INNOVATIONS IN DEVICE THERAPY:

Subcutaneous ICDs, Leadless Pacemakers, CRT Indications

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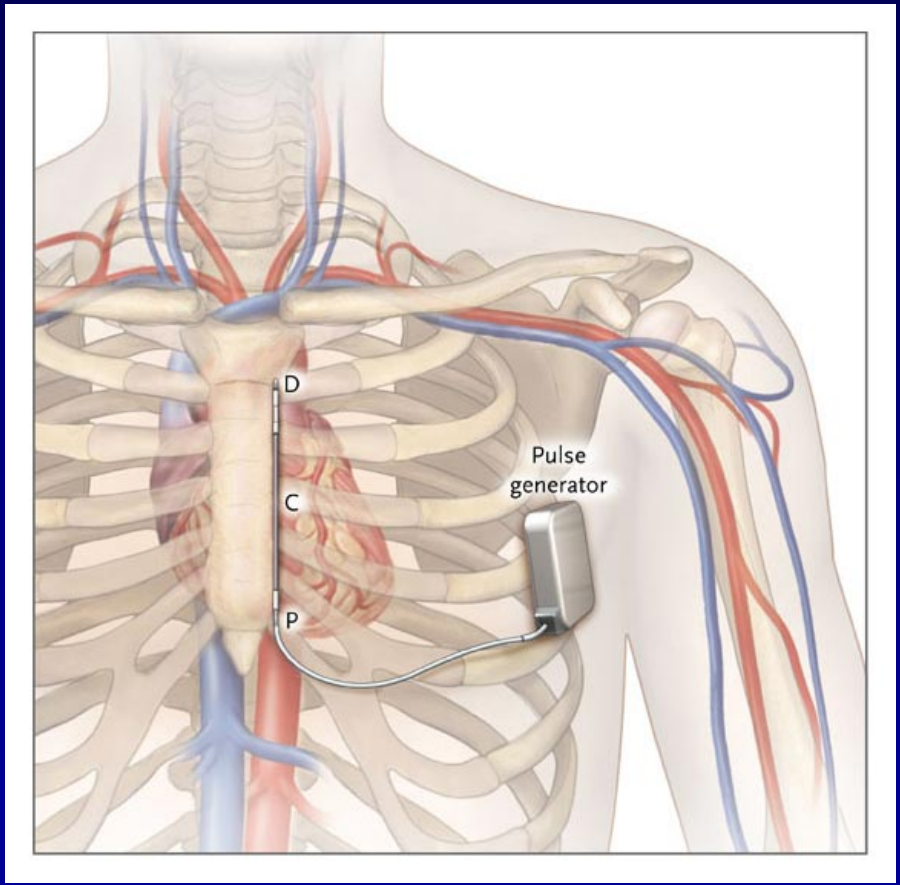
Disclosures: ACC Foundation: Consultant; Biosense / Webster: Consultant, Investigator; Medtronic: Consultant, Investigator

TRANSVENOUS ICD LEAD ISSUES

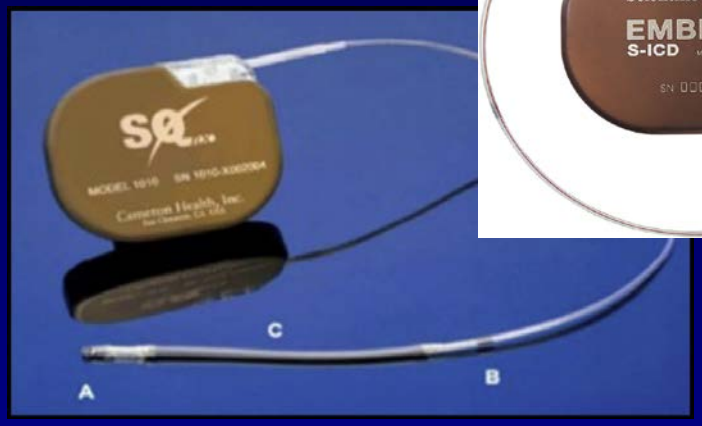
- TV ICD lead failure estimated at 0.68%-3.75% annually
  - Lead survival at 2 years: 91-99%
  - Lead survival at 5 years: 81-98%
  - Lead survival at 8 years: 60-95%
- Up to 1/10 PM implants associated with adverse events
  - Lead related (dislodgement, fracture, insulation failure, infection, cardiac perforation, venous occlusion, tricuspid regurgitation)
  - Surgical pocket or generator related (skin erosion, hematoma, infection)

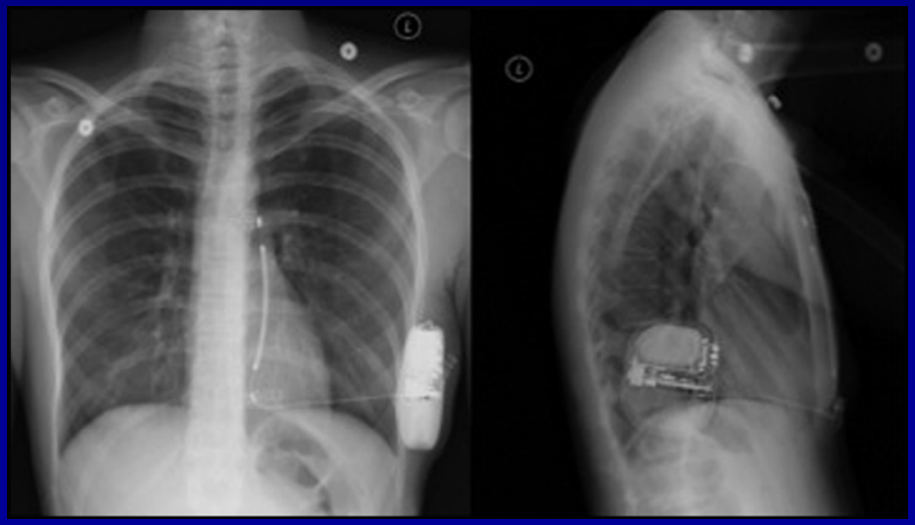
SUBCUTANEOUS ICD



- Indications
  - Current indication for ICD implantation
  - Not suited for pts who need
    - Pacing for bradycardia
    - Pacing for VT
    - CRT
- Initial target populations
  - Unfavorable anatomy, venous occlusion
  - Prior transvenous device infection or high risk for infection
  - Younger patients with need for lifelong therapy

