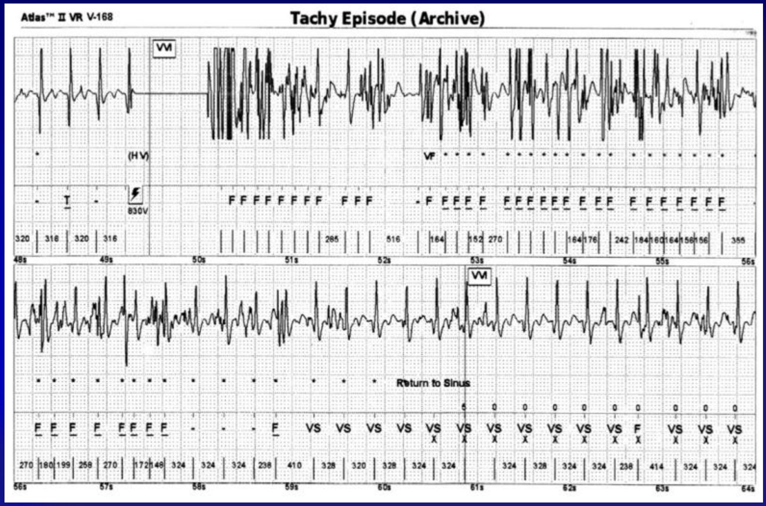
Ratika Parkash, MD, MS, FHRS,[*] Derek Exner, MD, MPH, FHRS,[†] Jean Champagne, MD,[‡] Iqwal Mangat, MD,[§] Bernard Thibault, MD,[¶] Jeffrey S. Healey, MD, MSc,[‖] Stanley Tung, MD,[#] Eugene Crystal, MD,[**] Christopher Simpson, MD,[††] Pablo B. Nery, MD,[‡‡] Laurence Sterns, MD,[§§] Sean Connors, MD,[¶¶] Doug Cameron, MD,[‖‖] Atul Verma, MD,[##] Marianne Beardsall,[##] Kevin Wolfe, MD,[***] Vidal Essebag, MD, PhD,[†††] Felix Ayala-Paredes, MD,[‡‡‡] Shubhayan Sanatani, MD,[§§§] Benoit Coutu, MD,[¶¶¶] Jennifer Fraser, XX,[‖‖‖] Satish Toal, MD,[###] Francois Philippon, MD, FHRS,[‡] Anthony S.L. Tang, MD,[§§] Raymond Yee, MD,[****] Andrew Krahn, MD, FHRS[††††]

Parkash R et al. Heart Rhythm 2013;10:692–695

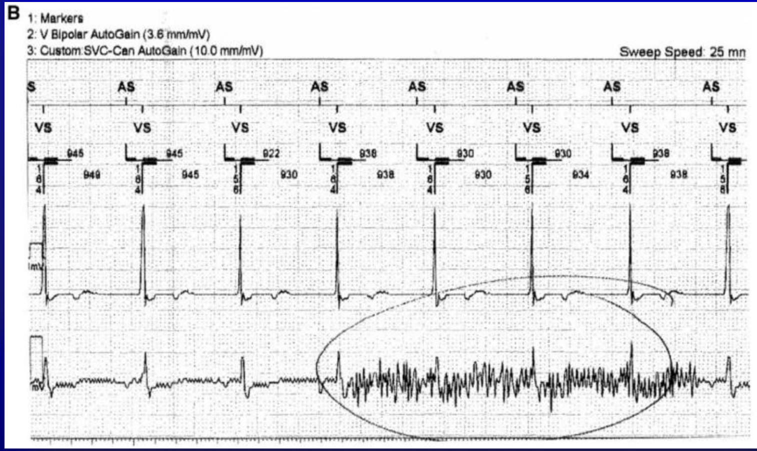
Table 2 Presentation of electrical failure

Clinical manifestation	n (%)	15xx	70xx
Increased threshold	88 (43.8)	67%	33%
Impedance rise or out of range	60 (29.9)*	55%	45%
Oversensing or nonsustained ventricular tachycardia	48 (23.9)	67%	33%
Inappropriate shock	32 (15.9)	72%	28%
More than 1 electrical abnormality	60 (29.9)	—	—
Cable externalization + electrical abnormality	16 (8.0)	—	—
Death	1 (0.50)	0%	1%

*Fourteen leads had an impedance change alone, with no other abnormality.



