



BEYOND AFFIRM: CONTEMPORARY MANAGEMENT OF ATRIAL FIBRILLATION

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 Cardiovascular Institute

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DISCLOSURES

Dr. Louis Miller, faculty for this educational activity, has no relevant financial relationships with ineligible companies* to disclose, and have indicated that the presentations or discussions will not include off-label or unapproved product.

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LEARNING OBJECTIVES

1. Evaluate and understand the evidence supporting early rhythm control of atrial fibrillation.
2. Describe an approach for selecting antiarrhythmic agents for atrial fibrillation, considering patient-specific factors.
3. Determine the appropriate scenarios in which an internist should refer a patient for atrial fibrillation catheter ablation.
4. (Bonus) Differentiate the clinical significance of atrial high-rate episodes from atrial fibrillation.

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A CASE

66-year-old man

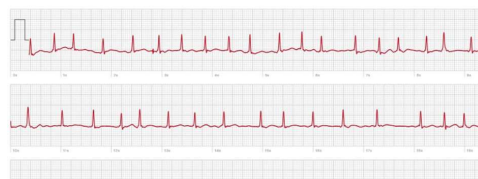
- Diabetes and hypertension
- Has received multiple irregular rhythm notifications from his wearable device
- Episodes last about 2-4 hours, but a few are longer than 24 hours
- Reports occasional palpitations but not during every episode
- Otherwise feeling fine

Blood pressure is 128/80mmHg

Regular heart rate at 65 bpm

He shows you one of the ECG recordings...

Atrial Fibrillation — 118 BPM Average
This ECG shows signs of AFib.
If this is an unexpected result, you should talk to your doctor.



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A CASE

66-year-old man

- Wearable alerts for "atrial fibrillation"
- Minimal symptoms
- Diabetes
- Hypertension

Blood pressure is 128/80mmHg

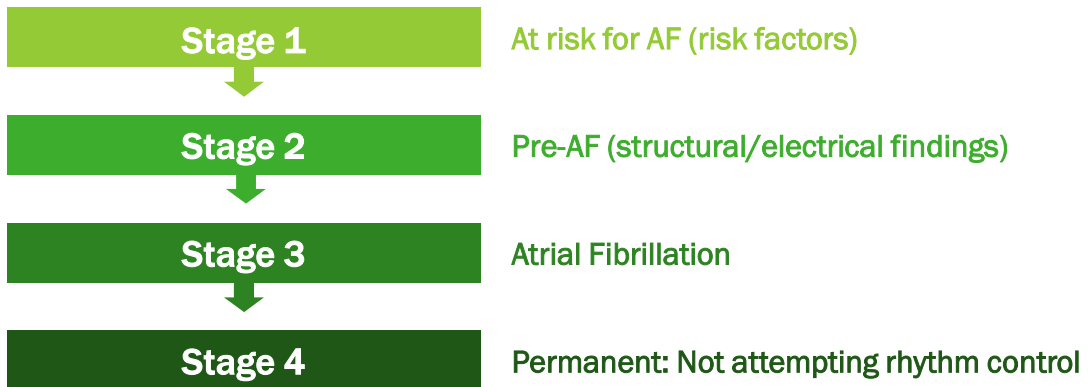
Regular heart rate at 65 bpm

Is this atrial fibrillation?



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STAGES OF ATRIAL FIBRILLATION



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ATRIAL HIGH-RATE EPISODES (AHRE)

- Sometimes referred to as Sub-clinical Atrial Fibrillation (SCAF)
- Generally, refers to:
 - Rare, intermittent, short bouts of atrial tachyarrhythmias
 - Resembling atrial fibrillation
 - Occurring in a patient without clinically diagnosed atrial fibrillation
- Detected by pacemakers, defibrillators, and implantable loop recorders
- Can also be detected by wearables
- Rates of detection are highly influenced by patient factors (age, comorbidities) and device factors (thresholds and algorithms).

