ΕΤΑΙΡΕΙΑ ΜΕΛΕΤΗΣ ΚΑΙ ΕΡΕΥΝΑΣ
ΤΗΣ ΚΑΡΔΙΑΚΗΣ ΑΝΕΠΑΡΚΕΙΑΣ

24ο ΠΑΝΕΛΛΗΝΙΟ ΣΥΝΕΔΡΙΟ
Καρδιακής Ανεπάρκειας

Αρρυθμιολογικός κίνδυνος σε ασθενείς με HFpEF

Τι να κάνουμε;

Γεώργιος Ανδρικόπουλος, MD, PhD, FESC,
Διευθυντής Α Καρδιολογικής Τμήματος /
Ηλεκτροφυσιολογίας - Βηματοδότησης
Ερρίκος Ντυνάν Hospital Center

3 - 5 ΦΕΒΡΟΥΑΡΙΟΥ 2023
Ξενοδοχείο DIVANI CARAVEL

Presenter Disclosure Information

The presenter has received honoraria for participation in lectures and advisory boards from the following pharmaceutical and biotechnology companies:

- *AstraZeneca,*
- *Bard,*
- *Bayer Healthcare,*
- *Boehringer Ingelheim,*
- *Boston Scientific,*
- *Bristol-Myers Squibb,*
- *ELPEN,*
- *Galenica,*
- *Lilly,*
- *Medtronic,*
- *Menarini,*
- *MSD,*
- *Pfizer,*
- *Sanofi,*
- *Servier,*
- *StJude,*
- *Unifarma,*
- *Vianex.*

Sudden Death and Ventricular Arrhythmias in Heart Failure With Preserved Ejection Fraction

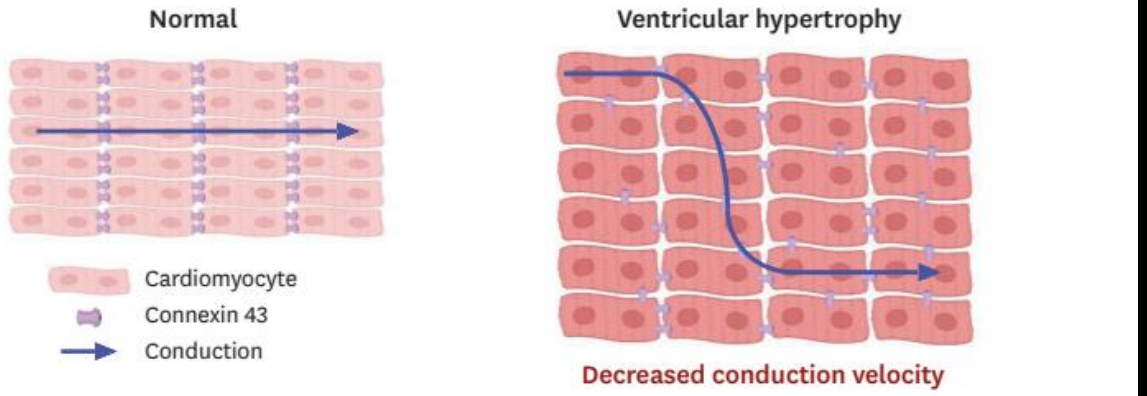


Figure 3. Ventricular hypertrophy in HFpEF reduces the conduction velocity and provides substrates for re-entry.
HFpEF = heart failure with preserved ejection fraction.

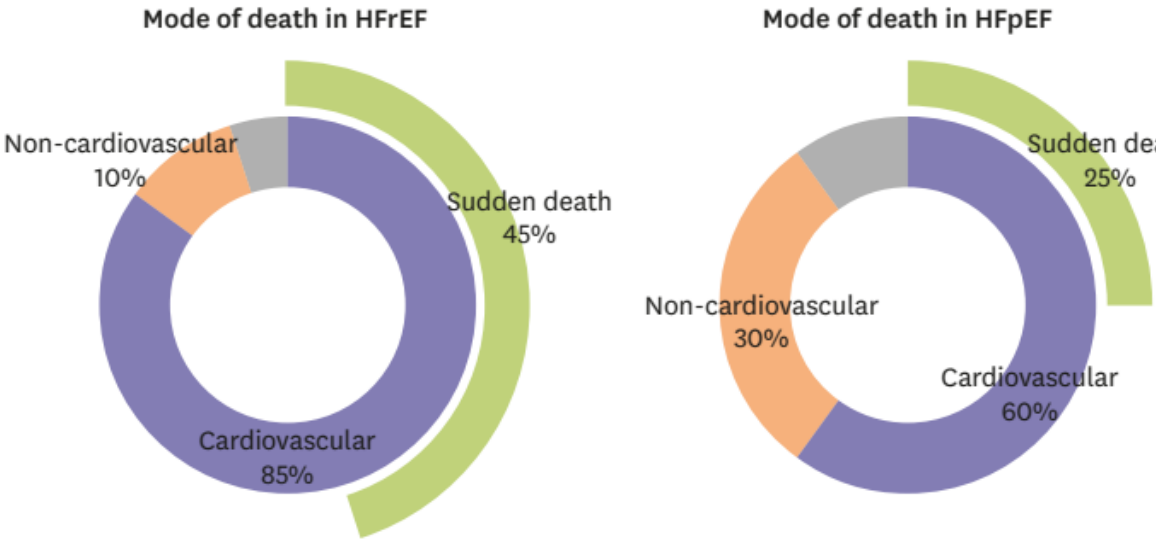
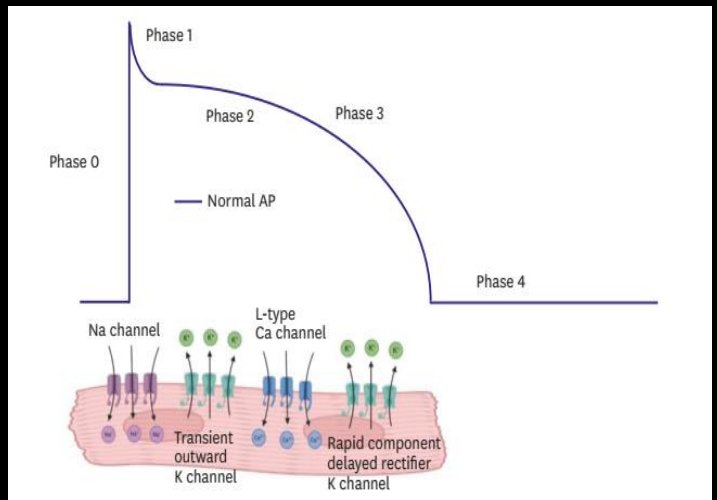


Figure 1. Mode of death in HFrEF and HFpEF patients.
HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction.



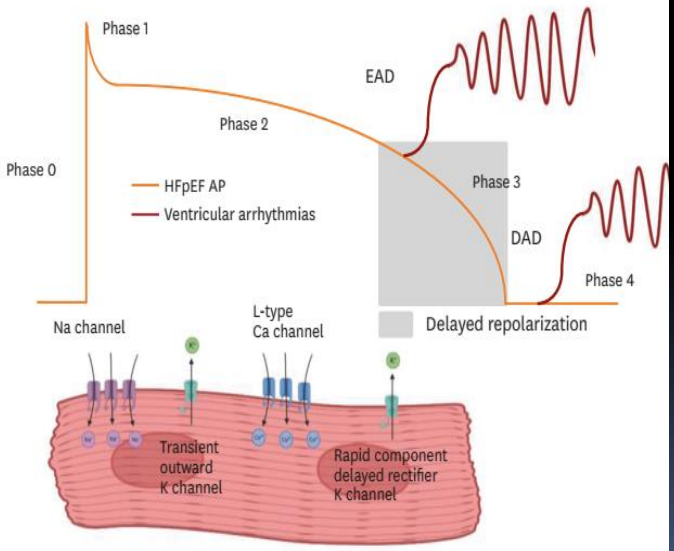
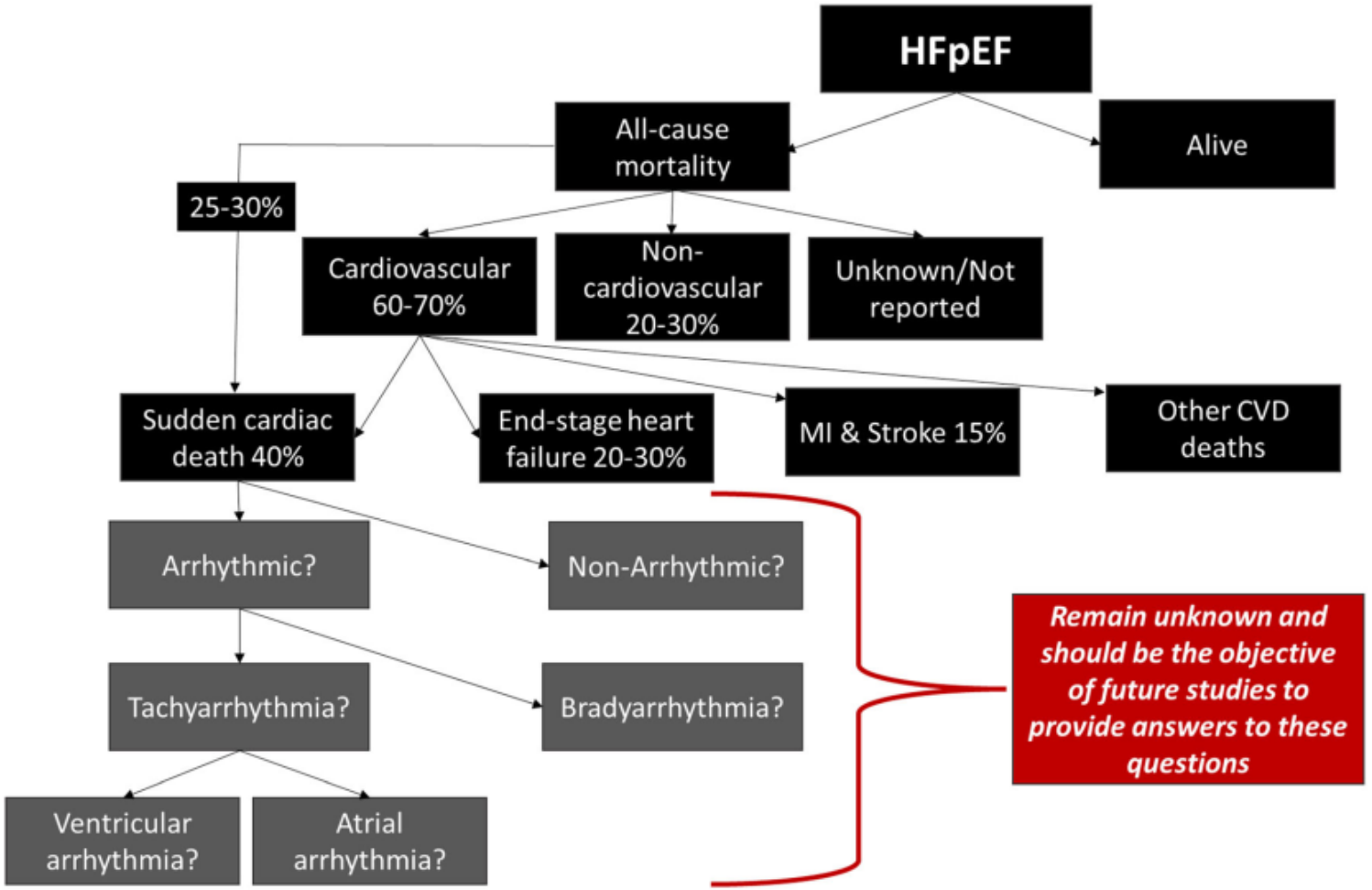


Figure 4. Delayed repolarization of HFpEF is caused by down-regulations of various potassium channels

Korean Circ J. 2022 Apr;52(4):251-264

Are arrhythmias the drivers of sudden cardiac death in heart failure with preserved ejection fraction? A review

Figure 1 Causes of mortality in heart failure with preserved ejection fraction (HFpEF).[12,18,20]



Yuyun MF, et al. ESC Heart Failure (2022) doi: 10,1002/ehf2.14248 (Brigham and Women's Hospital, Boston, USA)

Investigator-reported ventricular arrhythmias and mortality in heart failure with mildly reduced or preserved ejection fraction

Curtain JP, et al. British Heart Foundation Cardiovascular Research Centre, University of Glasgow

ESC European Society of Cardiology

Structured Graphical abstract

Baseline characteristics and rate of mortality in people with heart failure and an ejection fraction >40% who ...

