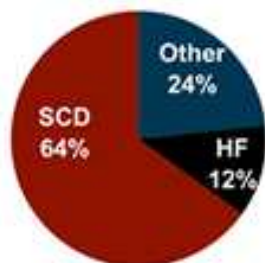# Treatment of VT in NYHA Class IV Heart Failure

Eun Kyoung Kim

Cardiology

Samsung Medical Center
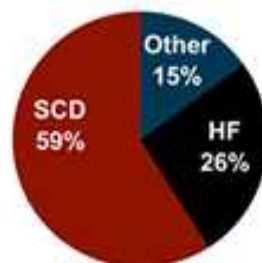
Sudden cardiac death (SCD) in HF

- **Rate of SCD (d/t VT/VF) in HF**
  - 12-15%: in patients with NYHA I-II
  - 50-60%: in patients with NYHA IV

- **Mode of death according to NYHA functional class**

NYHA II — Other 24%, SCD 64%, HF 12% — No. of deaths n = 103

NYHA III — Other 15%, SCD 59%, HF 26% — No. of deaths n = 232
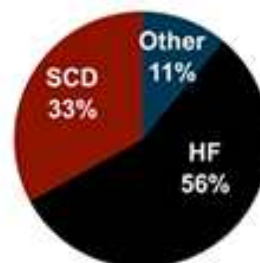
NYHA IV — Other 11%, SCD 33%, HF 56% — No. of deaths n = 27

* SCD prevention strategy

: mainly focused in patients
with mild to moderate CHF

Data from MERIT-HF

# VT management in NYHA IV HF

- **Heterogeneous group**

  - Transient state

  - Refractory state (stage D) : mortality < 1Y without HT

- **Little information regarding VT treatment**

  - *excluded from*

    VT ablation trial & observation study

    Randomized primary prevention ICD trial

  - *included in*

    small number in CRT-D trials

- Observational studies

   (non-randomized series of patients awaiting HT)

   : **increased survival with ICD**

Cumulative Survival
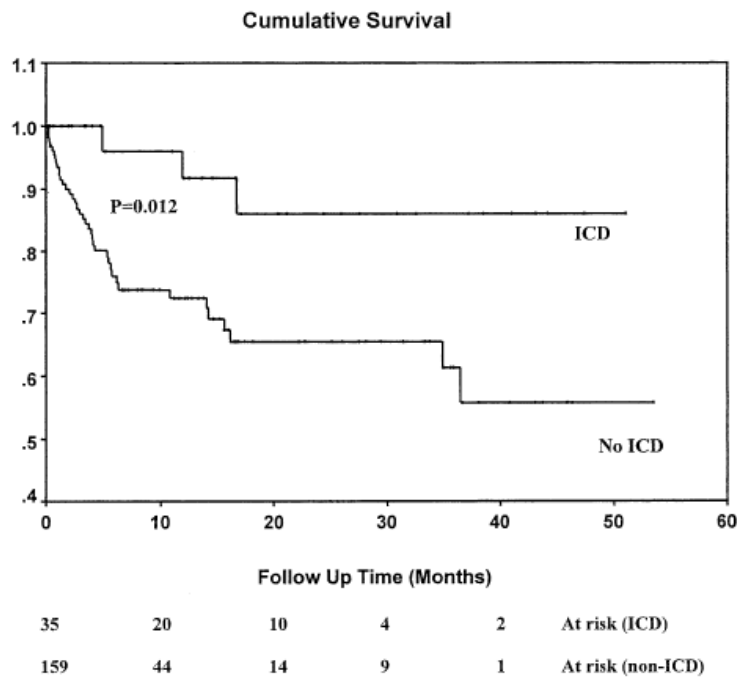
	Hazards ratio	p-value
Male gender	1.004	0.993
Age	0.998	0.876
Ejection fraction	0.984	0.425
Atrial fibrillation	1.420	0.374
Coronary artery disease	0.739	0.389
ACE inhibitors	0.433	0.045*
β-blockers	0.582	0.117
Amiodarone	1.153	0.762
Home inotropic therapy	0.804	0.846
Presence of assist device	1.398	0.510
Tx status 1A	0.779	0.744
Presence of ICD	0.222	0.018*

J Heart Lung Transplant. 2003;22(4):411.
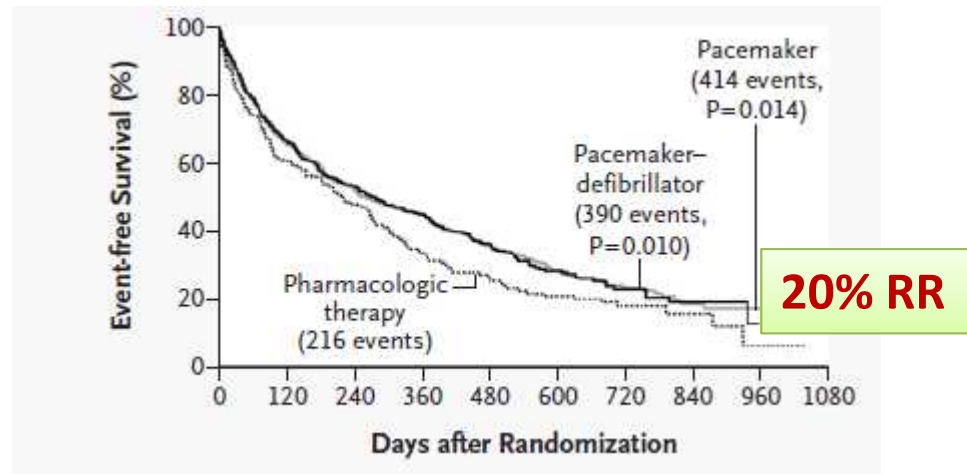
ICD may be considered as a bridging to HT

- **Ambulatory patients with NYHA class IV HF**

- **LVEF > 35%**

- **Narrow QRS complex**

- **Awaiting HT outside the hospital**

COMPANION trial

- 1520 patients with NYHA III/**IV patients** (**219, 14%**)

CRT-D in NYHA IV HF

Reduction of sudden cardiac death
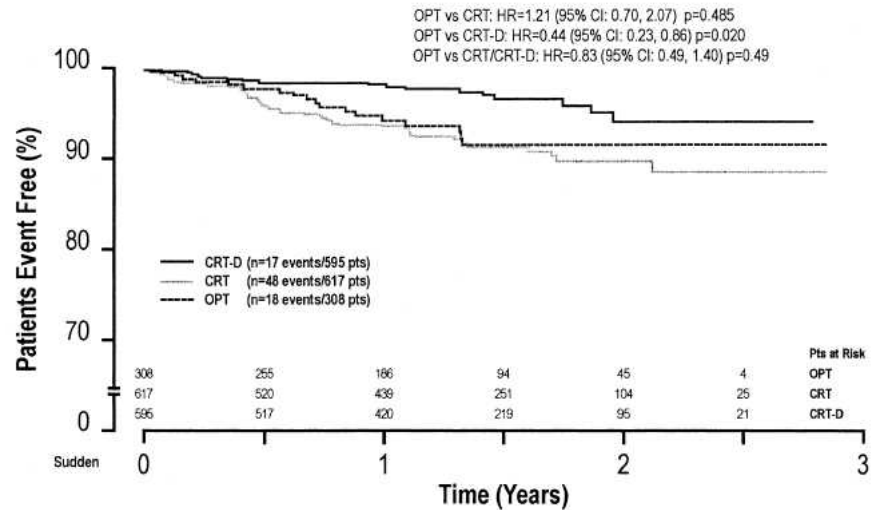
K-M for SCD

