MHIF FEATURED STUDY:

NanoCor

Currently Enrolling

EPIC message to *Research MHIF Patient Referral*

CONDITION:	PI:	RESEARCH CONTACTS:	SPONSOR:
Non-Ischemic Cardiomyopathy	Jay Traverse, MD Kasia Hryniewicz, MD	Jake Jensen – Jacob.Jensen@allina.com | 612-863-3818 Kari Thomas - Kari.M.Thomas@allina.com | 612-863-7493	AskBio

DESCRIPTION: an early phase, non-randomized study evaluating the safety of a single antegrade epicardial coronary artery infusion of NAN-101 in up to 12 subjects with non-ischemic cardiomyopathy and NYHA class III symptoms.

NAN-101 is a gene therapy product composed of a novel adeno-associated virus designed to target cardiomyocytes and deliver it's payload of I-1c transgene. This genetic material provides code for an upstream inhibitor of the SERC2a pathway, which has been identified as a primary pathogenic mechanism in heart failure. The goal is to improve calcium cycling within the heart

Preclinical studies have shown that constitutively activating I-1 within the failing rat heart improved not only contractility, but also reversed adverse remodeling by directly decreasing fibrosis and cardiac hypertrophy.

CRITERIA LIST/ QUALIFICATIONS:

Inclusion:

- Chronic non-ischemic cardiomyopathy
- LVEF of 30% or less
- NYHA III

Exclusion:

- Ischemic cardiomyopathy
- Restrictive cardiomyopathy/ infiltrative cardiomyopathy
- Renal failure

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MHIF FEATURED STUDY:

SOLVE-CRT

Stimulation **O**f the **L**eft **V**entricular **E**ndocardium for **C**ardiac **R**esynchronization **T**herapy in Non-Responders, Previously Untreatable and High-risk Upgrade Patients

Coming soon (~Feb. 16)!
EPIC message: *Research MHIF Patient Referral*

CONDITION:
Heart Failure with previously untreatable CRT or High-Risk Upgrades (HRU)*

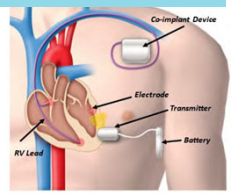
PI:
Jay Sengupta, MD

RESEARCH CONTACT:
Jessie Whelan
Jessica.Whelan@allina.com | 612-863-1661

SPONSOR:
EBR Systems

DESCRIPTION:

Three-part study that will work to demonstrate the safety and effectiveness of the WiSE CRT System. Two-part procedure (first implanting transmitter and battery and then implanting electrode in LV) followed by 5-year follow-up.



CRITERIA LIST/ QUALIFICATIONS:

Inclusion:

- Patient with a class I or IIa indication for implantation of a CRT device and one of the following:
  - CRT non-responder
    - EF remained unchanged or worsened since implant **AND**
    - Patient's clinical status has remained unchanged or worsened
  - Previously untreatable patient because CRT failed or programmed off
  - High-Risk Upgrade
- Patient is on stable Guideline Directed Medical Therapy
- Patient has suitable anatomy for implant
  - Adequate acoustic window, LV wall thickness in implant area >5mm, and absence of LV wall structural abnormalities)

Exclusion: (partial list)

- Pure RBBB
- LVEDD > 8 cm
- Non-ambulatory or unstable NYHA class IV
- Contraindications to heparin, chronic anticoagulants, or antiplatelet agents
- AF patients with RV pacing < 95% and/or have documented AF episode > 30 minutes or cardioversion within last 30 days
- Patients with prosthetic AV and non-viable transeptal approach, or patients with prosthetic MV and non-viable aortic approach for implant

**About 30% of patients have been found to not respond clinically to CRT.*

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MHIF FEATURED STUDY:

Myocardial perfusion and contraction assessed by cardiac MRI in acute and recovery takotsubo syndrome

OPEN AND ENROLLING* / EPIC message: *Research MHIF Patient Referral

CONDITION:	**PI:** Retu Saxena, MD **Co-I:** Scott Sharkey, MD	**RESEARCH CONTACTS:**	**SPONSOR:**
Takotsubo syndrome (TS)		Steph Ebnet stephanie.ebnet@allina.com | 320-291-8950 Sarah Schwager sarah.schwager@allina.com | 319-350-9643	MHIF IIR

DESCRIPTION: This study will use the new respiratory motion-corrected automated in-line perfusion mapping stress CMR protocol to quantify regional myocardial blood flow (MBF) and myocardial perfusion reserve (MPR) in TS patients resulting in a "myocardial perfusion map" which can be correlated with a "myocardial contraction map."