Key Question

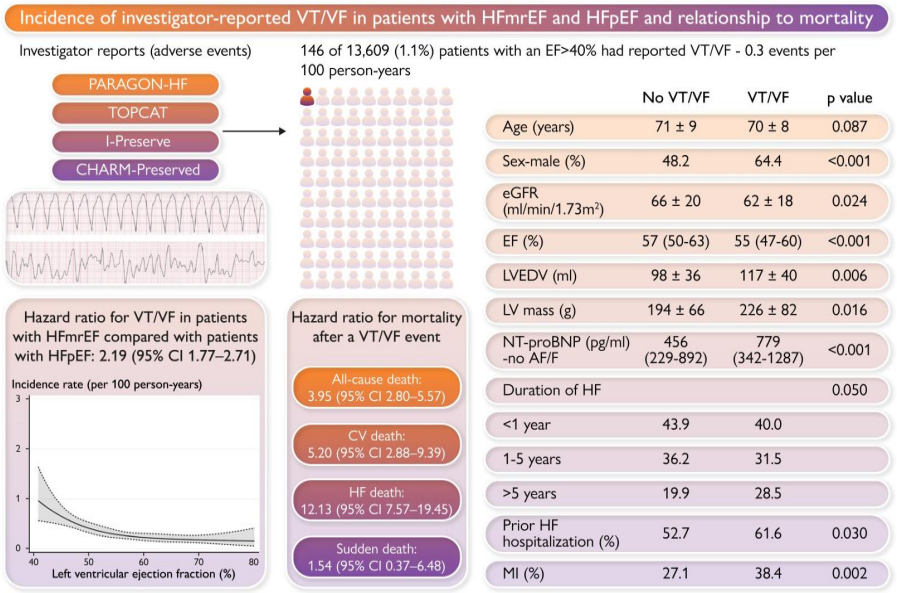
What is the incidence of ventricular tachycardia/fibrillation (VT/VF) and their relationship with subsequent mortality in patients with heart failure with mildly reduced ejection fraction (HFmrEF) or heart failure with preserved ejection fraction (HFpEF)?

Key Finding

Of 13,609 patients, 146 (1.1%) experienced investigator-reported VT/VF. The incidence rate of VT/VF was 0.3 per 100 person-years. VT/VF was associated with a three to five fold increase in all-cause and cardiovascular death but not sudden death.

Take Home Message

VT/VF is uncommon in patients with an EF>40% and appears to be more a marker of disease severity than risk of sudden death.



	No VT/VF	VT/VF	p value
Age (years)	71 ± 9	70 ± 8	0.087
Sex-male (%)	48.2	64.4	<0.001
eGFR (ml/min/1.73m²)	66 ± 20	62 ± 18	0.024
EF (%)	57 (50-63)	55 (47-60)	<0.001
LVEDV (ml)	98 ± 36	117 ± 40	0.006
LV mass (g)	194 ± 66	226 ± 82	0.016
NT-proBNP (pg/ml) -no AF/F	456 (229-892)	779 (342-1287)	<0.001
Duration of HF			0.050
<1 year	43.9	40.0	
1-5 years	36.2	31.5	
>5 years	19.9	28.5	
Prior HF hospitalization (%)	52.7	61.6	0.030
MI (%)	27.1	38.4	0.002

Eur Heart J, ehac801, https://doi.org/10.1093/eurheartj/ehac801

OXFORD UNIVERSITY PRESS

Investigator-reported ventricular arrhythmias and mortality in heart failure with mildly reduced or preserved ejection fraction

Data from the PARAGON-HF, TOPCAT, I-Preserve, and CHARM-Preserved trials were merged. VT/VF, reported as adverse events, were identified. Patients who experienced VT/VF were compared with patients who did not.

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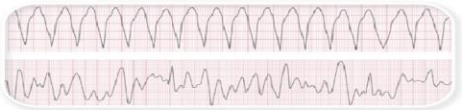
Take Home Message

VT/VF is uncommon in patients with an EF>40% and appears to be more a marker of disease severity than risk of sudden death.

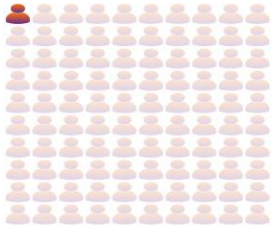
Incidence of investigator-reported VT/VF in patients with HFmrEF and HFpEF and relationship to mortality

Investigator reports (adverse events)

- PARAGON-HF
- TOPCAT
- I-Preserve
- CHARM-Preserved



146 of 13,609 (1.1%) patients with an EF>40% had reported VT/VF - 0.3 events per 100 person-years



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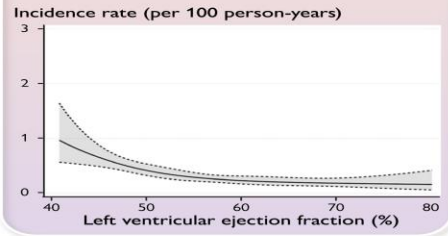
Prior HF hospitalization (%)	52.7	61.6	0.030
MI (%)	27.1	38.4	0.002

Hazard ratio for VT/VF in patients with HFmrEF compared with patients with HFpEF: 2.19 (95% CI 1.77–2.71)



Hazard ratio for mortality after a VT/VF event

- All-cause death: 3.95 (95% CI 2.80–5.57)
- CV death: 5.20 (95% CI 2.88–9.39)
- HF death: 12.13 (95% CI 7.57–19.45)
- Sudden death: 1.54 (95% CI 0.37–6.48)

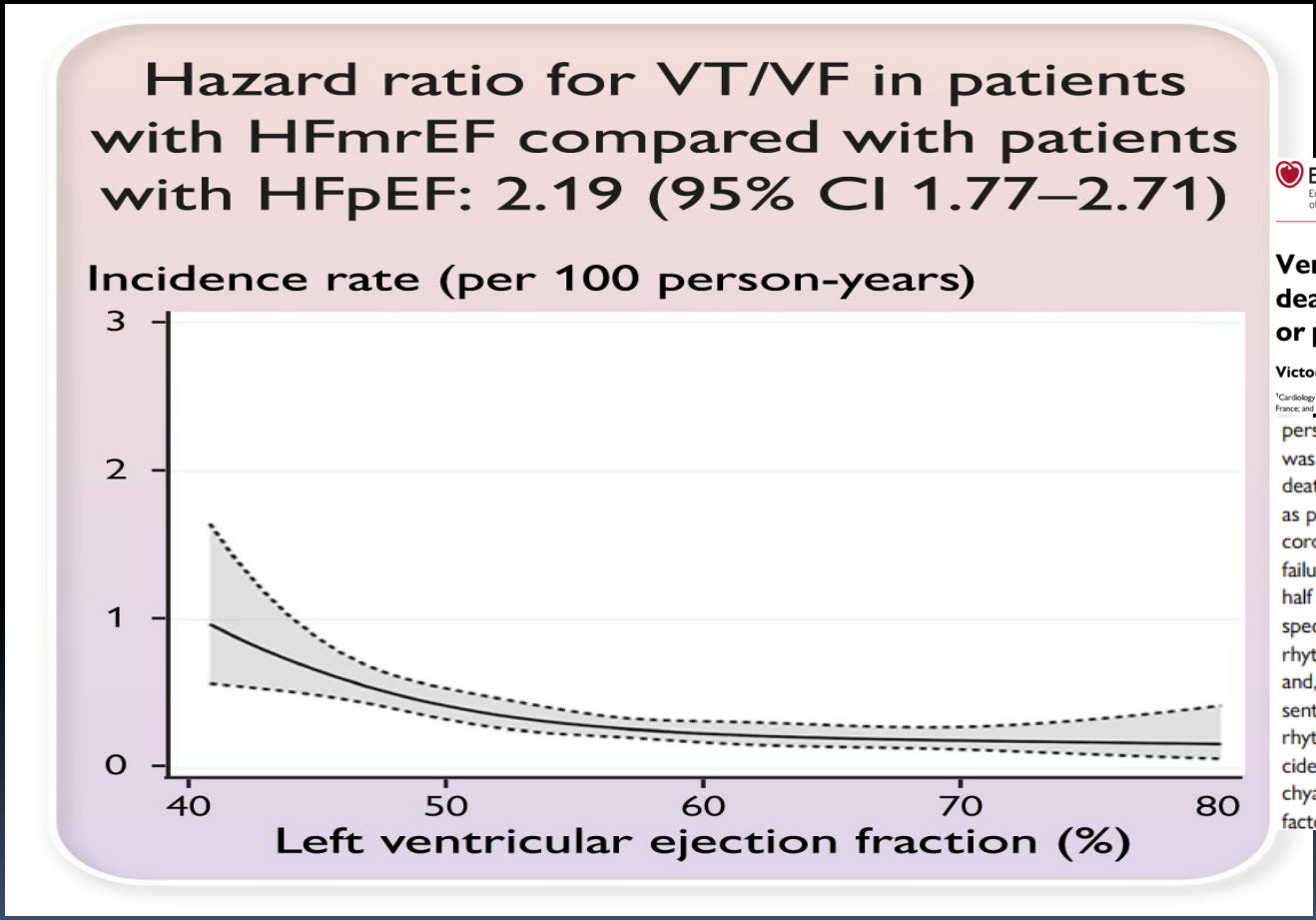
Conclusion: VT/VF was uncommon in patients with HFmrEF and HFpEF. However, such events were strongly associated with mortality and appear to be a marker of disease severity rather than risk of sudden death.

Curtain JP, et al. Eur Heart J 2023 Jan 12;ehac801. doi: 10.1093/eurheartj/ehac801. Online ahead of print.

Investigator-reported ventricular arrhythmias and mortality in heart failure with mildly reduced or preserved ejection fraction

Data from the PARAGON-HF, TOPCAT, I-Preserve, and CHARM-Preserved trials were merged. VT/VF, reported as adverse events, were identified. Patients who experienced VT/VF were compared with patients who did not.

