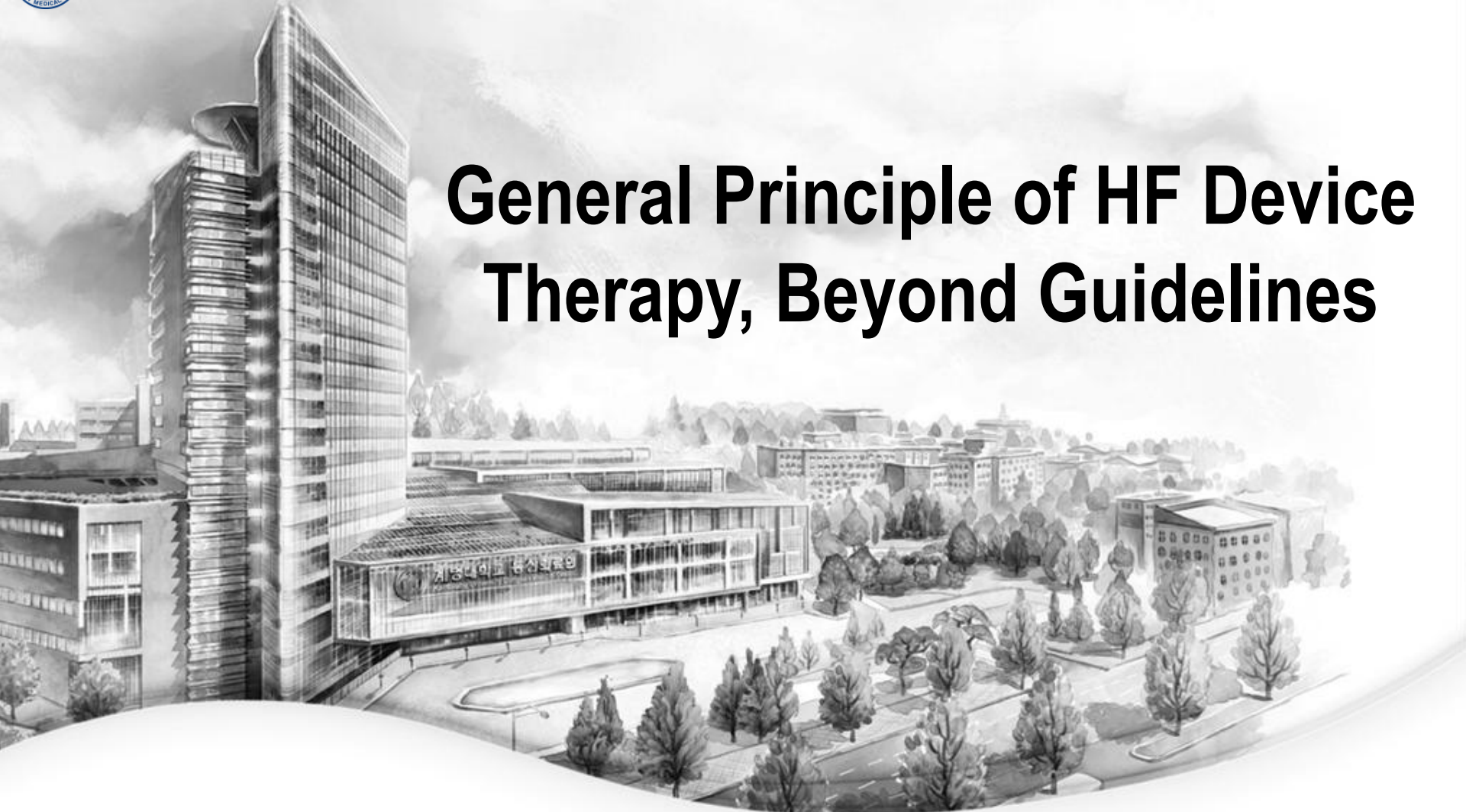




General Principle of HF Device Therapy, Beyond Guidelines



Seongwook Han, MD.PhD.

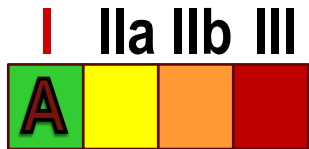
Professor of Medicine, Keimyung University School of Medicine
Arrhythmia Service, Cardiology, Dongsan Medical Center

Disclosure

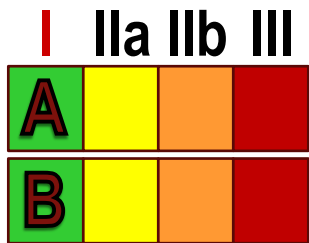
- **Served as a speaker or a consultant:** Bayer, Biosense Webster, Boehringer Ingelheim, Boston Scientific, Bristol-Myers Squibb, Daiichi-Sankyo, Pfizer, Servier, St. Jude Medical
- **Received research grants:** Servier, Yuhan
- **Served as a member of advisory board:** Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Pfizer, Boston Scientific, Daiichi-Sankyo



2013 ACCF/AHA Guideline for the Management of Heart Failure



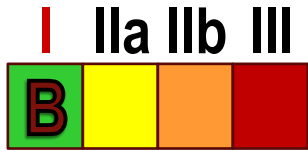
ICD therapy is recommended for **primary prevention of SCD** in selected patients with **HFrEF** at least 40 d post-MI with **LV EF $\leq 35\%$** and NYHA class **II or III** symptoms on chronic GDMT*, who are expected to live **>1 y**



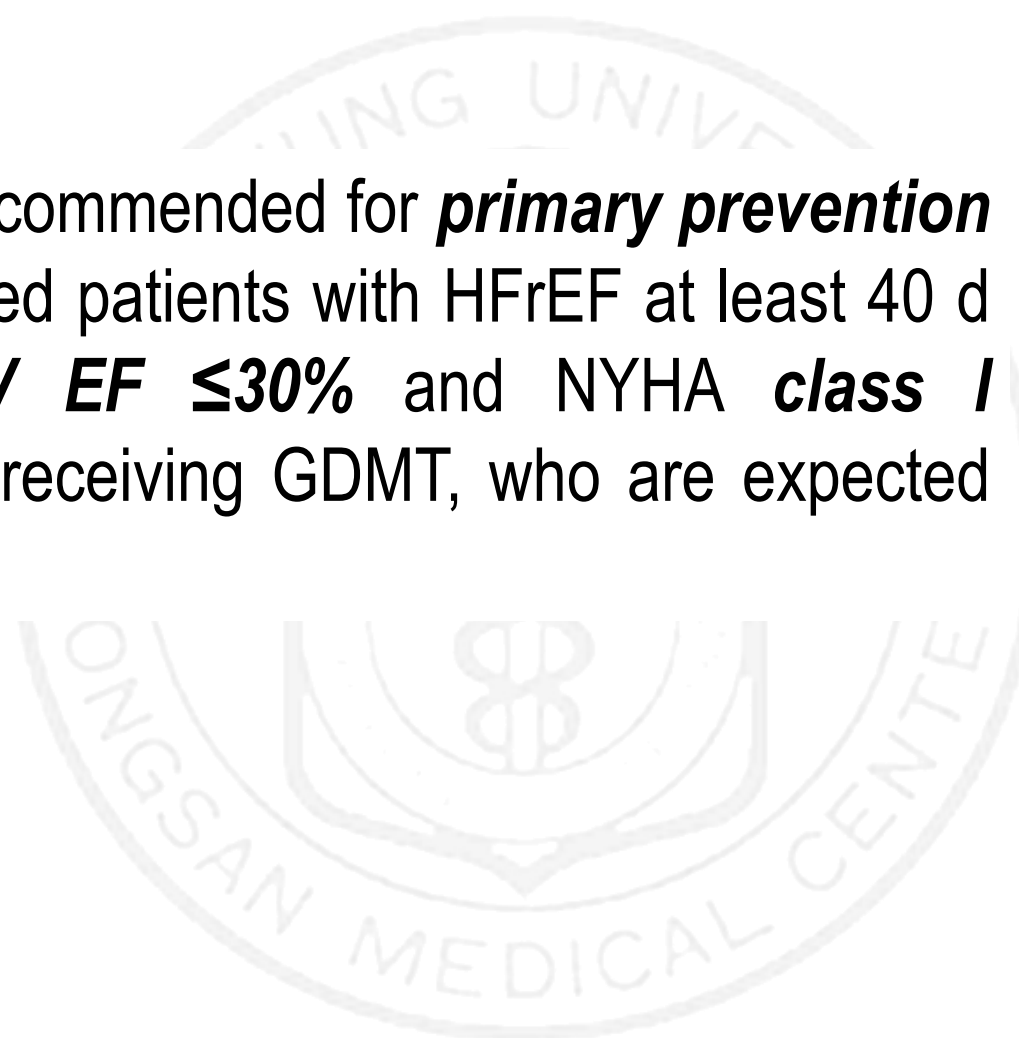
CRT is indicated for patients who have **LVEF $\leq 35\%$** , sinus rhythm, **LBBB** with a **QRS ≥ 150 ms**, & **NYHA class II, III, or ambulatory IV** symptoms on GDMT*

*Guideline-Directed Medical Therapy

2013 ACCF/AHA Guideline for the Management of Heart Failure



ICD therapy is recommended for **primary prevention of SCD** in selected patients with HFrEF at least 40 d post-MI with **LV EF $\leq 30\%$** and NYHA **class I** symptoms while receiving GDMT, who are expected to live **>1 y**



2013 ACCF/AHA Guideline for the Management of Heart Failure



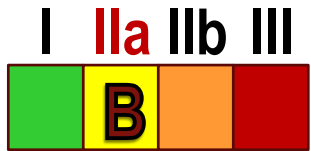
CRT can be useful for patients who have **LV EF \leq 35%**, **sinus rhythm**, a **non-LBBB** pattern with a **QRS \geq 150 ms** & NYHA class **III/ambulatory IV** symptoms on GDMT



CRT can be useful for patients who have **LV EF \leq 35%**, **sinus rhythm**, **LBBB** with a **QRS 120 to 149 ms**, & NYHA class **II, III, or ambulatory IV** symptoms on GDMT



2013 ACCF/AHA Guideline for the Management of Heart Failure



CRT can be useful in patients with **AF** and **LV EF \leq 35%** on GDMT if a) the patient **requires ventricular pacing or otherwise meets CRT criteria** and b) **atrioventricular nodal ablation or rate control allows near 100% ventricular pacing with CRT**



CRT can be useful for patients on GDMT who have **LVEF \leq 35%**, & are undergoing placement of a new or replacement device implantation with anticipated **ventricular pacing (>40%)**

2013 ACCF/AHA Guideline for the Management of Heart Failure



An **ICD** is of **uncertain benefit** to prolong meaningful survival in patients with a **high risk of non-sudden death** such as frequent hospitalizations, frailty, or severe comorbidities



CRT may be considered for patients who have **LV EF $\leq 35\%$** , **sinus rhythm**, a **non-LBBB** with a **QRS 120 to 149 ms**, and NYHA class **III/ambulatory IV** on GDMT

2013 ACCF/AHA Guideline for the Management of Heart Failure

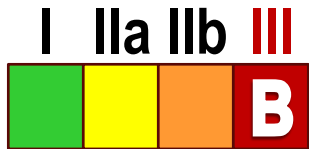


CRT may be considered for patients who have **LV EF** $\leq 35\%$, **sinus rhythm**, a **non-LBBB** with a **QRS** ≥ 150 ms, and NYHA **class II** symptoms on GDMT

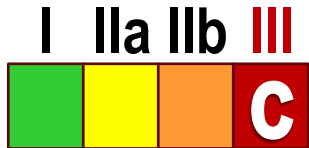


CRT may be considered for patients who have **LV EF** $\leq 30\%$, **ischemic** etiology of HF, **sinus rhythm**, **LBBB with QRS** ≥ 150 ms, and NYHA **class I** symptoms on GDMT

