AAD versus Ablation for VT

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FACULTY/PRESENTER DISCLOSURE

- Faculty: J. David Burkhardt
- Relationships with commercial interests:
  - Speakers Bureau/Honoraria: Biosense-Webster, St. Jude, Stereotaxis, Boeringer-Ingelheim

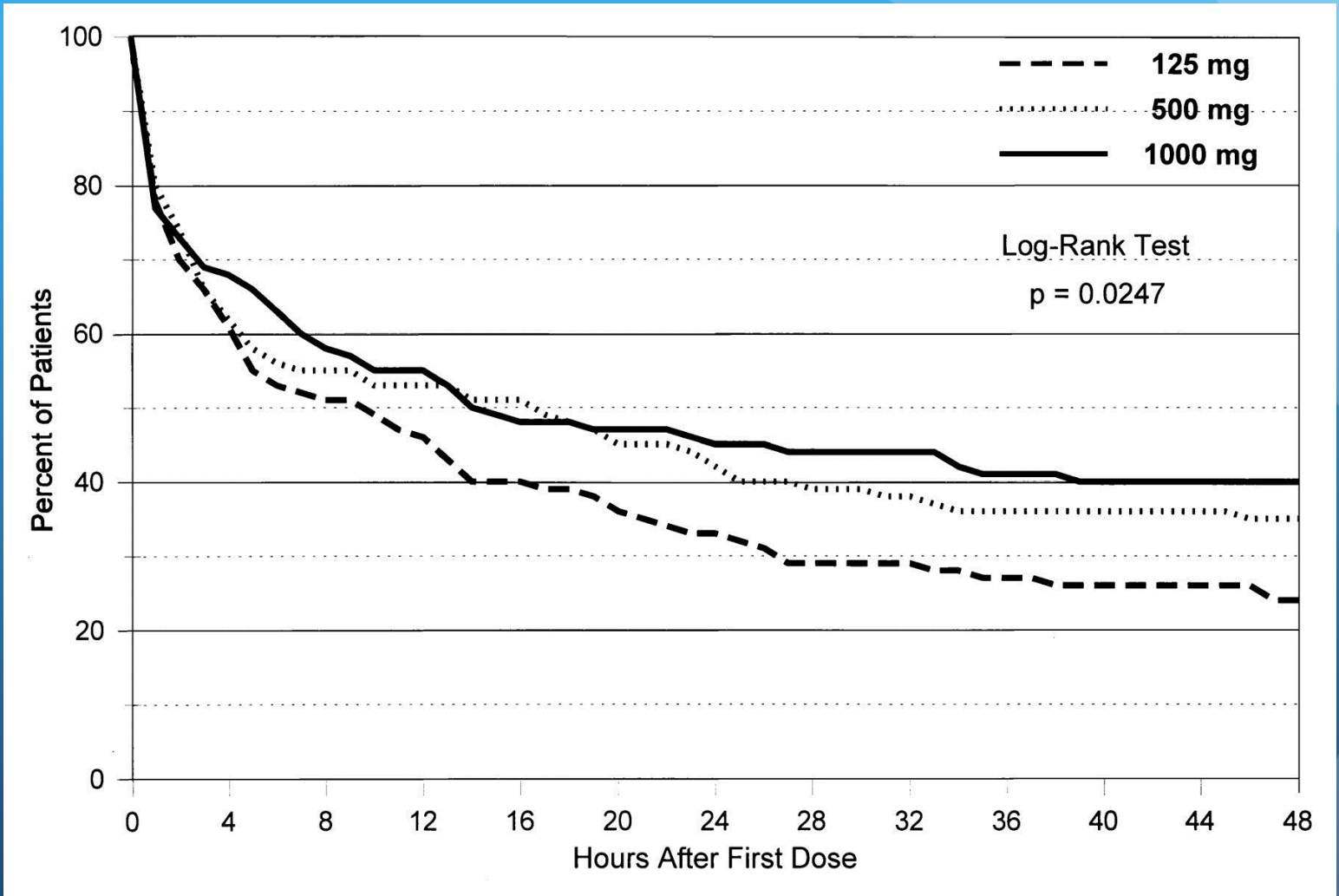

FAIL

Why Not AADs

- 1. They don’t work well
- 2. They kill you
- 3. They have bad side effects
- 4. They are not very cost effective

They Don’t Work Well

Graph of time to first event analysis demonstrates significant differences among the dose groups (P=.0247).



Scheinman M M et al. Circulation. 1995;92:3264-3272

American Heart Association.