Electrical near-feld noise in Larsen JM et al. Heart Rhythm 2013;10:821–827



Electrical far-field noise in Liu J et al. *Circ Arrhythm Electrophysiol* 2012;5;809-814

Conductor externalization at Fluoroscopy

Author/Study	Year	# Pts/screen	Techn.	DT	FU	CE %	8F/7F %	Risk Factors	Pref. site
Kodoth/Irish (1)	2012	212/165	F, 15 fps	62,7±13,4	3,98±1,43 yrs	15	26,9/4,7	Young age, DT, single-coil, MA	NA
Erkapic[(2)]	2011	357	R		42±24 mos	8	NA	niCMP, UA	TVc 20%
Schmutz/Bern (3)	2013	52	F		71±18 mos	11,5	NA	NA	TVc 100%
Liu/Pittsburgh[(4)]	2012	369/245	F, 15-30 fps	5,7±1,5 yrs		21,6		Younger age, DT, 8F UA	
Shen/Northwestern[(5)]	2012	189/84	F	67±25 mos		27.4		DT, septal position, additinal RV	
Parvathaneni/ Veteran Adm [(6)]	2012	x/87	F, 15 fps	5,9±3,4 yrs		43		DT, Riata 15xx, MA	TVc
Riata lead evaluation study[(7)]	2012	x/718	F, 15 fps	4,4 (7F single) to 6,7 (8F dual) yrs		18,7	24/9,3	8F dual -> 8F single -> 7F single	
Theuns, Netherlands[(8)]	2013	x/1029	F	59±7 mos		14,3	ST 7000: 5% 1582: 37,3%	DT UA	TVc 77%
Steinberg/Que…	2013	522/284	F	6 yrs		24,3	ST 7000: 7%	8F, DT MA	

Conductors’ externalization at Fluoroscopy

LIST OF ABBREVIATIONS

Year: year of publication; # Pts/screen: number of paients,/screened cohort, excluding dead and missed at FU; Techn. : thecnique employed to detect CE; F: fluoroscopy; DA: direct analysis of explanted leads; R: revision due to failure; FU/DT: follow up/dwelling time; CE: conductors’externalization; niCMP: non ischemic cardiomyopathy; UA univaruate analysis; MA: multivariate analyssis; Pref. site: preferential site of location of CE; NA not assesed; TV: tricuspid valve crossing

REFERENCES

1. Kodoth VN et al. PACE 2012;351498-504
2. Erkapic D, JCE 2011;22:1018-22
3. Schmutz M et al. Int J Cardio 2013;167:254-7
4. Liu et al. Cic Arrhythm Electrophysiol 2012;5:809-14
5. Shen et al.2012; JCE
6. Parvathaneni SV et al. Heart Rhythm 2012;9:1218 –1224
7. Riata lead evaluation study. 2012. http//riatacommunication.com
8. Theuns DAMJ et al. *Circ Arrhythm Electrophysiol* 2012;5;1059-1063
9. Steinberg C et al. Europace 2013;15, 402–408