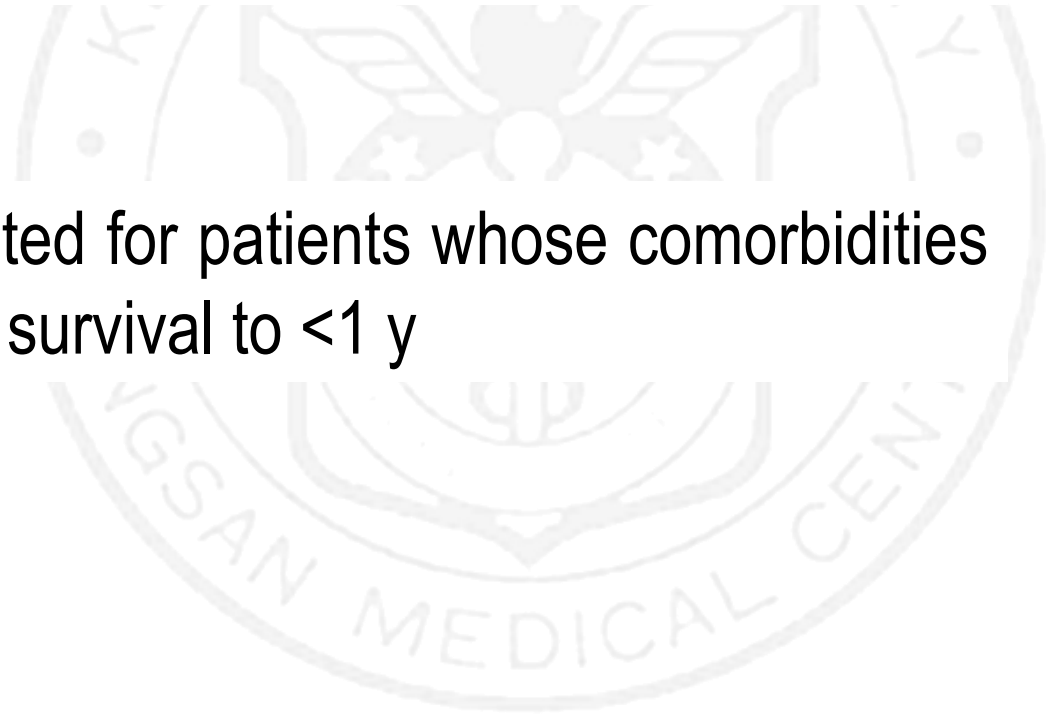
2013 ACCF/AHA Guideline for the Management of Heart Failure



CRT is not recommended for patients with NYHA *class I or II* symptoms and *non-LBBB* with a **QRS** <150 ms



CRT is not indicated for patients whose comorbidities and/or frailty limit survival to <1 y



2013 ACCF/AHA Guideline for the Management of Heart Failure

NYHA I

LVEF \leq 30%
QRS \geq 150ms
LBBB, sinus
Ischemic CM

QRS $<$ 150 ms
Non-LBBB

NYHA II

LVEF \leq 35%
QRS \geq 150ms
LBBB, sinus

LVEF \leq 35%
QRS 120-149ms
LBBB, Sinus

LVEF \leq 35%
QRS \geq 150ms
Non-LBBB, sinus

QRS \leq 150ms
Non-LBBB

NYHA III/Ambulatory IV

LVEF \leq 35%
QRS \geq 150ms
LBBB, Sinus

LVEF \leq 35%
QRS 120-149ms
LBBB, Sinus

LVEF \leq 35%
QRS \geq 150ms
Non-LBBB, Sinus

LVEF \leq 35%
QRS 120-149ms
Non-LBBB, Sinus

Special Ix

Anticipated to require frequent ventricular pacing ($>$ 40%)

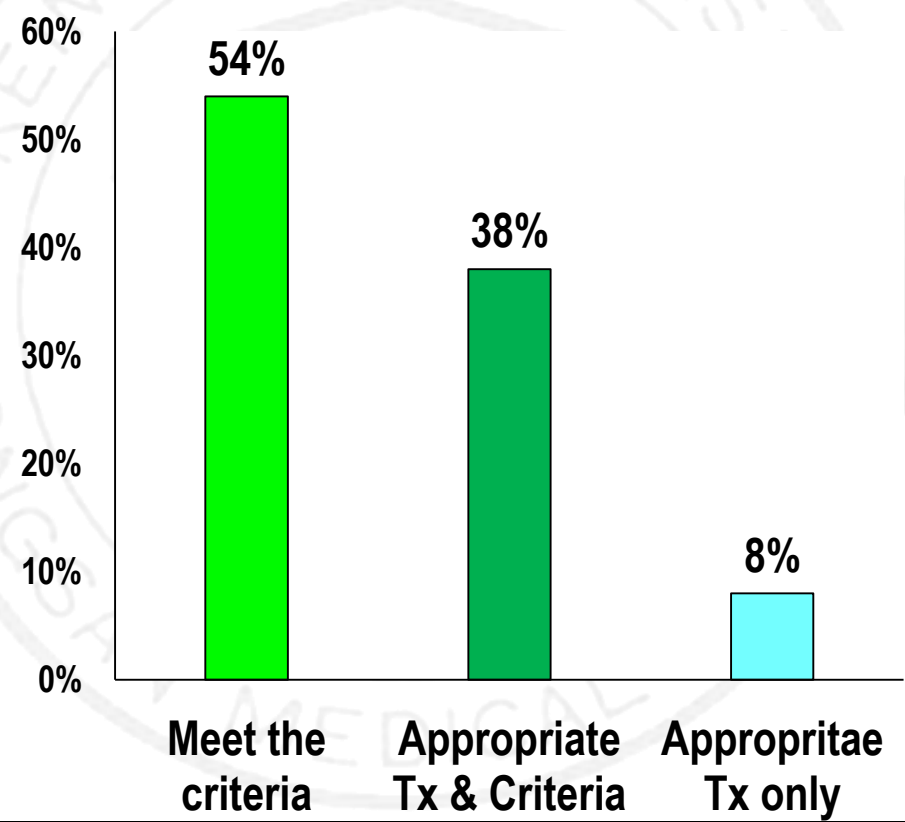
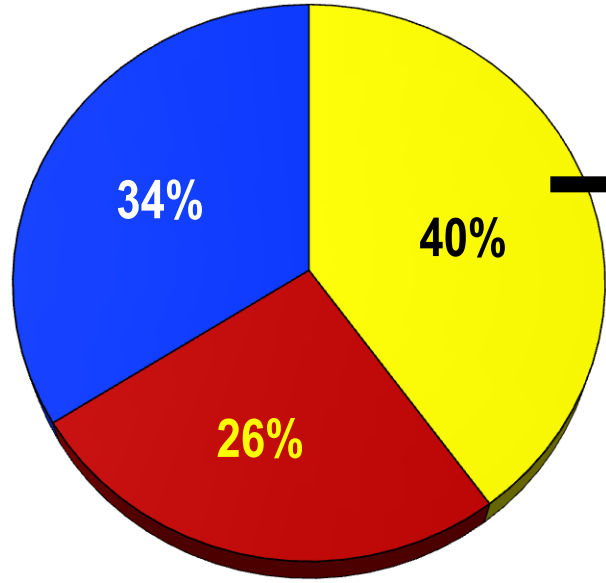
AF, if ventricular pacing is required & rate control will result in near 100% ventricular pacing with CRT

I **IIa** **IIb** **III**

Appropriateness of Primary Prevention ICDs at the Time of Generator Replacement

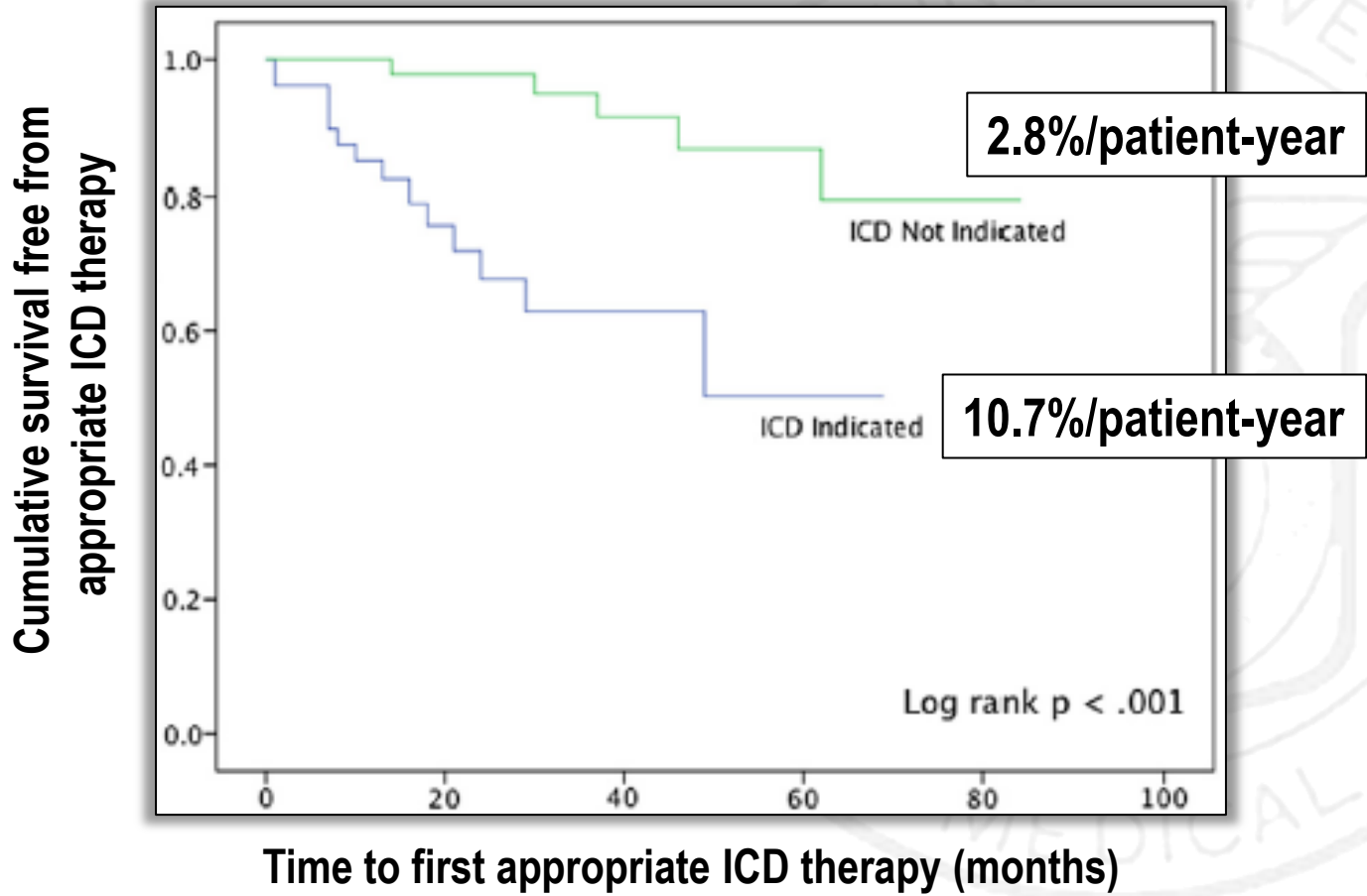
- To determine how often patients with 1° prevention ICD meets guideline-derived indications at the time of generator replacement
- 231 patients from 2 VA hospitals in the US: Retrospective review