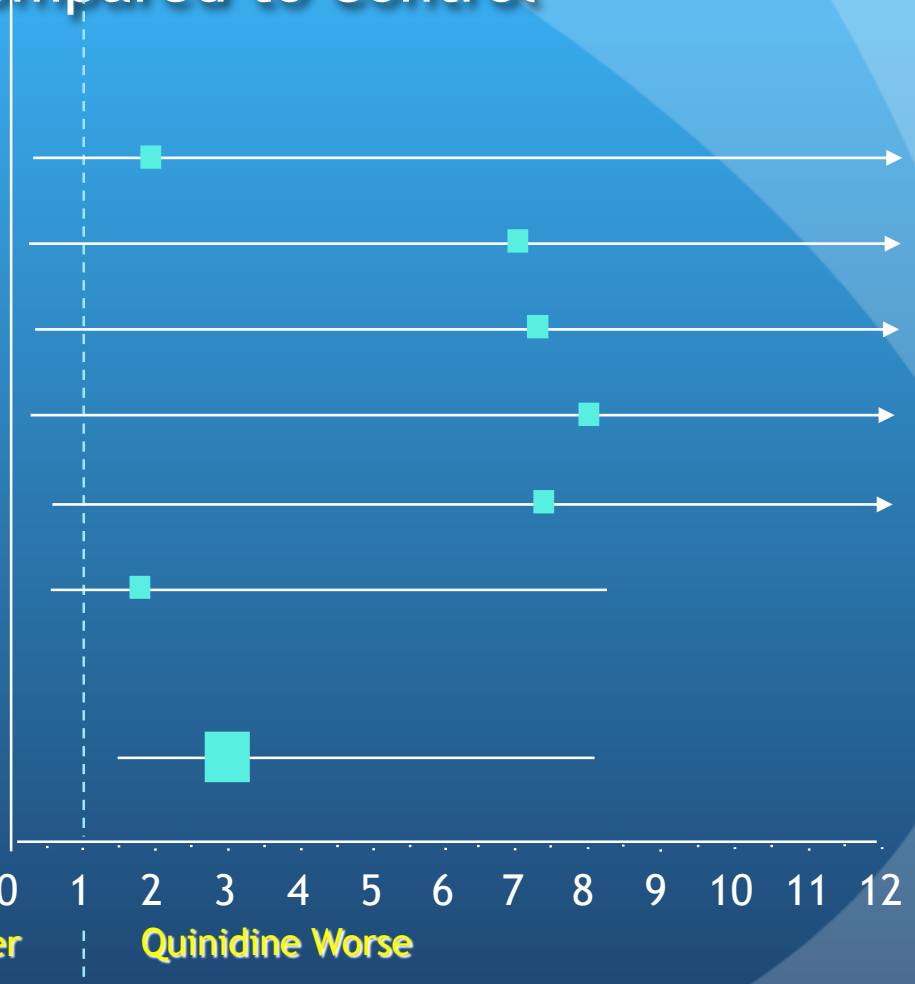
They Kill You


FAIL

Odds Ratio for Total Mortality for Patients Treated with Quinidine Compared to Control

RCT	n
Boissel	212
Byrne-Quinn	92
Hartel	175
Hillestad	100
Lloyd	53
Sodermark	176

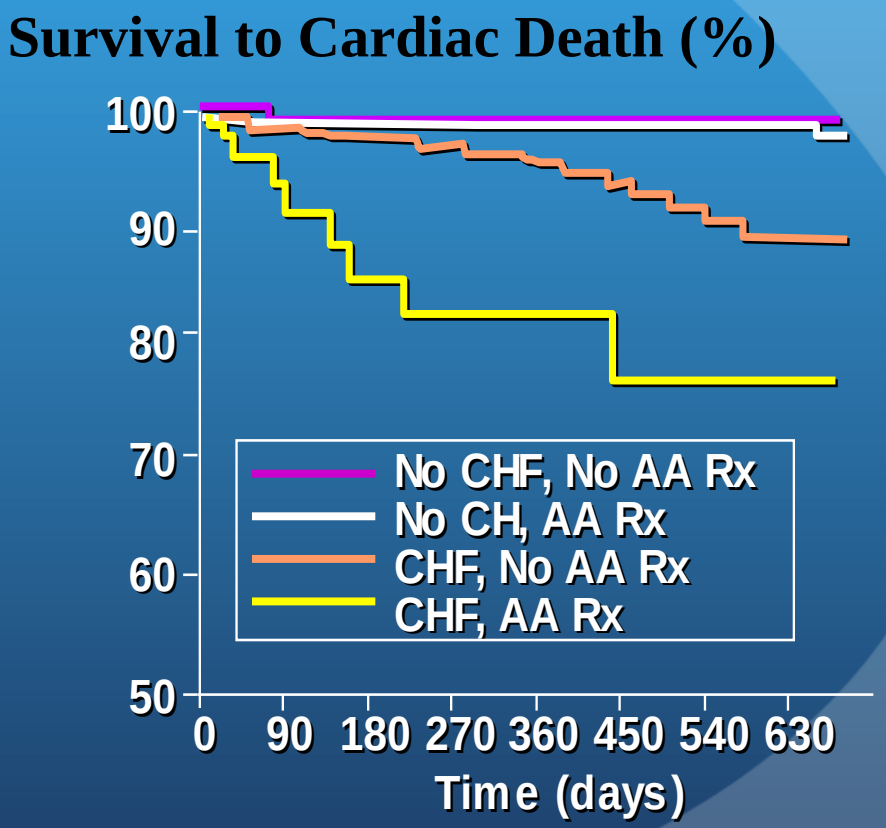
ALL STUDIES N = 808



Coplen SE. Circulation. 1990;82:1106-1116.

Antiarrhythmic Drug Risk
SPAF Trial

- 2.5X risk with antiarrhythmic treatment
- Arrhythmia deaths 2.6X
- CHF: cardiac death risk increased to 4.7X



Rhythm Control for Atrial Fibrillation:

Antiarrhythmic Drug Therapy

No Structural Heart Disease	LVH Without Ischemia or Conduction Defect	Ischemic Heart Disease	CHF
propafenone	propafenone†	sotalol	amiodarone
flecainide	flecainide†	dofetilide	dofetilide
disopyramide*	sotalol	amiodarone	+/- sotalol
sotalol	dofetilide	dronaderone	? Dronaderone
dofetilide	Amiodarone	avoid class 1C	avoid Class 1C
dronaderone	dronaderone		

They Have Bad Side Effects

From the FDA

- Cordarone has several potentially fatal toxicities, the most important of which is pulmonary toxicity (hypersensitivity pneumonitis or interstitial/alveolar pneumonitis) that has resulted in clinically manifest disease at rates as high as 10 to 17% in some series of patients with ventricular arrhythmias given doses around 400 mg/day, and as abnormal diffusion capacity without symptoms in a much higher percentage of patients. Pulmonary toxicity has been fatal about 10% of the time.

From the FDA

- Even in patients at high risk of arrhythmic death, in whom the toxicity of Cordarone is an acceptable risk, Cordarone poses major management problems that could be life- threatening in a population at risk of sudden death, so that every effort should be made to utilize alternative agents first.