146 of 13,609 (1.1%) patients with an EF>40% had reported VT/VF - 0.3 events per 100 person-years



(.....this study excluded ICD patients)

ESC European Society of Cardiology
European Heart Journal (2023) 00, 1–2
https://doi.org/10.1093/eurheartj/ehad001
EDITORIAL

Ventricular arrhythmias and sudden cardiac death in heart failure with mildly reduced or preserved ejection fraction: knowledge gaps

Victor Waldmann [1,2]*, Sergio Barra[2,3], and Eloi Marijon [1,2]

[1]Cardiology Department, European Georges Pompidou Hospital, 20 rue Leblanc, 75015, Paris, France; [2]Paris City University, INSERM U970, Paris Cardiovascular Research Center, Paris, France; and [3]Cardiology Department, Hospital da Luz Arrábida, V.N. Gaia, Portugal

person-years was reported, and the incidence of non-sustained VT was much higher (11.5 per 100 person-years).[5] Second, among 2420 deaths during follow-up, almost a quarter were SCDs not considered as potentially caused by VAs. While the rate of shockable rhythm recorded after sudden cardiac arrest may be lower in patients with heart failure and preserved ejection fraction, approximately a quarter and a half of patients with preserved or mildly reduced ejection fraction, respectively, still have a shockable rhythm recorded as presenting rhythm.[7] Moreover, these are rhythms recorded during resuscitation and, as asystole is the natural course even in patients who initially present with VT or VF, the proportion of SCDs caused by a shockable rhythm is undoubtedly greater.[8] In addition to underestimating the incidence of VAs, the non-consideration of these SCDs as potential tachyarrhythmia events may have also impacted the identification of factors associated with VT/VF.

Conclusion: **VT/VF was uncommon in patients with HFmrEF and HFpEF. However, such events were strongly associated with mortality and appear to be a marker of disease severity rather than risk of sudden death.**

Eur Heart J 2023 Jan 12;ehac801. doi: 10.1093/eurheartj/ehac801. Online ahead of print.

Ventricular tachyarrhythmia detection by implantable loop recording in patients with heart failure and preserved ejection fraction: the VIP-HF study

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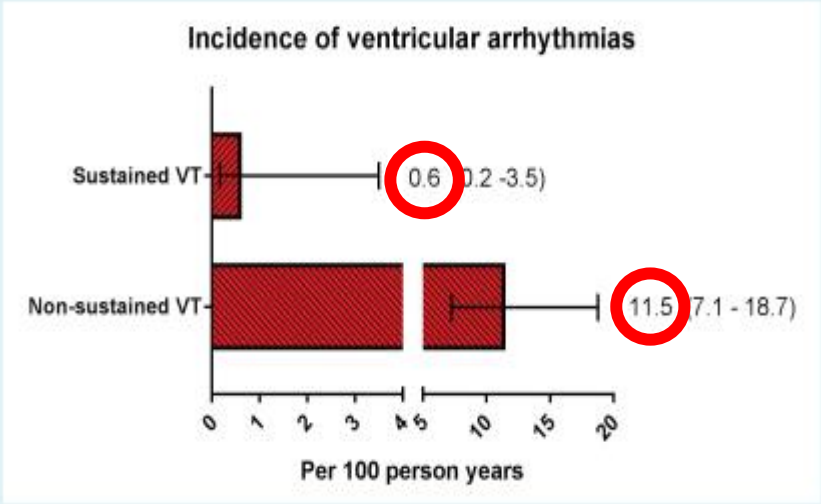

Figure 1 Bar graphs with 95% confidence intervals showing the incidence of sustained and non-sustained ventricular tachyarrhythmias (VT).

Table 1 Patient characteristics of the study population

	Total (n = 113)	HFpEF (n = 85, 75%)	HFmrEF (n = 28, 25%)	P-value
Age (years)	72.6 ± 8.1	73.7 ± 8.0	69.2 ± 7.7	0.01
Women	58 (51%)	50 (59%)	8 (29%)	0.005
Body mass index (kg/m^2)	29.7 ± 5.7	30.3 ± 5.7	28.3 ± 5.5	0.12
Comorbidities				
Hypertension	89 (78%)	70 (82%)	19 (68%)	0.10
Previous myocardial infarction	23 (20%)	15 (18%)	8 (29%)	
History of atrial fibrillation	64 (57%)	54 (64%)	10 (36%)	0.01
Diabetes mellitus	45 (40%)	35 (41%)	10 (36%)	0.6
Renal dysfunction[a]	54 (48%)	41 (48%)	13 (46%)	0.9
COPD	21 (19%)	15 (18%)	6 (21%)	0.7
NYHA HF class				0.2
II	61 (54%)	43 (51%)	18 (64%)	
III	52 (46%)	42 (49%)	10 (36%)	
Previous HF hospitalization	48 (43%)	35 (41%)	13 (46%)	0.6
Baseline laboratory values				
NT-proBNP (pg/mL)	1367 (710–2452)	1312 (687–2344)	1611 (744–2843)	0.9
Current medication				
Beta-blockers	99 (88%)	24 (86%)	75 (88%)	0.7
ACEi/ARB	72 (64%)	52 (61%)	20 (71%)	0.3
MRA	42 (37%)	30 (35%)	12 (43%)	0.5
Diuretics	102 (90%)	76 (89%)	26 (93%)	0.6
Holter data				
AF as basal rhythm	42 (37%)	35 (42%)	7 (25%)	0.12
Mean heart rate (bpm)	72 ± 13	73 ± 13	69 ± 12	0.3
PVC ≥1000/24 h	27 (24%)	19 (23%)	8 (29%)	0.5
Non-sustained VT	20 (18%)	12 (15%)	8 (29%)	0.09
Echocardiography				
LVEF (%)	54 ± 6	56 ± 5	45 ± 2	<0.001

This was an investigator-initiated, prospective, multicentre, observational study of patients with HF and left ventricular ejection fraction (LVEF) >40%. Patients underwent extensive phenotyping, after which an implantable loop recorder was implanted. We enrolled 113 of the planned 250 patients [mean age 73 ± 8 years, 51% women, New York Heart

Conclusion Despite the lower than expected number of included patients, the incidence of sustained VTs in HFmrEF/HFpEF was low. Clinically relevant bradyarrhythmias were more often observed than expected.

Veldhuisen DJ, et al. European Heart Journal (2021) 42, 3727–3738

Effect of dapagliflozin on ventricular arrhythmias, resuscitated cardiac arrest, or sudden death in DAPA-HF

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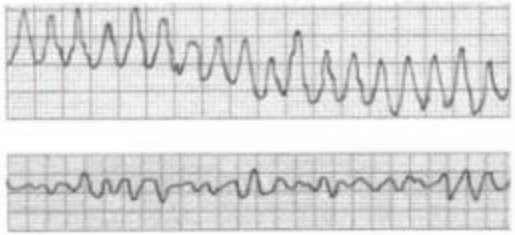
Investigator Reports (Serious Adverse Events)

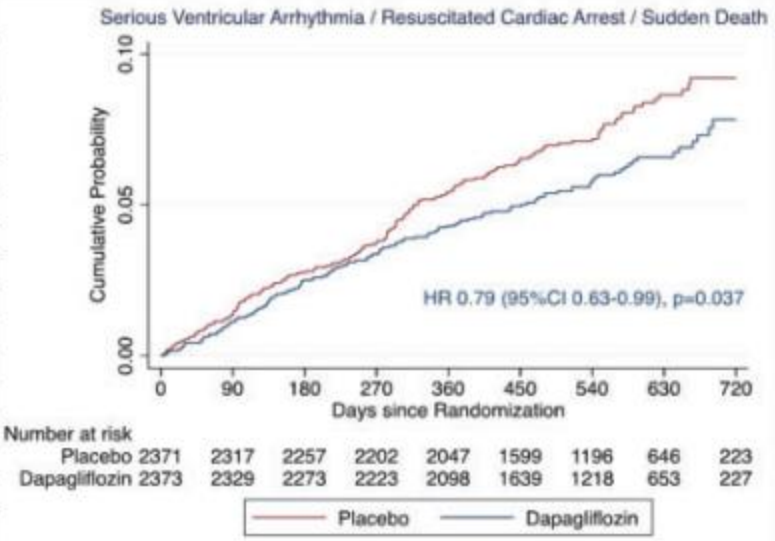
Median follow-up 18.2 months



Backward stepwise logistic regression multivariable model to predict any serious ventricular arrhythmia, resuscitated cardiac arrest or sudden death

Predictor Variable*	Odds Ratio (95% CI)	p Value**	χ2
Log-transformed NT-proBNP (per 1 unit increase)	1.54 (1.34 – 1.77)	<0.001	36.0
Previous Ventricular Arrhythmia	1.93 (1.41 – 2.64)	<0.001	16.8
LVEF (per 5% increase)	0.86 (0.78 – 0.94)	0.001	11.9
Systolic BP (per 10mmHg)	0.88 (0.81 – 0.96)	0.004	8.1
Previous MI	1.42 (1.11– 1.82)	0.005	7.8
Sex- male	1.53 (1.10 – 2.12)	0.012	6.3
BMI (per 1 kg/m^2 increase)	1.03 (1.00 – 1.05)	0.020	5.4
Sodium (per 1 mmol/L increase)	0.96 (0.92 – 0.99)	0.039	4.3
Non-white race	0.85 (0.72 – 0.99)	0.038	4.3
Dapagliflozin	0.80 (0.63 – 1.02)	0.067	3.4
Cardiac Resynchronization Therapy	0.64 (0.39 – 1.04)	0.070	3.3
Previous HF hospitalization	0.99 (0.78 – 1.27)	0.985	0.0

*Randomized treatment and history of heart failure hospitalization were fixed factors in the model. **The p-value threshold was set at p<0.1



Conclusions Dapagliflozin reduced the risk of any serious ventricular arrhythmia, cardiac arrest, or sudden death when added to conventional therapy in patients with HFrEF.

European Heart Journal (2021) 42, 3727–3738

DELIVER: Dapagliflozin in Heart Failure with Mildly Reduced and Preserved Ejection Fraction

Purpose:
To evaluate whether SGLT2 inhibitors (dapagliflozin) are effective in patients with heart failure and more than 40% left ventricular ejection fraction.

Trial Design: This was an international, multicenter, parallel-group, event-driven, randomized, double-blind, placebo-controlled study. N=6,263 patients with heart failure and a left ventricular ejection fraction of more than 40% were randomized in a 1:1 ratio to receive either dapagliflozin 10 mg or placebo.

Primary Endpoint: Time-to-event analysis of a composite of worsening heart failure (defined as unplanned hospitalization for heart failure or an urgent visit for heart failure) or cardiovascular death [over a median of 2.3 years].

Other Endpoints: Total number of worsening heart failure events and cardiovascular death, death from any cause, and change in total symptoms score of KCCQ at 8 months.

Results	Dapagliflozin	Placebo	P-value
Primary Composite Outcome – no.(%): Time to first occurrence of: 1) CV death; 2) Hospitalization for HF; 3) Urgent visit for HF	512 (16.4)	610 (19.5)	< 0.001
Total # of worsening HF events + Death	815	1057	< 0.001
Death from any cause – no. (%)	497 (15.9)	526 (16.8)	NA
Change in total symptom score of KCCQ at 8 months	Win ratio, 1.11; 95% CI, 1.03-1.21; P=0.009		

Results: Among individuals with heart failure and a mildly reduced or preserved ejection fraction, dapagloflozin reduced the combined risk of worsening heart failure or cardiovascular death.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

CONCLUSIONS
Dapagliflozin reduced the combined risk of worsening heart failure or cardiovascular death among patients with heart failure and a mildly reduced or preserved ejection fraction. (Funded by AstraZeneca; DELIVER ClinicalTrials.gov number,

RESULTS
Over a median of 2.3 years, the primary outcome occurred in 512 of 3131 patients (16.4%) in the dapagliflozin group and in 610 of 3132 patients (19.5%) in the placebo group (hazard ratio, 0.82; 95% confidence interval [CI], 0.73 to 0.92; P<0.001). Worsening heart failure occurred in 368 patients (11.8%) in the dapagliflozin group and in 455 patients (14.5%) in the placebo group (hazard ratio, 0.79; 95% CI, 0.69 to 0.91); cardiovascular death occurred in 231 patients (7.4%) and 261 patients (8.3%), respectively (hazard ratio, 0.88; 95% CI, 0.74 to 1.05). Total events and symptom burden were lower in the dapagliflozin group than in the placebo group. Results were similar among patients with a left ventricular ejection fraction of 60% or more and those with a left ventricular ejection fraction of less than 60%, and results were similar in prespecified subgroups, including patients with or without diabetes. The incidence of adverse events was similar in the two groups.