CRITERIA LIST/ QUALIFICATIONS:

Inclusion:

- Admitted with acute TS without significant coronary artery obstruction as defined on invasive coronary angiogram or CT coronary angiogram
- Typical apical or mid-ventricular ballooning pattern based on initial echocardiogram or left ventriculogram
- Age > 18 years

Exclusion:

- Significant acute or chronic renal disease (dialysis or estimated glomerular filtration rate <30 ml/min/m2)
- Contraindication to adenosine or gadolinium
- Decompensated acute heart failure (need for mechanical ventilation, vasopressor treatment of hypotension, mechanical circulatory support)
- Pregnancy or lactation
- Atrial fibrillation or sustained ventricular tachycardia/ventricular fibrillation
- Asthma requiring hospitalization or oxygen dependent COPD
- Bradycardia or advanced heart block unless pacemaker present

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2020 EP review for the non-EP

KRISTOPHER D KRUEGER, MD, PHD
CARDIAC ELECTROPHYSIOLOGIST

1

No Disclosures

2

My introduction to some at MHI:

3

Methods/Objectives

- Review of "important" articles from 2020
  - Purely subjective.
  - Avoided articles focusing on technical EP topics.
  - No COVID related articles.
- Objectives:
  - Identify advances and potential advances for implantable devices.
  - Identify limits in monitoring tech.
  - List some newer data on atrial fibrillation topics.

4

Devices: New and In the Pipeline

5

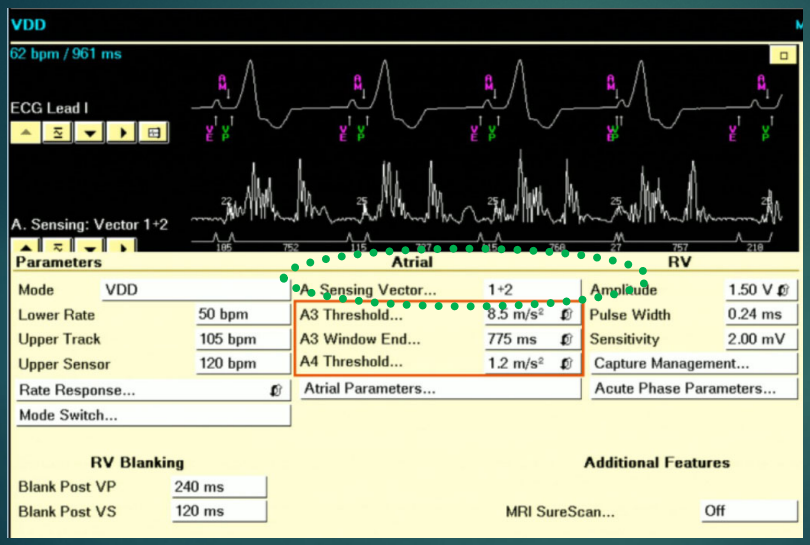
Atrioventricular Synchronous Pacing Using a Leadless Ventricular Pacemaker

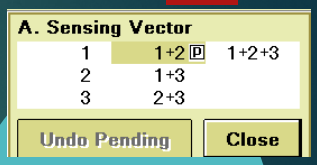
Results from the Marvel 2 Study (Steinwender et al, JACC EP, 2020; 6: 94-106).

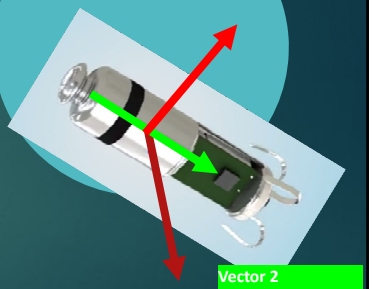
- Built off Marvel study (Chinitz et al., Heart Rhythm, 2018; 15: 1363-1371).
  - 64 patients (33 with high degree AV block).
  - Accelerometer-based atrial sensing is feasible and improves AVS.
- 75 patients from 12 centers. 40 had predominantly SR with CHB.
- Downloaded accelerometer-based algorithm.
- Primary efficacy objective was to demonstrate superiority of algorithm to provide AV synchronous (VDD) pacing versus VVI-50 pacing (SR with CHB).
- Safety endpoint: no pauses or heart rates of >100 bpm.