■ ICD indicated
■ ICD Not indicated
■ ICD Unclear indication



Appropriateness of Primary Prevention ICDs at the Time of Generator Replacement

Subsequent ICD therapies after elective generator replacement

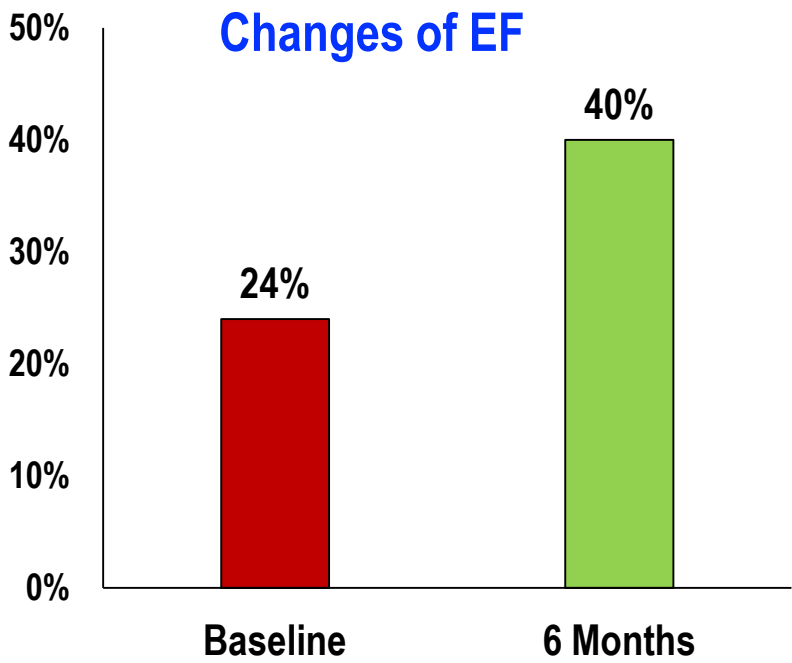


Appropriateness of Primary Prevention ICDs at the Time of Generator Replacement

- ❖ **Baseline LVEF of 30-35%** (compared with LVEF of < 30%) was the only significant characteristic associated with a **lower likelihood of meeting primary prevention ICD criteria** at the time of generator replacement (OR: 0.52; 95% CI: 0.3 to 0.88; p=0.01)
- ❖ Patients with **ICM tended to be more likely** than patients with NICM to meet criteria for ICD at the time of generator replacement (OR: 1.89; 95% CI: 0.90 to 3.95; p=0.09)

Clinical and Demographic Predictors of Outcomes in Recent Onset DCM: **IMAC-2**

- ❖ To determine clinical predictors of recovery of LV fx of recent onset CM
- ❖ 373 patients with LV EF $\leq 40\%$ & ≤ 6 mo duration of symptoms
- ❖ 10% Peripartum CM, 12% cardiac biopsy (inflammation 4%, myocarditis 2.6%)
- ❖ ACEi/ARB 91 \rightarrow 92%; Beta blocker 82 \rightarrow 94% @ 6 mo: A total of 4 yr FU



- 70% of patients had an absolute increase in LV EF of 10%
- 25% had complete or near-complete (LVEF > 50%) resolution of their CM



2013 ACCF/AHA Guideline for the Management of Heart Failure

HFrEF stage C, NYHA I-IV, treatment

I **IIa** **IIb** **III**

ACEi or ARB: Beta blocker

For all volume overload
NYHA II-IV

Add

Loop diuretics

For persistently symptomatic
African Americans
NYHA III-IV

Add

Hydralazine+nitrate

NYHA class II-IV
Estimated CrCl >30 mL/min
& K⁺ <5.0 mEq/dL

Add

Aldosterone antagonist

Things to Remember

GDMT (Guideline Directed Medical Therapy)

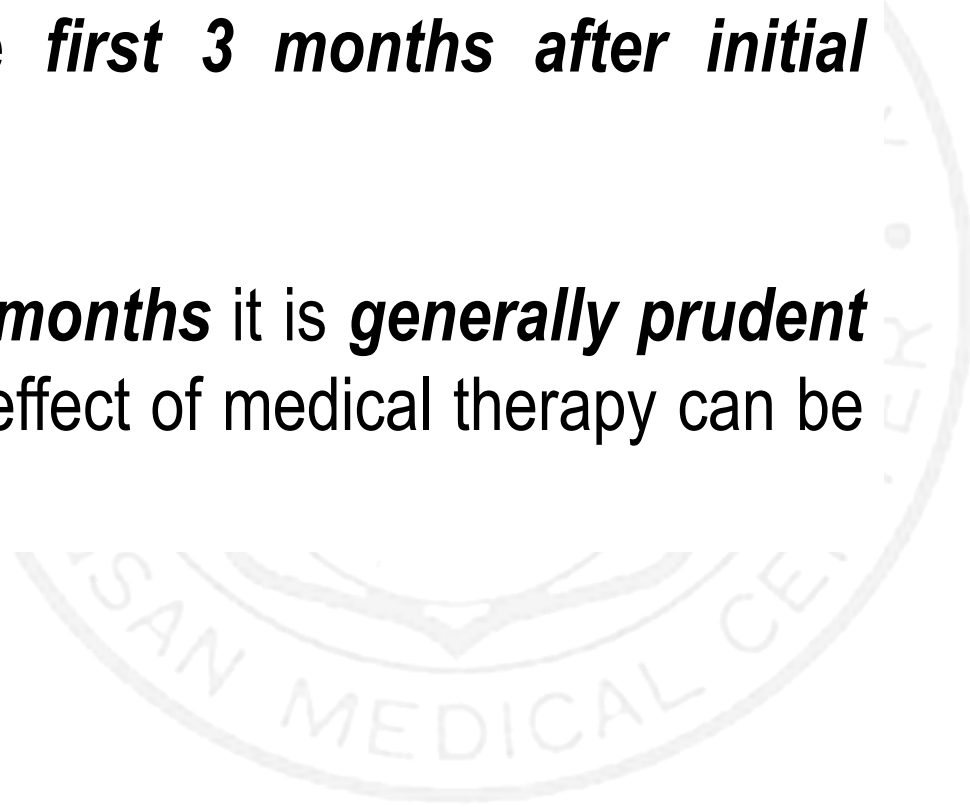
- ❖ Combination of an ***ACE inhibitor or ARB and beta blocker*** therapy adjusted to target doses as tolerated, with diuretics adjusted (the addition of ***aldosterone antagonists***)
- ❖ Clinical improvement during the ***first 3 to 6 months***
- ❖ ***GDMT should be provided for at least 3 months*** before planned reassessment of LV function to consider device implantation



Things to Remember

ICD implantation < 9 months from the initial Dx of NICM

- ❖ Implantation of an ICD for primary prevention is ***not recommended*** within the ***first 3 months after initial diagnosis*** of NICM
- ❖ In patients with ***NICM < 9 months*** it is ***generally prudent to delay ICD*** until the full effect of medical therapy can be evaluated



Things to Remember

ICD implantation within 90 days of revascularization

- ❖ **Survival benefit** with an ICD within the **first 90 days** after revascularization **is lacking** from the large, randomized, primary prevention trials
 - ✓ MADIT: excluded ≤ 2 mo after CABG, ≤ 3 mo after PTCA
 - ✓ MADIT II: excluded ≤ 3 mo after revascularization
- ❖ MADIT II: ICD was of benefit only at least 6 mo after revascularization
- ❖ CABG in patients with reduced LV EF: **30% improved LV function** on 9-12 Mo after surgery¹

Consequences of Frequent Shocks

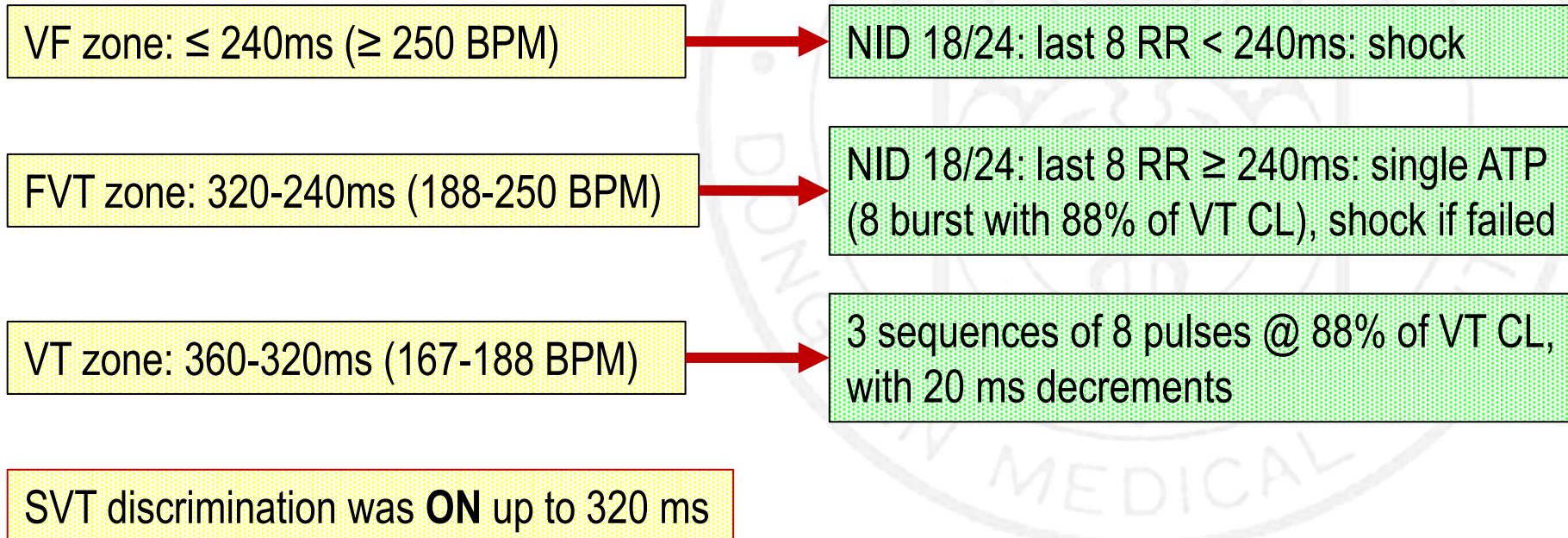
- Posttraumatic stress syndrome
- Decrease quality of life
- Acceleration of heart failure
- Proarrhythmia (rare)
- Mortality ?