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Abstract citation ID: ehac779.040

Efficacy of sodium glucose cotransporter 2 inhibitors for heart failure with preserved and mildly reduced ejection fraction: a systematic review and meta-analysis

Doctor RAB Cordovez, Doctor KA Rivera, Doctor RW Denila, Doctor MD Patricio

Vicente Sotto Memorial Medical Center, Cebu City, Philippines; Alaminos Doctors Hospital, Alaminos City, Philippines; Philippine Heart Center, Quezon, Philippines

Funding Acknowledgements: Type of funding sources: None.

Background: SGLT2 inhibition has been a breakthrough approach in the treatment for heart failure. A most recent trial of Dapagliflozin has shown its robust benefit in patients with HFpEF and HFmrEF. However, the positive outcomes of other SGLT2i have yet to be elucidated to establish its class effect.

Purpose: We evaluated the cardiovascular outcomes of SGLT2i for HFpEF and HFmrEF.

Methods: Randomized controlled trials on SGLT2i versus placebo in patients with left ventricular ejection fraction of more than 40% reporting CV outcomes were searched using Pubmed, CENTRAL, and ScienceDirect. Primary outcome was the composite of hospitalization for heart failure or CV death. Secondary outcomes were the individual HHF, CV death, as well as all-cause mortality. Pooled hazard ratios with 95% confidence intervals were used as effect estimates using fixed-effects model.

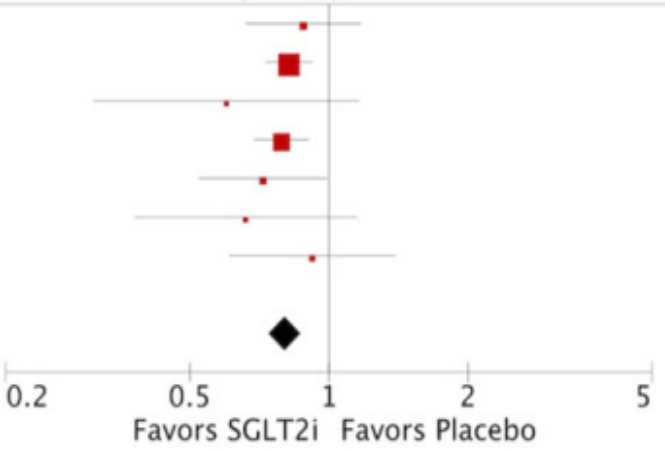
Results: Seven studies were included with a total of 16,713 patients. In the combined HFmrEF and HFpEF population, there was a significant reduction in composite of cardiovascular death and heart failure hospitalization in the SGLT2i group (HR 0.80, 95% CI 0.74-0.87, p<0.00001) compared to placebo, driven by a significant reduction in heart failure hospitalization (HR 0.75, 95% CI 0.68-0.83, p< 0.00001). In the distinct HFpEF population, there was a significant reduction in composite of cardiovascular death and heart failure hospitalization in the SGLT2i group (HR 0.77, 95% CI 0.67-0.87, p<0.0001) compared to placebo.

Conclusion: SGLT2i provides significant risk reduction in HF hospitalization or CV death among patients with HFpEF compared to placebo.

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
DECLARE TIMI 58	-0.1278	0.1468	7.5%	0.88 [0.66, 1.17]
DELIVER	-0.1985	0.0593	45.7%	0.82 [0.73, 0.92]
EMPA-REG	-0.5108	0.3369	1.4%	0.60 [0.31, 1.16]
EMPEROR-PRESERVED	-0.2357	0.0691	33.7%	0.79 [0.69, 0.90]
SCORED	-0.3285	0.1625	6.1%	0.72 [0.52, 0.99]
SOLOIST WHF	-0.4155	0.2817	2.0%	0.66 [0.38, 1.15]
VERTIS CV	-0.0825	0.2101	3.6%	0.92 [0.61, 1.39]
Total (95% CI)			**100.0%**	**0.80 [0.74, 0.87]**

Heterogeneity: $Chi^2 = 2.68$, df = 6 (P = 0.85); $I^2 = 0\%$

Test for overall effect: Z = 5.44 (P < 0.00001)



Ertugliflozin to reduce arrhythmic burden in ICD/CRT patients (ERASe-trial). a phase III study

Authors:
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On behalf: ERASe study group

Methods: Within a multicentre, national, randomized, double-blind, placebo-controlled, phase 3b trial we aim to enrol a total of 402 patients across Austria. Patients with HFrEF or HFmrEF and ICD±CRT therapy > 3 months and previous ventricular tachycardia (at least 10 documented non-sustained VT episodes within the last 12 months) are randomized in a 1:1 ratio to ertugliflozin (5mg once daily orally administered) or matching placebo.

Conclusion

The ERASe trial will be the first trial to test ertugliflozin in heart failure patients with non-preserved ejection fraction and ongoing ICD/CRT therapy regardless of their diabetic status. The ERASe trial may therefore extend the concept of SGLT2 inhibition to improve cardiac reverse remodelling, including reduced arrhythmic burden.

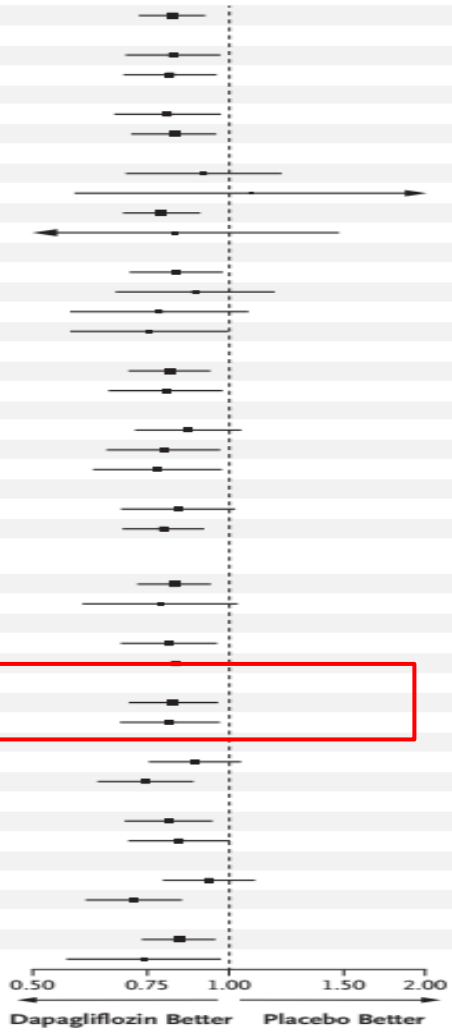
NEJM 2022

The NEW ENGLAND JOURNAL of MEDICINE

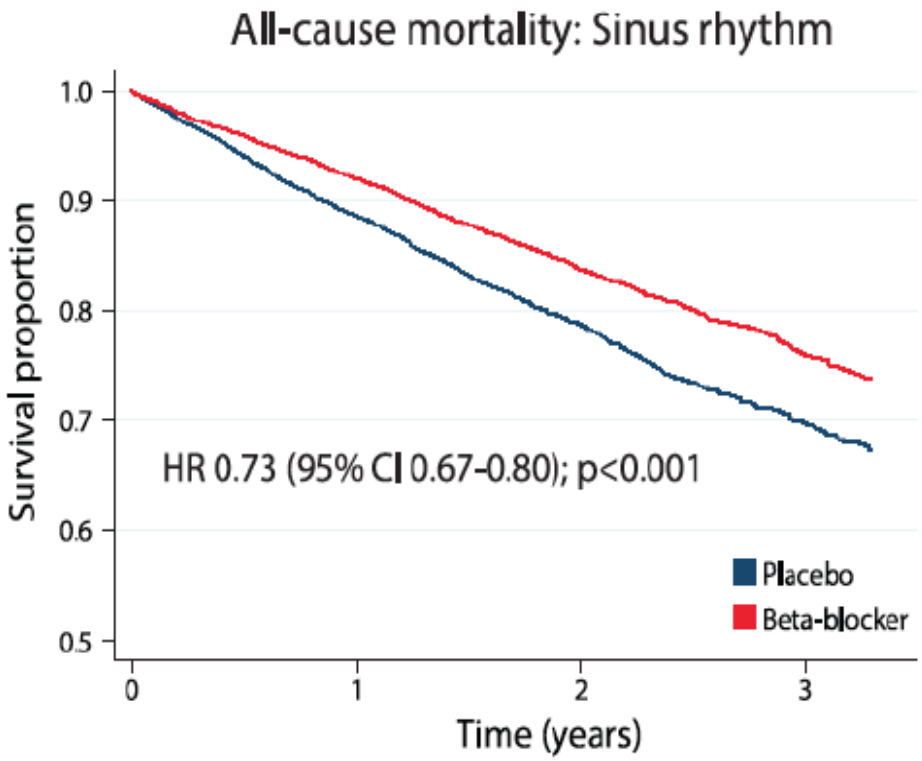
ORIGINAL ARTICLE

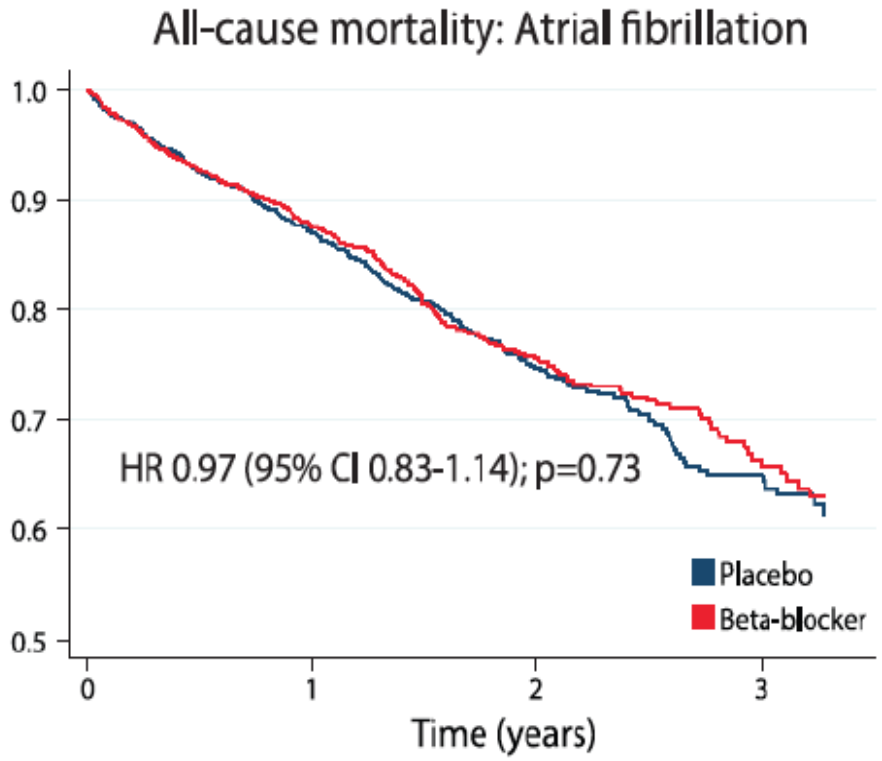
Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