K-M for all CD

JACC 2005:46:2329–34
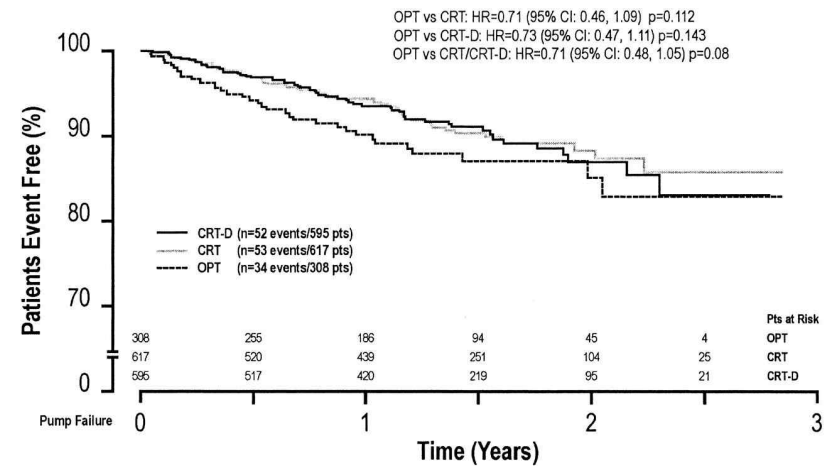
Management of VT in NYHA IV HF

- **Treatment of underlying CMP**

  : Addressing reversible factors

  : Optimizing HF status with maximal medical Tx

- **ICD, CRT-D: protection against SCD**

  But,, **Recurrent ICD shock**

  – increased long-term morbidity and mortality

- **Catheter ablation**

MERIT-HF trial

: 3991 patients with NYHA II-IV (**IV:145,3.6%**)

Reducing mortality

Reducing SCD

Metoprolol better   Placebo better

NYHA II

NYHA III

NYHA IV

Lancet 1999; 353: 2001–07

Bisoprolol on VT in NYHA IV HF

CIBIS-II trial

2647 symptomatic patients with NYHA III/IV (224, 17%)

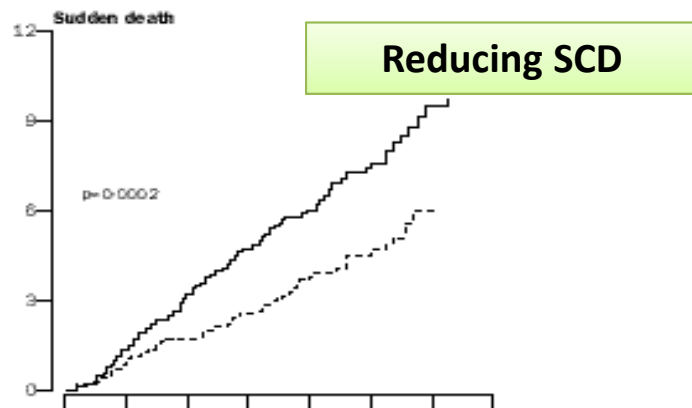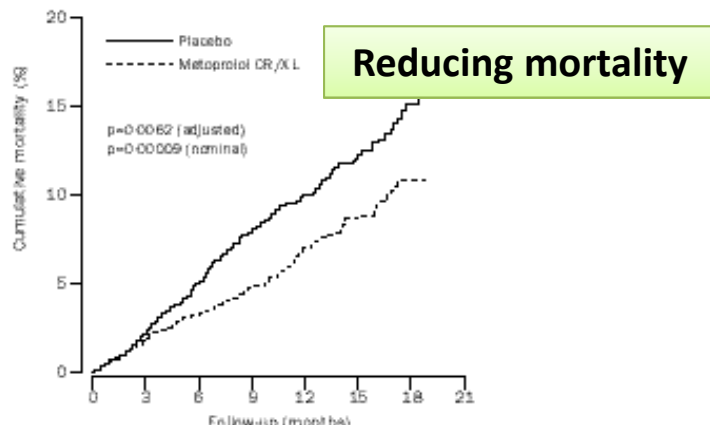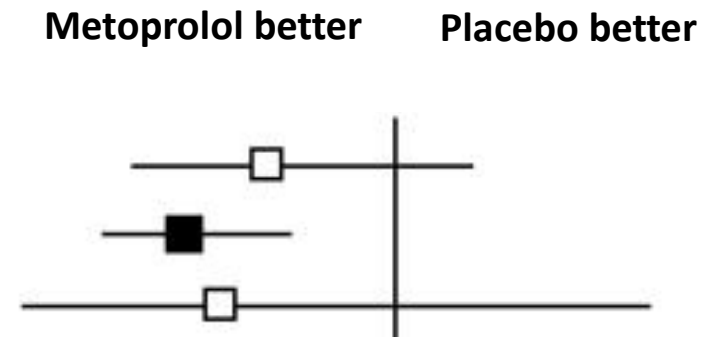|	Placebo (n=1320)	Bisoprolol (n=1327)	Hazard ratio (95% CI)	p
Primary endpoint				
All-cause mortality	228 (17%)	156 (12%)	0·66 (0·54–0·81)	<0·0001
Secondary endpoints				
All-cause hospital admission	513 (39%)	440 (33%)	0·80 (0·71–0·91)	0·0006
All cardiovascular deaths	161 (12%)	119 (9%)	0·71 (0·56–0·90)	0·0049
Combined endpoint	463 (35)	388 (29%)	0·79 (0·69–0·90)	0·0004
Permanent treatment withdrawals	192 (15%)	194 (15%)	1·00 (0·82–1·22)	0·98
Exploratory analyses				
Sudden death	83 (6%)	48 (4%)	0·56 (0·39–0·80)	0·0011
Pump failure	47 (4%)	36 (3%)	0·74 (0·48–1·14)	0·17
Myocardial infarction	8 (1%)	7 (1%)	0·85 (0·31–2·34)	0·75
Other cardiovascular	23 (2%)	28 (2%)	1·17 (0·67–2·03)	0·58
Non-cardiovascular deaths	18 (1%)	14 (1%)	0·75 (0·37–1·50)	0·41
Unknown cause of death	49 (4%)	23 (2%)	0·45 (0·27–0·74)	0·0012
Hospital admission for worsening heart failure	232 (18%)	159 (12%)	0·64 (0·53–0·79)	0·0001