shock cause this increase or simply marker of risk is unknown

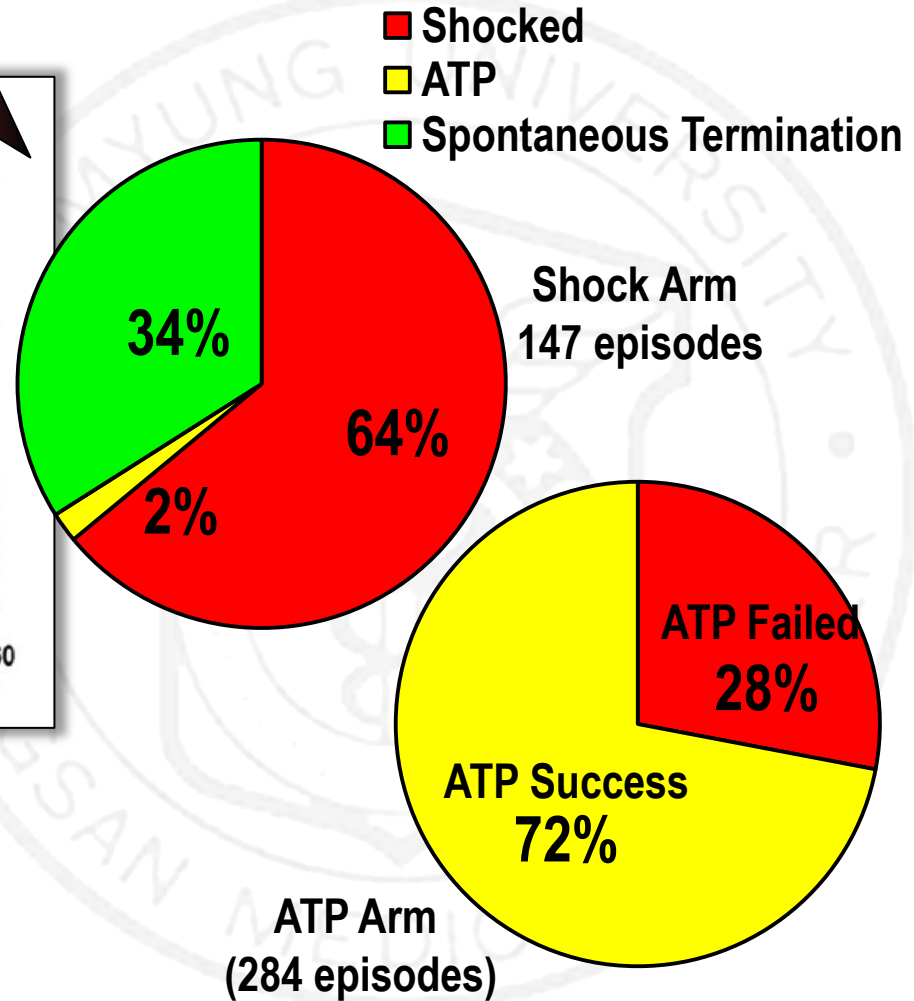
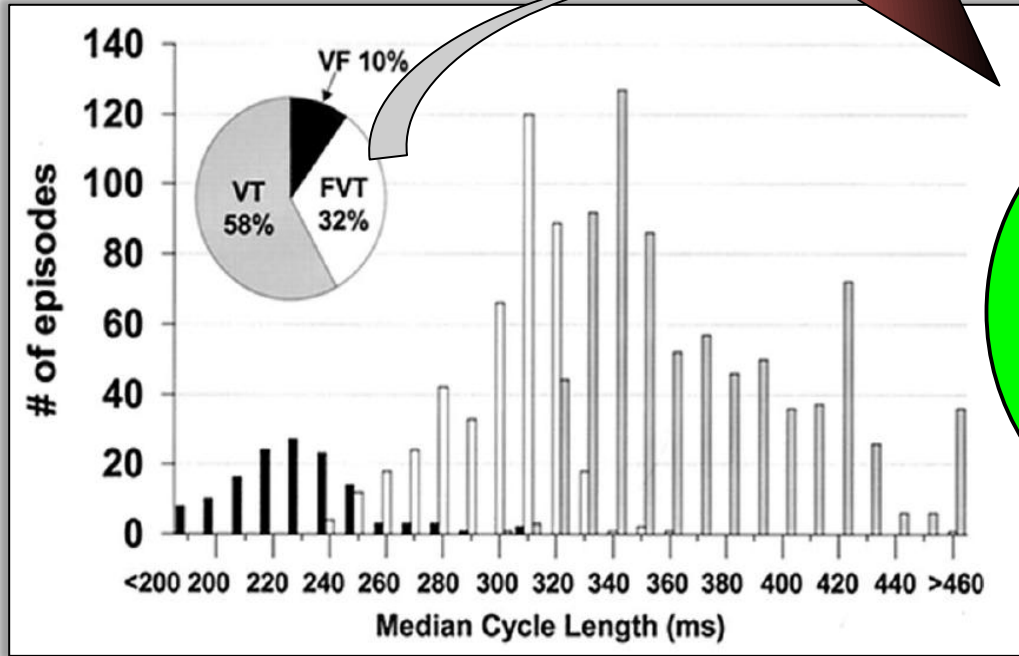


Pacing Fast Ventricular Tachycardia Reduces Shock Therapies (*PAINFREE II Rx*) Trial

- ❖ ATP terminates 78~94% of VTs <188-200 BPM with acceleration risk (2-4%)
- ❖ Fast VT (>200 BPM) is often treated by shock d/t safety concern
- ❖ **634 ICD** patients randomized to **ATP (n=313) vs shock (n=321)**
- ❖ **Efficacy, safety, QoL with Tx @ 11.2±3 Months FU**



Pacing Fast Ventricular Tachycardia Reduces Shock Therapies (*PAINFREE II Rx*) Trial



Pacing Fast Ventricular Tachycardia Reduces Shock Therapies (***PAINFREE II Rx***) Trial

- **FVT**: 32% of ventricular tachyarrhythmias & **76% of those that would be detected as VF & shocked with traditional ICD programming**
- Acceleration, episode duration, syncope, and sudden death were similar between arms
- **Conclusions** — Compared with shocks, ***empirical ATP for FVT is highly effective, is equally safe***, and ***improves quality of life. ATP may be the preferred FVT therapy*** in most ICD patients

Strategic Programming of Detection and Therapy Parameters In ICD Reduces in Shock in Primary Prevention Patients **PREPARE**

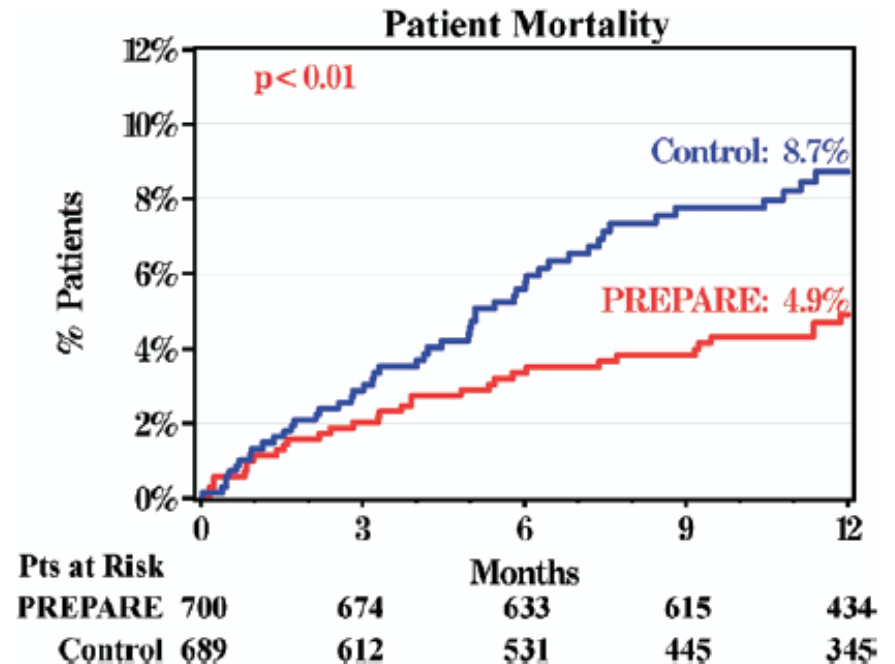
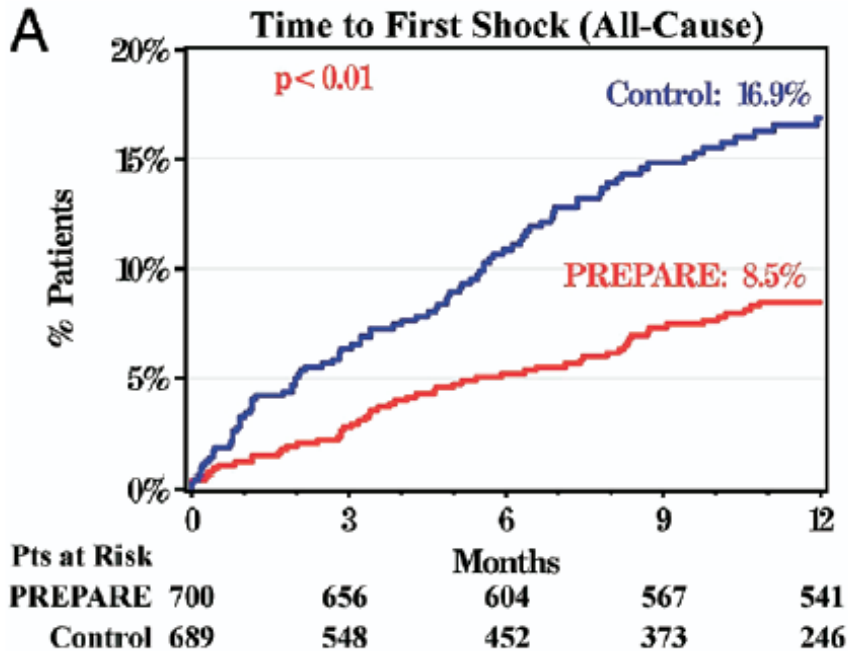
- 700 patients with primary prevention ICD: Followed for 1 year
- Control group: EMPIRIC & MIRACLE ICD trials
- **NID: 30 of 40, ATP is the first Tx for FVT (182-250 BPM), SVT discriminators were used for <200 BPM (300ms)**

Table 1 PREPARE VT/VF Programming Parameters

| | Detection | Threshold | Beats to Detect | Therapies |
|-----|-----------|---------------|-----------------|---|
| VF | On | 250 beats/min | 30 of 40 | 30 to 35 J (max output) × 6 |
| FVT | via VF | 182 beats/min | 30 of 40 | Burst (1 sequence), 30 to 35 J (max output) × 5 |
| VT | Monitor | 167 beats/min | 32 | Off |

Strategic Programming of Detection and Therapy Parameters In ICD Reduces in Shock in Primary Prevention Patients **PREPARE**

Conclusions Strategically chosen VT/VF detection and therapy parameters **can safely reduce shocks and other morbidities** associated with ICD therapy in patients receiving an ICD for primary prevention indications



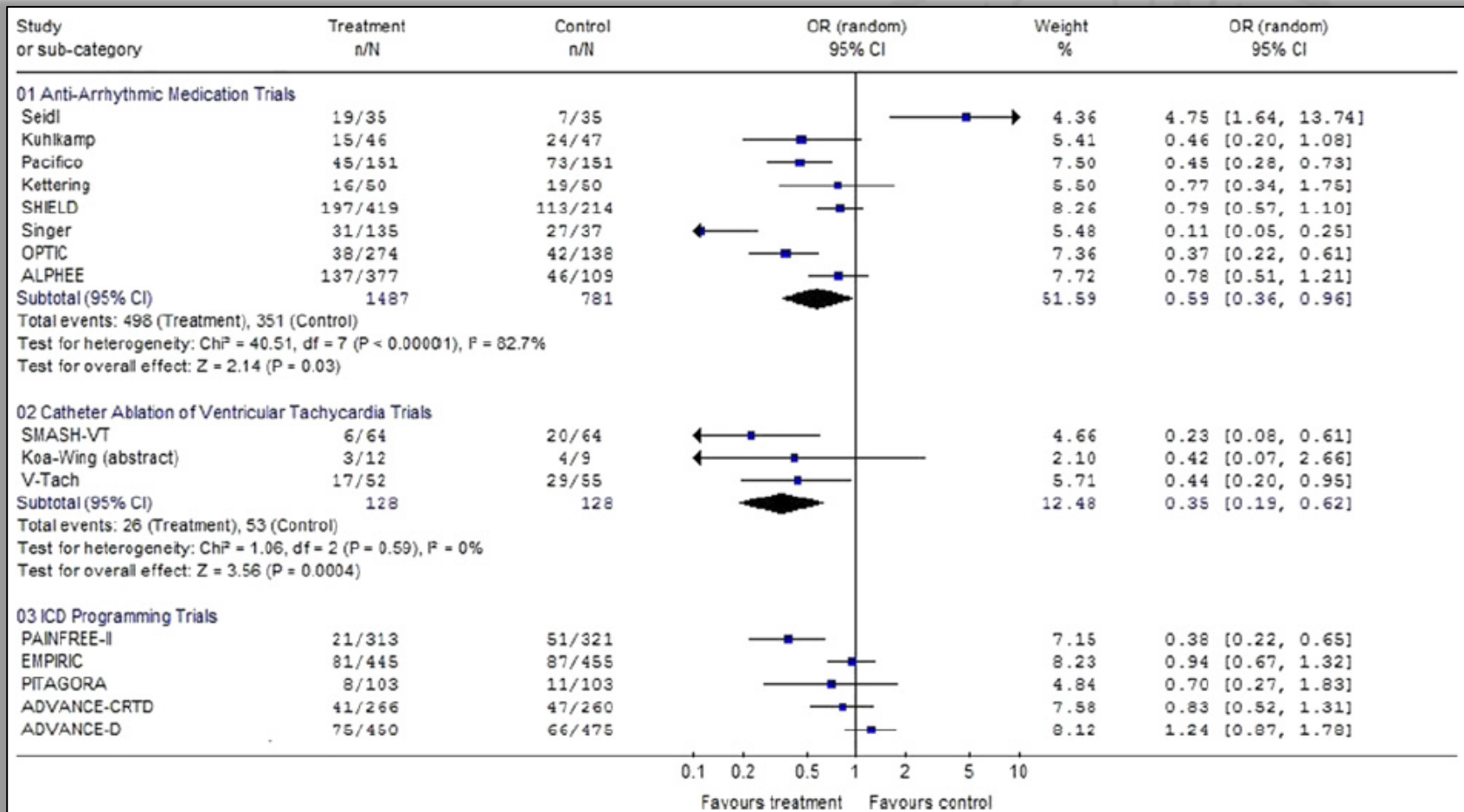
CONTEMPORARY REVIEW**Implantable cardioverter-defibrillator shock prevention does not reduce mortality: A systemic review**