Subgroup	Dapagliflozin	Placebo	Hazard Ratio (95% CI)
	no. of patients with events/total no.		
All patients	512/3131	610/3132	0.82 (0.73–0.92)
Age			
≤72 yr	247/1545	306/1604	0.82 (0.69–0.97)
>72 yr	265/1586	304/1528	0.81 (0.69–0.96)
Sex			
Female	195/1364	243/1383	0.81 (0.67–0.97)
Male	317/1767	367/1749	0.82 (0.71–0.96)
Race			
Asian	97/630	106/644	0.91 (0.69–1.21)
Black	21/81	19/78	1.08 (0.58–2.01)
White	372/2214	461/2225	0.79 (0.69–0.90)
Other	22/206	24/185	0.83 (0.46–1.48)
Geographic region			
Europe or Saudi Arabia	261/1494	309/1511	0.83 (0.70–0.98)
Asia	92/607	103/619	0.89 (0.67–1.18)
Latin America	70/602	87/579	0.78 (0.57–1.07)
North America	89/428	111/423	0.75 (0.57–1.00)
NYHA class at enrollment			
II	331/2314	411/2399	0.81 (0.70–0.94)
III or IV	181/817	198/732	0.80 (0.65–0.98)
LVEF at enrollment			
≤49%	207/1067	229/1049	0.87 (0.72–1.04)
50–59%	174/1133	211/1123	0.79 (0.65–0.97)
≥60%	131/931	170/960	0.78 (0.62–0.98)
NT-proBNP at enrollment			
≤1011 pg/ml	173/1555	208/1578	0.84 (0.68–1.02)
>1011 pg/ml	339/1576	402/1553	0.79 (0.69–0.92)
Enrollment during or within 30 days after hospitalization for heart failure			
No	419/2803	497/2806	0.82 (0.72–0.94)
Yes	93/328	113/326	0.78 (0.60–1.03)
Type 2 diabetes mellitus at enrollment			
No	242/1730	293/1727	0.81 (0.68–0.96)
Yes	270/1401	317/1405	0.83 (0.70–0.97)
Atrial fibrillation or flutter at enrollment ECG			
No	285/1803	339/1814	0.82 (0.70–0.96)
Yes	227/1327	271/1317	0.81 (0.68–0.97)
Body-mass index at enrollment			
<30	275/1734	302/1736	0.89 (0.75–1.04)
≥30	236/1395	308/1392	0.74 (0.63–0.88)
Estimated GFR at enrollment			
<60 ml/min/1.73 m²	289/1516	355/1554	0.81 (0.69–0.94)
≥60 ml/min/1.73 m²	223/1615	255/1577	0.84 (0.70–1.00)
Systolic blood pressure at randomization			
≤128 mm Hg	280/1568	300/1590	0.93 (0.79–1.10)
>128 mm Hg	232/1563	310/1542	0.71 (0.60–0.85)
Previous LVEF ≤40%			
No	420/2559	491/2553	0.84 (0.73–0.95)
Yes	92/572	119/579	0.74 (0.56–0.97)



Efficacy of β blockers in patients with heart failure plus AFib: an individual-patient data meta-analysis





Number at risk

Beta-blocker	7123	5014	1798	722	1521	997	331	113
Placebo	6819	4604	1530	561	1542	1020	346	115

Kotecha et al. Lancet 2014

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 11, 2014 VOL. 371 NO. 11

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

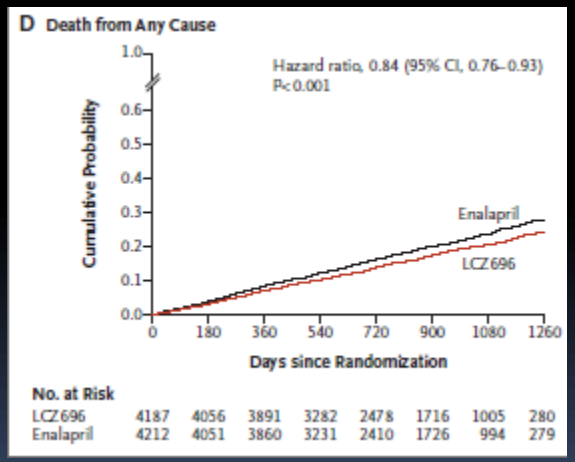
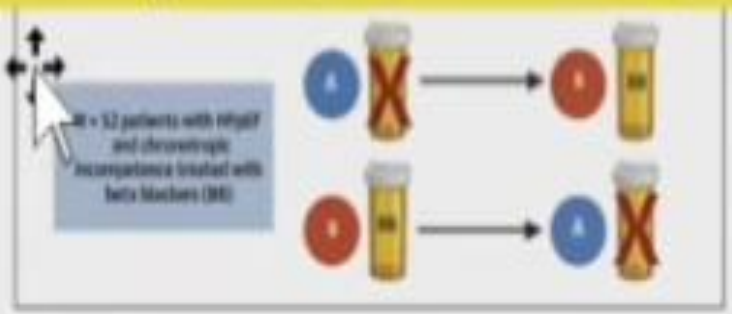


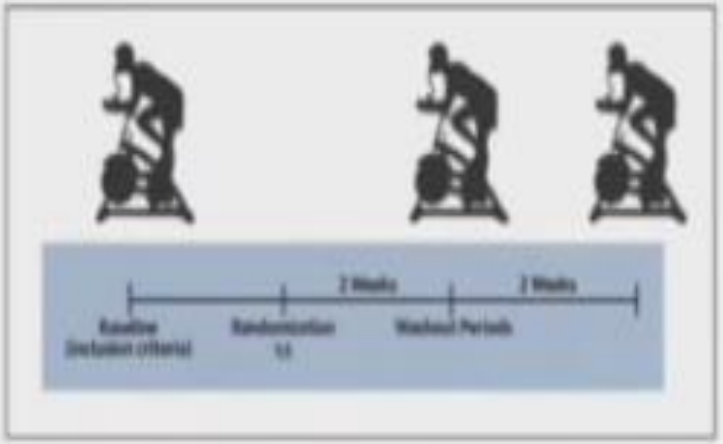
Table 2. Primary and Secondary Outcomes.*

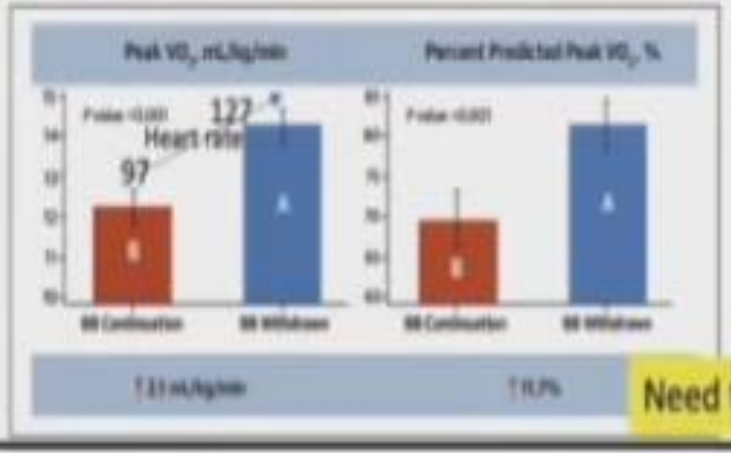
Outcome	LCZ696 (N=4187)	Enalapril (N=4212)	Hazard Ratio or Difference (95% CI)	P Value
Primary composite outcome — no. (%)				
Death from cardiovascular causes or first hospitalization for worsening heart failure	914 (21.8)	1117 (26.5)	0.80 (0.73–0.87)	<0.001
Death from cardiovascular causes	558 (13.3)	693 (16.5)	0.80 (0.71–0.89)	<0.001
First hospitalization for worsening heart failure	537 (12.8)	658 (15.6)	0.79 (0.71–0.89)	<0.001
Secondary outcomes — no. (%)				
Death from any cause	711 (17.0)	835 (19.8)	0.84 (0.76–0.93)	<0.001
Change in KCCQ clinical summary score at 8 mo†	−2.99±0.36	−4.63±0.36	1.64 (0.63–2.65)	0.001
New-onset atrial fibrillation‡	84 (3.1)	83 (3.1)	0.97 (0.72–1.31)	0.83
Decline in renal function§	94 (2.2)	108 (2.6)	0.86 (0.65–1.13)	0.28

Mc Murray JJ et al., NEJM 2014

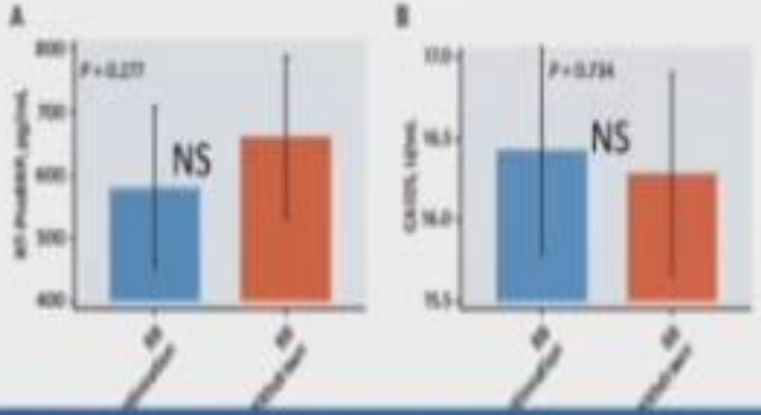
Impact of Beta Blocker Withdrawal (all at least by ½ dose) on Peak VO_2 in 52 patients with HFpEF and HR <65bpm at rest



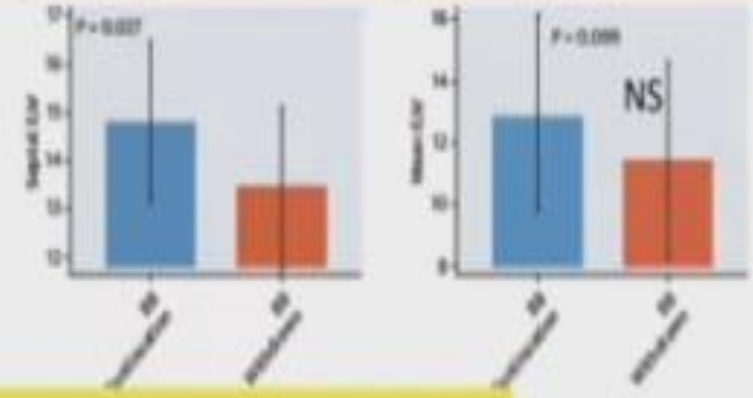




↑peak HR from mean of 97 to 127 bpm
(↑ ↑ increase in peak VO2)