AHRE increase stroke risk modestly ~1% per year
Anticoagulation management is controversial.

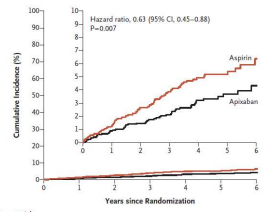


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ATRIAL HIGH-RATE EPISODES (AHRE)

ARTESIA

Apixaban versus Aspirin



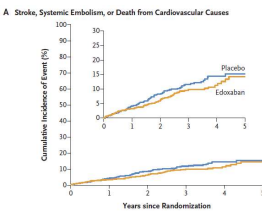
| No. at Risk | 1997 | 1777 | 1539 | 1120 | 780 | 468 | 200 |
|-------------|------|------|------|------|-----|-----|-----|
| Aspirin | 1997 | 1777 | 1539 | 1120 | 780 | 468 | 200 |
| Apixaban | 2015 | 1786 | 1558 | 1157 | 820 | 474 | 214 |

0.46% REDUCTION IN STROKE, EMOLISM

Healy JS et al. *NEJM* 2024;390:107-17.

NOAH-AFNET 6

Edoxaban versus Placebo



| No. at Risk (no. of events) | Edoxaban | 1270 (17) | 873 (20) | 559 (19) | 327 (3) | 148 (4) | 42 |
|-----------------------------|-----------|-----------|----------|----------|---------|---------|----|
| Edoxaban | 1270 (17) | 873 (20) | 559 (19) | 327 (3) | 148 (4) | 42 | |
| Placebo | 1266 (44) | 822 (19) | 534 (16) | 319 (7) | 137 (1) | 50 | |

NO DIFFERENCE IN CV DEATH, STROKE, EMOLISM

Kirchoff P et al. *NEJM* 2023;389:1167-79.

AHRE increase stroke risk modestly ~1% per year
Anticoagulation management is controversial.



Median CHA2DS2-VASc ~4
Most with duration < 6 hours

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A CASE

66-year-old man

- Wearable alerts for "atrial fibrillation"
- Symptomatic
- Some episode > 24 hours
- Diabetes
- Hypertension

Blood pressure is 128/80mmHg

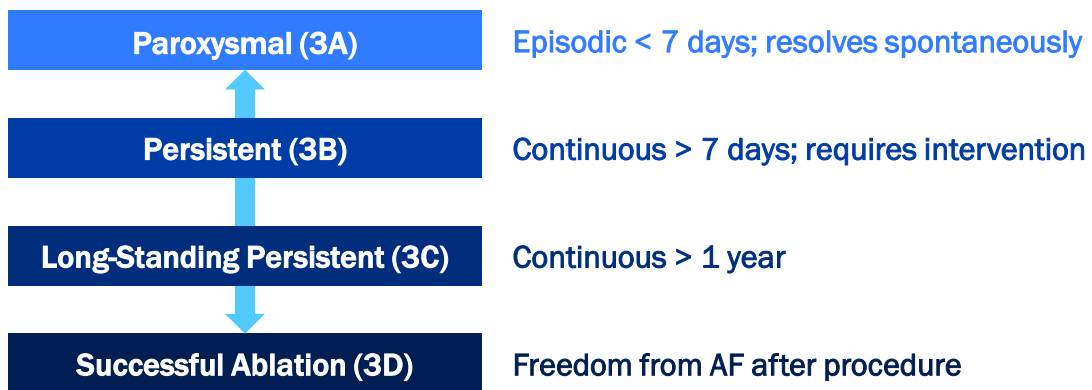
Regular heart rate at 65 bpm

Is this atrial fibrillation?



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SUB-STAGES OF ATRIAL FIBRILLATION (STAGE 3)



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A CASE

66-year-old man

- New diagnosis of atrial fibrillation
- Minimal symptoms
- Diabetes
- Hypertension

Blood pressure is 128/80mmHg

Regular heart rate at 65 bpm

Would this patient benefit more from a rhythm or rate control treatment strategy?