	Bisoprolol (n/total)	Placebo (n/total)
Ischaemia	75/662	121/654
Primary DCM	13/160	15/157
Undefined	68/505	92/509
NYHA III	116/1106	173/1096
NYHA IV	40/221	55/224
Total		

Relative risk 0·4 0·6 0·8 1·0 1·2 1·4 1·6 1·8

Lancet 1999; 353: 9–13
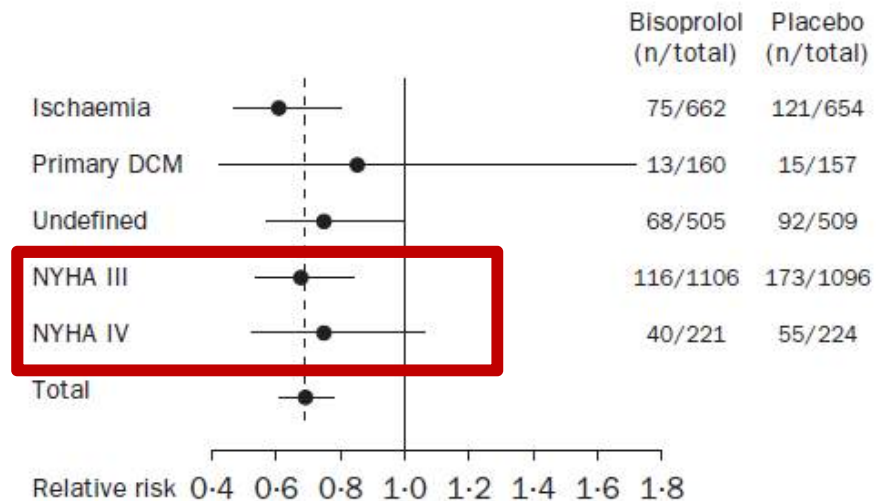
Carvedilol on VT in NYHA IV HF

CAPRICORN trial

: 1959 patients with MI & LVEF < 40%
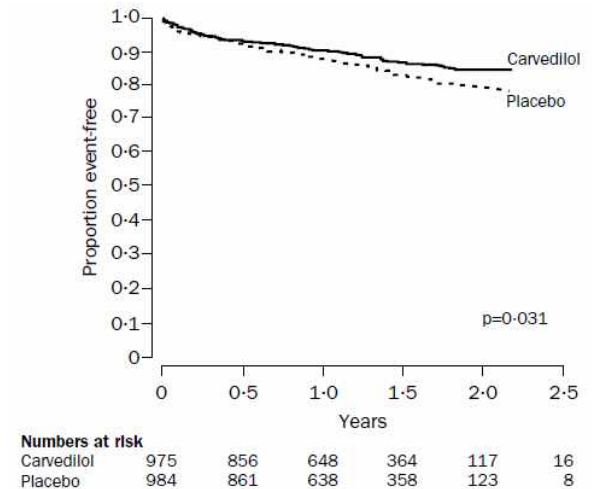
Reducing VT/VF

	Carvedilol group (n=975)	Placebo group (n=984)	Hazard ratio (95% CI)	p
Primary endpoints				
All-cause mortality	116 (12%)	151 (15%)	0·77 (0·60–0·98)	0·031
All-cause mortality or cardiovascular-cause hospital admission	340 (35%)	367 (37%)	0·92 (0·80–1·07)	0·296
Secondary endpoints				
Sudden death	51 (5%)	69 (7%)	0·74 (0·51–1·06)	0·098
Hospital admission for heart failure	118 (12%)	138 (14%)	0·86 (0·67–1·09)	0·215
Other endpoints				
Cardiovascular-cause mortality	104 (11%)	139 (14%)	0·75 (0·58–0·96)	0·024
Death due to heart failure	18 (2%)	30 (3%)	0·60 (0·33–1·07)	0·083
Non-fatal myocardial infarction	34 (3%)	57 (6%)	0·59 (0·39–0·90)	0·014
All-cause mortality or non-fatal myocardial infarction	139 (14%)	192 (20%)	0·71 (0·57–0·89)	0·002

Lancet 2001; 357: 1385–90

COPERNICUS trial

: 2289 patients with HF symptoms at rest or on minimal exertion, who were clinically euvolemic, and who had an EF< 25%

Reducing VT/VF
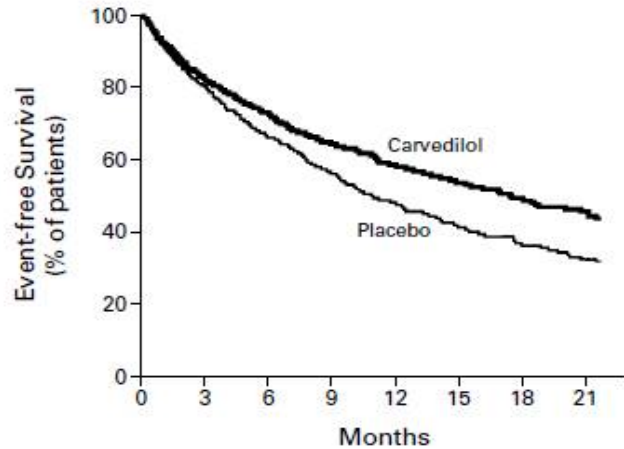
N Engl J Med 2001;344:1651-8
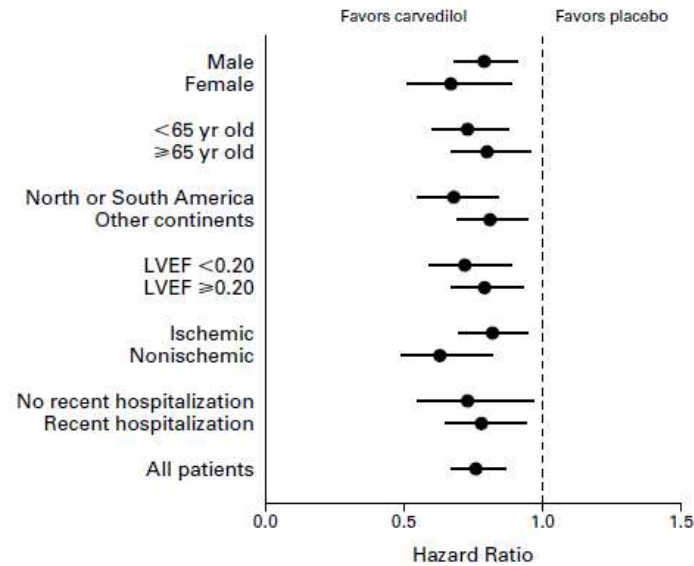
AAD – class I