Secondary Endpoint of Biomarkers and Echo parameters No Ill effect



Need to get rid of Afib to reduce beta blockers

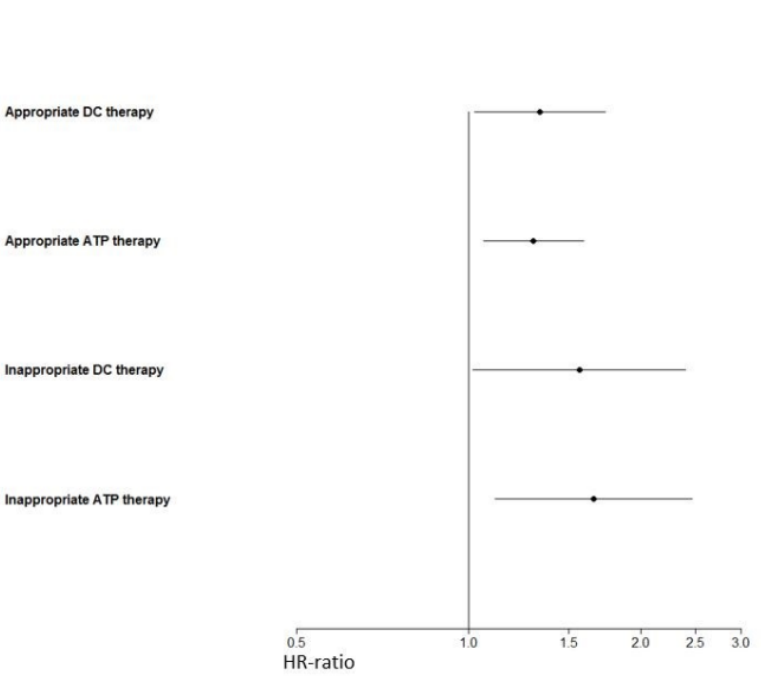
Palau P JACC 2021;78:2042–2056

History of betablocker treatment breaks and risk of ventricular tachyarrhythmias among patients with heart failure and implantable cardioverter defibrillator: a nationwide cohort study

Background: Beta-blockers have in randomized clinical trials been shown to reduce the risk of life-threatening arrhythmias and sudden cardiac death (SCD) in patients with heart failure (HF), and treatment is a class 1A recommendation in current guidelines. Thus, beta-blocker treatment breaks (i.e. planned break, beta-blocker related side-effects, or poor adherence) may increase risk of life-threatening arrhythmias and SCD. Whether patients with HF and a history of beta-blocker treatment breaks before implantable cardioverter defibrillator (ICD) is associated with increased risk of device related therapy and mortality is largely unknown.

Kjaer E, et al. Danish Pacemaker and ICD Registry - 9,239 patients with HF and an ICD

Figure 1. Beta-blocker treatment breaks >60 days and 1-year risk of appropriate and inappropriate shocks and anti-tachycardia pacing according to multivariable Cox regression analysis

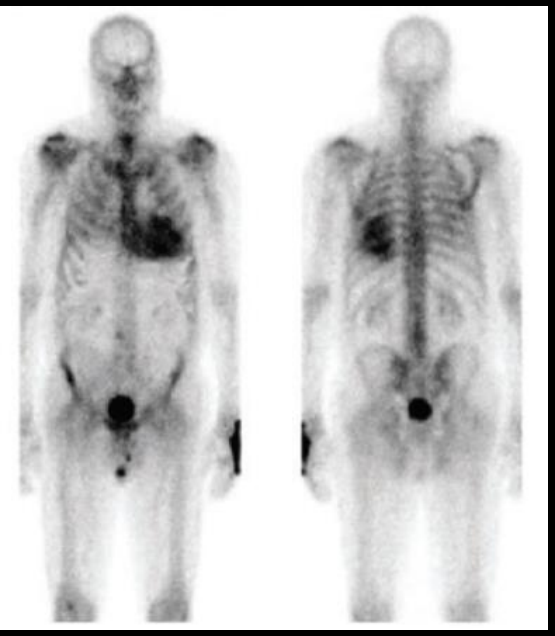


Adjusted for sex, 5-year increment in age, year of implantation, indication for implantation, device type, atrial fibrillation, chronic renal failure, diabetes, hypertension, ischemic heart disease, use of loop diuretics, renin angiotensin system inhibitors and lipid lowering drugs.

Conclusion: Patients with heart failure who had a history of treatment breaks with beta-blockers prior to ICD implantation was associated with a higher 1year risk of appropriate and inappropriate shocks and anti-tachycardia pacing, but not all-cause mortality

ESC 2022

Heart failure with preserved ejection fraction, atrial fibrillation, and the role of senile amyloidosis



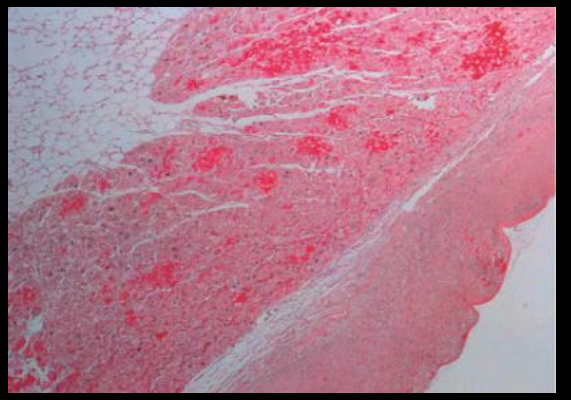
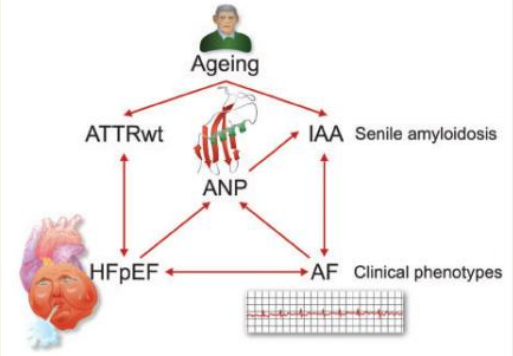


Table I Frequency of atrial fibrillation in different types of cardiac amyloidosis

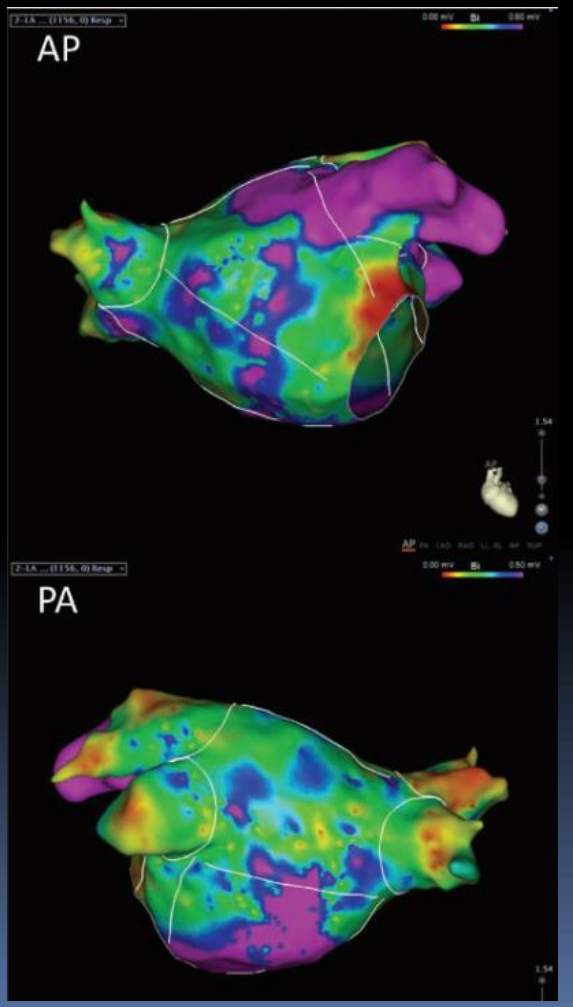
	N	AL amyloidosis (%)	ATTRm (%)	ATTRwt (%)
Rapezzi *et al.*[10]	233	12	5	27
Longhi *et al.*[11]	262	9	11	40
Pinney *et al.*[12]	138	16	NA	43
Kristen *et al.*[13]	216	16	18	30
Grogan *et al.*[14]	360	NA	NA	62



Take home figure Intricate interrelations exist between HFpEF, AF, and senile amyloidosis, potentially leading to detrimental vicious circles.

Conclusions

Heart failure with preserved ejection fraction and AF are very common diseases that also often occur in combination, further aggravating each other. Senile amyloidosis, either due to TTR (ATTRwt) or ANP (IAA) appears to play an important role in both diseases and in their interaction. In terms of diagnostics, bone scintigraphy has become available and affords an easy and reliable way to establish the presence of cardiac ATTRwt. Moreover, pharmacological options are now available or under development to treat ATTRwt and possibly also IAA, thereby potentially stopping, or even reversing, the downhill course of some patients with HFpEF and AF.



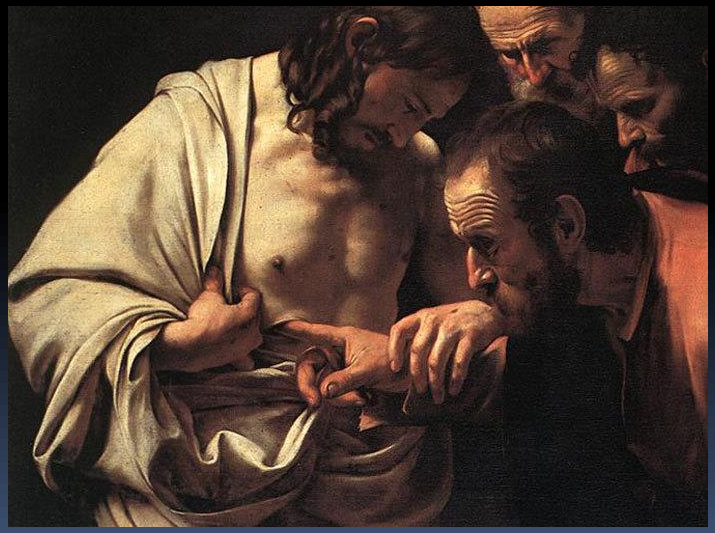
Maarten P, et al. European Heart Journal (2019) 40, 1287–1293

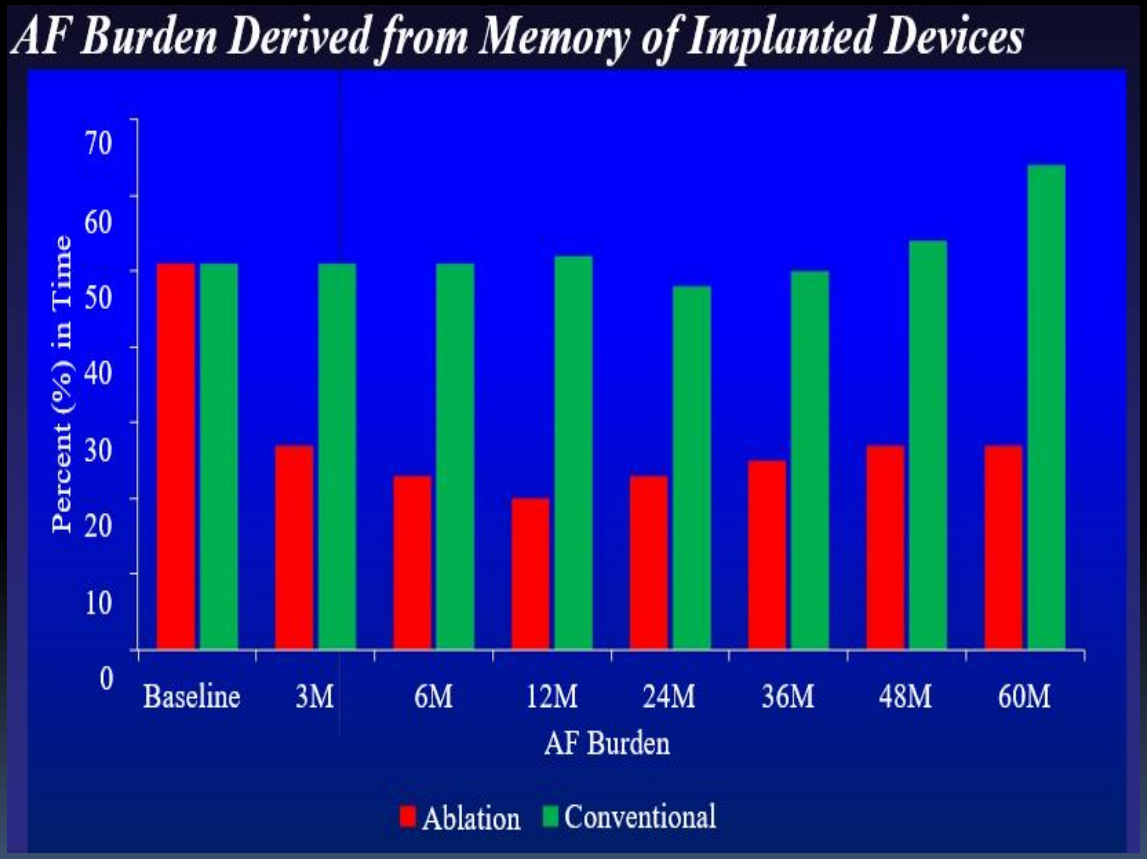
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 1, 2018 VOL. 378 NO. 5