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AFFIRM

The New England Journal of Medicine

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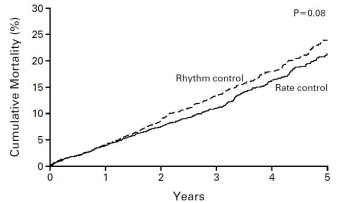
A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

THE ATRIAL FIBRILLATION FOLLOW-UP INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) INVESTIGATORS*

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AFFIRM

What you remember about AFFIRM



| No. of DEATHS | number (percent) | | | |
|----------------|------------------|--------|---------|----------|
| Rhythm control | 0 | 80 (4) | 175 (9) | 257 (13) |
| Rate control | 0 | 78 (4) | 148 (7) | 210 (11) |
| | | | | 314 (18) |
| | | | | 275 (16) |
| | | | | 352 (24) |
| | | | | 306 (21) |

Figure 1. Cumulative Mortality from Any Cause in the Rhythm-Control Group and the Rate-Control Group. Time zero is the day of randomization. Data have been truncated at five years.

RATE CONTROL = RHYTHM CONTROL

AFFIRM Investigators *NEJM* 2002;347:1825-33.

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What you might have forgotten



Predictors of Death

Antiarrhythmic drugs

Digoxin

Predictors of Survival

Anticoagulation

Sinus rhythm

AFFIRM Investigators *Circulation* 2004;109:1509-1513.

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EAST-AFNET4

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812

OCTOBER 1, 2020

VOL. 383 NO. 14

Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

P. Kirchhof, A.J. Camm, A. Goette, A. Brandes, L. Eckardt, A. Elvan, T. Fetsch, I.C. van Gelder, D. Haase, L.M. Haegeli, F. Hamann, H. Heidbüchel, G. Hindricks, J. Kautzner, K.-H. Kuck, L. Mont, G.A. Ng, J. Rekosz, N. Schoen, U. Schotten, A. Suling, J. Taggeselle, S. Themistoclakis, E. Vettorazzi, P. Vardas, K. Wegscheider, S. Willems, H.J.G.M. Crijns, and G. Breithardt, for the EAST-AFNET 4 Trial Investigators*

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EAST-AFNET 4

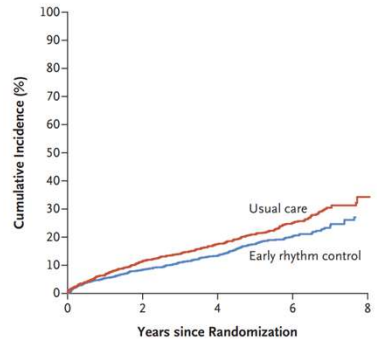
Early rhythm versus rate control
 Early = diagnosis within the last year

Primary composite endpoint:

- CV death
- Stroke
- HF hospitalization
- ACS hospitalization

Early rhythm control significantly reduced both CV death and stroke.

EARLY RHYTHM CONTROL > RATE CONTROL



| No. at Risk | 0 | 2 | 4 | 6 | 8 |
|----------------------|------|------|-----|-----|----|
| Usual care | 1394 | 1169 | 888 | 405 | 34 |
| Early rhythm control | 1395 | 1193 | 913 | 404 | 26 |

Kirchhoff P et al. *NEJM* 2020;383:1305-16.

THE PARADIGM IS SHIFTING

AFFIRM



RATE CONTROL = RHYTHM CONTROL

EAST-AFNET4



EARLY RHYTHM CONTROL > RATE CONTROL

THE PARADIGM IS SHIFTING

| RATE CONTROL = RHYTHM CONTROL | | | | ➔ | RHYTHM CONTROL > RATE CONTROL | | | |
|-------------------------------|------|-------|-----------|---|-------------------------------|------|-------|-----------|
| Trial | Year | N | Follow-up | | Trial | Year | N | Follow-up |
| AFFIRM | 2002 | 4,060 | 3.5 years | | EAST-AFNET4 | 2020 | 2,789 | 5 years |
| PIAF | 2000 | 252 | 1 year | | CASTLE-AF | 2018 | 398 | 3 years |
| RACE | 2002 | 522 | 2 years | | ATHENA | 2009 | 4,628 | 2 years |
| STAF | 2003 | 200 | 3 years | | CABANA | 2019 | 2,204 | 4 years |
| AF-CHF | 2008 | 1,376 | 3 years | | | | | |
| J-RHYTHM* | 2009 | 885 | 2 years | | | | | |