Andrew H. Ha, MD,^{*} Inje Ham, BSc,^{*} Girish M. Nair, MBBS,[†] Stuart J. Connolly, MD,[†] Paul Dorian, MD,[‡] Carlos A. Morillo, MD, FHRS,[†] Jeff S. Healey, MD, MSc, FHRS[†]

- ❖ Meta analysis with trials assessing the efficacy of intervention to prevent ICD shocks
- ❖ 5875 patients from 17 randomized trials

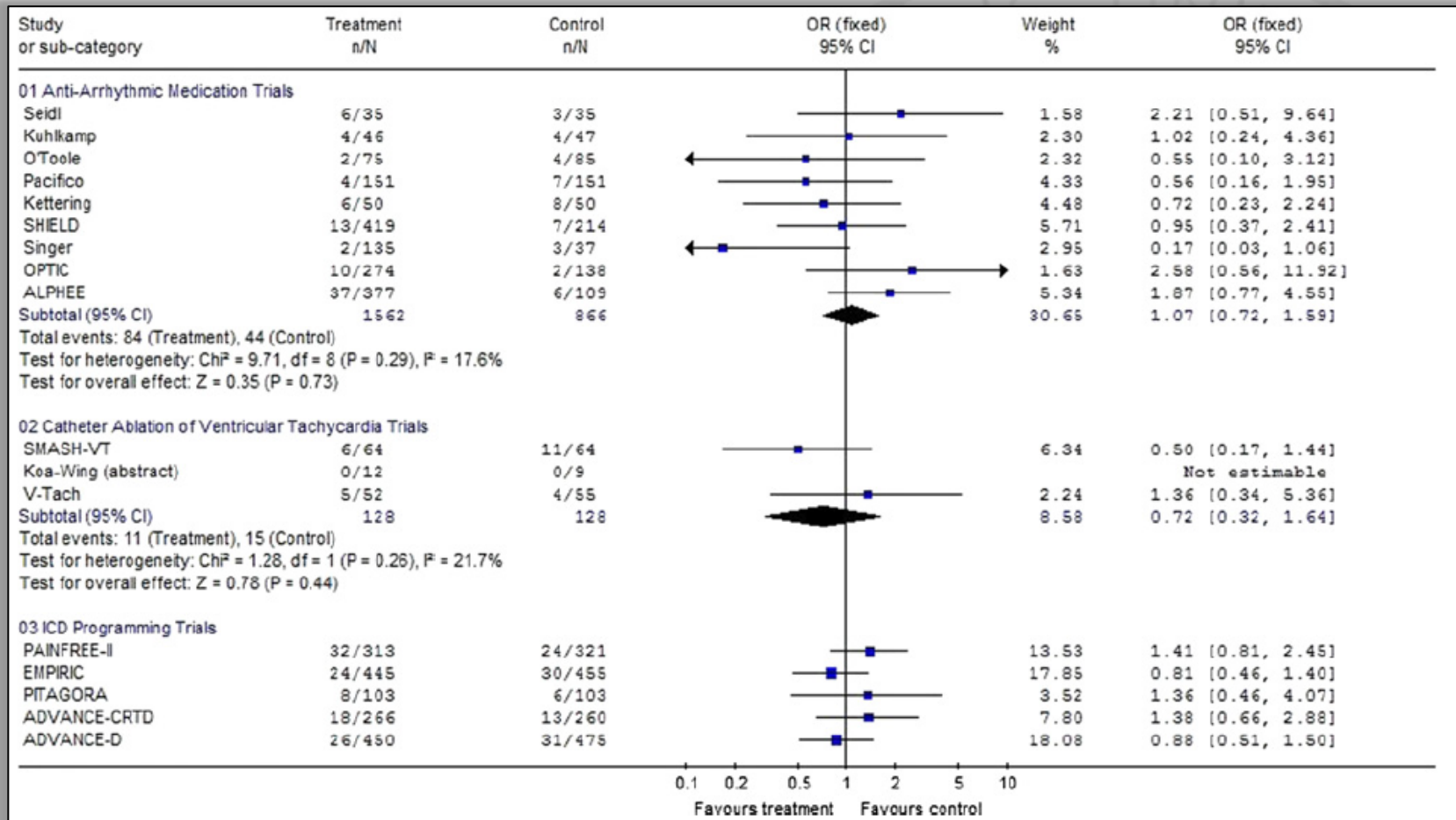
Implantable cardioverter-defibrillator shock prevention does not reduce mortality: A systemic review

Shock reductions were achieved by AAA & Catheter ablation



Implantable cardioverter-defibrillator shock prevention does not reduce mortality: A systemic review

No significant reduction in mortality



CONTEMPORARY REVIEW

Implantable cardioverter-defibrillator shock prevention does not reduce mortality: A systemic review

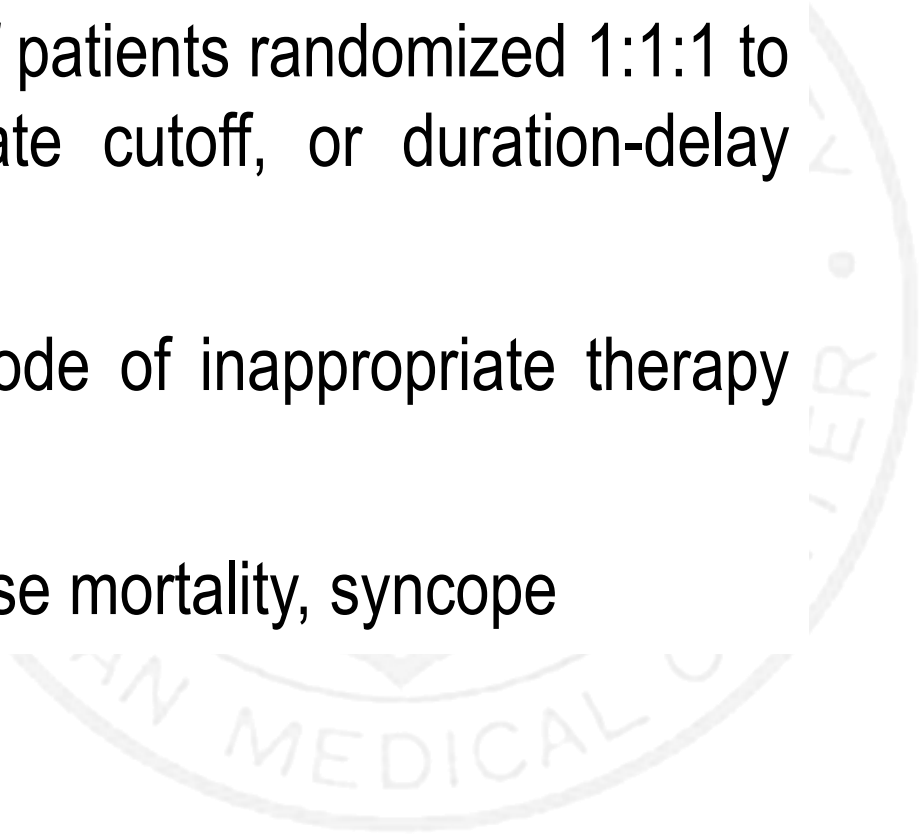
Andrew H. Ha, MD,* Inje Ham, BSc,* Girish M. Nair, MBBS,[†] Stuart J. Connolly, MD,[†] Paul Dorian, MD,[‡] Carlos A. Morillo, MD, FHRS,[†] Jeff S. Healey, MD, MSc, FHRS[†]

- ❖ 5 ICD programming trials had sufficiently heterogeneous intervention that pooling of their results was not performed
- ❖ Only PAINFREE II trial reduced ICD shocks (OR 0.38, 95% CI 0.22-0.65) but not mortality (OR 0.41, 95% CI 0.81-2.45)

Conclusion: There is ***no compelling evidence that existing interventions that reduce ICD shocks significantly improve survival***

Reduction In Inappropriate Therapy and Mortality through ICD programming. ***MADIT-RIT trial***

- ❖ 1500 patients with a primary-prevention indication
- ❖ Randomized, 3-arm study of patients randomized 1:1:1 to either conventional, high-rate cutoff, or duration-delay programming
- ❖ Primary endpoint: first episode of inappropriate therapy (shock or ATP)
- ❖ Secondary endpoint: All cause mortality, syncope