Catheter Ablation for Atrial Fibrillation with Heart Failure

«Άπιστος Θωμάς»
Michelangelo Merisi da Caravaggio
(1571–1610)



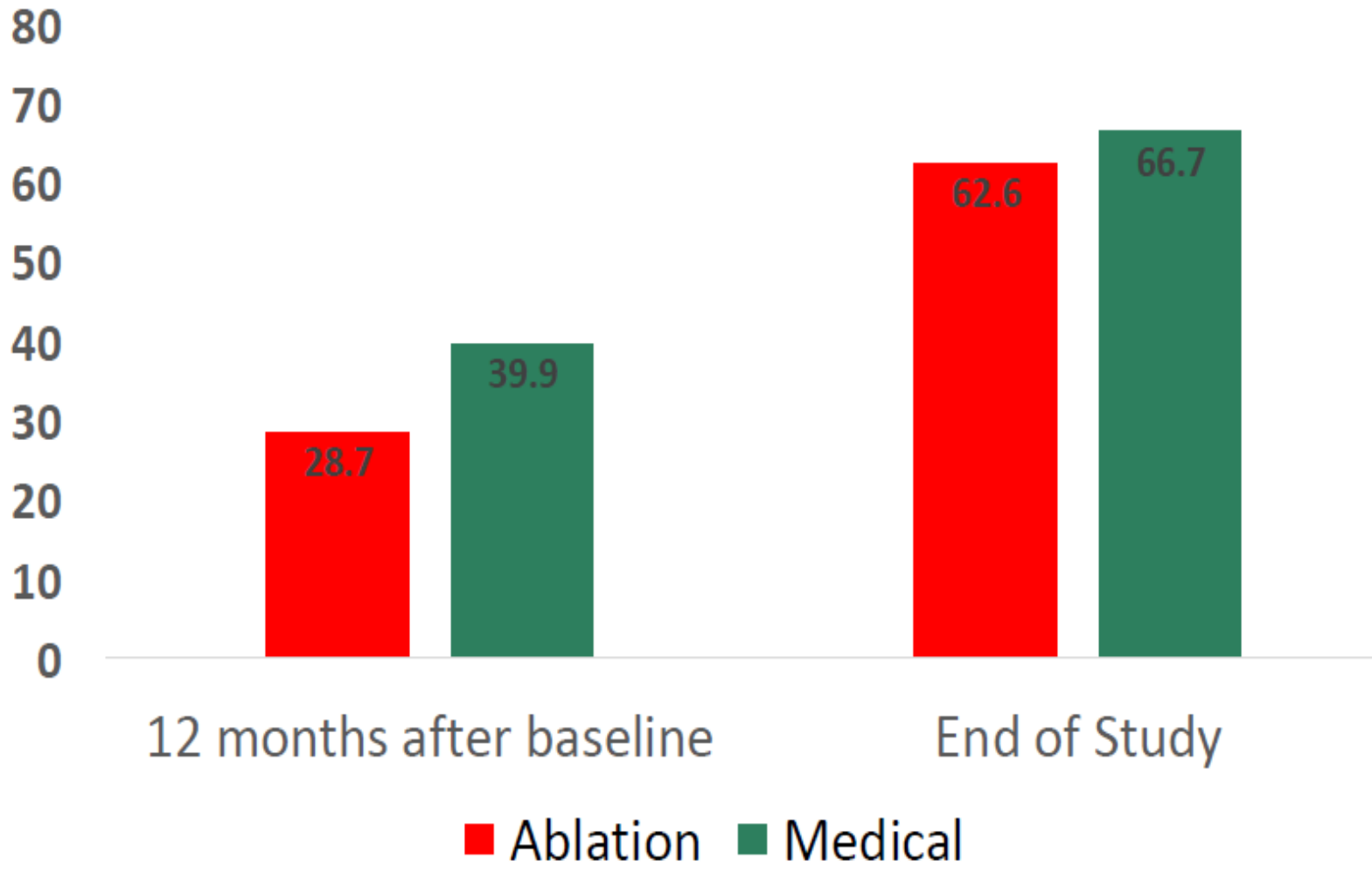


Marrouche H, et al. New Eng J Med 2018:378(5);417-427

ESC 2018
Johannes Brachmann
Klinikum Coburg, Germany

Results CASTLE AF

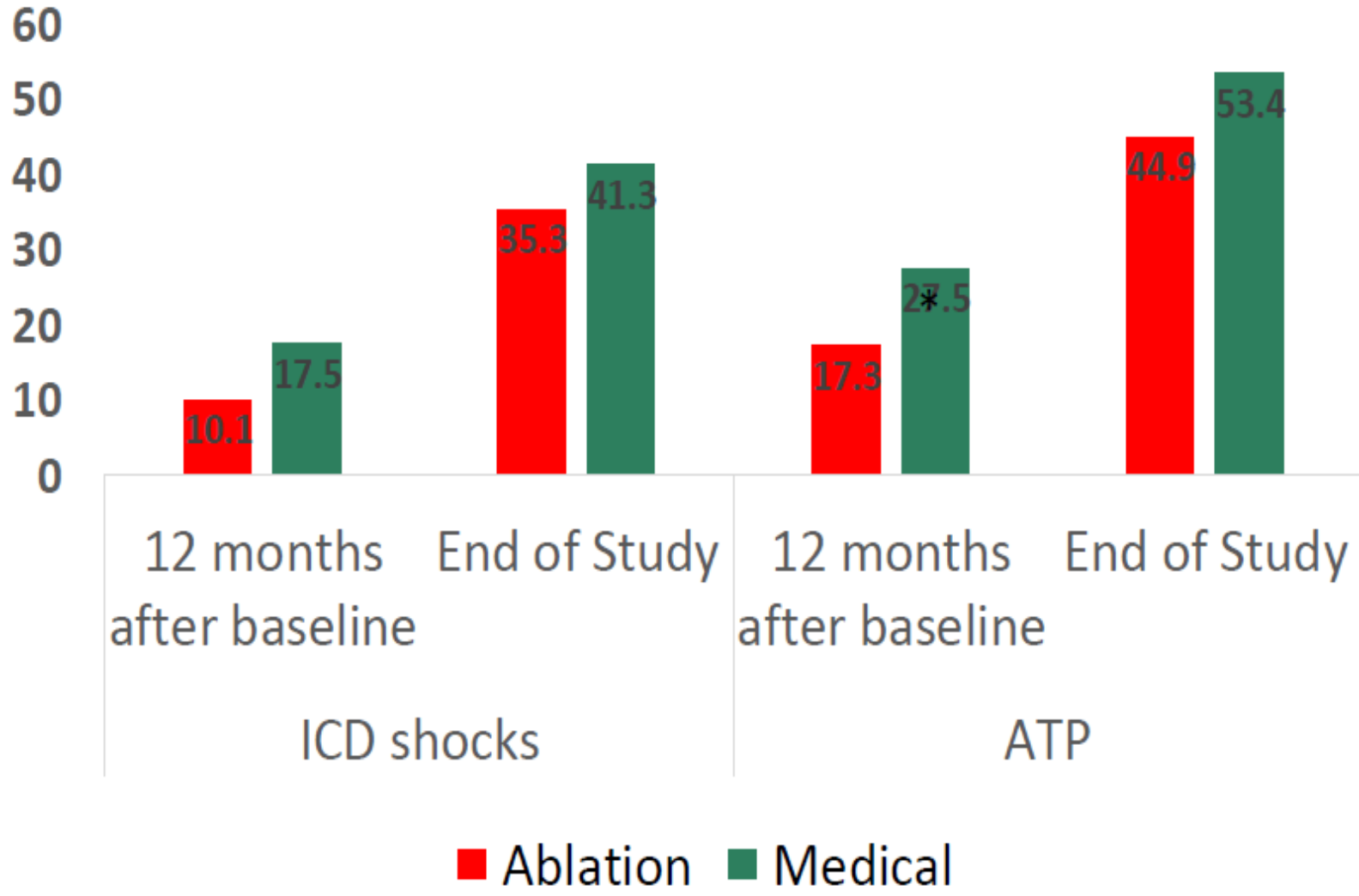
Device-detected VT/VF (%)



Johannes Brachmann
Klinikum Coburg, Germany

Results-CASTLE AF

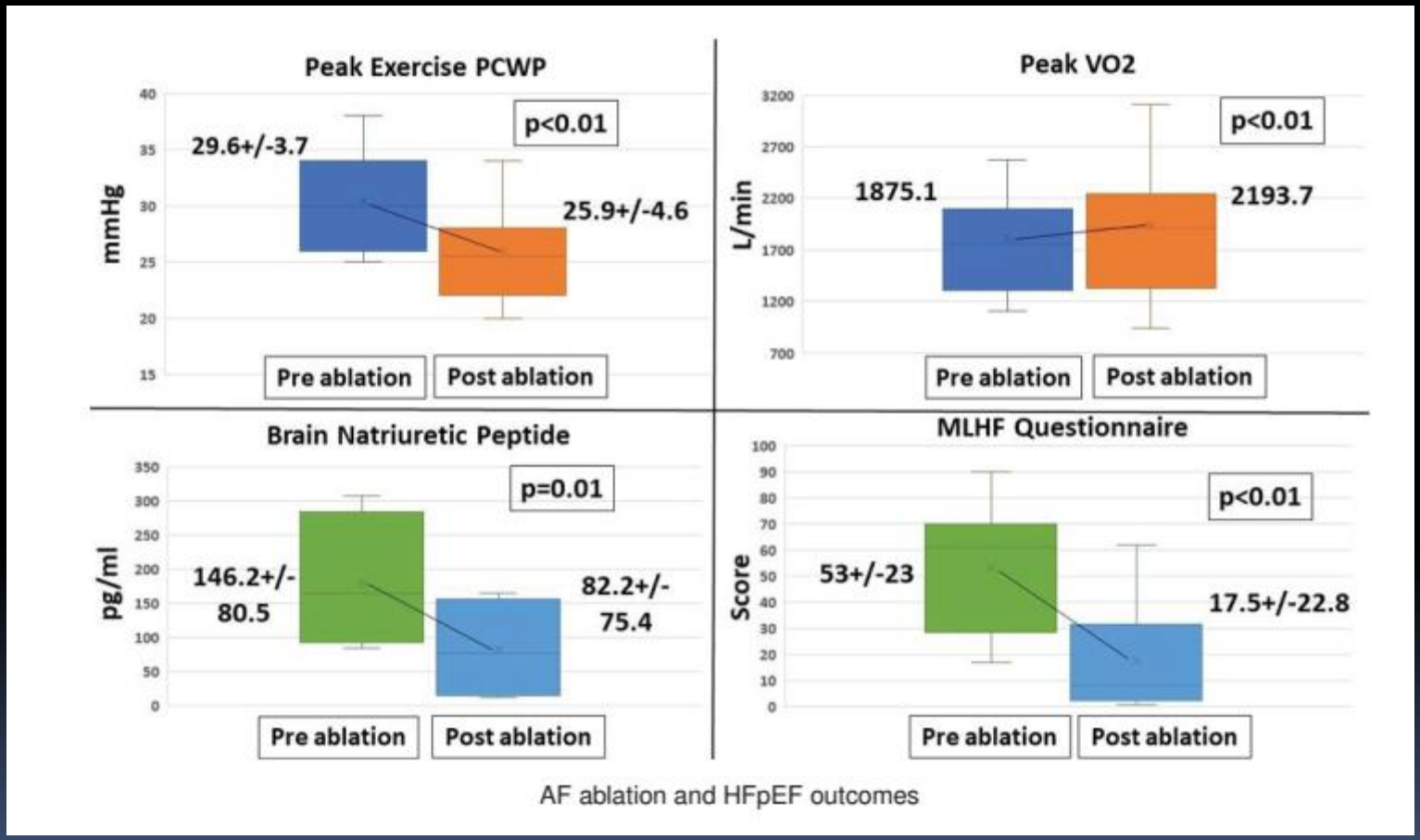
ICD Shocks and ATPs (%)