DEVICE / IMPLANT CONSIDERATIONS





- Surface ECG screening
- Sensing vectors
- Minimal programming
  - Unconditional zone
  - Conditional zone – morphology algorithms to discriminate SVT, cardiac signal oversensing
- DFT testing at 65 J
  - Device delivers 80J
- Large PG size (60-70 cc)
- Can provide 30 s post shock demand pacing
- Episode EGM storage (not remote monitoring)

EFFORTLESS REGISTRY: REAL WORLD EXPERIENCE

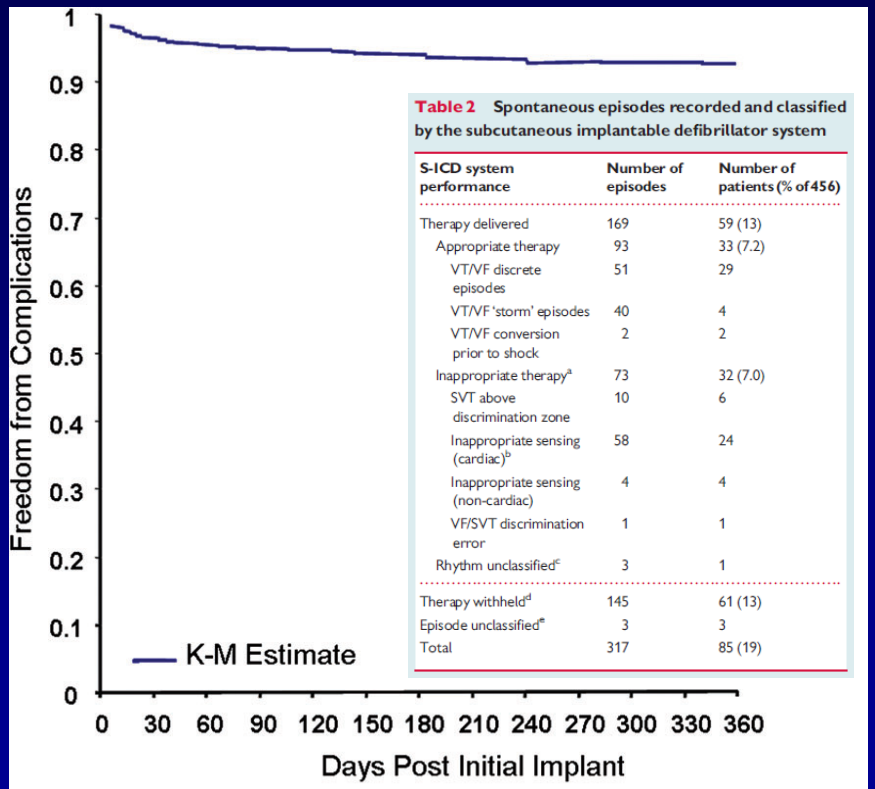


Table 2 Spontaneous episodes recorded and classified by the subcutaneous implantable defibrillator system

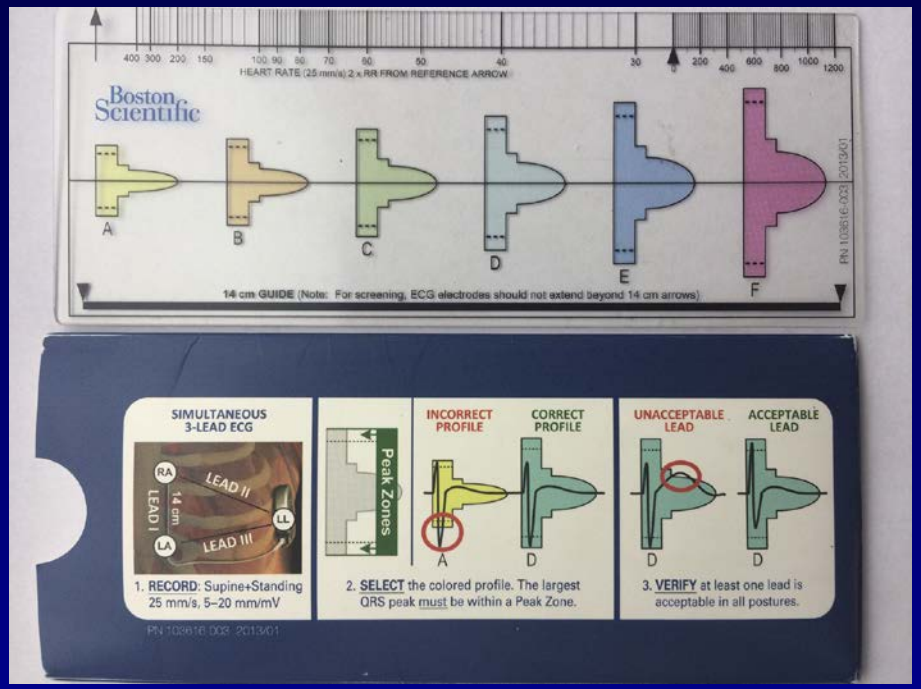
S-ICD system performance	Number of episodes	Number of patients (% of 456)
Therapy delivered	169	59 (13)
Appropriate therapy	93	33 (7.2)
VT/VF discrete episodes	51	29
VT/VF 'storm' episodes	40	4
VT/VF conversion prior to shock	2	2
Inappropriate therapy[a]	73	32 (7.0)
SVT above discrimination zone	10	6
Inappropriate sensing (cardiac)[b]	58	24
Inappropriate sensing (non-cardiac)	4	4
VF/SVT discrimination error	1	1
Rhythm unclassified[c]	3	1
Therapy withheld[d]	145	61 (13)
Episode unclassified[e]	3	3
Total	317	85 (19)

	Day 30	Day 180	Day 360
KM Rate	97%	94%	94%
At Risk	453	381	290
Failed	14	26	28
Censored	3	62	148
Remaining	439	368	280