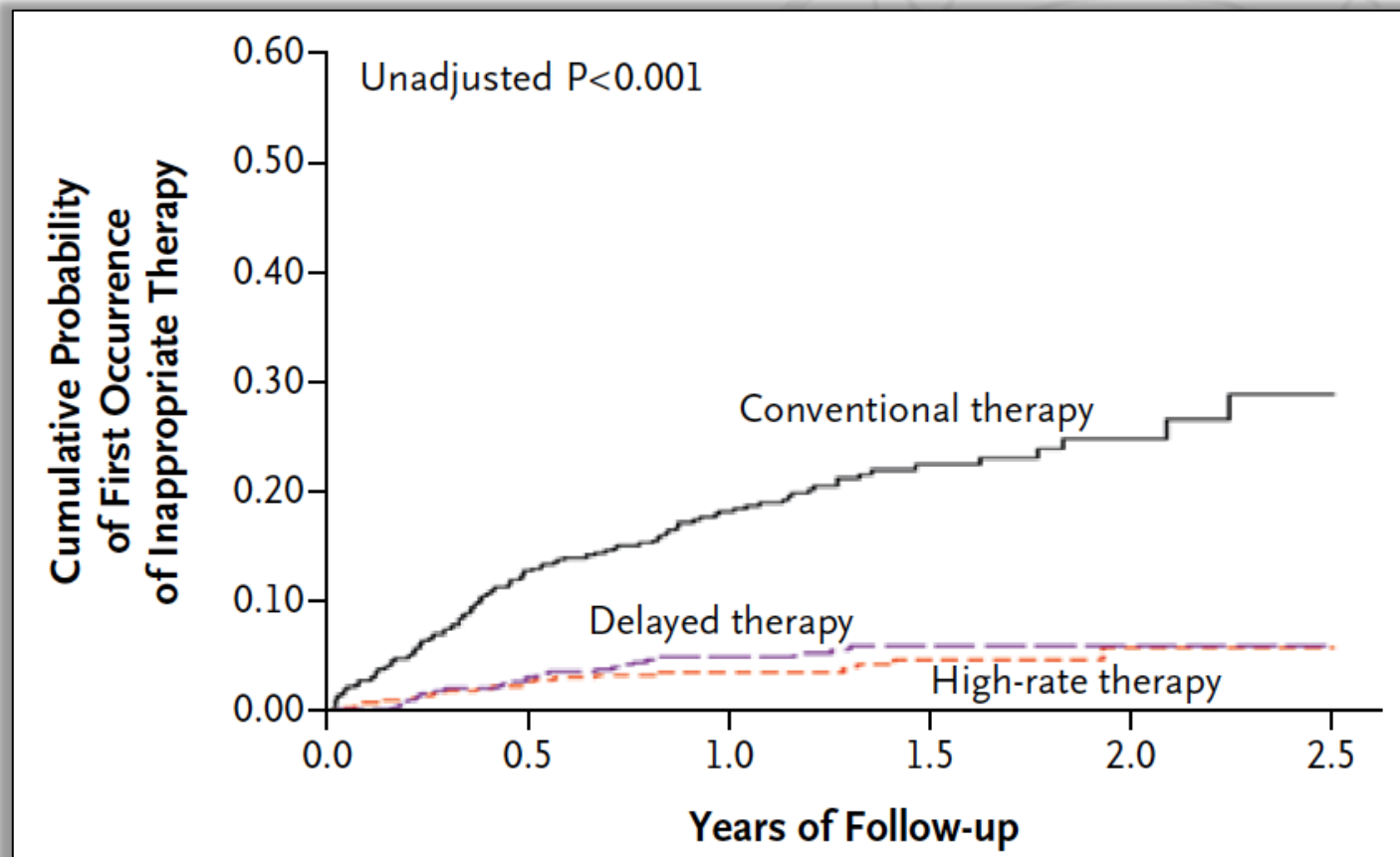


MADIT-RIT: ICD Programming

| Arm A (Conventional) | Arm B (High-rate) | Arm C (Duration-delay) |
|--|---|---|
| <p align="center"><u>Zone 1</u></p> <p>≥170 bpm, 2.5s delay Onset/Stability Detection Enhancements ON</p> <p>ATP + Shock</p> | <p align="center"><u>Zone 1</u></p> <p>170 bpm Monitor only</p> | <p align="center"><u>Zone 1</u></p> <p>≥170 bpm, 60s delay Rhythm ID[®] Detection Enhancements ON</p> <p>ATP + Shock</p> |
| <p align="center"><u>Zone 2</u></p> <p>≥200 bpm, 1s delay Quick Convert™ ATP</p> <p>Shock</p> | <p align="center"><u>Zone 2</u></p> <p>≥200 bpm, 2.5s delay Quick Convert™ ATP</p> <p>Shock</p> | <p align="center"><u>Zone 2</u></p> <p>≥200 bpm, 12s delay Rhythm ID[®] Detection Enhancements ON</p> <p>ATP + Shock</p> |
| | | <p align="center"><u>Zone 3</u></p> <p>≥250 bpm, 2.5s delay Quick Convert™ ATP + Shock</p> |

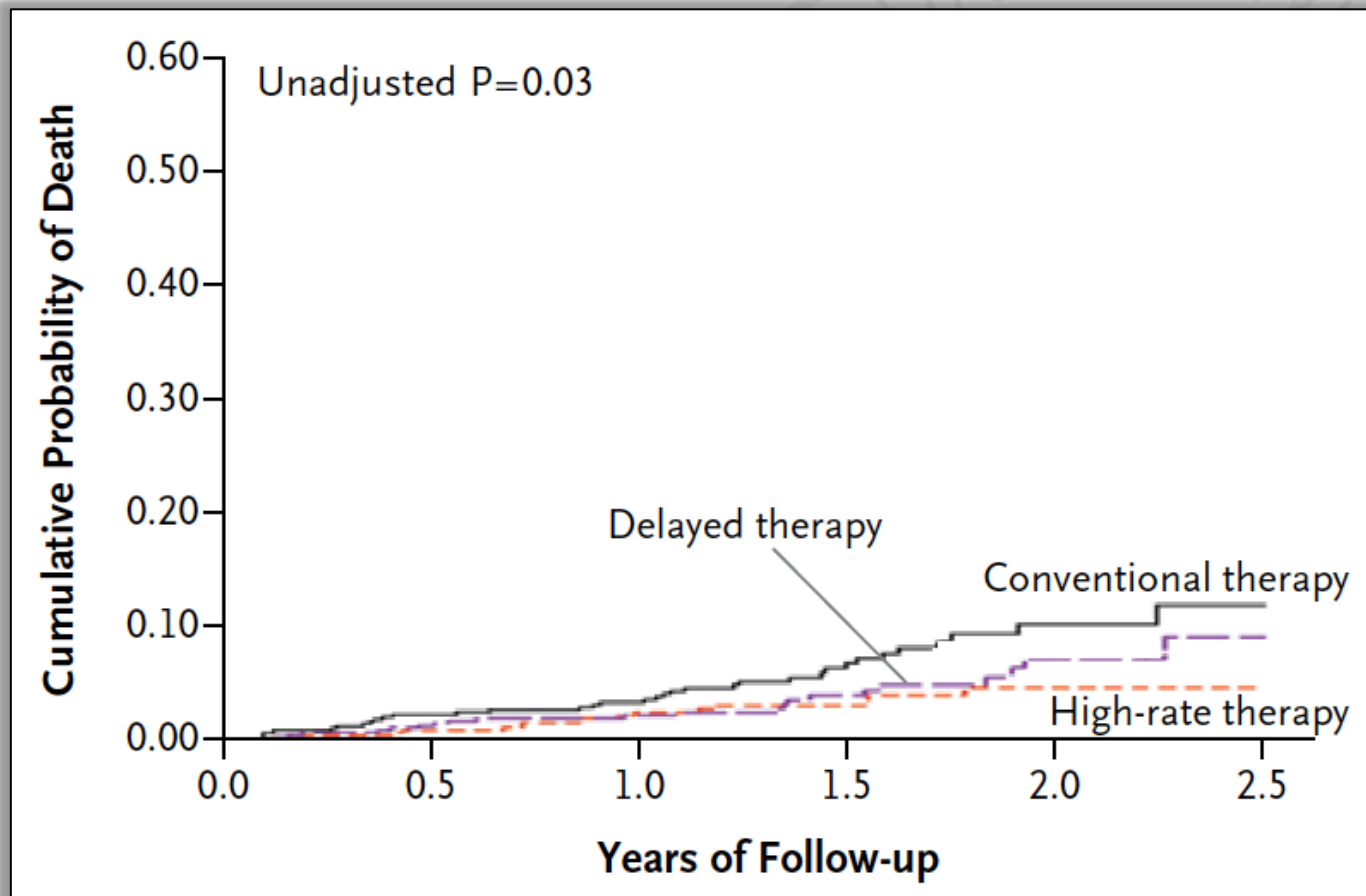
Reduction In Inappropriate Therapy and Mortality through ICD programming. *MADIT-RIT trial*

Cumulative Probability of First Occurrence of Inappropriate Tx



Reduction In Inappropriate Therapy and Mortality through ICD programming. *MADIT-RIT trial*

Cumulative Probability of Death



Reduction In Inappropriate Therapy and Mortality through ICD programming. **MADIT-RIT trial**

Table 3. Hazard Ratios for a First Occurrence of Inappropriate Therapy, Death, and a First Episode of Syncope According to Treatment Group.

| Variable | Conventional Therapy (N = 514) | High-Rate Therapy (N = 500) | Delayed Therapy (N = 486) | High-Rate Therapy vs. Conventional Therapy | | Delayed Therapy vs. Conventional Therapy | |
|---|-----------------------------------|--------------------------------|------------------------------|--|---------|--|---------|
| | | | | Hazard Ratio (95% CI) | P Value | Hazard Ratio (95% CI) | P Value |
| | <i>no. of patients</i> | | | | | | |
| First occurrence of inappropriate therapy | 105 | 21 | 26 | 0.21 (0.13–0.34) | <0.001 | 0.24 (0.15–0.40) | <0.001 |
| Death | 34 | 16 | 21 | 0.45 (0.24–0.85) | 0.01 | 0.56 (0.30–1.02) | 0.06 |
| First episode of syncope | 23 | 22 | 22 | 1.32 (0.71–2.47) | 0.39 | 1.09 (0.58–2.05) | 0.80 |

CONCLUSIONS

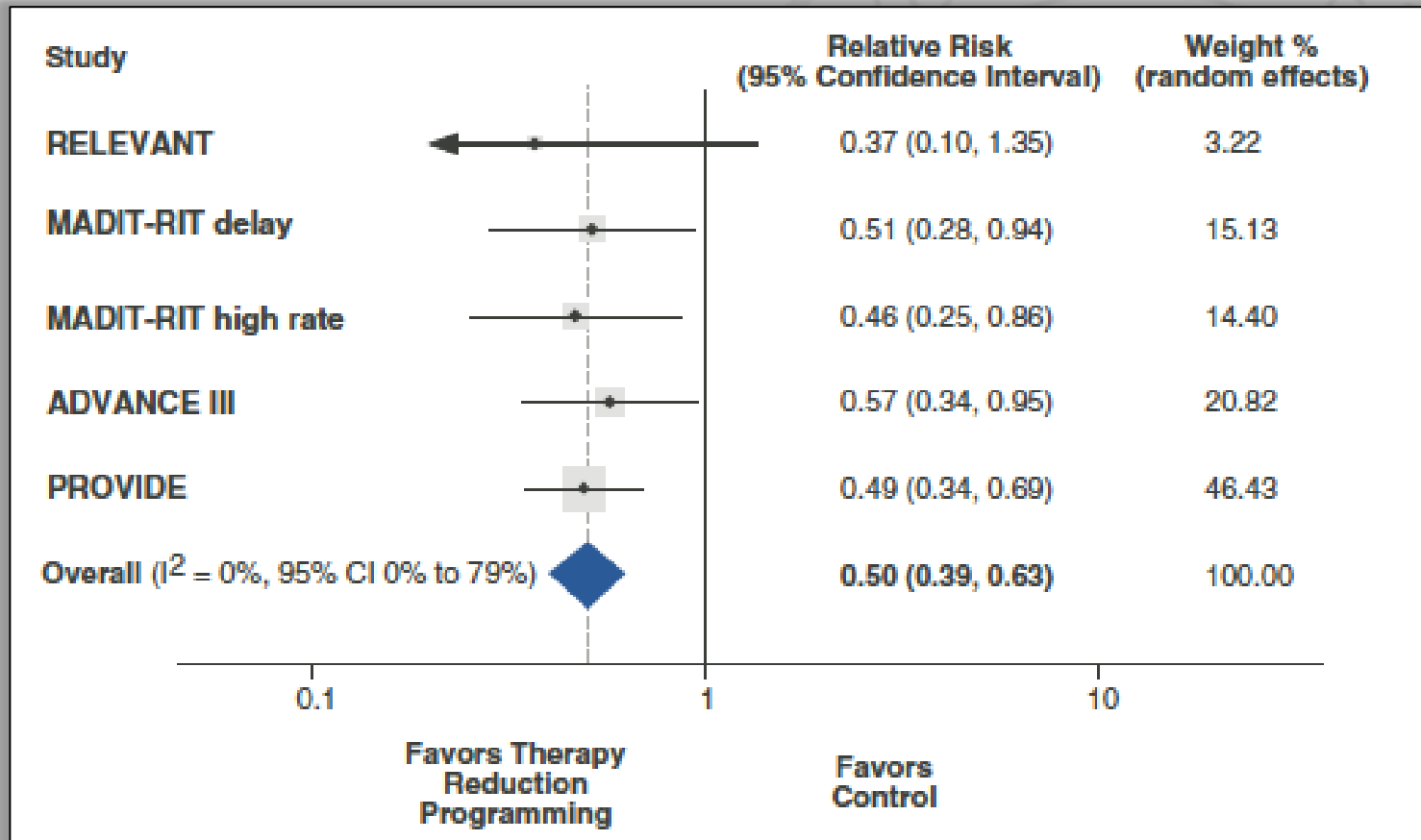
Programming of ICD therapies for tachyarrhythmias of ≥ 200 BPM or with a prolonged delay in therapy at ≥ 170 beats BPM was associated with reductions in inappropriate therapy and all-cause mortality

