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A Review of Common Clinical Scenarios in the Management of Atrial Fibrillation

Updates in Hospital Medicine
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HARVARD MEDICAL SCHOOL

Disclosures

- No relevant disclosures

Learning objectives

- Manage thrombotic risk appropriately in patients with AF who are elderly, those with prosthetic valves and those with recurrent bleeding
- Appropriately utilize pharmacology in rate control of AFib
- Understand the impact of lifestyle modification on Afib
- Utilize cardiac CT in the exclusion of LA thrombi prior to DCCV
- Appropriately refer patients for an early rhythm control strategy
- Understand indications for PPM implantation in AFib

Case 1

History of the Present Illness:

90F with a history of hypertension (well managed with hydrochlorothiazide), bioprosthetic mitral valve replacement 10 years prior for endocarditis in the setting of known mitral valve prolapse (now on aspirin 81 mg daily only) presenting with 3 days of cough with upper respiratory symptoms and shortness of breath who is found to be in atrial fibrillation. She drinks 2-3 glasses of wine weekly. She remains fully independent and prior to this acute illness was walking 1 mile daily. She has no symptoms of thyroid dysfunction.

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Case 1

Exam:

- HR 116 bpm, BP 140/92, RR 14, O2 Sat 98% on Room Air, Weight 50 kg
- Comfortable appearing, appears much younger than stated age
- Erythematous posterior oropharynx and nasal mucosa, lungs clear
- Jugular venous pressure 6 cm H_2O, heartrate is irregularly irregular without murmurs, S3 not present, extremities warm and no edema

Testing

- BMP, CBC, LFTs and TSH notable for GFR ~45 ml/min/1.73 m^2
- ECG reveals atrial fibrillation without significant ST/T changes
- TTE shows normal biventricular function, normal functioning bioprosthetic mitral valve and moderate LA dilation

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Question*

In addition to rate control therapy, would you recommend anticoagulation?

A. Yes, her CHA_2DS_2-Vasc score is elevated
B. No, while her CHA_2DS_2-Vasc score is elevated, given her age, her bleeding risk is high and outweighs the ischemic benefit

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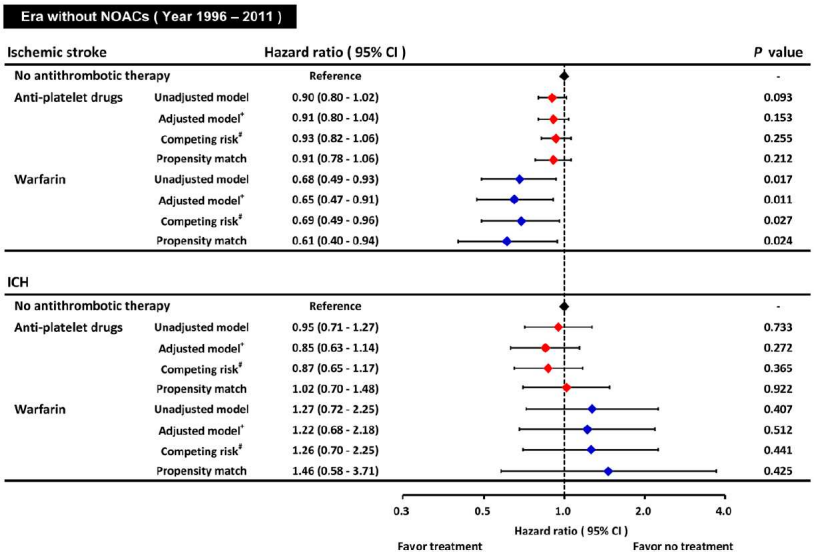
Is there an age cutoff for anticoagulation?



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Chao et al. Circulation 2018.

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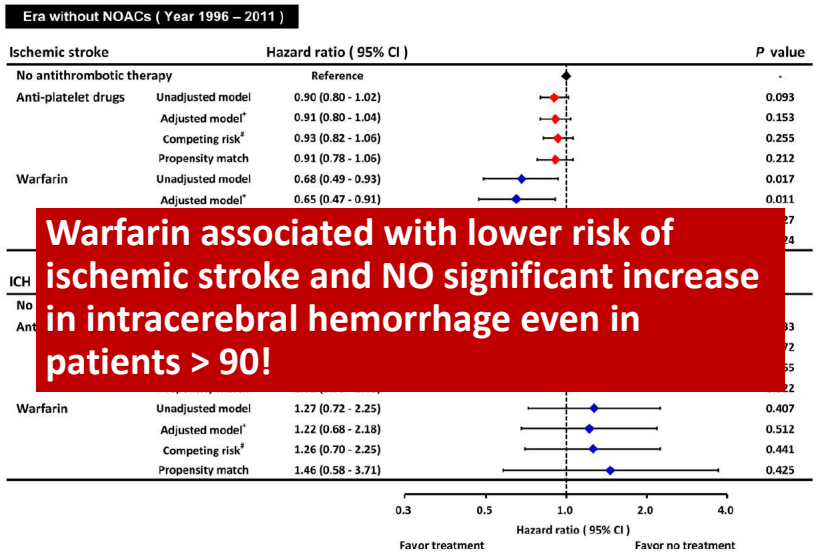

Warfarin associated with lower risk of ischemic stroke and NO significant increase in intracerebral hemorrhage even in patients > 90!