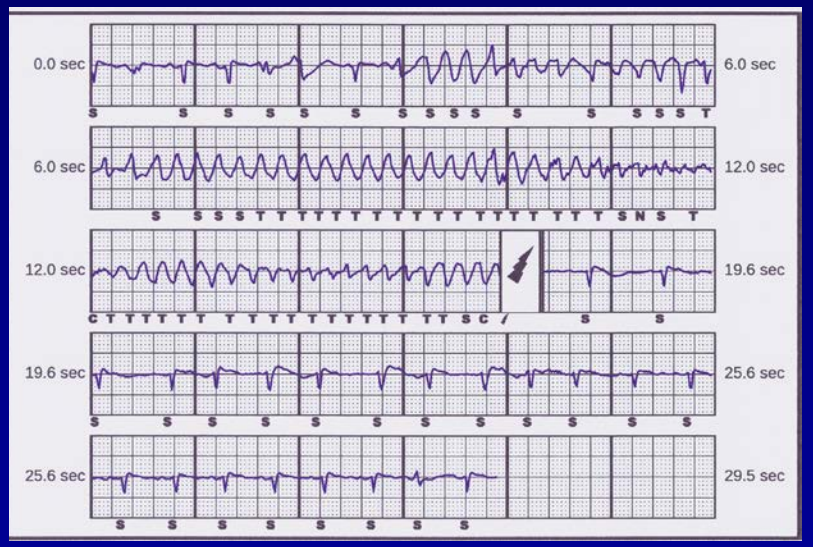
- 472 pts, mean 18 mo f/u
- Age 49±18 yr
- LVEF 42±19%
- 63% primary prevention
- Heart disease:
  - Ischemic (37%)
  - Channelopathy/IVF (21%)
  - HCM (8%)
  - Other nonischemic CM (23%)
- Device infection 4%, 2.2% required explant
- One arrhythmic death

Lambiase et al, EHJ 2014; 35:1657-1665

S – ICD FUNCTION



- pocket hematomas 0.4% of pts
- Superficial infection treated conservatively in 0.3% of pts
- infection requiring device removal or revision occurred in 1.7% of pts



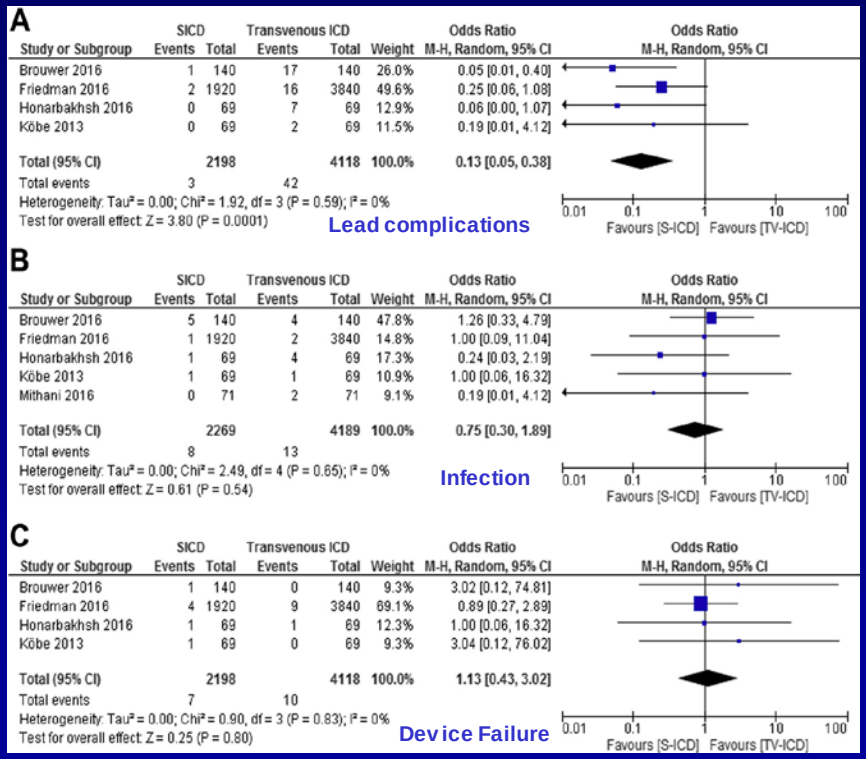
- 882 pts followed for mean of 651 days
- A total of 111 VT/VF episodes treated in 59 patients.
- Single shock successful in terminating VF in 90.1% of episodes, and 98.2% of
- VT/VF episodes after 5 shocks

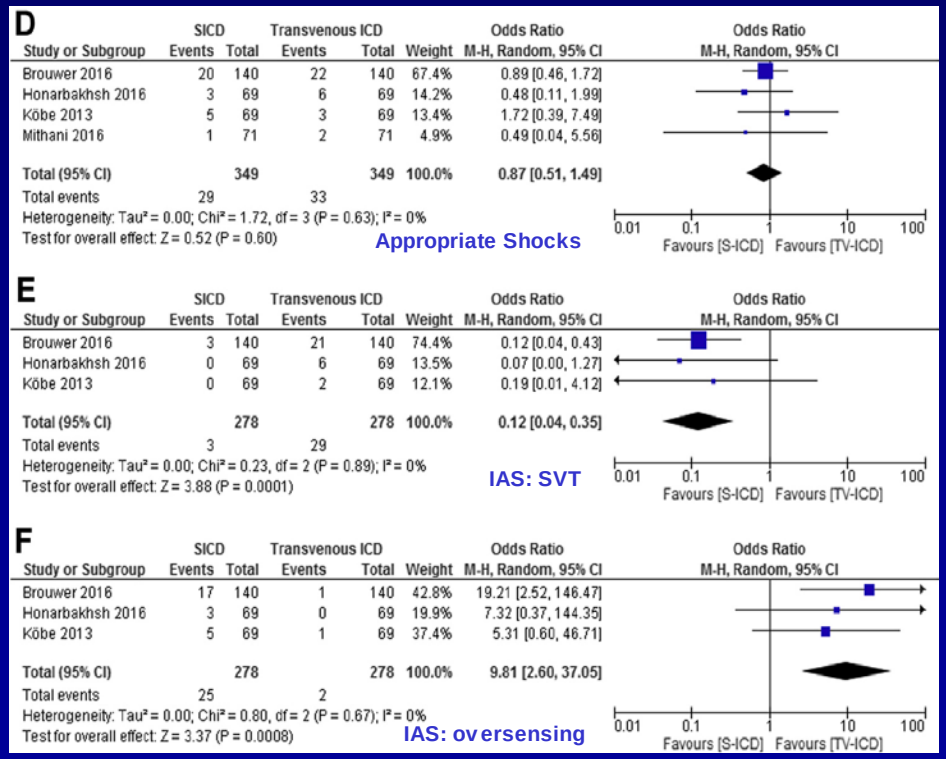
Burke et al, J Am Coll Cardiol 2015. 60:1605-1650