Impact of Programming Strategies Aimed at Reducing Nonessential Implantable Cardioverter Defibrillator Therapies on Mortality

- ❖ 7687 patients from 6 trials: 3598 conventional vs 4089 Therapy reduction programming
- ❖ EMPIRIC, MADIT-RIT, ADVANCE-III, PROVIDE, RELEVANT, PREPARE
- ❖ No significant heterogeneity among studies was observed (P =0.6)
- ❖ No significant difference in the risk of syncope (P =0.5)

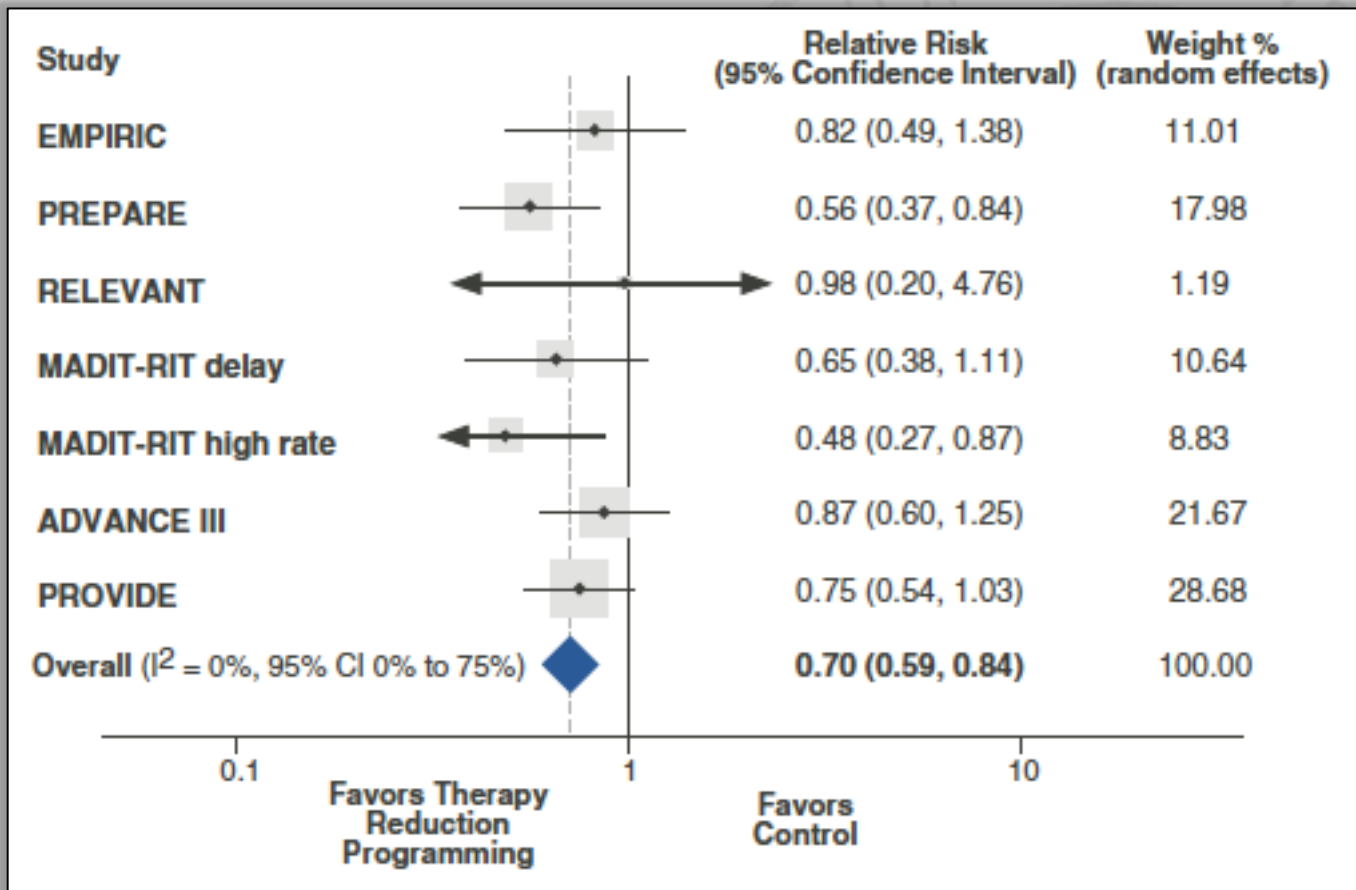
Impact of Programming Strategies Aimed at Reducing Nonessential Implantable Cardioverter Defibrillator Therapies on Mortality

Risk of Inappropriate ICD Shocks



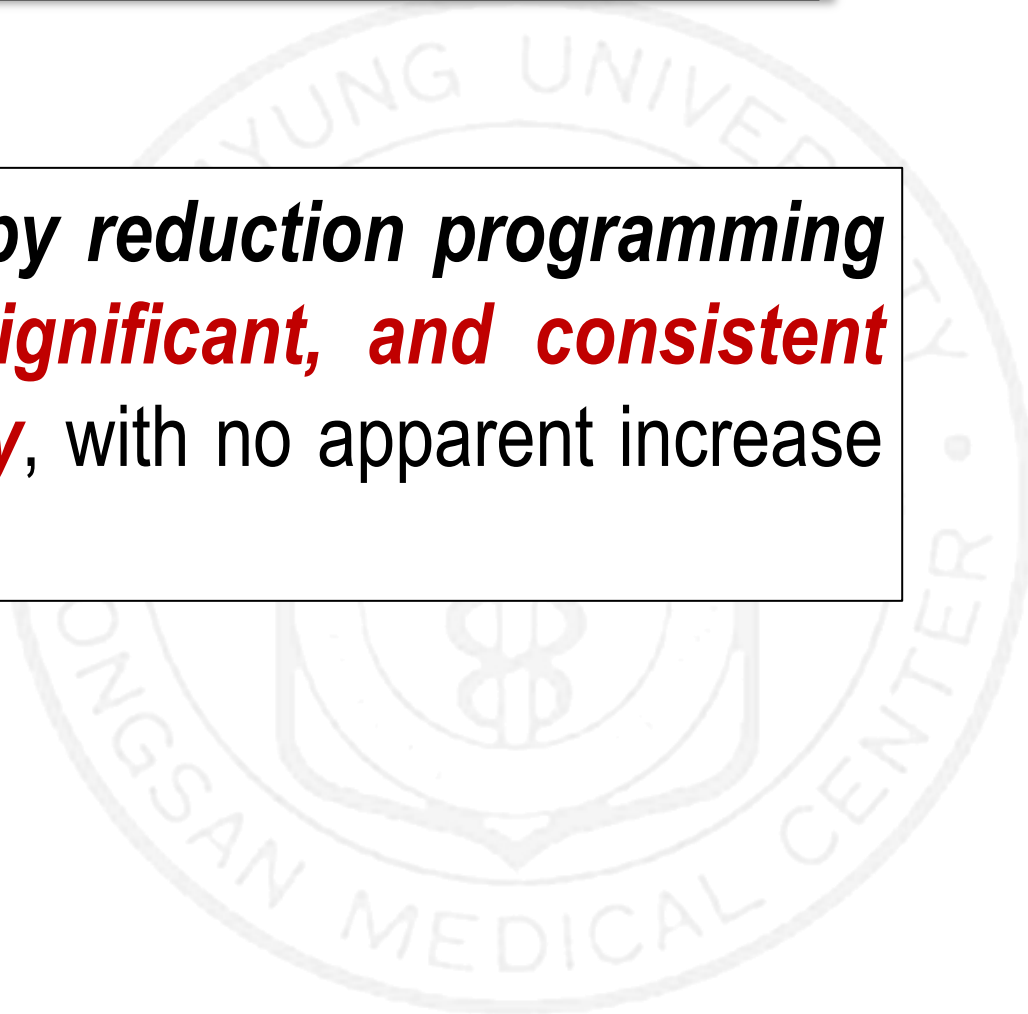
Impact of Programming Strategies Aimed at Reducing Nonessential Implantable Cardioverter Defibrillator Therapies on Mortality

Effects on the outcome of All-cause Mortality



Impact of Programming Strategies Aimed at Reducing Nonessential Implantable Cardioverter Defibrillator Therapies on Mortality

Conclusions—*Therapy reduction programming* results in a ***large, significant, and consistent reduction in mortality***, with no apparent increase in the risk of syncope



Suggested ICD Programming

| Condition | Arrhythmia | Programming |
|-----------------------------|--------------------|---|
| Primary Prevention | VF: ≥ 200 BPM | Longer detection time or 30/40 NID |
| | FVT: 170-199 BPM | Monitor only |
| Secondary Prevention | VF: ≥ 200 BPM | 30/40 NID Use 1-2 sequences of burst |
| | FVT: 170-199 BPM | Use multiple sequences of ATP |
| | VT < 170 BPM | Monitor only |

Recommended ICD Programming

| zone | Primary Prevention | | | Secondary prevention | | |
|------------|--------------------|---|----------------------|----------------------|--|---------------------------------|
| | Lower rate (BPM) | Duration | Tx | Lower rate (BPM) | Duration | Tx |
| VF | 220-250 | 32 intervals 16 intervals 5 seconds | ≥ 30J X 6 | 220-250 | 18/24 intervals 16 intervals 5 seconds | ≥ 30J X 6 |
| FVT | 182 | 30/40 intervals 16-20 intervals 7 seconds SVT ON | 1 burst* ≥30J X 5 | 200 | 18/24 intervals 9-12 intervals 5 seconds SVT ON | 1 burst* ≥30J X 5 |
| VT | 167 | 30/40 intervals 16-20 intervals 7 seconds SVT ON | Off (Monitor) | 150 | 16 intervals 16 intervals 7 seconds SVT ON | 3 bursts 20J X 1 ≥30J X 3 |

2012 EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: implant and follow-up recommendations and management



Electrocardiogram Evaluation of the CRT patients

- ✓ Atrial rhythm—NSR or atrial paced vs. atrial fibrillation
- ✓ Evidence of appropriate atrial sensing or capture
- ✓ Presence of ventricular pacing
- ✓ Presence, frequency, and morphology of PVCs
- ✓ Evidence of appropriate ventricular sensing or capture
- ✓ Morphology of paced QRS—evidence of LV capture
- ✓ Paced QRS width
- ✓ Evidence of pacing fusion or pseudo-fusion in QRS

2012 EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: implant and follow-up recommendations and management

Use of Device Diagnostic Data

- ❖ ***Ventricular pacing***
 - > 95% (Ideally near to 100%)
 - Make sure it's BiV pacing through ECG
- ❖ ***Ventricular sensing***
 - Should be close to 0%
- ❖ ***PVC/NSVT***
 - Reduce the time in effective CRT; should be suppressed
- ❖ ***AT/AF episodes/Mode switch***
 - Promote native AV conduction: depends on burden

Radiofrequency Ablation of Premature Ventricular Ectopy Improves the Efficacy of Cardiac Resynchronization Therapy in Nonresponders