Study population

Retrospective multicentre study

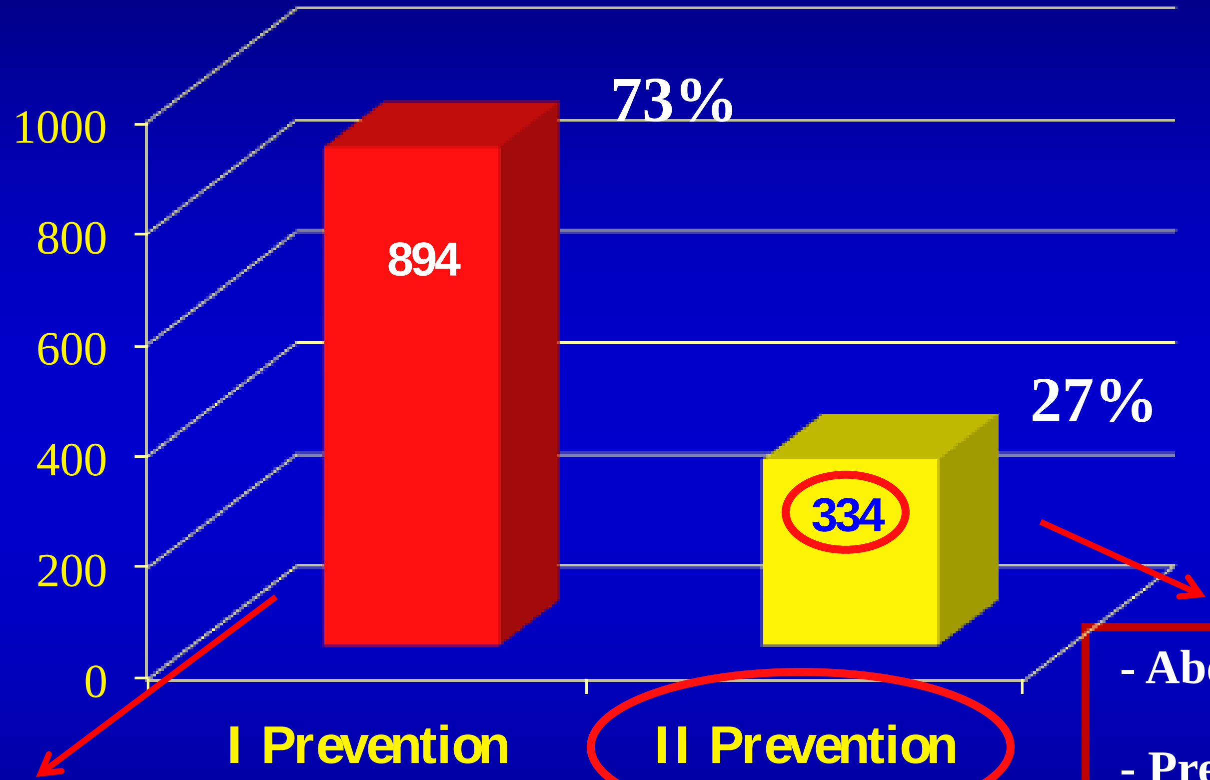
ICD implantations, I and II prevention
from 1/01/2005 ato31/12/2010

Azienda Città della Salute e della Scienza di Torino
University and Hospital Cardiology

ASTI | **BIELLA** | **PINEROLO** | **ORBASSANO**

1228 Pts

1228 patients



At risk of SCD, LV dysfunction, no previous arrhythmia

FOLLOW-UP
Median 34 mos
(25-75pct:18-52)

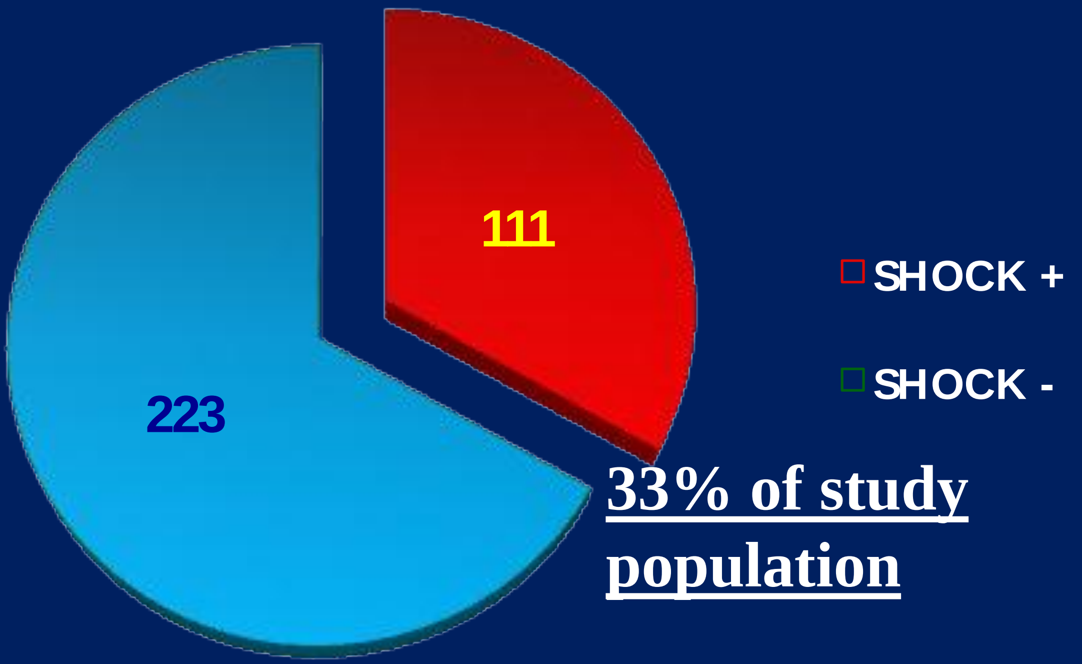
- Aborted SD
- Previous unstable sVT
- Syncope and + EPS