- Not to mention liver, eye, thyroid, skin, and drug interactions.

- Drug Withdrawal is 29% in All VT Trials that include Amiodarone.

It is Not Cost Effective

Calkins et al. Amiodarone VS Ablation Cost Effectiveness Circ 2000

- The favorable cost-effectiveness ratios appear to be due, in part, to the high crossover rate from amiodarone to ablation and the costs associated with amiodarone-related adverse events. These factors contribute toward increasing the 5-year costs and decreasing the quality of life associated with amiodarone.

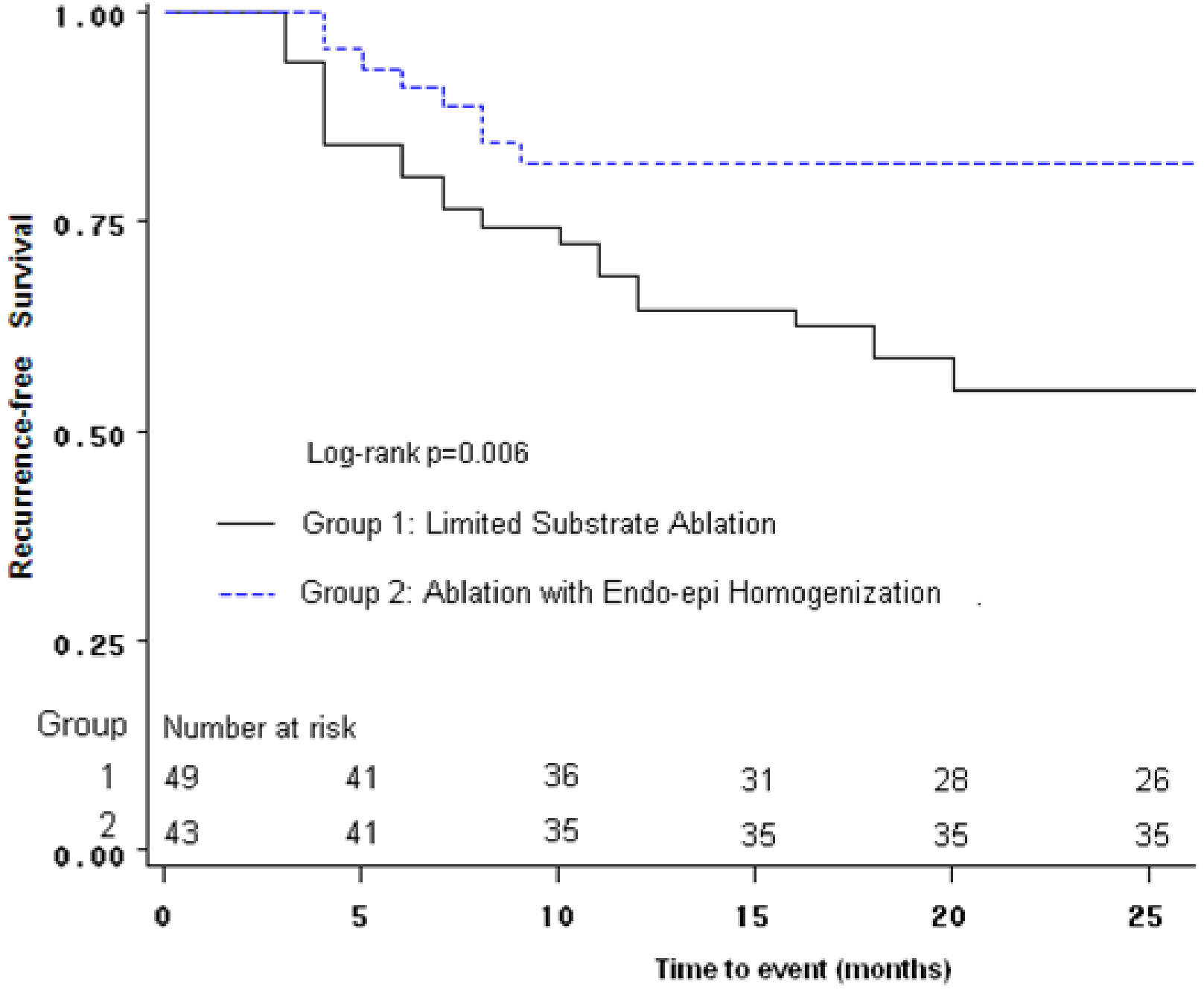
Why Ablation

- 1. It works
- 2. It continues to improve

Trials

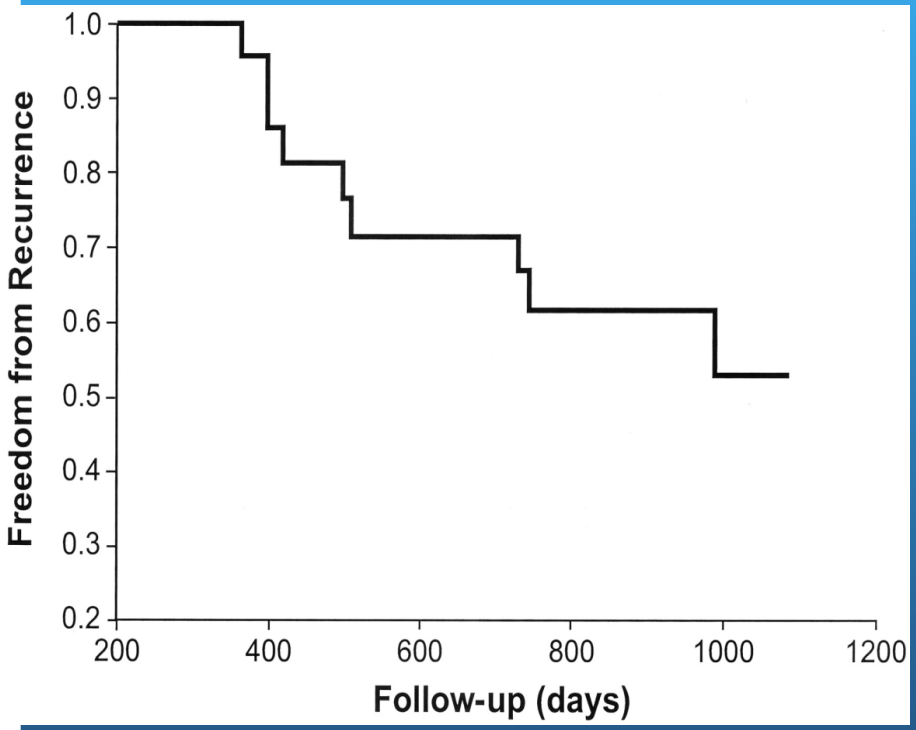
- No good head to head trials
- Consider that most VT Ablation trials are in patients who have failed drugs.