6

How does algorithm work? Sensing Vectors



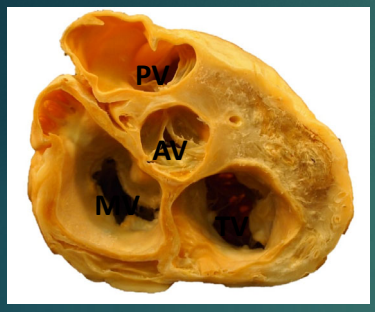


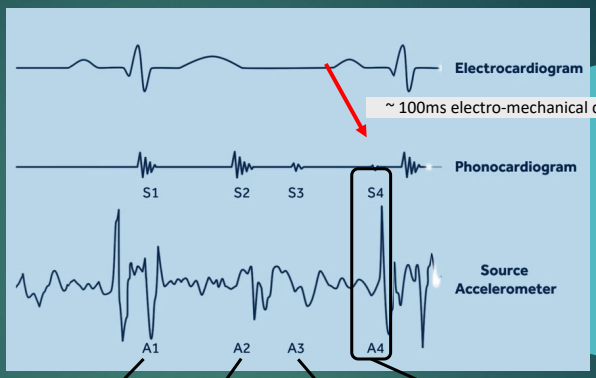


Vector 2 (longitudinal) best overall for picking up the atrial kick (A4)

7

ACCELEROMETER CAN DETECT MECHANICAL ACTIVITY: ACCELEROMETER SIGNALS CORRESPOND TO HEART SOUND TIMING & KNOWN CARDIAC ACTIVITY





A1 A-V valves close

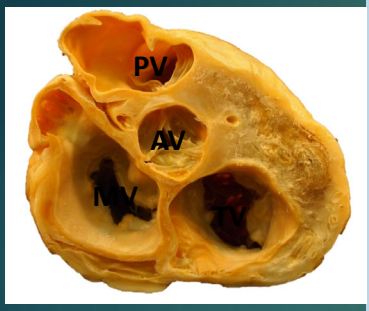
A2 Aortic & Pulmonary valves close

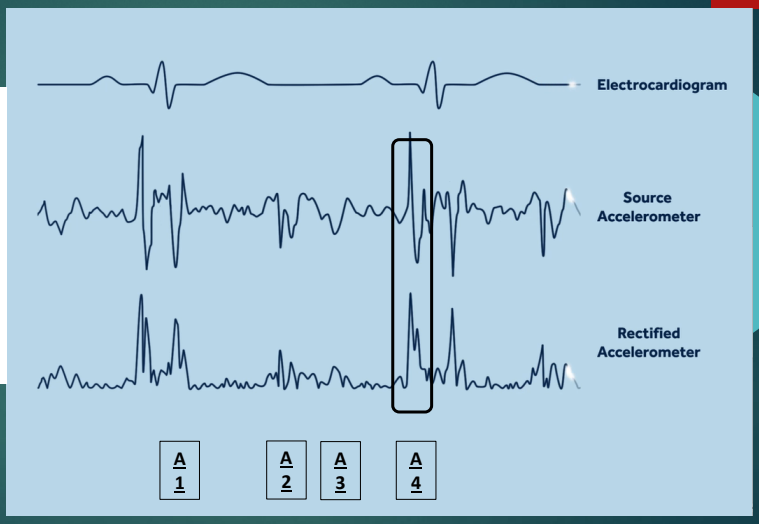
A3 A-V valves open (passive flow, atria to ventricles)

A4 Atrial kick (active flow)

8

NOTE THAT ACCELEROMETER SIGNALS CORRESPOND TO HEART SOUND TIMING & KNOWN CARDIAC ACTIVITY

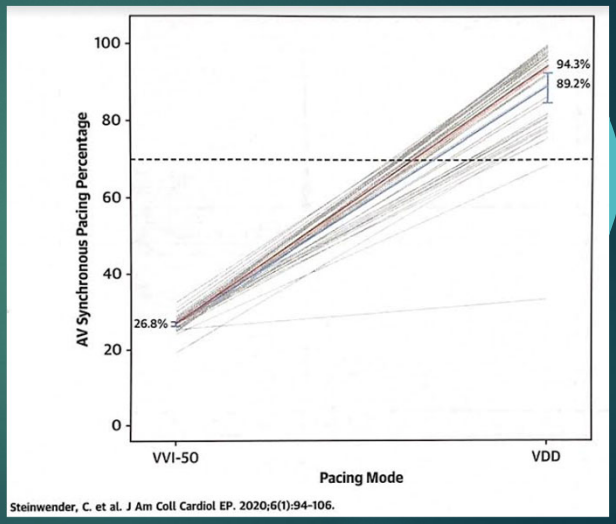




9

AV Synchronous Pacing %

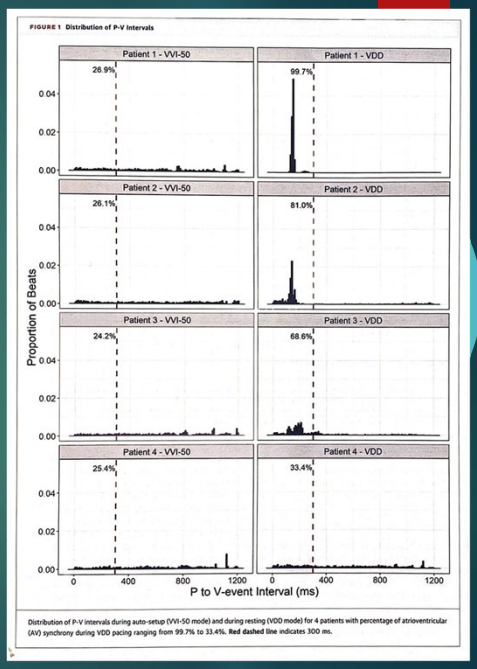
- Mean AV synchrony pacing % from 26.8% → 89.2% with VDD pacing.
- 94.3% median AV synchrony at rest.
- 95% of patients (38/40) had >/=70% AV synchrony.
- 8.8% improvement in SV (based on LVOT VTI).