Descriptive statistics

Overall characteristics	N°	%
# of Patients (M/F)	334 (277/57)	82,9%/17,1%
Age, yrs mean ± SD	69,6 ± 12,6	
HR, mean ± SD	70,9 ± 13,7	
EF, %, mean ± SD	37,3 ± 12,7	
EF < 35%	165	49,4%
NYHA I-II	254	76,1
NYHA III-IV	80	23,9
Normal Sinus Rhythm	273	80,5%
Previous AF	97	29%
AF at follow-up	38	12,2%
Hypertension	193	58,3%
Dyslipidemia	101	30,5%
Diabetes	69	20,8%

Shock incidence

At least one shock
(appropriate or inappropriate ones)

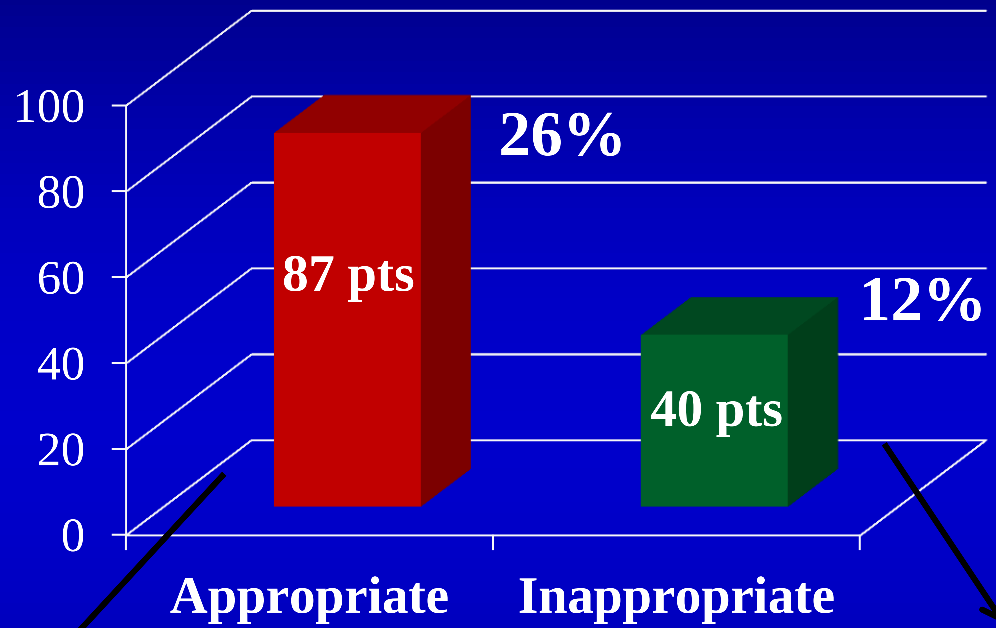


33% of study population

Tot 334

Mean number of shocks per pt: 1,14

Incidence of appropriate and inappropriate shocks



VT	61 (70%)
VF	26 (30%)

AF	27 (67,5%)
SVT	6 (15%)
Oversensing	3 (7,5%)
Noise	2 (5%)
EGM NA	2 (5%)