It Works


1.00
0.75
0.50
0.25
0.00
Recurrence-free Survival
Log-rank p=0.006
Group 1: Limited Substrate Ablation
Group 2: Ablation with Endo-epi Homogenization
Group
Number at risk
1 49 41 36 31 28 26
2 43 41 35 35 35 35
0
5
10
15
20
25
Time to event (months)

It Continues to Improve

Catheter Ablation of Ventricular Tachycardia in ARVD: Endocardial Substrate Based Ablation

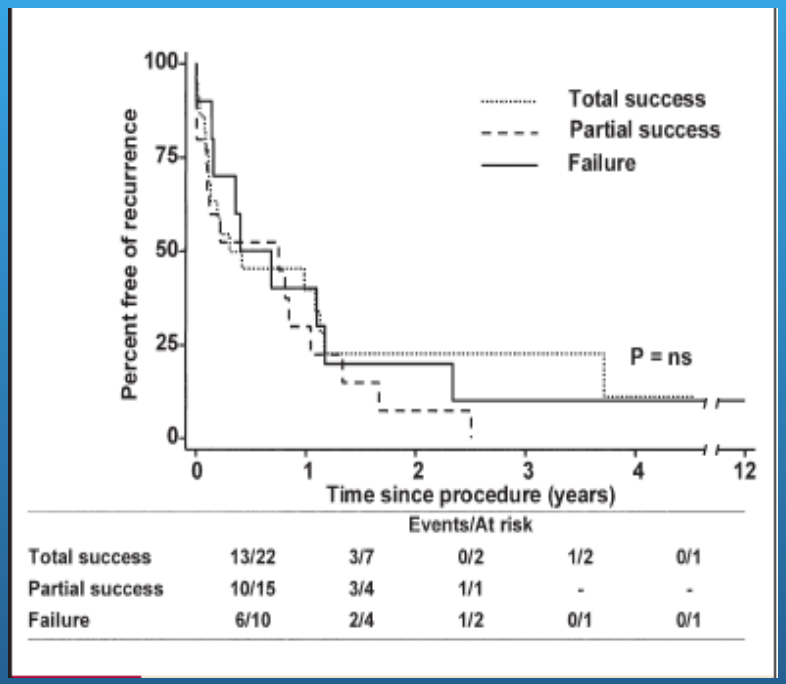


- 22 ARVD patients
- ICD implanted in 18
- Success with elimination of VTs = 53%
- Follow-up = 3 years

In patients with ARVD, freedom from ventricular arrhythmias (VAs) after endocardial ablation is limited at the long term follow-up.

Verma, Natale et al. Circulation 2005;111:3209-3213

Long-Term Efficacy of Catheter Ablation of Ventricular Tachycardia i Patients With Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopa



	Events/At risk				
Total success	13/22	3/7	0/2	1/2	0/1
Partial success	10/15	3/4	1/1	-	-
Failure	6/10	2/4	1/2	0/1	0/1

- 48 ARVD patients
- 75% Success rate after 1.5 months
- 50% Success rate after 5 months
- 25% Success rate after 14 months
- No difference between procedural success, mapping technique and repeat procedure.

This study shows a high rate of recurrence in ARVD/C patients undergoing RFA of VT. This likely reflects the fact hat ARVD/C is a diffuse cardiomyopathy with progressively evolving electrical substrate.