- Should be avoided in Advanced HF d/t

    Negative inotropic effect

    Potential proarrhythmic action

- **Quinidine** : minimal negative inotropic property

    Mexilletine : can be used with class III

- Increasing SVR, Decreasing CO/SV

AAD – class III

Random trials of class III AAD
: Amiodarone, sotalol, azimilide, celivarone

First Author, Year (Ref. #)	N Included		Age, yrs		ICM		Ejection Fraction		ICD Appropriate Therapy		Deaths	
	AAD	CTRL	AAD	CTRL	AAD	CTRL	AAD	CTRL	AAD	CTRL	AAD	CTRL
Kühlkamp et aL, 1999 (112)	46	47	59 ± 18	64 ± 17	31 (67)	28 (60)	35 ± 8	38 ± 19	15 (33)*	24 (51)*	4 (9)	3 (6)
Pacifico et al., 1999 (43)	151	151	63 ± 11	61 ± 11	110 (73)	100 (66)	37 ± 12	39 ± 14	33 (22)*	49 (32)*	4 (3)	7 (5)
Kettering et al., 2002 (113)	50	50	59 ± 12	60 ± 9	35 (70)	38 (76)	38 ± 15	38 ± 14	30 (60)	33 (66)	6 (12)	8 (16)
Dorian et aL, 2004 (42)	419	214	63 ± 12	62 ± 12	266 (63)	141 (66)	35 ± 13	34 ± 14	247 (59)*	136 (64)*	13 (3)	7 (3)
Singer et al.. 2004 (44)	135	37	66 ± 12	65 ± 11	109 (81)	30 (81)	30 ± 13	34 ± 14	NA	NA	2 (2)	3 (8)
Connolly et al., 2006 (41)												
Amiodarone	140	138	64 ± 11	63 ± 10	111 (79)	111 (80)	34 ± 12	34 ± 12	15 (11)*	45 (33)	6 (4)	2 (1)
Sotalol	134		66 ± 9		109 (81)		34 ± 12		38 (28)		4 (3)	
Kowey et aL, 2011 (114)												
Celivarone	324	109	64 ± 10	65 ± 12	225 (69)	86 (79)	29 ± 8	29 ± 8	194 (59)	66 (61)	28 (9)	6 (6)
Amiodarone	53		67 ± 8		36 (68)		29 ± 8		20 (38)*		9 (17)	

AAD – class III

8 studies, 2,268 patients, 15 months f/u for recurrent VT
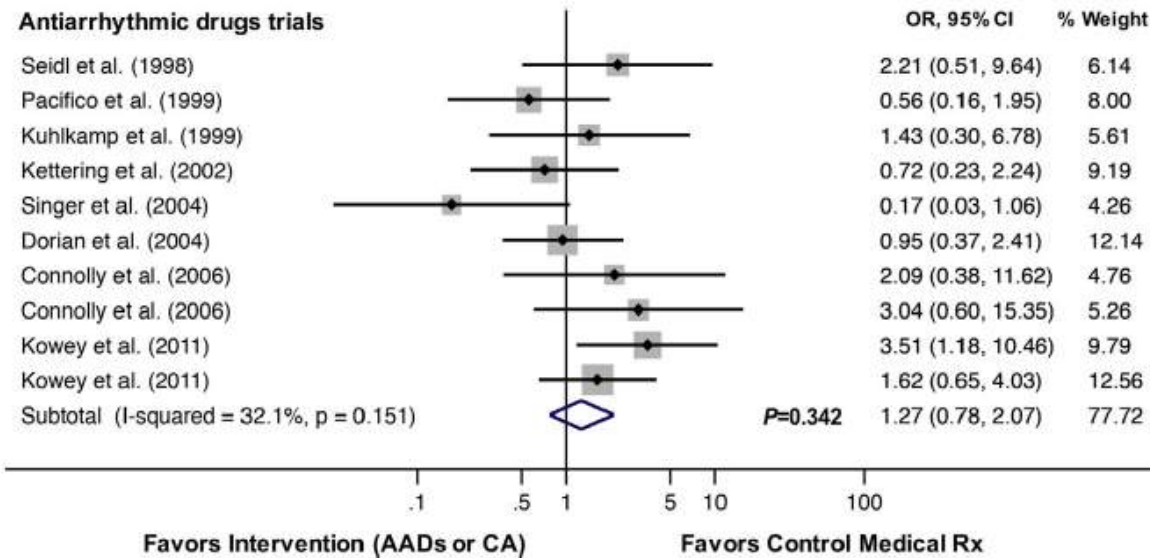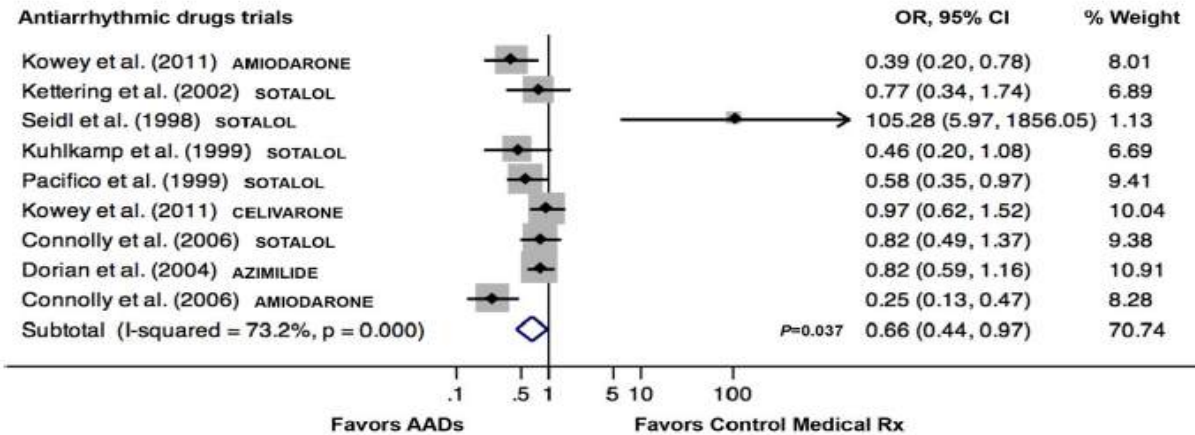
AAD – no data of Amiodarone in NYHA IV HF

- **Reducing all-cause ICD shock**
- **Reducing incidence of SCD**
- **No change of all-cause mortality**

- **Multi-organ side effect**
  : thyroid, skin, pulmonary, hepatic, neuromuscular
- **Potential for symptomatic bradycardia**