Catheter ablation in atrial fibrillation and heart failure with preserved ejection fraction improves peak pulmonary capillary wedge pressure, exercise capacity and quality of life: RCT STALL HFpEF

D. Chieng[1], H. Sugumar[1], L. Segan[1], A. Al-Kaisey[2], J. Hawson[2], S. Prabhu[1], A. Voskoboinik[1], J.B. Morton[2], G. Lee[2], J. Mariani[3], A. La Gerche[1], P.M. Kistler[1], J.M. Kalman[2], D.M. Kaye[1], L.H. Ling[1]

[1]Baker Heart and Diabetes Institute, Melbourne, Australia; [2]Royal Melbourne Hospital, Cardiology, Melbourne, Australia; [3]The Alfred Hospital, Melbourne, Australia

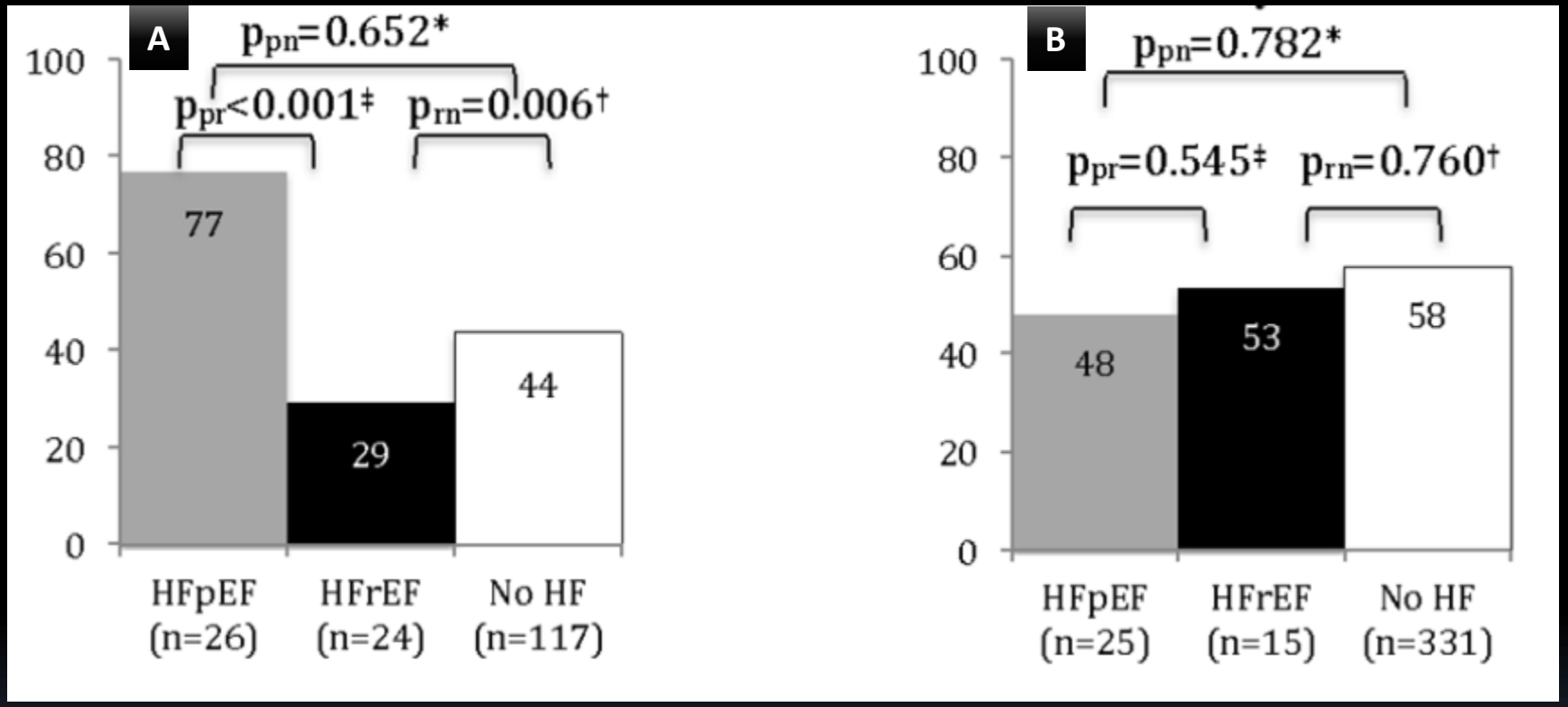


AF ablation and HFpEF outcomes

ESC Congress 2022 – Barcelona, Spain
26–29 August 2022

Comparison of Outcomes After Ablation of Atrial Fibrillation in Patients With Heart Failure with Preserved Versus Reduced Ejection Fraction

Freedom from atrial arrhythmias by atrial fibrillation subtype over all follow-up



A) Freedom from atrial arrhythmias on or off antiarrhythmic drugs in patients with persistent AF

B) Freedom from atrial arrhythmias on or off antiarrhythmic drugs in patients with paroxysmal AF

In conclusion, there were no significant differences in arrhythmia-free survival between patients with HFpEF and HFrEF undergoing catheter ablation of AF.

Am J Cardiol. 2020 December 01; 136: 62–70. doi:10.1016/j.amjcard.2020.09.018.

New Online | Views 2,771 | Citations 0 | Altmetric 143

Original Investigation

ONLINE FIRST

February 1, 2023

Effect of Personalized Accelerated Pacing on Quality of Life, Physical Activity, and Atrial Fibrillation in Patients With Preclinical and Overt Heart Failure With Preserved Ejection Fraction

The myPACE Randomized Clinical Trial

Margaret Infeld, MD, MS[1]; Kramer Wahlberg, MD[1]; Jillian Cicero, BS[1]; et al

» Author Affiliations

JAMA Cardiol. Published online February 1, 2023. doi:10.1001/jamacardio.2022.5320

Objective: To assess the effects of a moderately accelerated personalized backup heart rate compared with 60 bpm (usual care) in patients with preexisting pacemaker systems that limit pacemaker - mediated dyssynchrony.

Design, Setting, and Participants : This blinded randomized clinical trial enrolled 107 patients with stage B and C HFpEF from the University of Vermont Medical Center pacemaker clinic between June 2019 and November 2020.

Results Overall, 107 participants were randomly assigned to the personalized accelerated pacing (n = 50) or usual care (n = 57) groups. The median (IQR) age was 75 (69-81) years, and 48 (48%) were female. Over 1-year follow-up, the median (IQR) pacemaker-detected heart rate was 75 (75-80) bpm in the personalized accelerated pacing arm and 65 (63-68) bpm in usual care. MLHFQ scores improved in the personalized accelerated pacing group (median [IQR] baseline MLHFQ score, 26 [8-45]; at 1 month, 15 [2-25]; at 1 year, 9 [4-21]; $P < .001$) and worsened with usual care (median [IQR] baseline MLHFQ score, 19 [6-42]; at 1 month, 23 [5-39]; at 1 year, 27 [7-52]; $P = .03$). In addition, personalized accelerated pacing led to improved changes in NT-proBNP levels (mean [SD] decrease of 109 [498] pg/dL vs increase of 128 [537] pg/dL with usual care; $P = .02$), activity levels (mean [SD], +47 [67] minutes per day vs −22 [35] minutes per day with usual care; $P < .001$), and device-detected atrial fibrillation (27% relative risk reduction compared with usual care; $P = .04$) over 1-year of follow-up. Adverse clinical events occurred in 4 patients in the personalized accelerated pacing group and 11 patients in usual care.

Personalized Pacing: A New Paradigm for Patients With Diastolic Dysfunction or Heart Failure With Preserved Ejection Fraction (myPACE)

ClinicalTrials.gov Identifier: NCT04721314

Recruitment Status : Completed
First Posted : January 22, 2021
Last Update Posted : February 9, 2022

View this study on Beta.ClinicalTrials.gov

Why did b-blockade therapy fail?

Study Type :	Interventional (Clinical Trial)
Actual Enrollment :	123 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Intervention Model Description:	Patients are randomized to either a personalized pacemaker lower heart rate setting based on a resting heart rate algorithm or to the conventional pacemaker lower rate setting of 60bpm.
Masking:	Double (Participant, Investigator)
Masking Description:	All investigators are blinded to patient randomization. To assess subject blinding, participants are asked at 1 month and 12 month follow up if they believed that their pacemaker lower rate was changed.
Primary Purpose:	Treatment
Official Title:	Personalized Pacing: A New Paradigm for Patients With Diastolic Dysfunction or Heart Failure With Preserved Ejection Fraction
Actual Study Start Date :	July 17, 2019
Actual Primary Completion Date :	October 30, 2021
Actual Study Completion Date :	December 5, 2021

ΕΤΑΙΡΕΙΑ ΜΕΛΕΤΗΣ ΚΑΙ ΕΡΕΥΝΑΣ
ΤΗΣ ΚΑΡΔΙΑΚΗΣ ΑΝΕΠΑΡΚΕΙΑΣ

24ο ΠΑΝΕΛΛΗΝΙΟ ΣΥΝΕΔΡΙΟ
Καρδιακής Ανεπάρκειας

Αρρυθμιολογικός κίνδυνος σε ασθενείς με HFpEF

Τι να κάνουμε;

Γεώργιος Ανδρικόπουλος, MD, PhD, FESC,
Διευθυντής Α Καρδιολογικής Τμήματος /
Ηλεκτροφυσιολογίας - Βηματοδότησης
Ερρίκος Ντυνάν Hospital Center

3 - 5 ΦΕΒΡΟΥΑΡΙΟΥ 2023
Ξενοδοχείο DIVANI CARAVEL

- Αιτιολογική αντιμετώπιση HFpEF όπου είναι εφικτό
- SGLT2 ανταγωνιστές (?)
- ICD στη δευτερογενή πρόληψη
- Ablation KM
- Accelerating Pacing (???)