Subcutaneous Versus Transvenous Implantable Defibrillator Therapy

A Meta-Analysis of Case-Control Studies

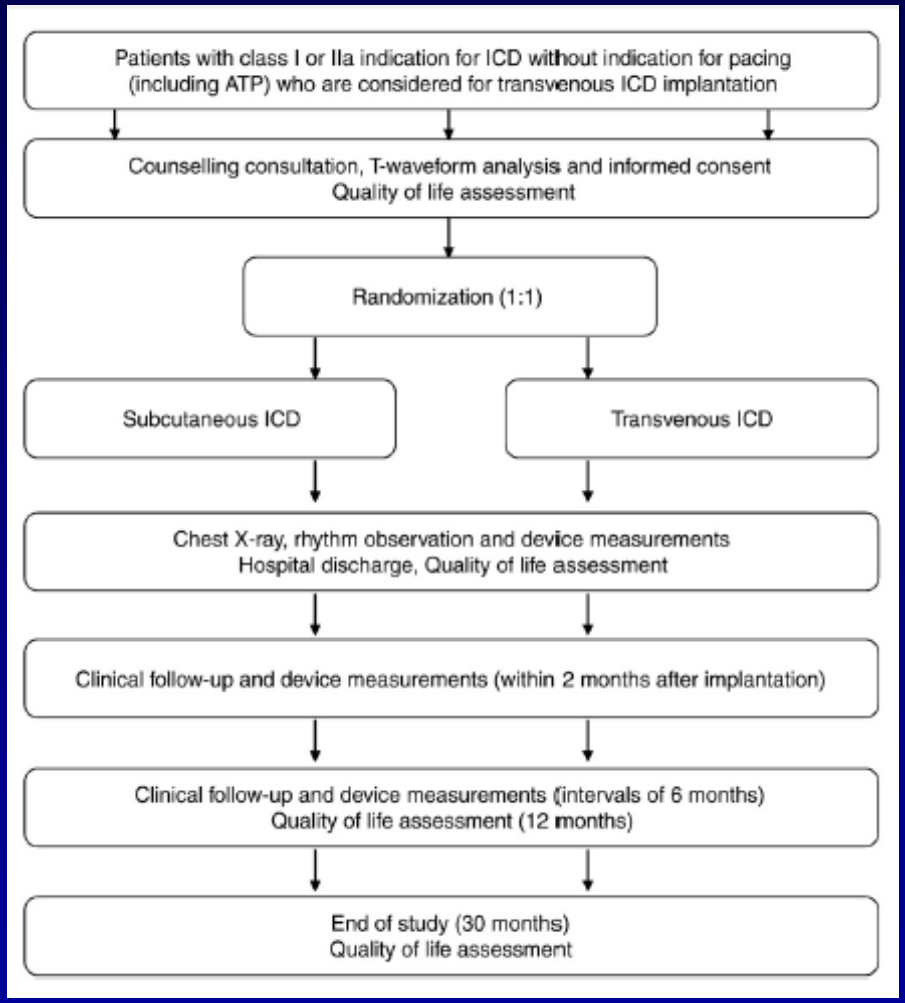
Indranill Basu-Ray, MD,[a] Jing Liu, MD,[b] Xiaoming Jia, MD,[b] Michael Gold, MD,[c] Kenneth Ellenbogen, MD,[d] James DiNicolantonio, PharmD,[e] András Komócsi, MD,[f] András Vorobcsuk, MD,[g] Jitae Kim, BS,[h] Hamid Afshar, MD,[i] Wilson Lam, MD,[i] Nilesh Mathuria, MD,[a] Mehdi Razavi, MD,[a] Abdi Rasekh, MD,[a] Mohammad Saeed, MD[a]





JACCEP 2017: online before print

PRAETORIAN TRIAL



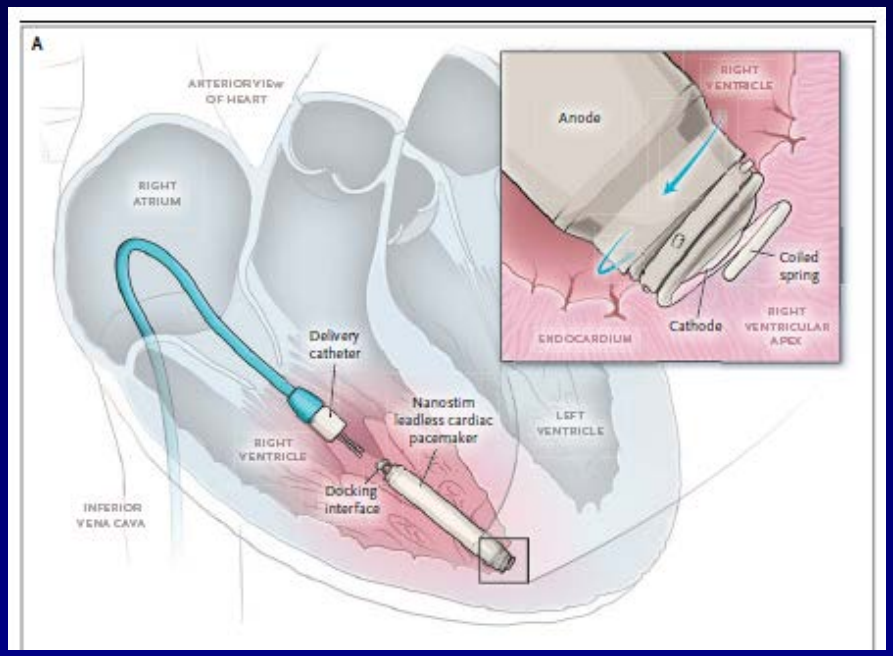
Olde Nordkamp et al Am Heart J, 2012; 163:753-760