Dronedarone

- **All-cause mortality and hospitalization**

- **Warning in NYHA IV or II-III with recent decompensated HF**
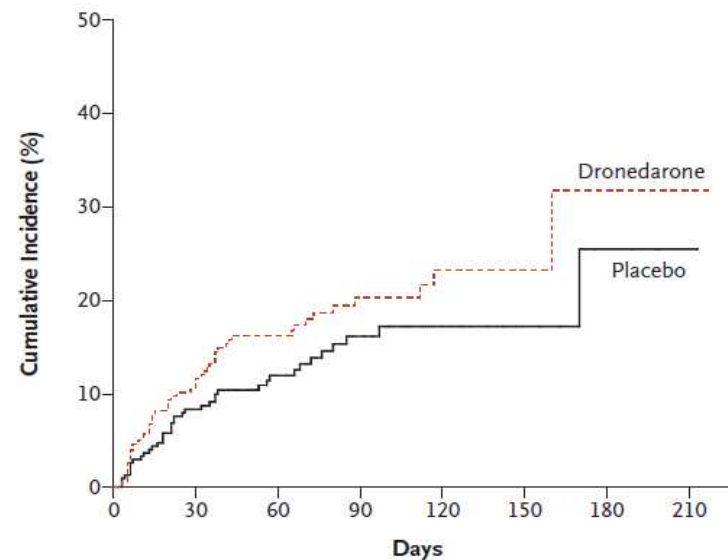
ANDROMEDA, N Engl J Med 2008; 358:2678-2687

Ranolazine

- Inhibits late phase of inward Na+ channel during ischemia
  At higher concentrations, the rapid delayed rectifier K+ channel.

- <u>Anti-ischemic and antiarrhythmic effects</u>

- Multicenter case reports
  in patients with AAD-refractory ICD
  shocks
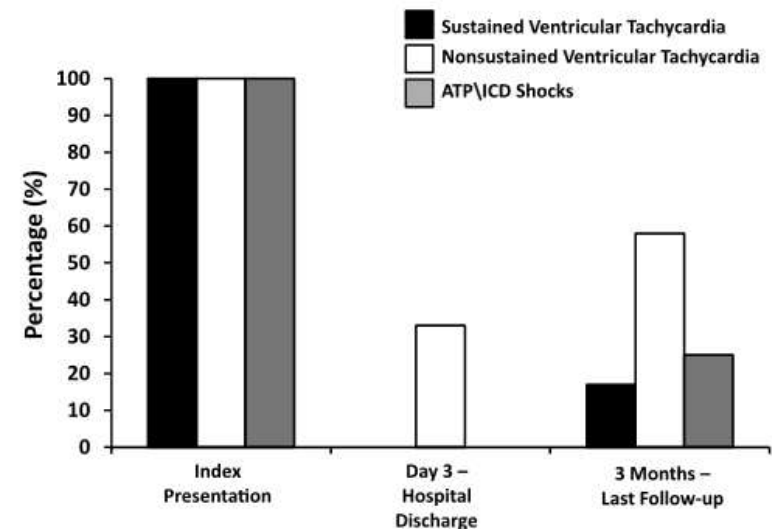
→ **effective in reducing the recurrence of ICD shocks?**

Curr Opin Cardiol 2013, 28:337–343
PACE 2011; 34:1600–1606

Circulation. 2018;138:e272–e391.
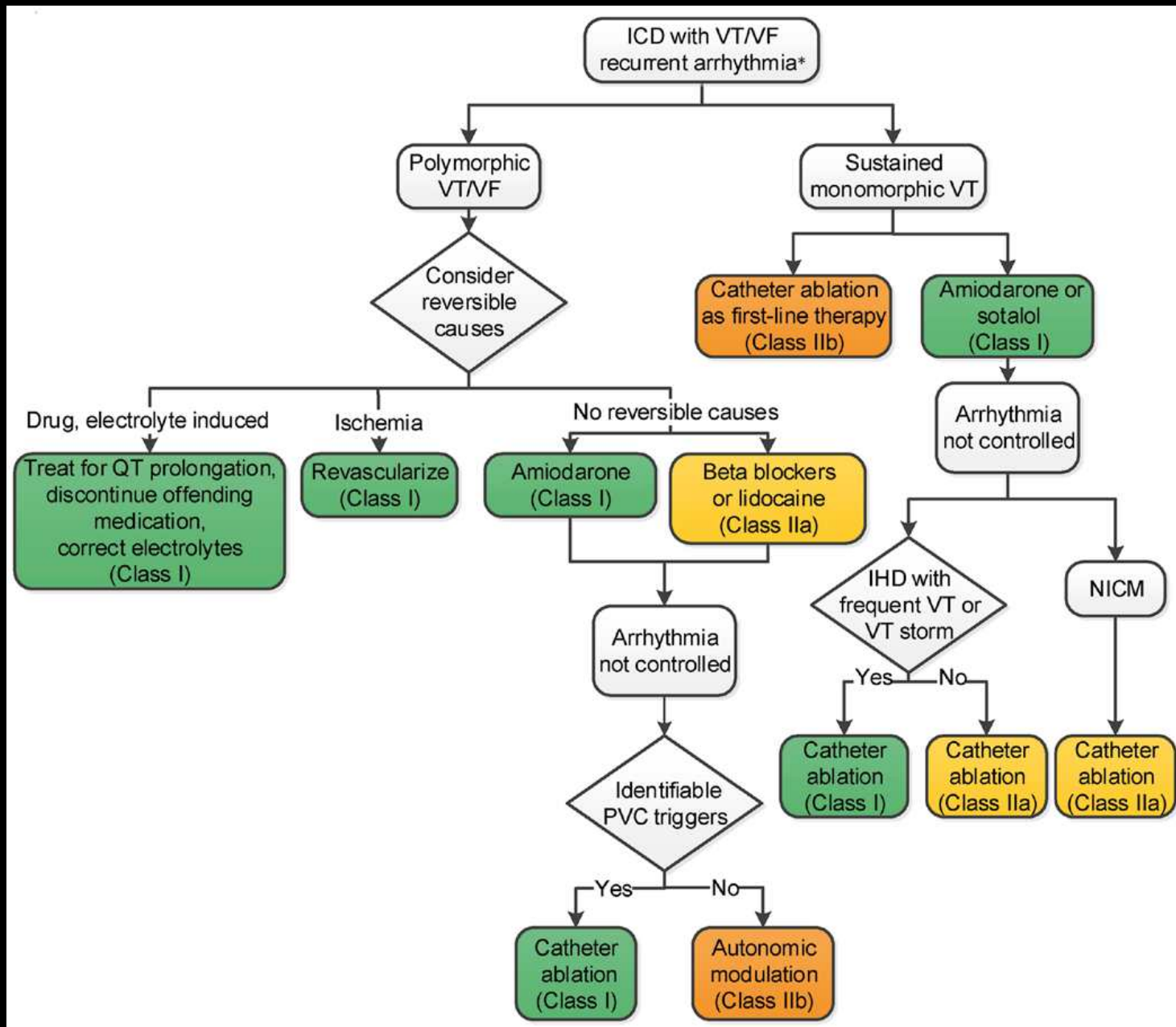
Catheter ablation (CA)

- Adjunctive treatment in patients with frequent VT & ICD shock despite medication

- **Benefit of CA**

  - Location of the circuit

  - Underlying substrate

  - Arrhythmia inducibility

  - NYHA HF status

- **6Y Arrhythmia free-survival rate after CA**

  - 54±4% in ICMP, 38±4% in non-ICMP

Catheter ablation (CA)