*Favored rhythm control on QoL endpoint

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A CASE

52-year-old man

- New diagnosis of atrial fibrillation
- Minimal symptoms
- Diabetes
- Hypertension

Blood pressure is 128/80mmHg

Regular heart rate at 65 bpm

Would this patient benefit more from a rhythm or rate control treatment strategy?



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SHARED DECISION MAKING

RATE CONTROL

- 75-85% of patients
- **Safer medications**
- **Fewer hospitalizations**
- Most prior studies show similar stroke/death with rhythm control
- Based on older studies
- **Requires anticoagulation**

RHYTHM CONTROL

- 15-25% of patients
- More toxic medications and/or
- Invasive procedures
- More hospitalizations
- **Improved quality of life/symptoms**
- **New studies suggest less stroke/death**
- **Requires anticoagulation**

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A CASE

52-year-old man

- New diagnosis of atrial fibrillation
- Minimal symptoms
- Diabetes
- Hypertension

Blood pressure is 128/80mmHg

Regular heart rate at 65 bpm

Would this patient benefit more from a rhythm or rate control treatment strategy?



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A CASE

- 52-year-old man
- New diagnosis of atrial fibrillation
 - Minimal symptoms
 - Diabetes
 - Hypertension

Hemodynamically stable
HR 160-180s

*He goes back into atrial fibrillation
with rapid ventricular response.*



You send him to the ER.

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A CASE

- 52-year-old man
- Paroxysmal atrial fibrillation
 - Minimal symptoms
 - Diabetes
 - Hypertension

Hemodynamically stable
HR 160-180s overnight

*Sinus rhythm is spontaneously
restored by morning rounds.*



*He tells you he strongly prefers
to stay out of atrial fibrillation.*

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A CASE

52-year-old man

- Paroxysmal atrial fibrillation
- Minimal symptoms
- Diabetes
- Hypertension

Blood pressure is 128/80mmHg

Regular heart rate at 65 bpm

How should sinus rhythm be maintained?



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SHARED DECISION-MAKING FOR RHYTHM CONTROL

AADs

Antiarrhythmic Drugs

- Each have toxicities and contraindications
- **Choice is guided mostly by safety**
- **Efficacy is modest** (30-50% at 1 year)
- Asymptomatic recurrences are common
- Most can worsen underlying conduction disease
- Amiodarone is a last-line agent
- **Anticoagulation should be continued**

Ablation

Catheter Ablation

- **Procedural risks are low < 3%**
- Used as first-line or after drug failure
- Decreases use of antiarrhythmic drugs
- **Decreases recurrences**
- **Improves quality of life and symptoms**
- Improves mortality in HF with reduced EF
- **Anticoagulation should be continued**

CONSULTATION WITH A CARDIOLOGIST IS APPROPRIATE AT THIS TIME.