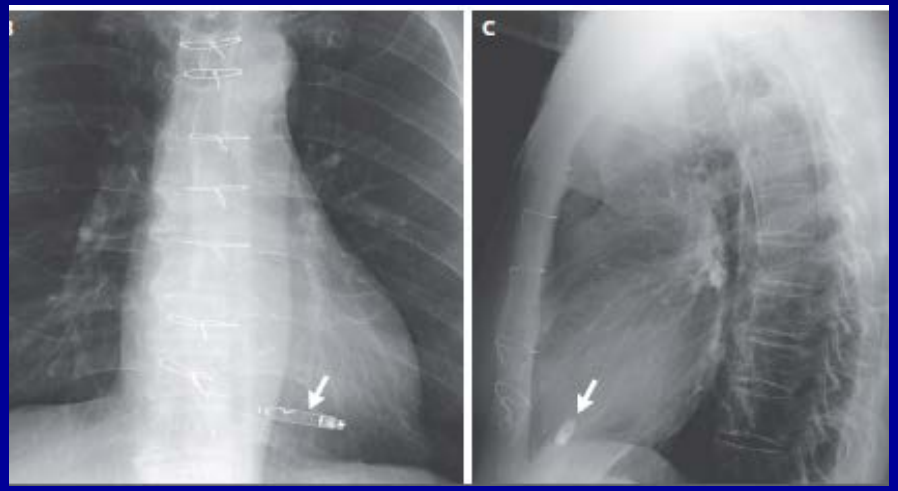
- Noninferiority randomized comparison of single chamber TV-ICD vs S-ICD
- Primary endpoint: composite of device-related complications and inappropriate shocks
- Secondary endpoints:
  - Device related complications
  - Inappropriate shocks
  - Appropriate shocks
  - QOL, MACE, death, syncope
- Target enrollment 700 pts
- First enrollment 2/2011
- Estimated completion 2018

LEADLESS TRANSVENOUS PACING

- Up to 1/10 PM implants associated with adverse events
  - Lead related (dislodgement, fracture, insulation failure, infection, cardiac perforation, venous occlusion, tricuspid regurgitation)
  - Surgical pocket or generator related (skin erosion, hematoma, infection)