10

Variable Response to Algorithm

- Bottom tile shows no response but some degree of "AV synchrony"
  - Some pts have periods of AV synchrony.
  - Some P waves fortuitously fall just before V pacing.
- Garweg et al., Heart Rhythm, 2020; 17: 2037-2045.
  - Looked at 64 patients in MARVEL 2 with visible P waves.
  - High AVS = good A4 signal (good atrial mechanical function).
  - Predictors of good A4 signal amplitude
    - E/A ratio <0.94
    - Low sinus rate variability.



11

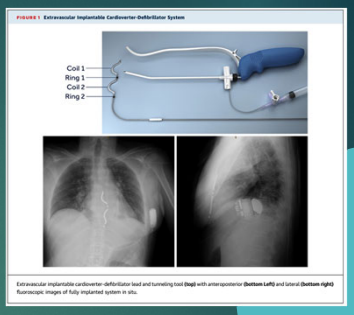
Appropriate Micra AV Patients

- Lack of atrial pacing indications.
- Infrequent pacing.
- Vascular access issues.
- Sedentary patients.
- Other comorbidities.

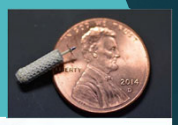
12

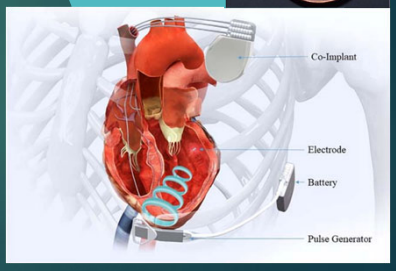
Current and Planned CRM Studies at MHI

- EV-ICD: Subcutaneous ICD
  - PI: Dr. Gornick
- SOLVE-CRT: Endocardial LV pacing
  - PIs: Dr. Moore and Dr. Sengupta
- LEADR: 4FR ICD lead.
  - PI: Dr. Zakaib

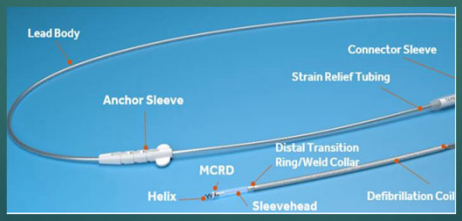


Crozier et al., JACC: Clinical Electrophysiology, 2020; 6 (12): 1527.





Singh et al., Americal Heart Journal, 2019; 217: 13.



13

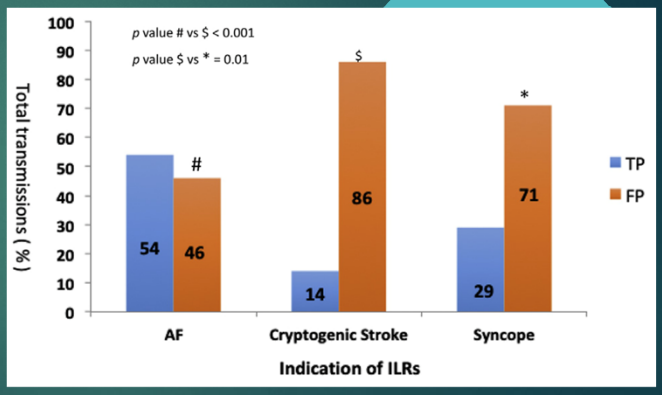
Implantable Loop Recorders

14

Incidence of false (+) transmissions during remote monitoring with ILRs

Afzal et al., Heart Rhythm, 2020: 17: 75-80.