Darshan D, Calkins H et al. JACC : 2007;50, 422-440

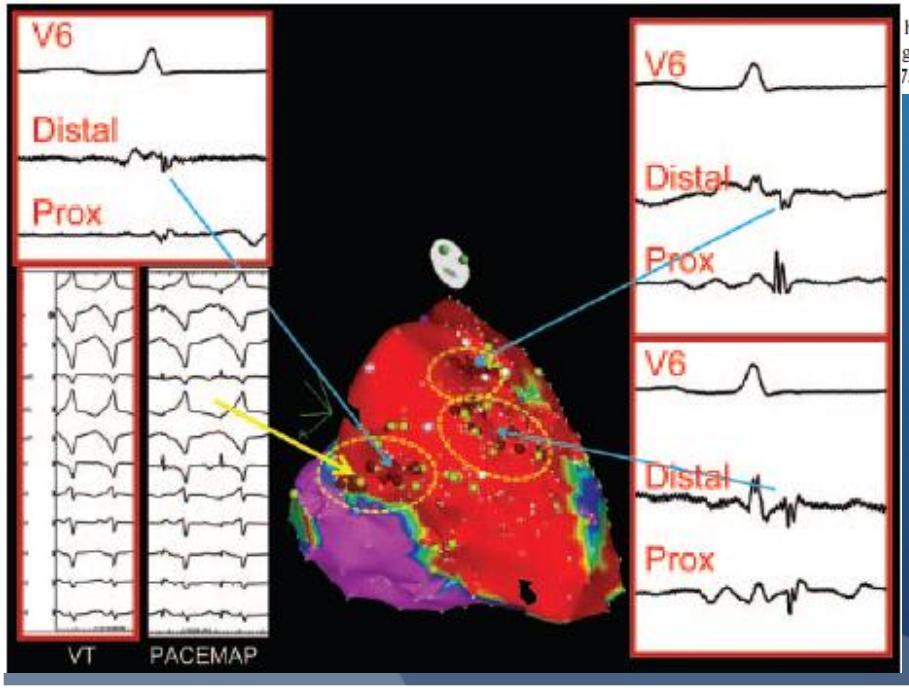
Arrhythmia/Electrophysiology

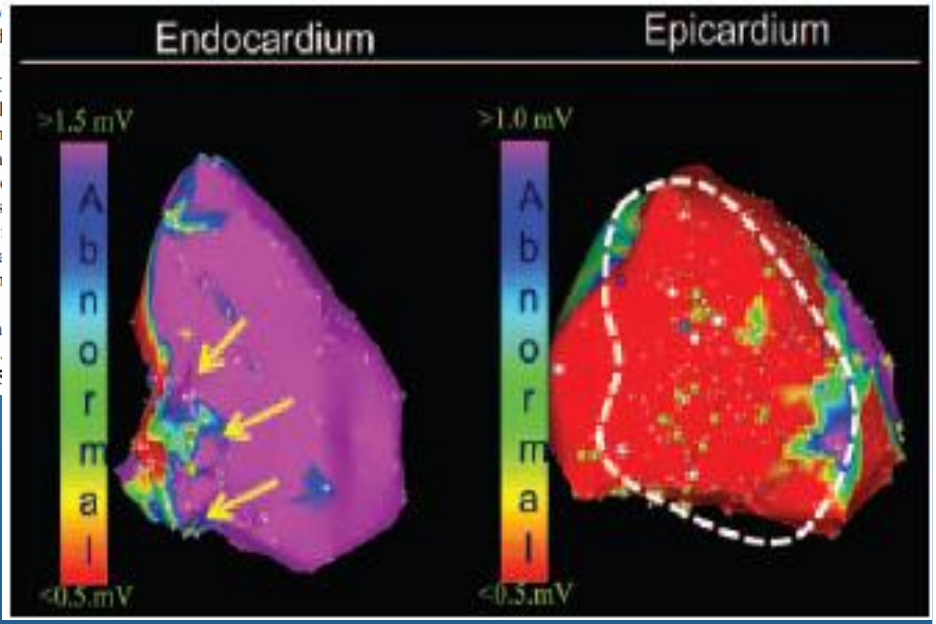
Epicardial Substrate and Outcome With Epicardial Ablation of Ventricular Tachycardia in Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia

Fermin C. Garcia, MD; Victor Bazan, MD; Erica S. Zado, PA-C;
Jian-Fang Ren, MD; Francis E. Marchlinski, MD

Background—Efficacy of endocardial ventricular tachycardia (VT) ablation in arrhythmogenic right ventricular cardiomyopathy/dysplasia may be limited by epicardial VT, right ventricular thickening, or both. We so the endocardial versus epicardial substrate, measure right ventricular free wall thickness, and d ablation efficacy in patients with right ventricular cardiomyopathy/dysplasia.

Methods and Results—Thirteen consecutive patients (3 female; aged 43±15 years; range, 17 to 7(endocardial and epicardial sinus rhythm voltage mapping and epicardial VT ablation after fail ablation were included. In each patient, the low bipolar voltage area (<1.0 mV for epicardium endocardium) was more extensive on the epicardium (95±47 versus 38±32 cm^2; $P<0.001$) and wa by multicomponent and late electrograms. The basal right ventricular thickness assessed by electr >10 mm in 6 of 13 patients compared with 5 to 10 mm in 4 reference patients without structural dis VTs were targeted on the epicardium with the use of activation, entrainment, or pace mapping with and targeting of late potentials. Epicardial VTs were targeted opposite normal endocardium in 10 pa opposite ineffective endocardial ablation sites in 11 patients (85%). During 18±13 months, 10 of th





ABLATION OF VENTRICULAR ARRHYTHMIAS IN RIGHT VENTRICULAR DYSPLASIA: ARRHYTHMIAS FREE SURVIVAL AFTER ENDO-EPICARDIAL SUBSTRATE BASED MAPPING AND ABLATION

AIM OF THE STUDY

We compared the long term freedom from recurrent VAs by using endocardial substrate based ablation versus endo-epicardial substrate based ablation.

Di Biase L., Burkhardt, Natale A et al. AHA 2009

Methods

- 42 patients with ARVD undergoing ablation of VAs have been included.
- All patients had an ICD.
- Conventional and 3D mappings were utilized to identify area of “scar”.
- Clinical VAs were induced with pacing maneuvers or administration of isoproterenol.
- In all cases ablation was performed with 3.5 mm open irrigated catheter.
- In the first 23 patients ablation was performed only endocardially (group 1),