- Small (1cc) self contained devices with encapsulated battery, electronics, and electrodes have been developed
- Implantation via a transfemoral venous delivery-retrieval device with fixation in the RV
- Current devices for single chamber pacing indication only

LTP: SJM NANOSTIM

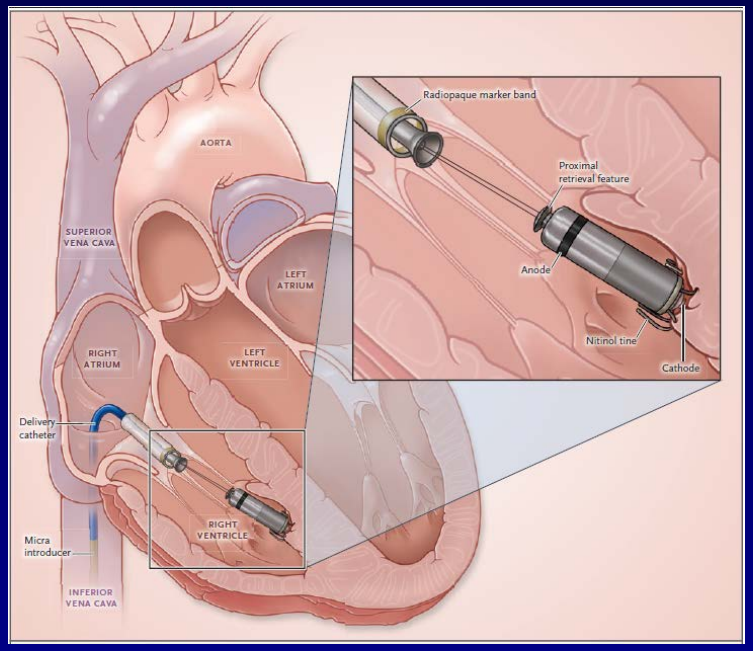




- Dimension 4.2 X 0.6 cm
- Active fixation, rate adaptive
- Successful implant 504/526 pts (96%)
  - Implant time 47±25 min
- 6 mo adverse event rate 6.7%
  - 1.6% perforation
  - 1.1% dislodgement
  - 0.8% new device for elevated pacing threshold

Reddy et al, New Engl J Med 2015; 373 (12):1125-1135

LTP: MEDTRONIC MICRA



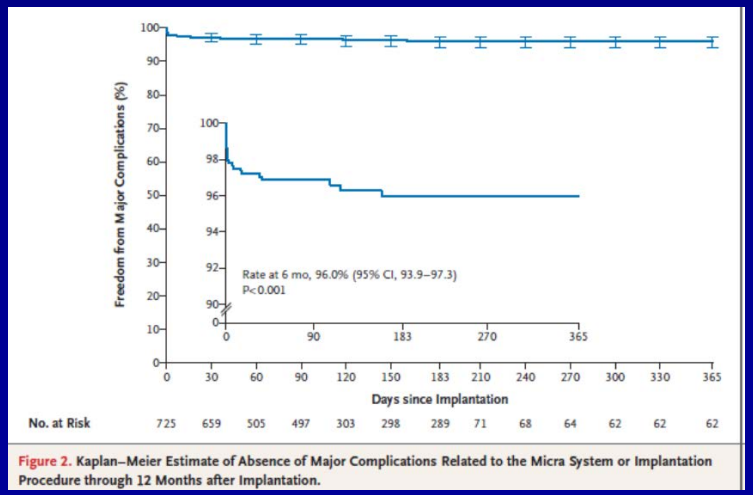
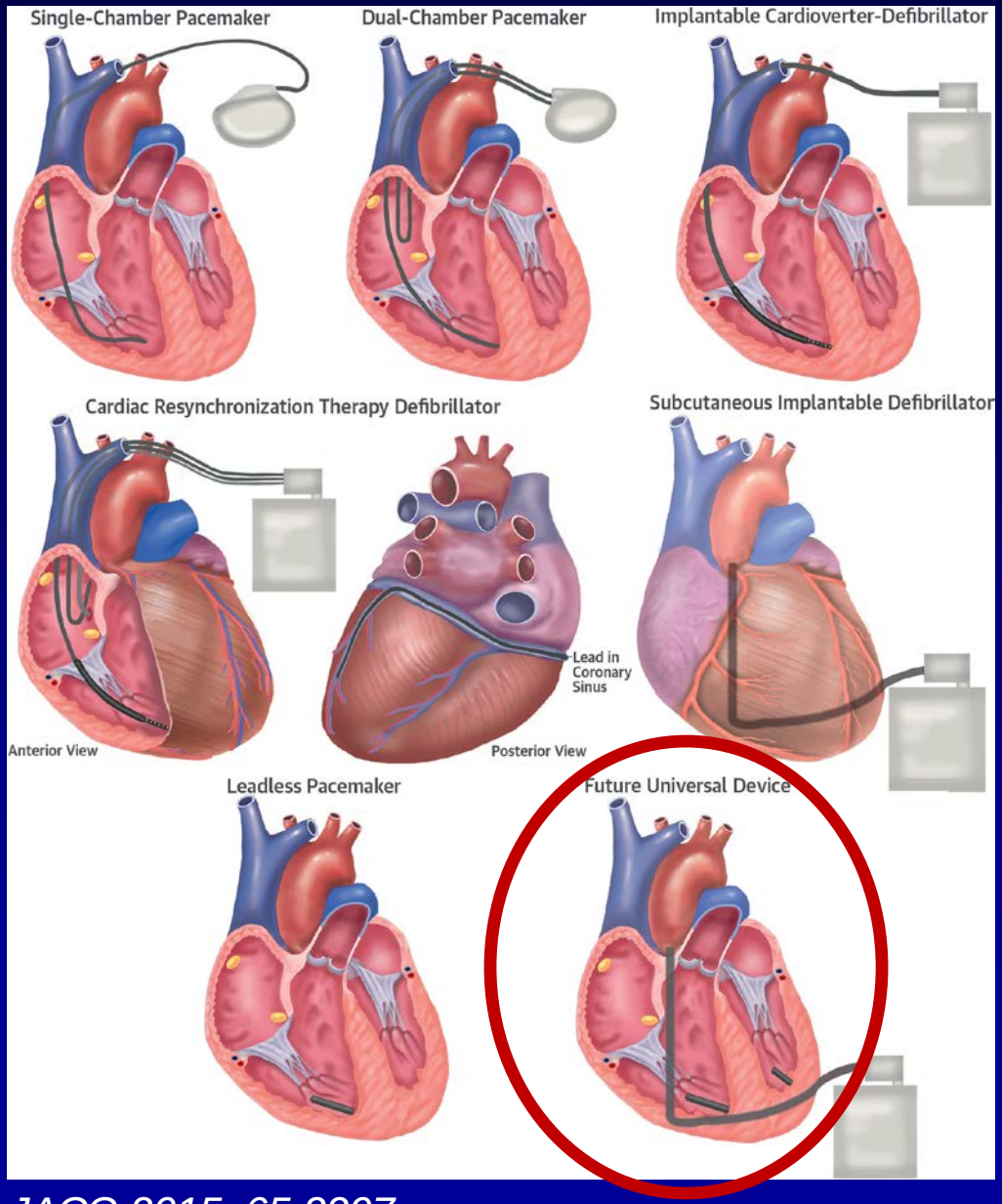