Shock predictive factors

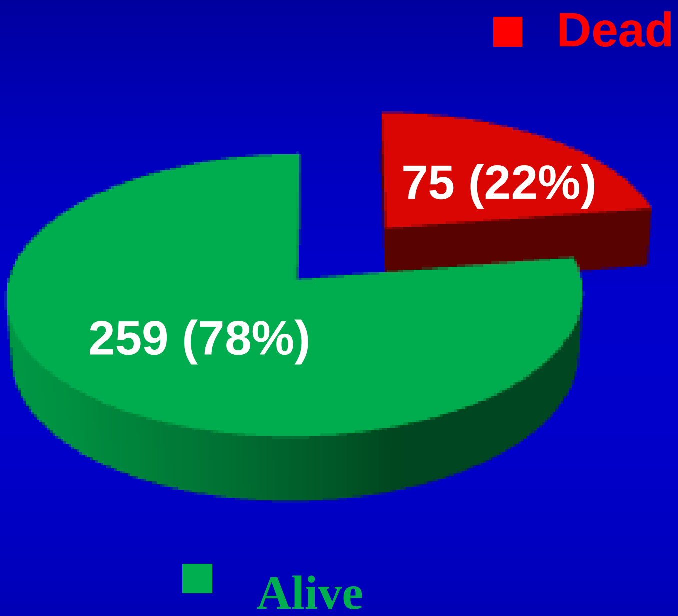
Appropriate Shocks

Variable	R.R.	χ 2	95% CI
Age > 65 yrs	1,09	p = 0,74	0,62-1,92
NYHAClass IV (vs III)	1,95	p = 0,37	0,33-11,39
Previous AMI	1,47	p = 0,13	0,88-2,44
Chronic renal failure	1,47	p = 0,17	0,84-2,57
EF < 30%	1,08	p = 0,79	0,59-1,95
Valvular HD	1,26	p = 0,42	0,71-2,22

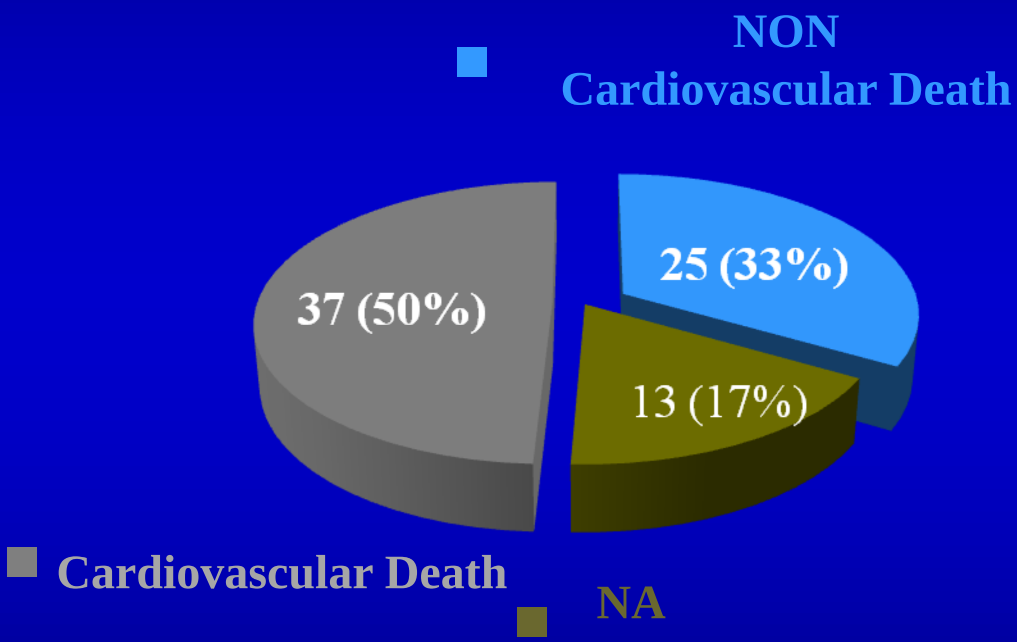
Inappropriate Shocks

Variable	R.R.	χ 2	95% CI
Female gender	1,92	p = 0,09	0,88-4,22
CAD (vs DCM)	3,46	p = 0,08	0,78-15,38
NYHA IV (vs III)	1,95	p = 0,44	0,33-11,39
Hypertension	1,32	p = 0,43	0,65-2,68
EF < 30%	1,91	p = 0,07	0,92-3,95
Previous AF	4,93	p=0,0001	2,12-11,44