- **No mortality reduction in advanced HF**

Catheter ablation trials

Study		RR (95% CI)	Weight %
Epstein et al (1998)		0.43 (0.03, 7.11)	1.95
Reddy et al. (2007)		0.50 (0.17, 1.44)	10.18
Kuck et al. (2010)		1.36 (0.34, 5.36)	6.90
Al-Khatib et al. (2015)		1.09 (0.13, 9.12)	3.26
Koa-Wing et al. (2004)		(Excluded)	0.00
Subtotal (I-squared = 0.0%, p = 0.671)	P=0.423	0.74 (0.35, 1.56)	22.28
Overall (I-squared = 21.0%, p = 0.225)	P=0.546	1.13 (0.76, 1.69)	100.00

.1   .5 1   5 10   100

Favors Intervention (AADs or CA)   Favors Control Medical Rx

- **Limited data on the use of CA in NYHA IV HF**
  - High mortality rate
  - Safety concern

CA in NYHA IV HF patients

- **12 International Ventricular Tachycardia Ablation Center Collaboration Analysis (NYHA IV vs. NYHA II-III)**

Variable	NYHA II and III (n=1254)	NYHA IV (n=111)	P Value
Age, y	64±12	65±11	0.317
Male sex	1113 (89)	95 (86)	0.350
Ischemic cardiomyopathy	741 (59)	68 (61)	0.688
LVEF	30±11	21±7	<0.001
Hypertension	663 (53)	57 (61)	0.132
Hyperlipidemia	695 (55)	59 (69)	0.018
Atrial fibrillation	357 (32)	39 (40)	0.116
Diabetes mellitus	280 (22)	45 (42)	<0.001
Chronic kidney disease	432 (34)	58 (52)	<0.001

ICD type			0.006
None	133 (11)	5 (5)	
Single or Dual Chamber	731 (58)	56 (51)	
CRT	390 (31)	49 (45)	
VT storm/incessant VT	447 (36)	74 (67)	<0.001
ICD shocks	750 (60)	75 (72)	0.016
Syncope	114 (9)	8 (19)	0.055
Previous ablation	478 (38)	40 (36)	0.685
Previous cardiothoracic surgery	409 (34)	36 (33)	0.916
Use of antiarrhythmic drug	959 (81)	96 (91)	0.008
Amiodarone	706 (60)	86 (82)	<0.001
Sotalol	139 (12)	4 (4)	0.009
≥2	239 (20)	27 (26)	0.209
β-Blocker	1022 (83)	99 (90)	0.046

Circ Arrhythm Electrophysiol. 2017;10:e004494

CA in NYHA IV HF patients

- **Procedure-related data**

  - **-** More hemodynamic cardiac
    supporting device
  - More VTs induction
  - Slower VT cycle lengths

  - **No change of**
    epicardial ablation
    procedural time
    acute noninducibility
    acute complication

Variable	NYHA II and III (n=1254)	NYHA IV (n=111)	P Value
Use of hemodynamic support device	67 (7)	17 (22)	<0.001
Epicardial mapping	335 (29)	29 (27)	0.823
Surgical epicardial access	25 (2)	6 (6)	0.036
No. of VTs induced	2.2±2.0	2.6±2.3	0.057
No. with unmappable VT	497 (57)	56 (58)	0.764
Fastest VT cycle length, ms	351±87	376±90	0.016
Slowest VT cycle length, ms	420±110	458±110	0.005
Procedure time, min	285±116	280±120	0.691
Noninducible or inducible for nonclinical VT on final PES	1028 (82)	88 (79)	0.521
Final PES not performed	54 (5)	12 (11)	0.010
Complications	82 (7)	11 (10)	0.246

Circ Arrhythm Electrophysiol. 2017;10:e004494

CA in NYHA IV HF patients

Procedure-related complication according to NYHA class

	NYHA II-III (n=1254)	NYHA IV (n=111)
Vascular access-related bleeding	31 (2.5%)	2 (1.8%)
Pericardial effusion		
Pericardiocentesis	27 (2.2%)	3 (2.7%)
Surgical repair	3 (0.2%)	-
Thromboembolic event	6 (0.5%)	3 (2.7%)
Intraprocedural cardiac arrest	5 1 – ECMO 4 – LVAD	-

Clinical outcomes according to NYHA class

Survival Following VT Recurrence By NYHA Classification

Variable	NYHA II and III (n=1254)	NYHA IV (n=111)	P Value
In-hospital mortality	35 (3)	19 (17)	<0.001
Recurrent VT in 1 y	357 (29)	40 (36)	0.102
Time to VT recurrence, d	283±357	67±94	<0.001
Early (≤1 mo) VT recurrence	130 (10)	21 (19)	0.011
Cardiac transplantation in 1 y	50 (4)	12 (11)	0.003
One-y mortality	320 (26)	53 (48)	<0.001
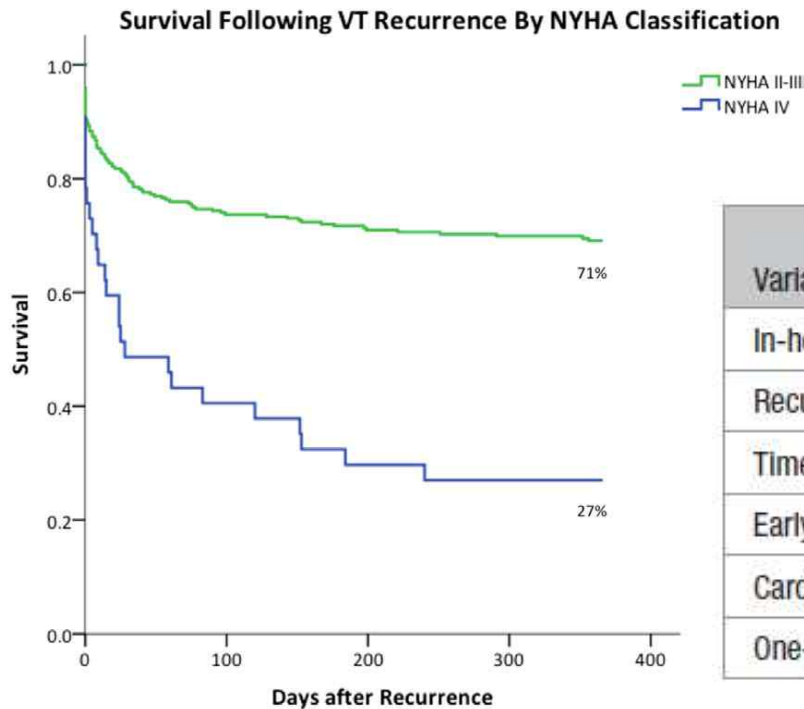
Number At Risk