while

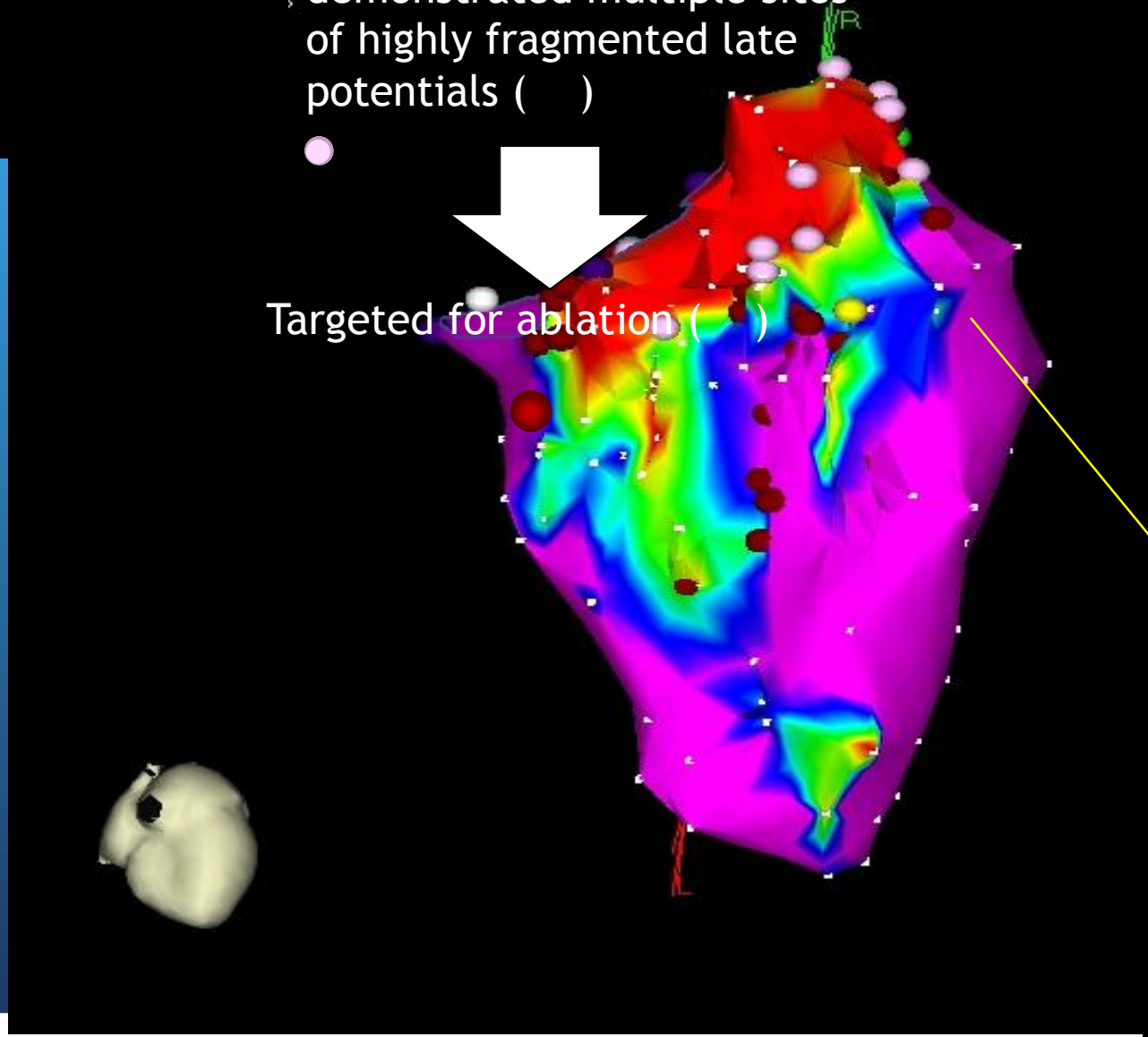
- the remaining 19 underwent endo-epicardial ablation after either failed endocardial ablation (10 pts) or at the time of the first procedure (9 pts) (group 2).

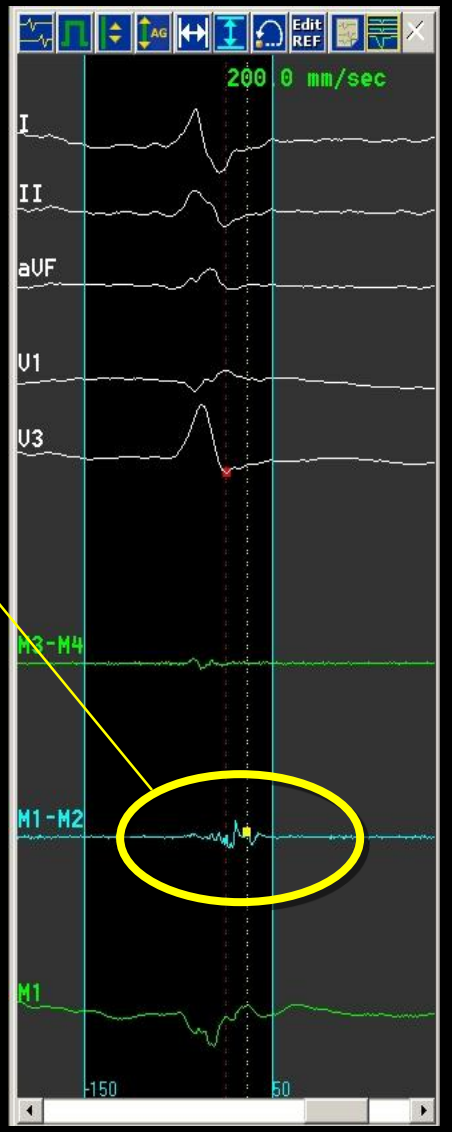
Di Biase L., Burkhardt J D, Natale A et al. AHA 2009

LATE POTENTIALS

Basal inferior wall scar demonstrated multiple sites of highly fragmented late potentials ( )

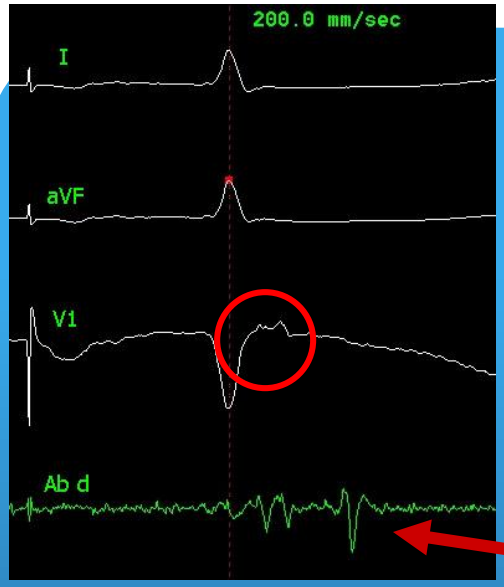
Targeted for ablation ( )