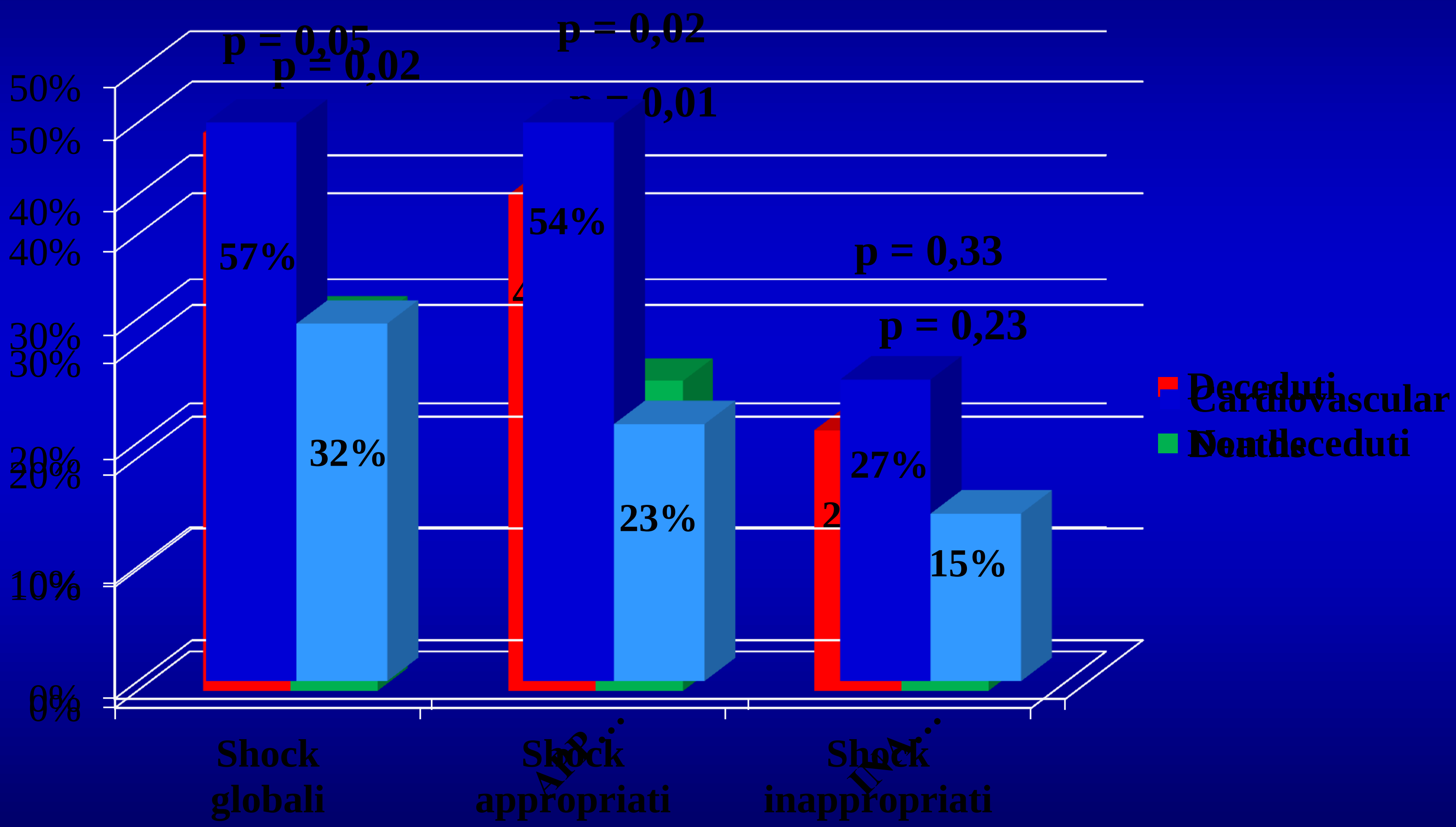
Deaths



Cause of Death



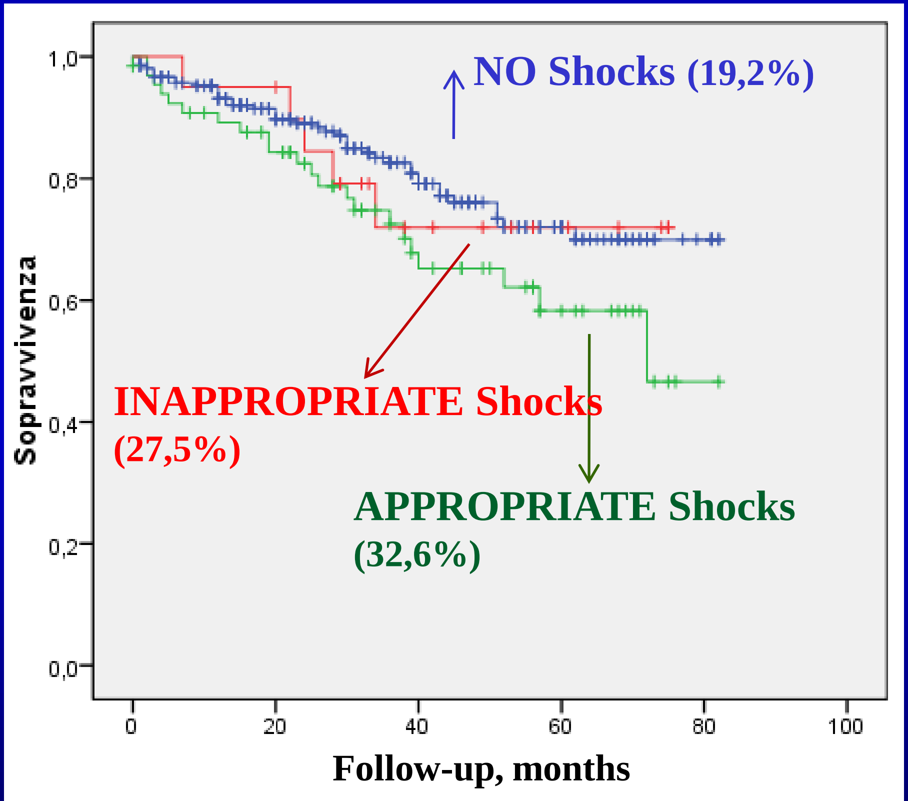
Mortality and shocks



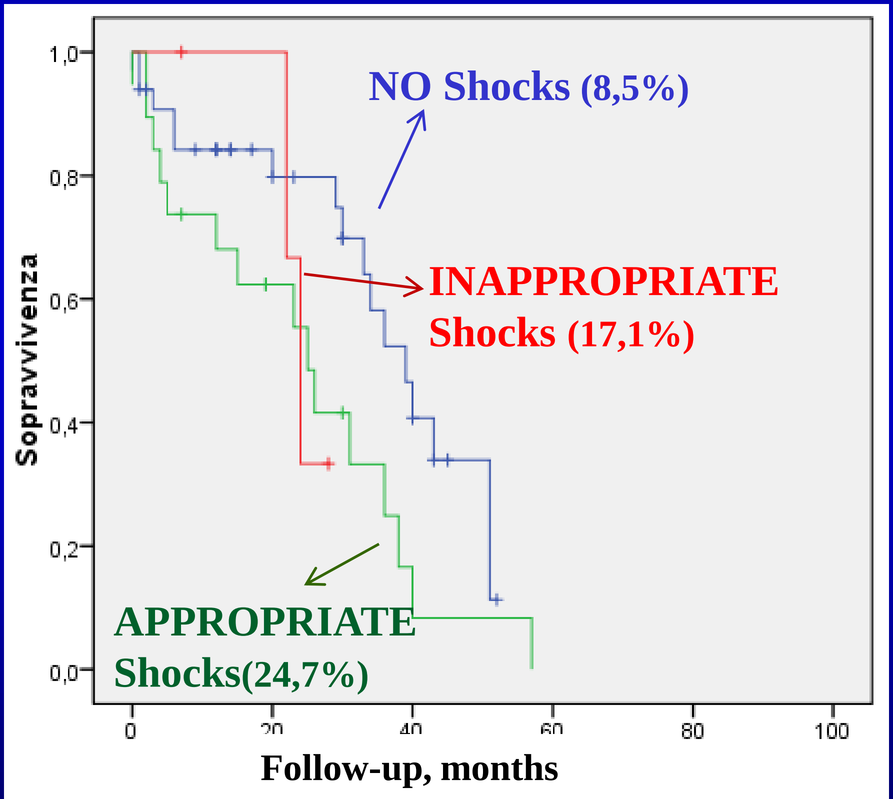
Mortality and Shocks

Kaplan-Meyer Actuarial Survival Curves

All-cause Mortality



Cardiovascular mortality