- 695 remote transmissions on 559 pts over 4 weeks
  - AF surveillance: 321
  - Cryptogenic stroke: 168
  - Syncope: 70
- Primary reason for FP:
  - Scheduled: signal dropout and undersensing.
  - Alert: ectopy.
- ADJUDICATION!!!
  - 30-45 min for device RN+EP



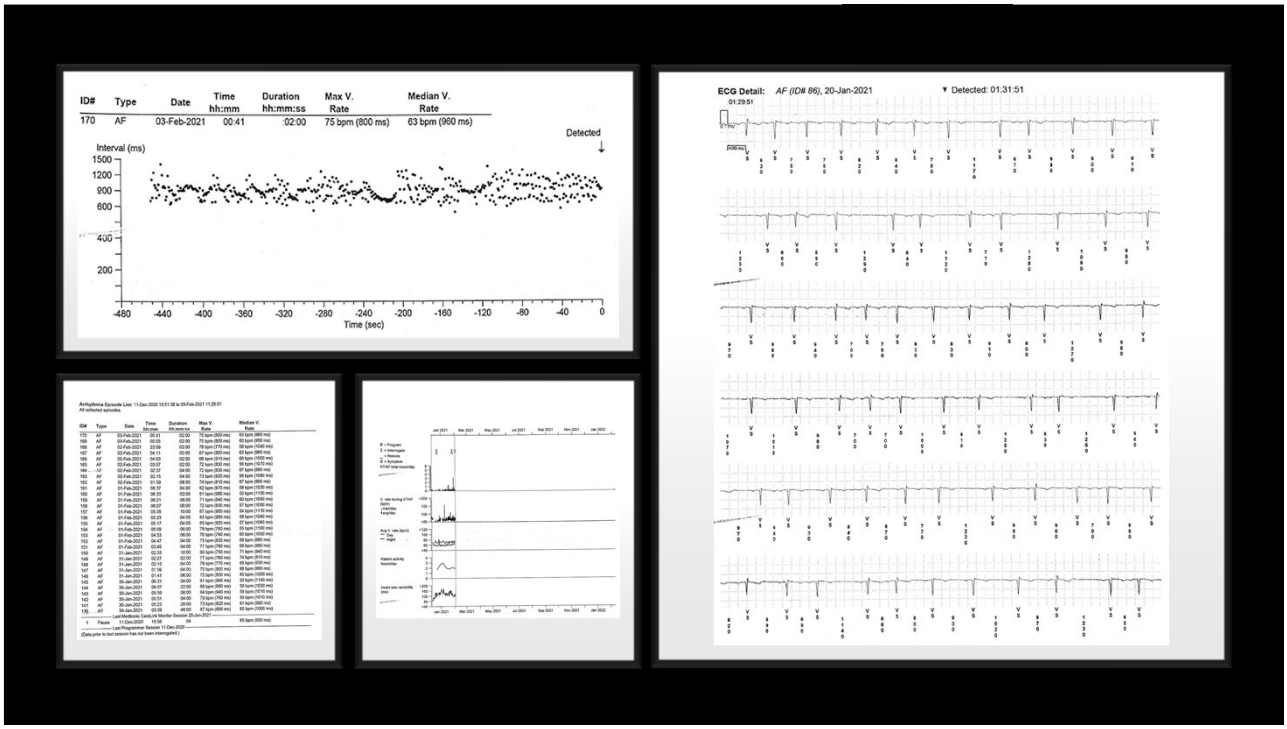
15

ILR False positive

70 y/o female admitted to ANW hospital on 12/9/2020.

- Left sided facial droop and worsening upper/lower extremity weakness.
- CTA with occlusion at origin of M2 branch of right MCA
- Outside of tPA window and not a mechanical thrombectomy candidate.
- ILR placement on 12/11/2020 for CS.

16


ID# Type Date Time hh:mm Duration hh:mm:ss Max V. Rate Median V. Rate
170 AF 03-Feb-2021 00:41 :02:00 75 bpm (800 ms) 63 bpm (960 ms)
Detected
Interval (ms)
1500
1200
900
600
400
200
-480 -440 -400 -360 -320 -280 -240 -200 -160 -120 -80 -40 0
Time (sec)
ECG Detail: AF (ID# 86), 20-Jan-2021
Detected: 01:31:51
01:29:51

17

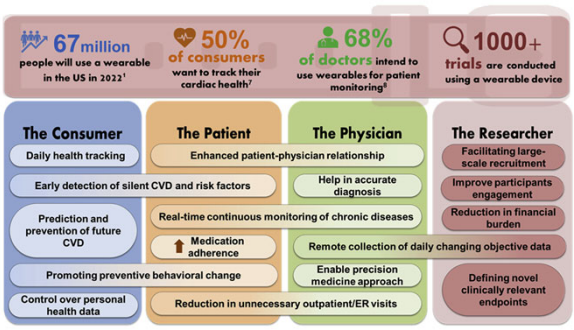

Wearable Tech

18

"It all started when I got my Apple Watch."

Wearables:

- Market of 27.49 billion in 2026.
- 9% in 2014 → 33% in 2018.
- By 2022: estimated 67 million users in US.



Dagher et al., Heart Rhythm, 2020; 17: 889.

19

Table 5

Summary of validity, representing sensitivity and specificity of eligible studies.