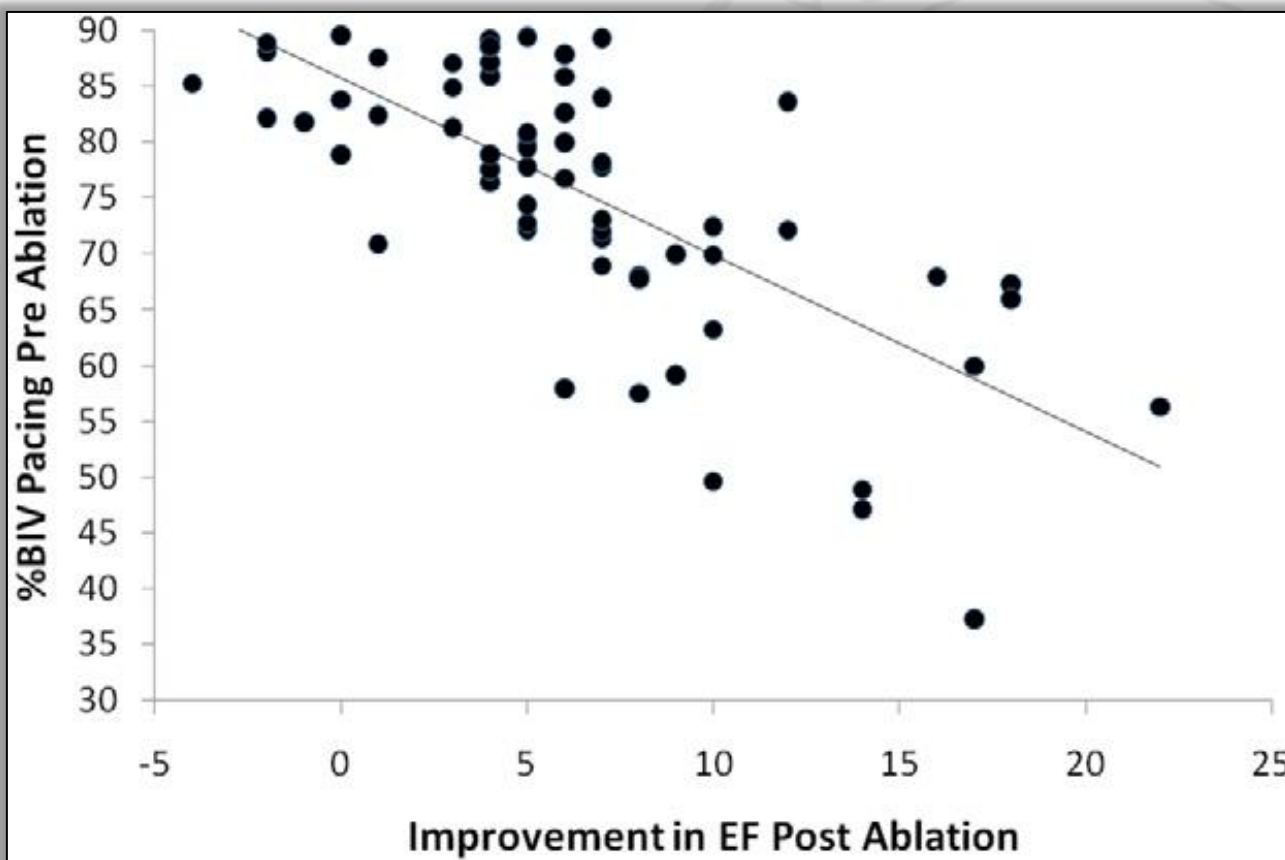
- ❖ 65 patients, CRT nonresponders with PVC > 10,000/24h
- ❖ Underwent PVC ablation
- ❖ Acute & long-term success: 91% & 88% in 12 ± 4 Mo FU

Changes in Various Echo Parameters Before and After PVC Ablation

| Change in Echo Parameters | Pre-Ablation | Post-Ablation | Mean Improvement | p Value |
|---------------------------|--------------|---------------|------------------|---------|
| Δ EF | 26.2 ± 5.5 | 32.7 ± 6.7 | 6.42 ± 5.26 | <0.001 |
| Δ LVEDD | 6.83 ± 0.83 | 6.51 ± 0.91 | -0.32 ± 0.26 | <0.001 |
| Δ LVESD | 5.83 ± 0.55 | 5.62 ± 0.32 | -0.31 ± 0.23 | <0.001 |
| Δ LVESV | 178 ± 72 | 145 ± 23 | -33.17 ± 22.94 | <0.001 |
| Δ LVEDV | 242 ± 85 | 212 ± 63 | -30.65 ± 21.63 | <0.001 |

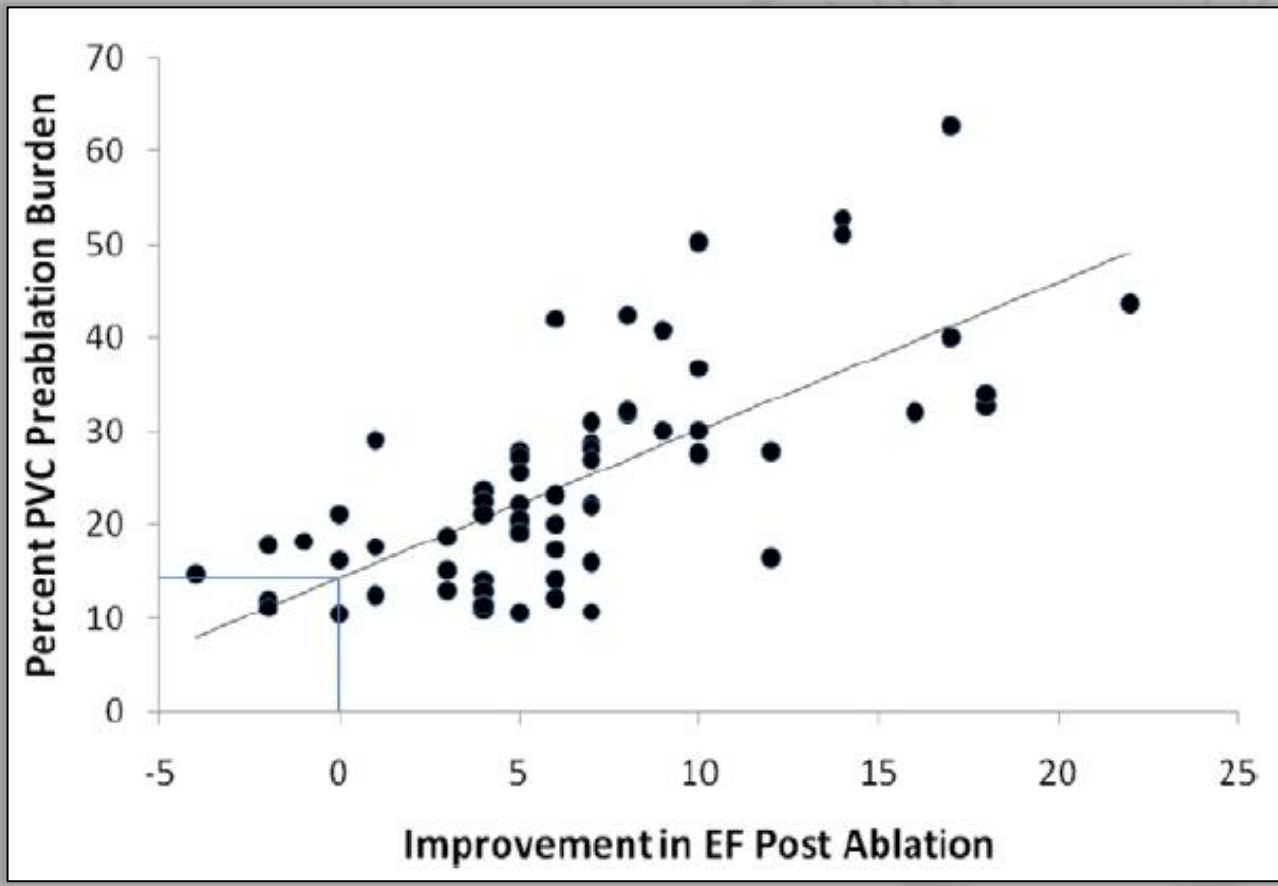
Radiofrequency Ablation of Premature Ventricular Ectopy Improves the Efficacy of Cardiac Resynchronization Therapy in Nonresponders

Correlation Between Pre-Ablation BIV Pacing % & Post-Ablation Improvement in EF



Radiofrequency Ablation of Premature Ventricular Ectopy Improves the Efficacy of Cardiac Resynchronization Therapy in Nonresponders

Correlation Between PVC Burden & EF Change Following Ablation

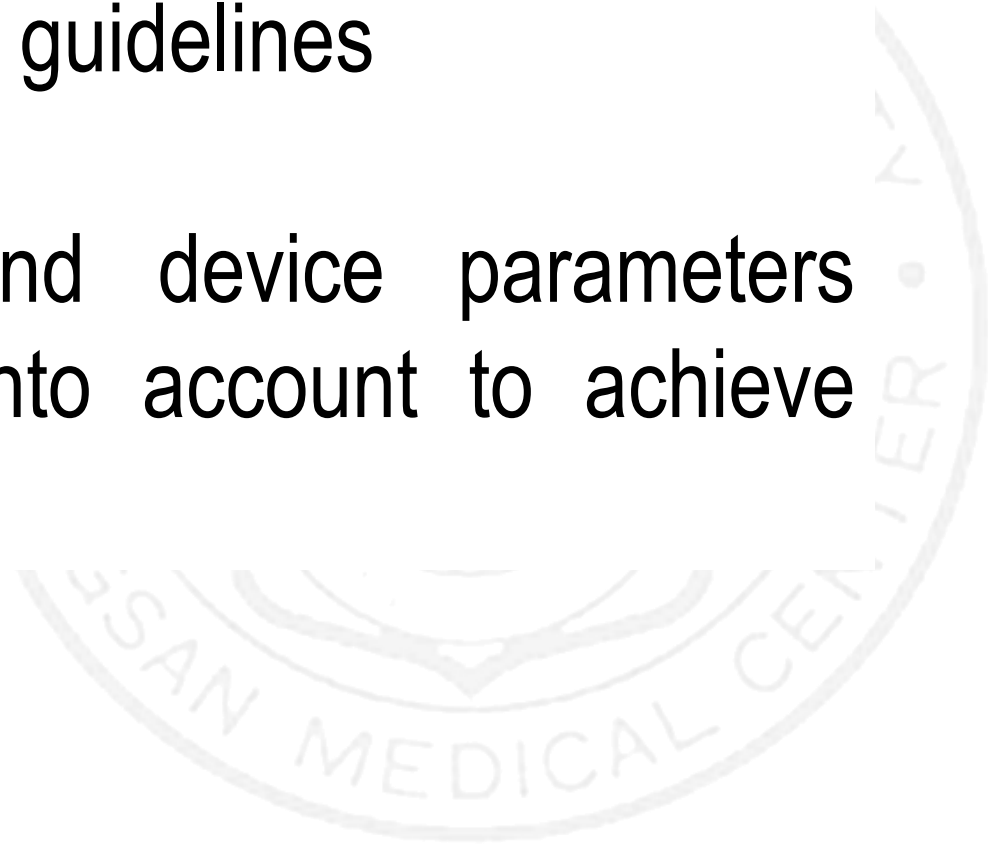


Radiofrequency Ablation of Premature Ventricular Ectopy Improves the Efficacy of Cardiac Resynchronization Therapy in Nonresponders

- ❖ **Sites of PVC: LV (75%) vs RV (25%)**
 - ✓ LV submitral annulus: 28.94%, the rest of LV: (46.06%)
 - ✓ RVOT: 15.78%, the rest of RV: 9.22%
- ❖ **Pre-ablation PVC burden (>22%/24h)** revealed an improvement in ejection fraction
- ❖ **Conclusions:** PVC ablation may be used to enhance CRT efficacy in nonresponders with significant PVC burden

Summary

- It is important to choose right patients according to current guidelines
- Several clinical and device parameters should be taken into account to achieve adequate results





Thank You for Your Attention !



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