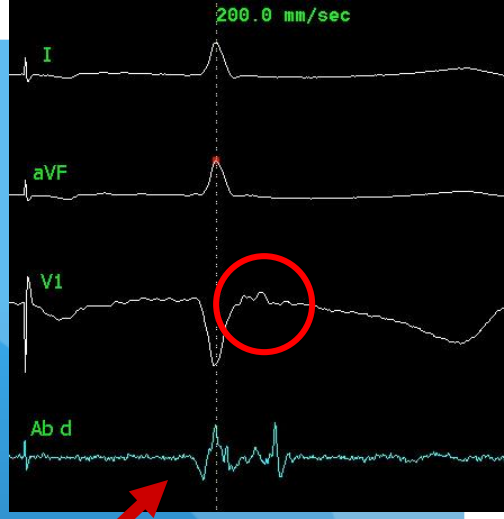


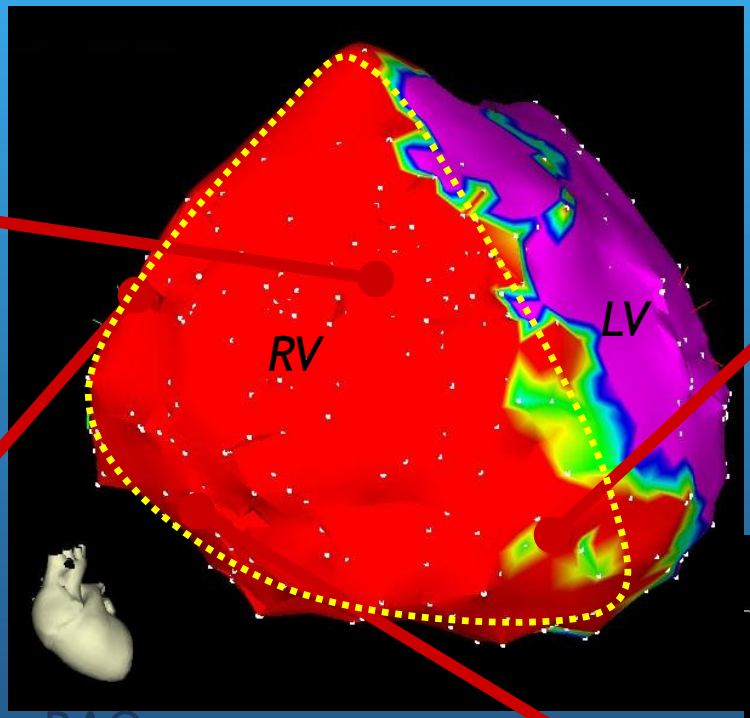


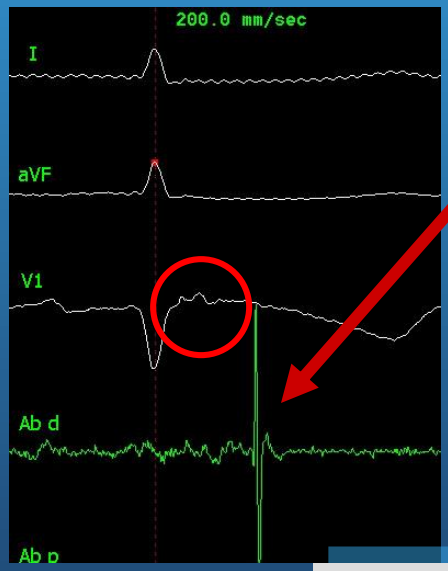
Epicardial SR Voltage Map

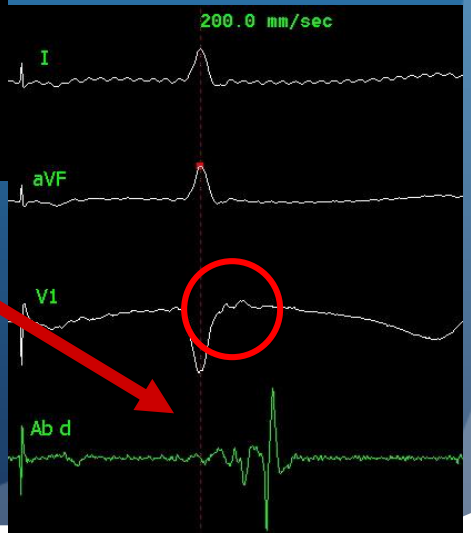
(Color Range – 1.0–0.52 mV







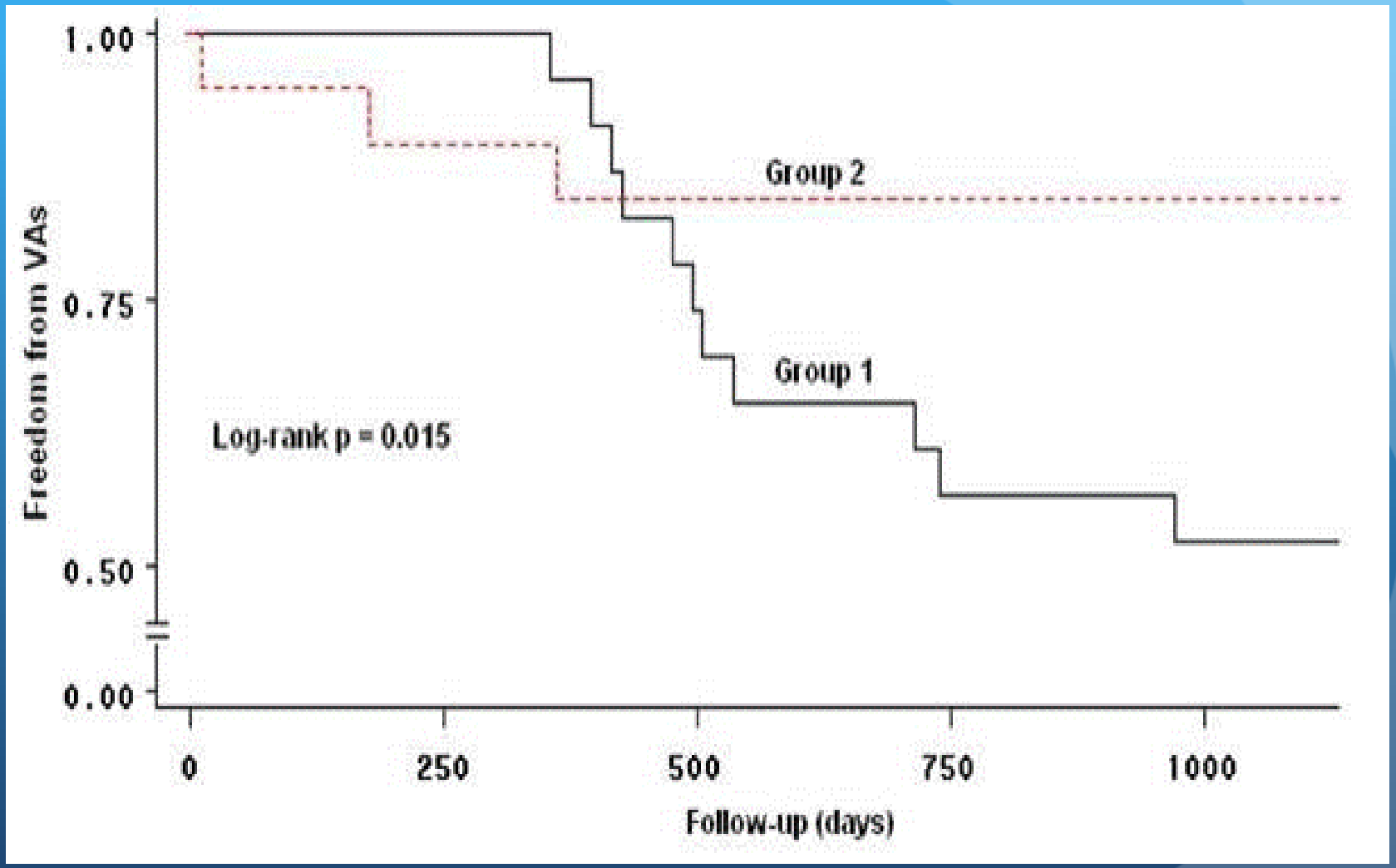




Late and Fractionated

RV Epicardial Electrograms

Results



Di Biase L.,Burkhardt, Natale A et al. AHA 2009

Results

- Out of the 3 patients reporting VA ablation failure in group 2,
  - ✓ one pt had an ICD shock 2 weeks after the procedure,
  - ✓ one had a VT treated with ATP at 6 months follow up,
  - ✓ one had an ICD shock after one year when discontinuing antiarrhytmic drugs (AADs).

- In addition, group 2 patients were more likely to have discontinued AADs (21% in group 1 versus 68% in group 2 $p<0.001$).

Di Biase L.,Burkhardt, Natale A et al. AHA 2009

A story of AADs in VT

Circ 1992

Efficacy of Antiarrhythmic Drugs in Patients With Arrhythmogenic Right Ventricular Disease

Results in Patients With Inducible and Noninducible Ventricular Tachycardia

Thomas Wichter, MD; Martin Borggrefe, MD; Wilhelm Haverkamp, MD;
Xu Chen, MD; and Günter Breithardt, MD, FESC, FACC

AADs in ARVD VT.

- 81 patients with ARVD and documented VT.
- Mean follow up of 34 +/- 25 months
- 26.2% considered drug refractory