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ANTIARRHYTHMIC PEARLS

Flecainide & Propafenone **DO NOT USE WITH CAD, MI, CHF, LVH**

- Use with AV nodal blocker – risk of 1:1 conduction of atrial flutter
- Rare non-cardiac side effects – dizziness, blurred vision, metallic taste (propafenone)



Sotalol & Dofetilide **DO NOT USE WITH CKD (GFR < 40)**

- Prolongs QT interval – associated with torsade de pointes, monitor
- Avoid other QT prolonging drugs



Dronedaron **DO NOT USE WITH CHF**

- Liver toxicity, anorexia, nausea, but less toxic (and effective) than amiodarone
- Bradycardia

Amiodarone **DO NOT USE FIRST LINE**

- Thyroid, liver, pulmonary toxicity, ocular and skin discoloration
- Prolongs QT – but rare torsade de pointes
- Sinus bradycardia

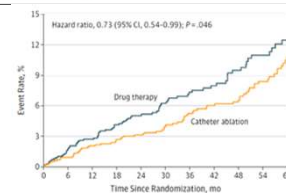
WHO SHOULD BE REFERRED FOR ABLATION

JAMA | Original Investigation

Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation The CABANA Randomized Clinical Trial

Douglas L. Packer, MD, Daniel B. Mark, MD, MPH, Richard A. Robb, PhD, Kristi H. Monahan, RN, Tristram D. Bahnson, MD, Jeanne E. Poole, MD, Peter A. Noseworthy, MD, Yves D. Rosenberg, MD, MPH, Neal Jeffries, PhD, L. Brent Mitchell, MD, Greg C. Flaker, MD, Evgeny Pokushalov, MD, Alexander Romanov, MD, T. Jarek Bunch, MD, Gregg Roscher, MD, Andrey Arbidshew, MD, Anton Reboldtke, MD, David J. Wilber, MD, Riccardo Cappato, MD, Karl Heinz Kusik, MD, Gerhard Hindricks, MD, D. Wyn Davies, MD, Peter R. Kowey, MD, Gerald V. Naccarelli, MD, James A. Reffel, MD, Jonathan P. Piccini, MD, MHS, Adam P. Silverstein, MS, Hassan R. Al-Khalidi, PhD, Kerry L. Lee, PhD, for the CABANA Investigators

Figure 2. Kaplan-Meier Estimates of the Incidence of the Primary End Point



CABANA

Ablation versus medical therapy

- Primary endpoint: death, disabling stroke, serious bleeding, cardiac arrest
- Secondary endpoint: death, cardiovascular hospitalization

ABLATION > MEDICATIONS?

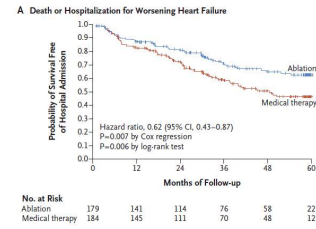
- Intention-to-treat analysis:
 - No difference for primary endpoint
 - 6.4% ARR for secondary endpoint
- Per-protocol (as-treated) analysis:
 - Benefit in the ablation group at 1 year (but not 6 months). HR 0.73, P=0.046

WHO SHOULD BE REFERRED FOR ABLATION



Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heibert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*



CASTLE-AF

- NYHA 2-4, LVEF ≤ 35% w/ ICD or CRT-D
- Primary endpoint: death from any cause or unplanned overnight hospitalization for worsening heart failure

ABLATION > MEDICATIONS

- 16.1% ARR for primary endpoint
- Significant reductions of death, CV death and heart failure hospitalizations
- No significant reduction of stroke

WHO SHOULD BE REFERRED FOR ABLATION



- **Patients with asymptomatic long-standing persistent atrial fibrillation, and other co-morbidities.**
- **HFrEF patients, particularly with rapid rates or recent admissions attributed to atrial fibrillation.**
 - Including patients with tachycardia-induced cardiomyopathy.
- **Patients with recently diagnosed atrial fibrillation.**
- **Patients with symptomatic paroxysmal atrial fibrillation.**

SUMMARY

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TAKE HOME POINTS

- Newer trials suggest a paradigm shift for the management of atrial fibrillation.
- Rhythm control may be preferred in select patients:
 - Newly diagnosed
 - Heart failure with reduced LV function
- Involve a cardiologist, particularly if considering a rhythm control strategy.
- Avoid amiodarone, especially in younger patients if possible.
- Regardless of rate or rhythm control, continue anticoagulation!

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