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Chao et al. Circulation 2018.

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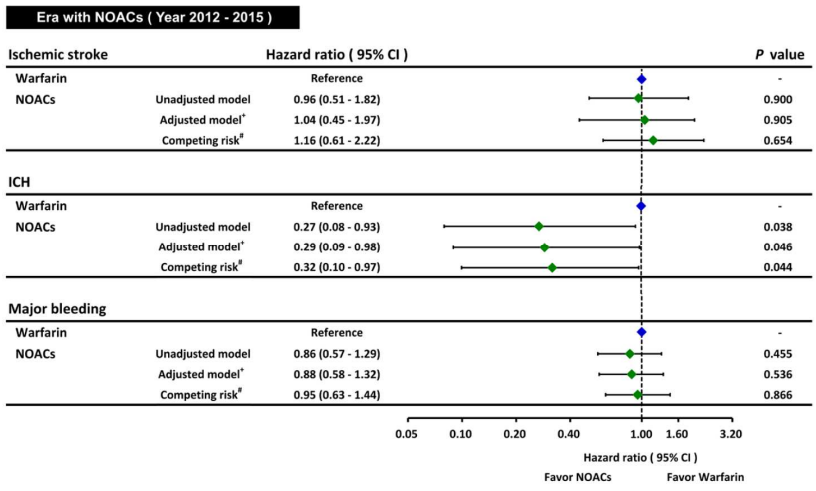

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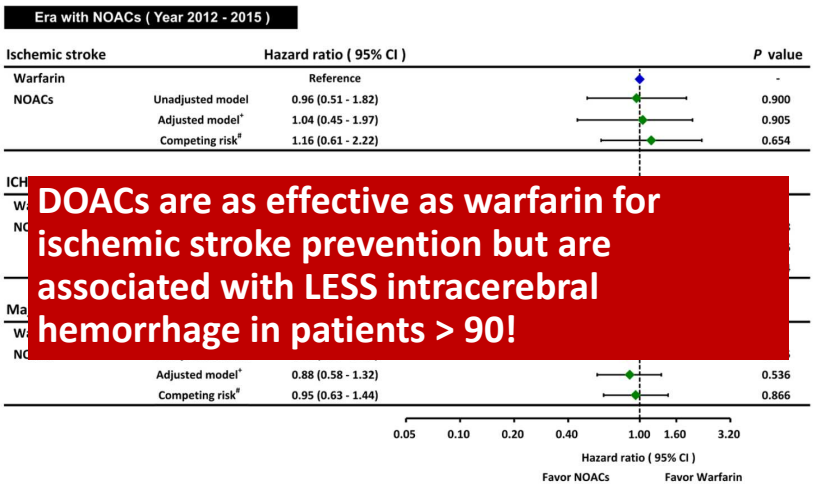

DOACs are as effective as warfarin for ischemic stroke prevention but are associated with LESS intracerebral hemorrhage in patients > 90!

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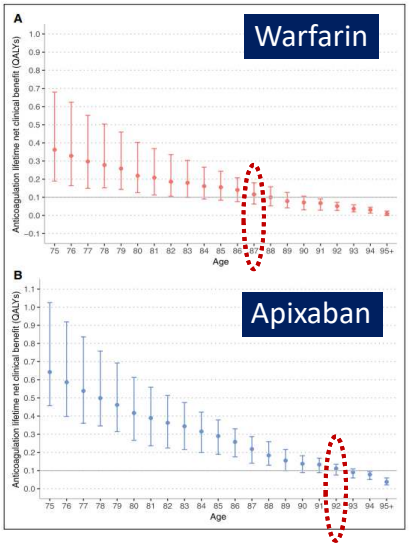
Chao et al. Circulation 2018.

There is a net reduction in benefit with aging!



- Net clinical benefit of anticoagulation decreases with age
- < 0.1 QALY:
  - 87: Warfarin
  - 92: Apixaban
- Competing risks diminishes net clinical benefit

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Shah et al. Circ Cardiovasc Qual Outcomes 2019.