- 23.8% of the inducible VT underwent ablation (Before 1992!)

TABLE 3. Drugs and Dosages Used in Patients With Inducible Ventricular Tachycardia

Class	Drug	No. of patients	Dosage (mg/day)
Ia	Disopyramide	10	594±138
	Quinidine	1	600
Ib	Tocainide	1	800
	Mexiletine	16	700±135
Ic	Propafenone	20	728±196
	Flecainide	17	250±50
	Aprindine	8	113±23
	Prajmaline	7	107±41
	Lorcainide	3	333±153
	Diprafenone	1	600
	Barucainide	1	450
III	Sotalol	38	459±100
	Amiodarone	13	400±155*
IV	Verapamil	5	300±120

TABLE 5. Efficacy of Antiarrhythmic Drugs in Patients With Inducible Ventricular Tachycardia

Drug	No. of patients	Overall efficacy		Complete suppression		Partial response	
		No.	%	No.	%	No.	%
Class Ia/b	18	1	5.6	0	0	1	5.6
Class Ic	25	3	12.0	1	4.0	2	8.0
β-Blockers	7	0	0				
Sotalol	38	26	68.4	22	57.9	4	10.5
Amiodarone	13	2	15.4	2	15.4	0	0
Verapamil	5	0	0				
Combinations	26	4	15.4	2	7.7	2	7.7
Two class I drugs	5	0	0				
Class I+β-blocker	7	0	0				
Class I+sotalol	10	2	20.0	2	20	0	0
Class I+amiodarone	4	2	50.0	0	0	2	50.0

Side Effects for Discontinuation

- 9.3% Class1 (GI)
- 5.5% Sotalol (Brady, hypotension, Torsades, CHF)
- Amiodarone 29.4% (thyroid, liver, eye)

Conclusions

- Ablation is superior to AADs in VT
  - More effective
  - Fewer side effects
  - Cost Effective
  - Continues to improve, while drugs drop off.