328	224	202	186	172
36	15	11	9	6

CA in NYHA IV HF patients

Mortality among NYHA IV patients

Variable	Univariable Analyses		Multivariable Analysis	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Age	0.99 (0.96–1.01)	0.245		
Ischemic cardiomyopathy	0.63 (0.36–1.10)	0.103		
LVEF	0.99 (0.96–1.03)	0.673		
Presence of CRT-D	1.22 (0.73–2.04)	0.440		
VT storm/incessant VT	1.01 (0.56–1.81)	0.973		
Hypertension	1.65 (0.84–3.24)	0.146		
Diabetes mellitus*	1.62 (0.92–2.88)	0.098	1.79 (0.92–3.49)	0.088
Chronic kidney disease*	1.80 (1.01–3.21)	0.047	1.39 (0.71–2.72)	0.334
Antiarrhythmic drug use	2.52 (0.61–10.41)	0.201		
Amiodarone use	1.93 (0.76–4.88)	0.166		
β-Blocker use	0.54 (0.24–1.20)	0.131		
Use of hemodynamic support device*	2.37 (1.21–4.66)	0.012	1.20 (0.59–2.45)	0.619
Epicardial and endocardial mapping	1.26 (0.93–1.72)	0.133		
Partial success on final PES	0.68 (0.36–1.31)	0.251		
Inducible at final PES	1.80 (0.71–4.54)	0.216		
VT recurrence†	7.03 (3.68–13.42)	<0.001	4.72 (2.25–9.91)	<0.001
Early (≤1 mo) VT recurrence*	10.31 (4.99–21.29)	<0.001	8.30 (3.53–19.50)	<0.001

Early VT recurrence group showed >8-fold increased risk of mortality

Survival Based on Early VT Recurrence Following Ablation and by NYHA Class
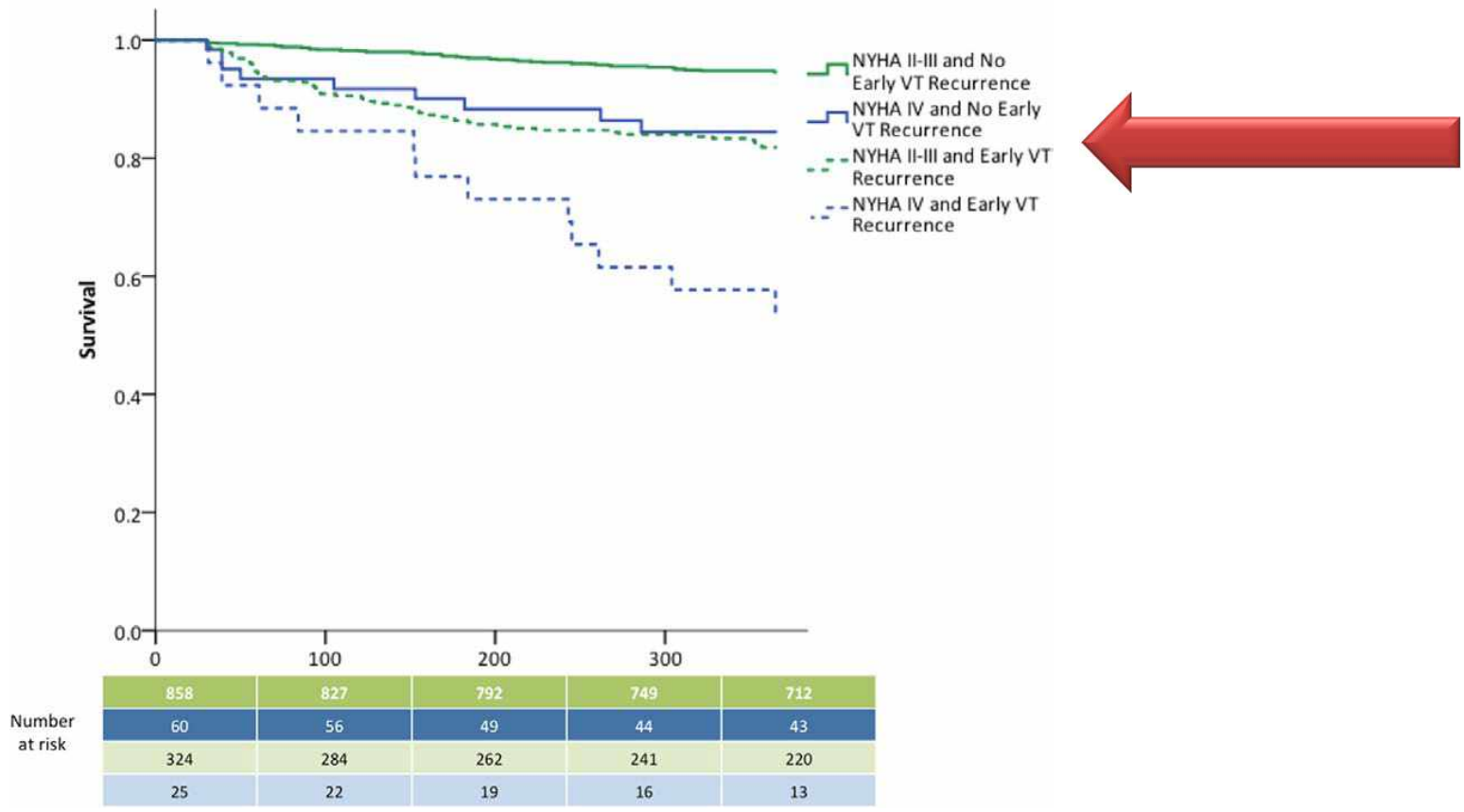
VT recurrence among NYHA IV patients

Variable	Univariable Analyses		Multivariable Analysis	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Age*	0.98 (0.94–1.01)	0.230	1.00 (0.96–1.05)	0.891
Ischemic cardiomyopathy	0.70 (0.37–1.33)	0.273		
LVEF*	0.93 (0.87–1.00)	0.050	0.90 (0.78–1.05)	0.176
Presence of CRT-D*	0.52 (0.27–0.98)	0.045	0.33 (0.13–0.84)	0.020
VT storm/incessant VT	1.03 (0.51–2.10)	0.935		
Hyperlipidemia*	3.46 (1.28–9.35)	0.014	2.76 (0.75–10.12)	0.126
Atrial fibrillation*	0.50 (0.24–1.02)	0.056	0.46 (0.13–1.66)	0.235
Diabetes mellitus	1.63 (0.83–3.21)	0.160		
Chronic kidney disease	0.63 (0.33–1.22)	0.172		
Antiarrhythmic drug use	0.71 (0.25–2.05)	0.530		
Use of hemodynamic support device*	2.98 (1.19–7.44)	0.020	4.23 (1.08–16.66)	0.039
Partial success on final PES*	0.52 (0.26–1.06)	0.070	0.72 (0.25–2.08)	0.539
Inducible at final PES	1.23 (0.93–1.63)	0.145		

- Significant intermediate-benefit

- Strategy <u>for minimizing hemodynamic instability</u> compared to patients with mild to moderate HF