Research	Sensitivity	Specificity
Chan & Choy[11]	98%	29.2%
Chan et al[12]	75% (95% CI 70–80%)	98.2% (95% CI 59.3–70.5
Desteghe et al[13]	54.5%–78.9%	97.5%–97.9%
Evans et al[14]	Unreported	Unreported
Halcox et al[15]	Unreported	Unreported
Lown et al[16]	87.8% (95% CI 78.7%–93.9%)	98.8% (95% CI 96.9%–99.6%)
Lowres et al[6]	98.5%	91.4%
Lowres et al[17]	94.6% (95% CI, 85.1–98.9)	92.9% (95% CI, 92.0–93.8
Soni et al[18]	Unreported	Unreported
Soni et al[19]	Unreported	Unreported
Tarajki et al[20]	100%	97%

CI = confidence interval.

Effectiveness of AliveCor (Kardia mobile) device for AF screening

Hall et al., Medicine, 2020; 99: 30

-Rates of AF detection: 0.8-36%
-Rather good.
-Does not pick everything up and may still be wrong: patient education!

20

Wearable Accuracy in SVT

Sequeria ta al., Heart Rhythm, 2020; 17: 854-859

- Device placed on wrist during EPS for SVT on 52 patients.
- All devices inaccurate at HR detection of short SVT.
- If an elevated heart rate is detected, it is likely real.
- Some devices are accurate at detecting elevated HRs during longer SVT.

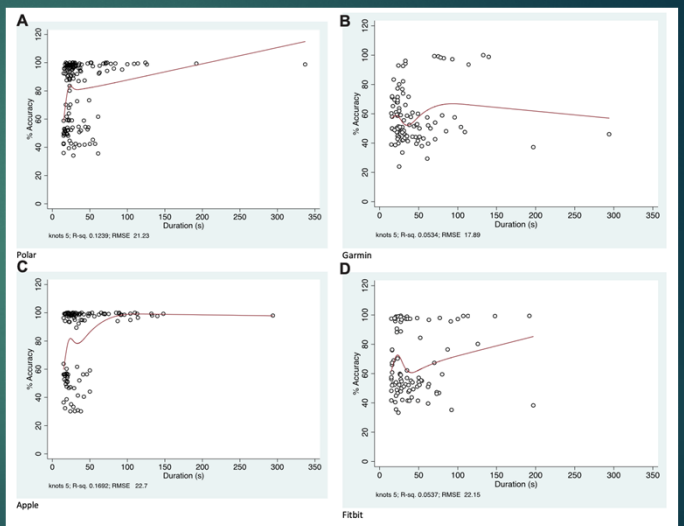


Figure 1 Supraventricular tachycardia duration vs device accuracy. Model fit for restricted cubic splines for each wearable device. **A:** Apple: $r^2 = 0.1692$. **B:** Fitbit: $r^2 = 0.0537$. **C:** Garmin: $r^2 = 0.0534$. **D:** Polar: $r^2 = 0.1239$. RMSE = root mean square error.

21

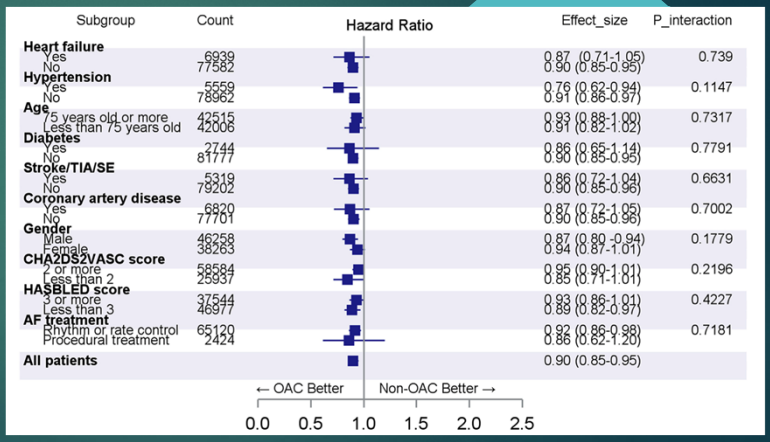
Topics in Atrial Fibrillation

22

Reduced Risk of Dementia/CI with OAC for AF

Mongkhon et al., Heart Rhythm, 2020; 17: 706713

- Retrospective cohort study.
  - UK 1° care data 2000-2017.
  - 84521 with AF
    - 35245 on OAC
    - 49276 not
- 10% lower risk in patients on OAC versus not.
- No difference in warfarin vs DOACs
- Increased risk of dementia in patients on OAC/antiplatelet Rx