Figure 2. Kaplan–Meier Estimate of Absence of Major Complications Related to the Micra System or Implantation Procedure through 12 Months after Implantation.

- Dimension 2.6 X 0.7 cm
- Rate adaptive, APC
- Passive fixation
- Successful implant 719/725 pts (99%)
- 6 mo adverse event rate 4%
- Perforation or effusion 1.6%, elevated threshold
- requiring revision 0.2%
- no dislodgements

Reynolds et al, New Engl J Med 2015; *DOI 10.10561*

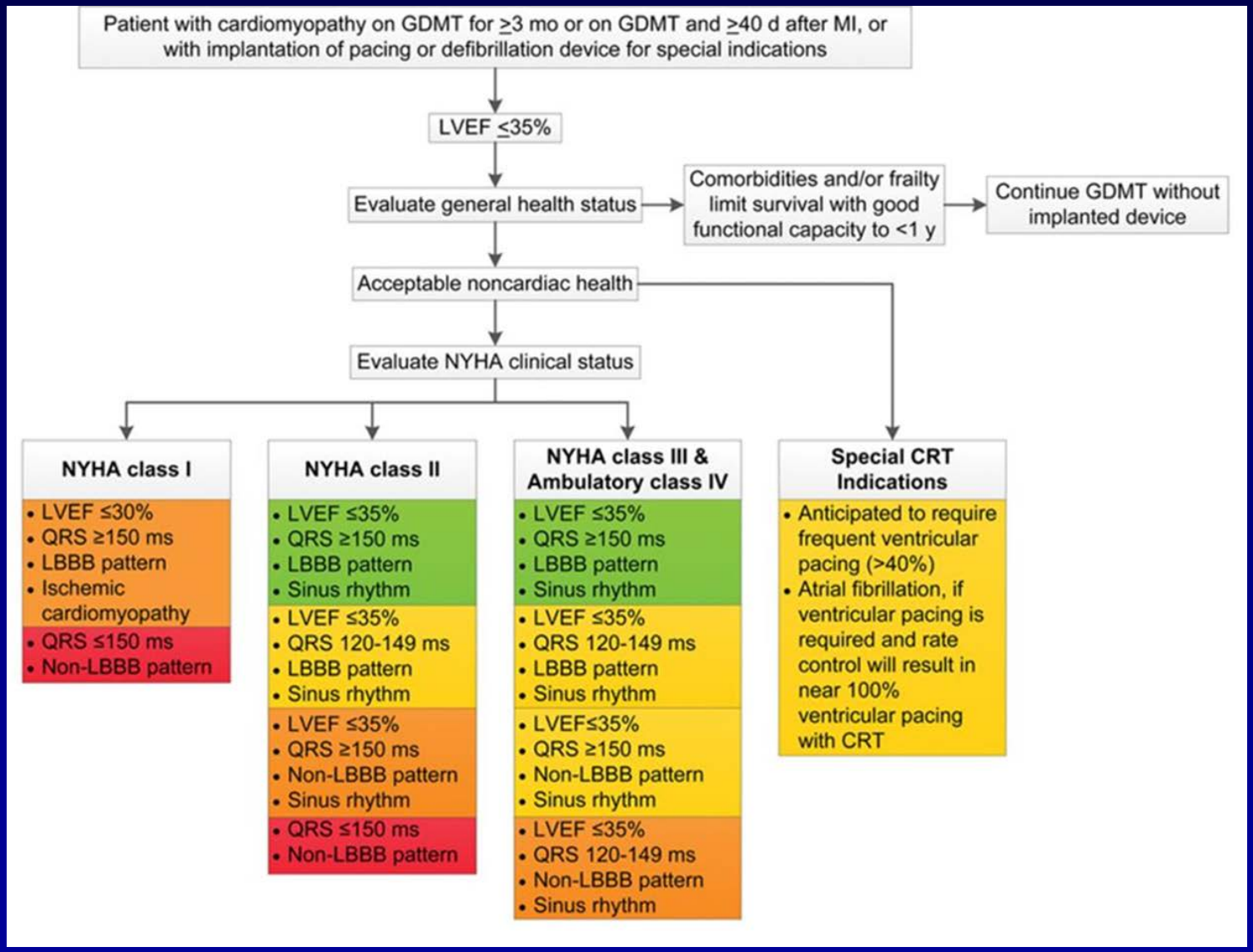


JACC 2015; 65:2207

FUTURE PERSPECTIVES

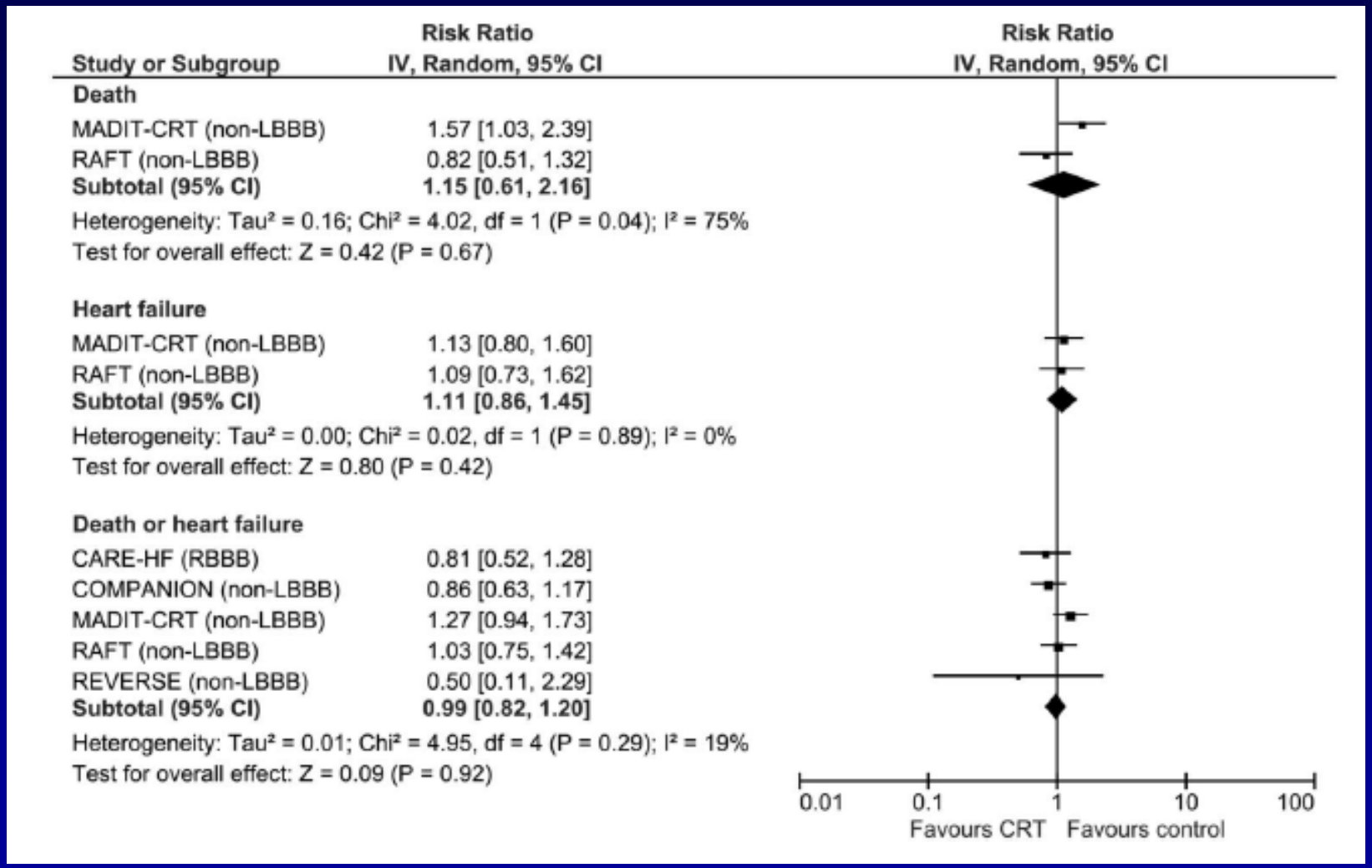
- Unresolved issues:
  - Battery longevity
  - Long-term stability of pacing parameters
  - Long-term ease of removal
- Potential integration into more complex devices