Patient selection and preparation

Predictors of AHD – *PAAINESD* Score
N = 193 patients w/ scar-related VT

Incidence of Acute Hemodynamic Decompensation (AHD)*

*Sustained hypotension (SBP <80-90 mm Hg) despite increasing doses of vasopressors and requiring mechanical hemodynamic support or procedure discontinuation.
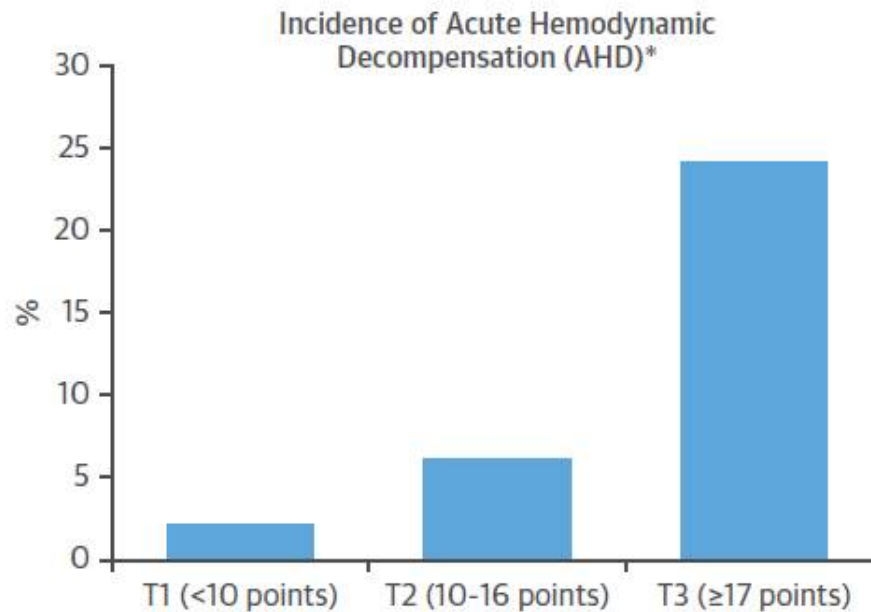
PAAINESD RISK SCORE	
VARIABLE	SCORE
Pulmonary disease [chronic obstructive] – COPD	5
Age >60 years	3
Anesthesia [general]	4
Ischemic cardiomyopathy	6
NYHA class III or IV	6
Ejection fraction <25%	3
Storm [VT]	5
Diabetes mellitus	3

Patients with either:

Severely decreased left ventricular systolic function or

NYHA class IV symptoms with ventricular arrhythmias and are refractory to antiarrhythmic drugs

Is there evidence of hemodynamic decompensation by clinical examination?

Y

RFA

RFA: Radiofrequency ablation

No RFA

Right heart (RH) catheterization to optimize and determine which platform to use for temporary circulatory support (ECMO or percutaneous LVAD)

Is patient successfully weaned from temporary circulatory support after RF ablation?

Y

N

Reattempt weaning with hemodynamic-guided inotropic support

Continue to monitor closely post-RF ablation

If patient meets criteria, consider evaluation for heart transplant or durable LVAD

If not a candidate for advanced therapies, consider palliative care and hospice

N

Is temporary circulatory support required?

Y

N

RH catheterization; consider IABP, ECMO, or percutaneous LVAD

RFA

Proceed with RF ablation

Is patient successfully weaned from temporary circulatory support?

Y

N

RFA

Proceed with RF ablation

Continue to monitor closely post-RF ablation

Prophylactic mechanical support

- **High PAAINESD score**

- Diuretics, inotropic or vasodilation ..

<table>
<tr><td>

<< Optimal goal >>

CVP < 8mmHg
PCWP <15mmHg
CI >2.4 l/min/m2
Maximum recovery of EOD

</td><td>

<< NYHA IV HF with VT >>

High arrhythmic burden
Severe pump failure
High co-morbidities
Refractory VT

</td></tr>
</table>
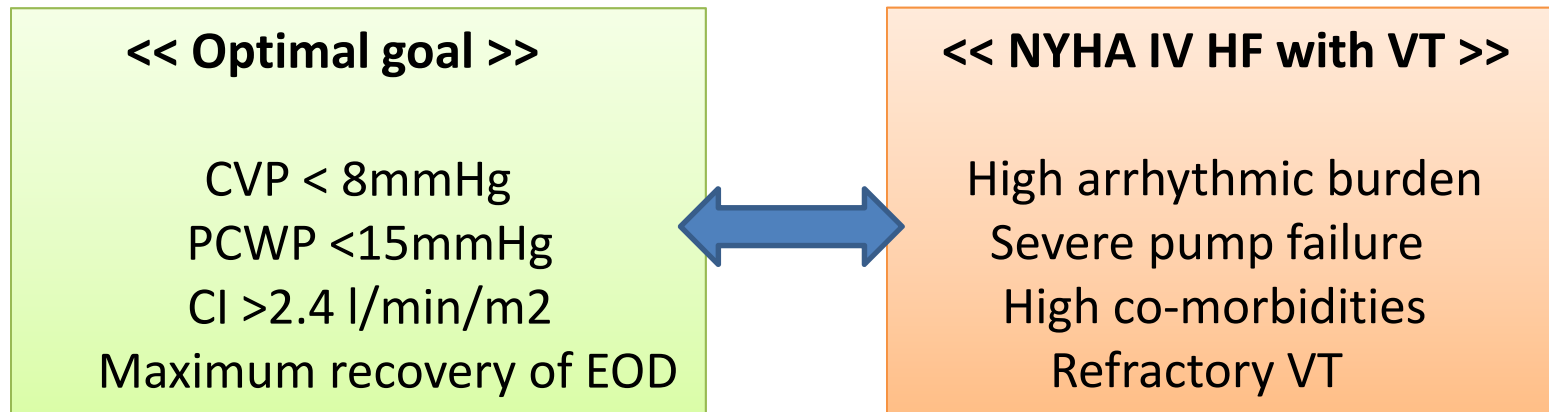
- **Rt. Heart catheterization**

  : Determining temporary circulatory support

  : ECMO, VAD..

CA with mechanical support

- **Maintenance of vital organ perfusion**

- **Reduction of intra-cardiac filling pressures**

- Reduction of LV volumes, wall stress, and myocardial consumption of oxygen

- Improvement of coronary perfusion
- **Support of systemic circulation & reduction of cardiac stunning** due to multiple VT inductions for mapping and during ablation.

Summary

- **AAD**

  : main stay for suppression of VT

  : no mortality benefit beyond BB

- **Catheter ablation as adjunctive to AAD**

  : reduce ventricular arrhythmia

  : no impact on mortality

- **In NYHA IV HF**

  : high VT burden (multiple ICD shock, more comorbidities)

  : reduced response rate

  : Individualization of treatment strategy

   (considering underlying disease substrate in HF)

Thank you for attention