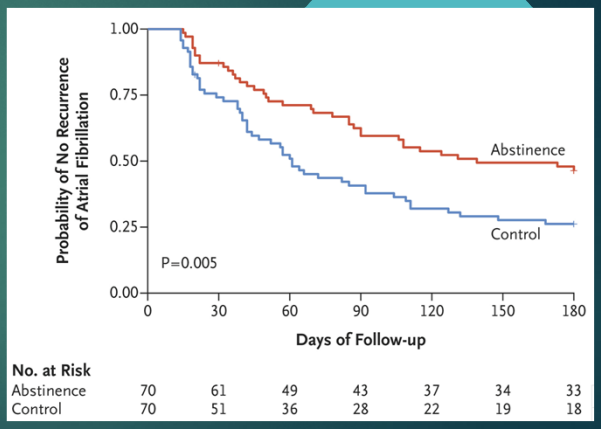


23

EtOH Moderation and AF Recurrence

Voskoboinik et al., NEJM, 2020; 382: 20-28

- Prospective, randomized 6 hospitals in Australia, 140 patients.
  - AF and 10+ EtOH drinks/week.
    - Abstinence: 16.8±7.7 → 2.1 ± 3.7 (complete: 61%)
    - Control: 16.4±6.9 → 13.2 ± 6.5
  - Endpoints after 2 week blanking period
    - Freedom from AF recurrence at 6 months.
      - Abstain: 53% versus 73%
    - AF burden over 6 months.
      - Abstain: 0.5% versus 1.2%



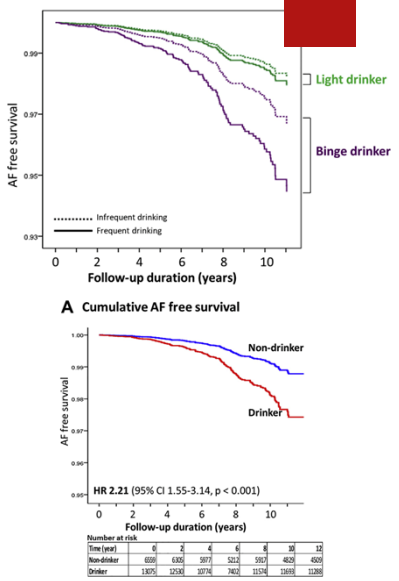
24

EtOH and AF Risk in Healthy Adults

Cha et al., Heart Rhythm, 2020; 17: 2086-2092

19634 patients 2007-2015 in South Korea

- Retrospective screening of healthy pts, no AF
- Excluded those with any medical/surgical history.
- Average follow-up: 7.0±2.8 years.
- Any EtOH use increased risk of AF.
- Highest risk was for frequent, binge drinkers.



25

Impact of Bariatric Surgery on AF Type

Donnellan et al., Circulation: Arrhythmia and Electrophysiology, 2020; 13 (2): 106

- Retrospective 440 consecutive morbidly obese patients (2007-2013).
- 220 Control
  - 10.1% weight loss
  - No AF reversal
- 220 underwent BS (loss%/AF reversal%)
  - Gastric bypass: 25/70
  - Sleeve gastrectomy: 19/56
  - Gastric banding: 16/50
- No benefit in long-standing or permanent AF.

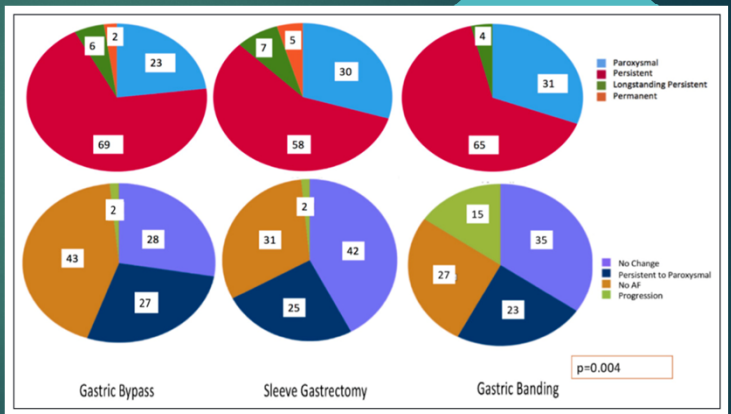


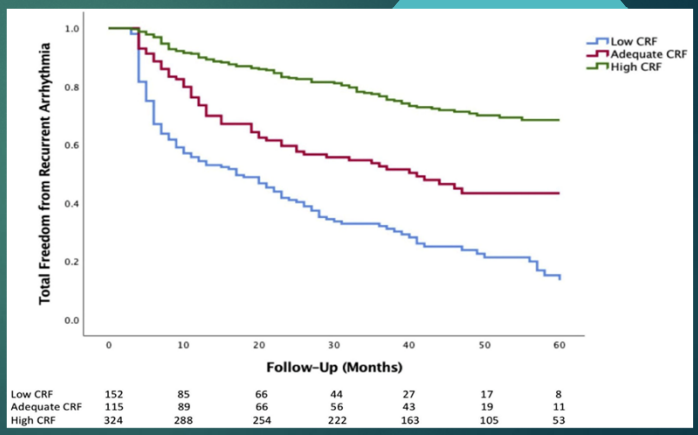
Figure. Pie charts demonstrating changes in atrial fibrillation (AF) type between groups; *P*=0.004 for between-group differences in AF reversal.