CURRENT CRT INDICATIONS



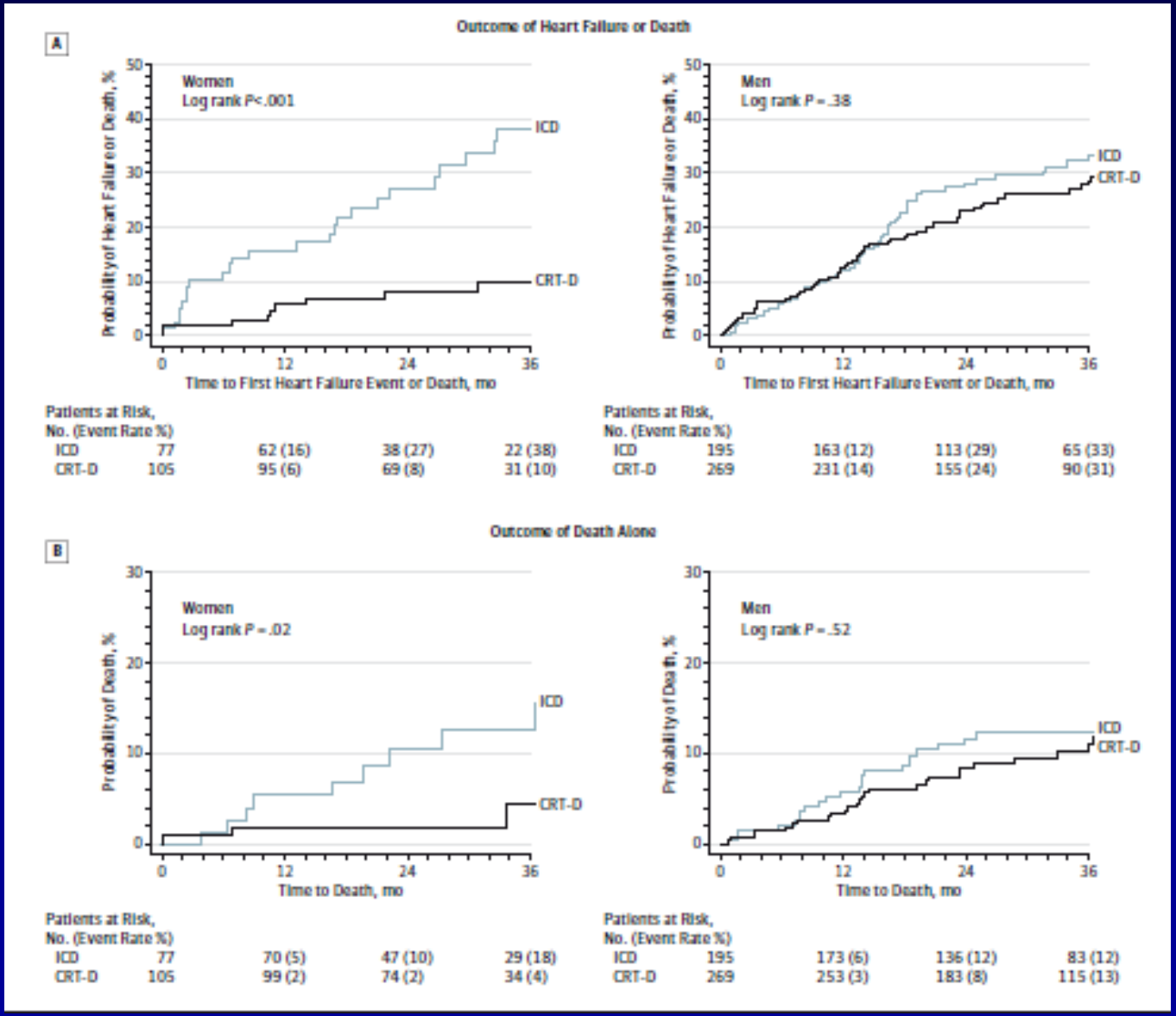
J Am Coll Cardiol 2012. 60:1297-313

CRT BENEFIT IN NON-LBBB



Cunnington et al, Heart 2015; 101: 1456-1462

WOMEN AND CRT



Zusterzeel et al, JAMA Intern Med 2014; 174:1340-1348

CRT FOR NON-LBBB AND LONG PR INTERVALS

Table 3. CRT-D Versus ICD therapy on HF/Death, HF Only, and All-Cause Mortality in Non-LBBB Patients by Baseline PR Interval

End Point*	Hazard Ratio	95% Confidence Interval	*P* Value	Interaction *P* Value
HF or death (141 events/478 patients)				
CRT-D: ICD in PR <230 ms (112 events)	1.45	0.96–2.19	0.078	<0.001
CRT-D: ICD in PR ≥230 ms (29 events)	0.27	0.13–0.57	<0.001	
HF only (117 events/478 patients)				
CRT-D: ICD in PR<230 ms (91 events)	1.31	0.84–2.05	0.235	<0.001
CRT-D: ICD in PR ≥230 ms (26 events)	0.25	0.11–0.57	<0.001	
All-cause mortality (67 events/478 patients)				
CRT-D: ICD in PR< 230 ms (55 events)	2.14	1.12–4.09	0.022	<0.001
CRT-D: ICD in PR ≥230 ms (12 events)	0.19	0.06–0.63	<0.001	

CRT-D indicates cardiac resynchronization therapy with defibrillator; HF, heart failure; ICD, implantable cardioverter defibrillator; and LBBB, left bundle branch block.

*Data were available in 478 of 534 patients with non-LBBB. Model is adjusted for age dichotomized at 65 years, diabetes mellitus, left ventricular end-systolic volume index at baseline, HF hospitalization before enrollment, diastolic blood pressure, atrial arrhythmia before enrollment, glomerular filtration rate ≥60, and smoking at baseline.

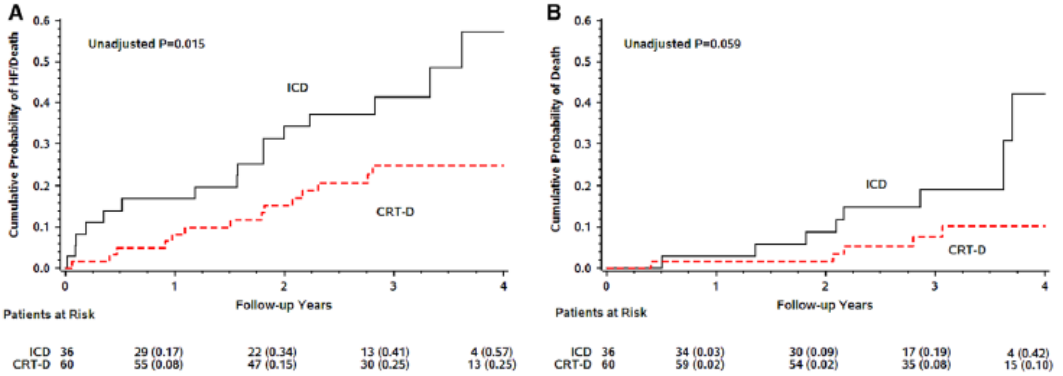


Figure 2. Kaplan–Meier estimates of the cumulative probability of (**A**) heart failure (HF)/death episodes in patients with PR ≥230 ms, (**B**) all-cause mortality in patients with PR ≥230 ms, (**C**) HF or death in patients with PR <230 ms, and (**D**) all-cause mortality in patients with PR <230 ms. CRT-D indicates cardiac resynchronization therapy with defibrillator; and ICD, implantable cardioverter defibrillator.

MADIT CRT SUBSTUDY

Kutyifa et al, Circulation A&E 2014; 7:645-651

NEW DIRECTIONS IN CRT

- Clinical response rate ~ 70%, objective indices (LVEF improvement, reduced ventricular volumes) in ~ 50%
- Practical considerations
  - % biventricular pacing as close to 100% as possible
  - Major issues are ventricular ectopy and AF
  - Assure LV contribution to pacing on surface ECG
- Quadripolar leads improve transvenous lead placement success, may be associated with reduced mortality
- Targeted placement at site of latest LV activation (electrogram timing) or contraction (LV strain imaging)
- Endocardial lead placement appears to produce better hemodynamic response, and allows tailoring to individual abnormal contraction patterns (AL-SYNC, WISE-CRT)

SUMMARY

- Use of Subcutaneous ICD expanding rapidly
  - High effectiveness for sensing and terminating ventricular arrhythmias has been maintained
  - Adverse events declining with experience
- Initial experience with leadless pacemakers promising, longer follow-up needed, size of target population unclear
- CRT: new twists
  - Gender interaction with QRS duration and efficacy
  - Possible benefit in non-LBBB with long PR intervals