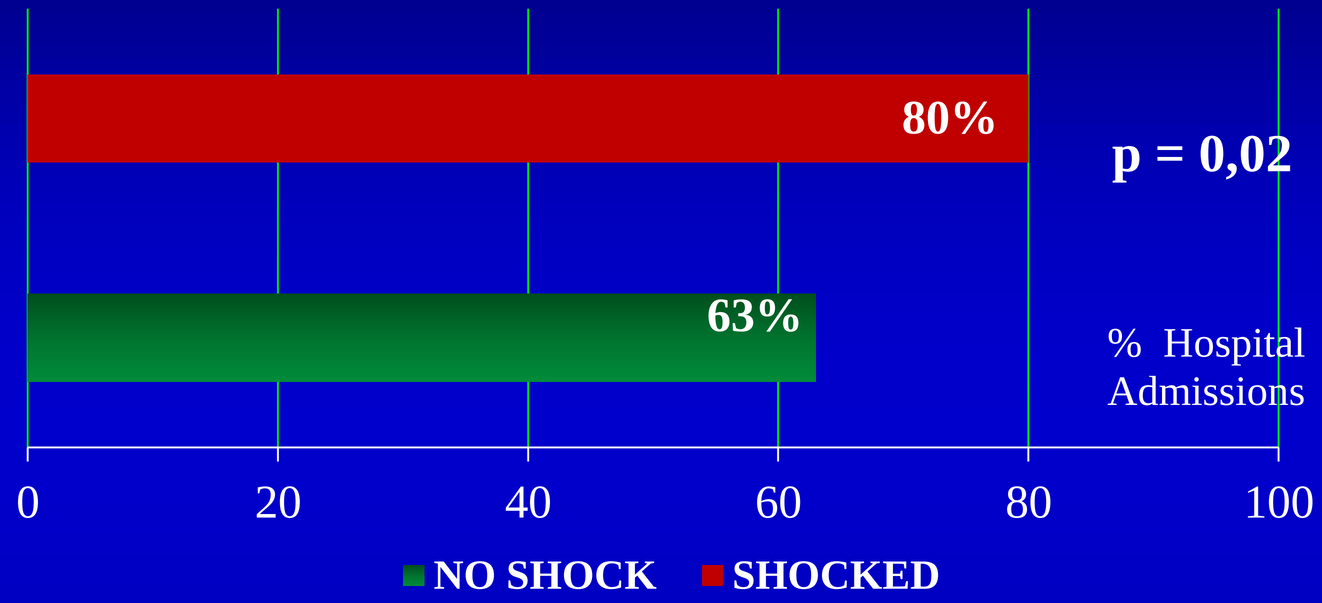


Mortality Predictive Factors

Multivariate Analysis

Variable	R.R.	χ 2	95% CI
APPROPRIATE Shocks	2,07	p = 0,027	1,08-3,95
NYHA Class III-IV	2,05	p = 0,037	1,04-4,01
EF < 35%	1,85	p = 0,05	0,97-3,52
Age > 65 years	1,60	p = 0,23	0,73-2,81
Chronic Renal Failure	2,18	p = 0,017	1,15-4,14
Hypertension	1,43	p = 0,29	0,73-2,81
B-Blocker Therapy	0,36	p = 0,007	0,17-0,75

Shocks and Hospital Admissions



Overall incidence of any shock (appropriate and inappropriate ones) increases Hospital Admissions