26

Higher Cardiopulmonary Fitness Associated with Lower Recurrence after AF ablation

Donnellan et al., Heart Rhythm, 2020; 17: 1687-1693.

- 591 consecutive patients
  - Retrospective 1/2012-1/2018.
  - Undergoing ablation for AF.
  - Had exercise stress test within 12 months prior to ablation.
- 3 groups
  - Low CRF: <85% predicted METs
  - Adequate CRF: 85-100%
  - High CRF:>100%
  - Similar patient characteristics between 3 groups.
- Outcomes: mean f/u 32 months.
  - Arrhythmia recurrence: 79%, 54% and 27.5%
  - Death: 11%, 4% and 2.5%

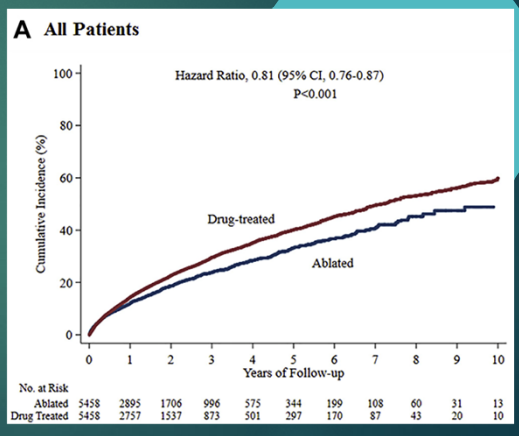


27

Generalizability of CASTLE-AF Trial: Does it apply to general practice?

Noseworth et al., Heart Rhythm, 2020: 17: 1057-1065

- Large retrospective database
  - 289831 AF/HF patients
  - 7465 Rx with ablation
  - 282366 Rx with medical therapy.
- CASTLE-AF applicable population?
  - 7.8% met CASTLE-AF eligibility
  - 91% failed inclusion criteria.
  - 15.5% failed exclusion criteria.
- Primary endpoint: composite of death and HF hospitalization.
  - 18% reduction
  - 38% reduction in CASTLE-AF.



28

Early Rhythm Control of Atrial Fibrillation Camm et al., NEJM, 2020, 383: 1305

- Randomized 2789 patients (135 centers)
  - Diagnosed within last year.
  - 75 or older, prior TIA/stroke or at least 2 criteria (CHADSVASc +CKD and LVH)
  - Median time since diagnosis: 36 days.
  - Early rhythm control (abl or AAD) versus usual care (Rx guided by symptoms)
  - Primary endpoints
    - Composite of CV death, stroke or hospitalization for CHF or ACS.
    - Hospitalization days.
- Results
  - No difference in hospital days.
  - 249 versus 316 patient events favoring early rhythm control (HR: 0.79, p=0.005).

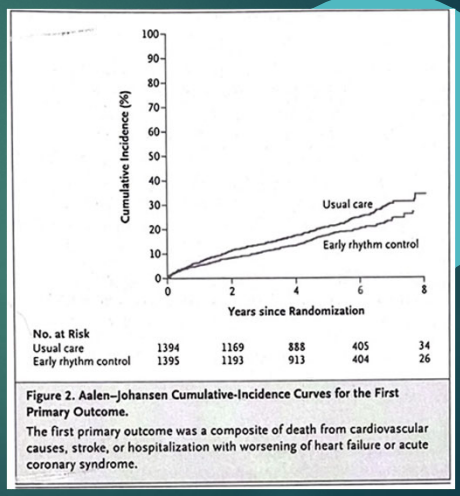


Figure 2. Aalen–Johansen Cumulative-Incidence Curves for the First Primary Outcome.
The first primary outcome was a composite of death from cardiovascular causes, stroke, or hospitalization with worsening of heart failure or acute coronary syndrome.

29

Conclusions:

- CRM: Pacing and ICD options continue to expand.
- ILR and wearable tech:
  - Adjudication of any of these results important.
  - Wearable tech options are expanding and have clear limitations.
  - Importance of patient education.
- Atrial fibrillation:
  - Multiple studies have confirmed reduction of dementia with OAC in AF.
  - Risk factor modification needs to be emphasized: EtOH, weight loss (BS) and fitness.
  - Benefit of ablation in some AF patients with CHF.
  - Early rhythm control important.

30