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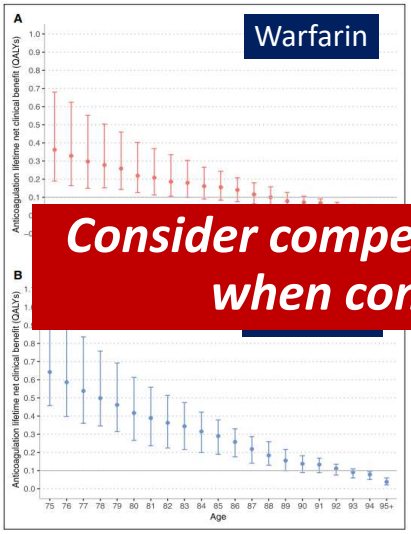

- Net clinical benefit of anticoagulation decreases with age

Consider competing mortality risks when considering AC!

- Competing risks diminishes next clinical benefit

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Shah et al. Circ Cardiovasc Qual Outcomes 2019.

Is there an age cutoff for anticoagulation?

Take-home

- Age alone should not dissuade you from anticoagulation
- There is evidence of net clinical benefit even in the very elderly population
- Clinical benefit decreases with age
- Competing mortality risks significantly impacts benefit

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Question*

What anticoagulant would you choose in this 50 kg 90 year old woman with a bioprosthetic AVR with an EGFR of 45 45 ml/min/1.73 m^2?

A. Rivaroxaban 20 mg daily
B. Dose-adjusted warfarin for goal INR 2-3
C. Apixaban 5 mg twice daily
D. Apixaban 2.5 mg twice daily

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DOACs in Valvular AF

- Valvular atrial fibrillation = atrial fibrillation with moderate to severe MS, valve replacement or valve repair
- Native AS, AI, MR and TR are NOT considered valvular AF
- DOACs with mechanical valves are absolutely contraindicated!
- DOACs should not be used with moderate to severe MS

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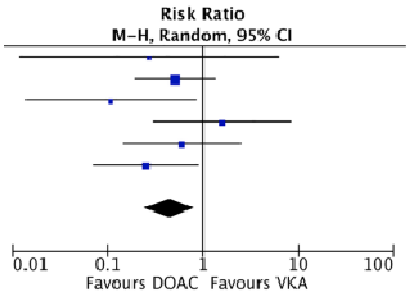
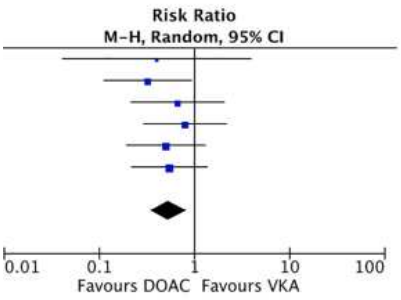
DOACs with Bioprosthetic Valves?

Embolic risk



Bleeding Risk



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Lacy et al. Catheter Cardiovasc Interv. 2021.

DOACs with Bioprosthetic Valves?

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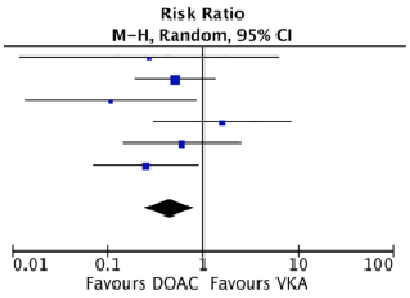

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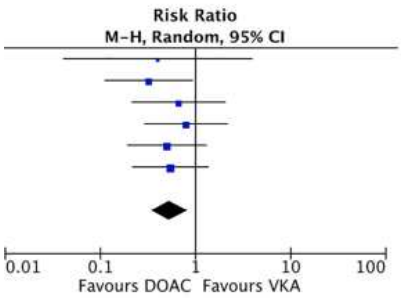

DOACs probably safe among patients with bioprosthetic valves.

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Lacy et al. Catheter Cardiovasc Interv. 2021.

DOACs with Bioprosthetic Valves?

- Warfarin preferred in first 3-6 months after bioprosthetic valve replacement
- After 3-6 months, DOACs can be considered (ACC/AHA class IIb recommendation) among patients with bioprosthetic valves or valve repair and Afib
- If initial indication for bioprosthetic MVR was mitral stenosis, warfarin still preferred

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Case 2

History of the Present Illness:

65M with history of paroxysmal atrial fibrillation and flutter status post ablation presenting with pAF in the setting of AKI and viral gastroenteritis. Active at baseline. Plays recreational hockey, does yoga, and jogs 3-4 miles 2-3x per week. He drinks espresso twice daily and 1-2 glass of alcohol on the weekend.

He is on apixaban 5 mg twice daily though he has missed a few doses recently and is also on metoprolol 50 mg every 6 hours.

Case 2 continued

Exam:

On exam, he is tachycardic to 128, blood pressure is 110/67 and he is saturating well on room air. He has dry mucous membranes. His jugular venous pressure is < 5 cm H2O. On cardiovascular exam, he is irregularly irregular without murmurs or S3. Lungs are clear and her extremities are warm without any peripheral edema.

Case 2 continued

Workup:

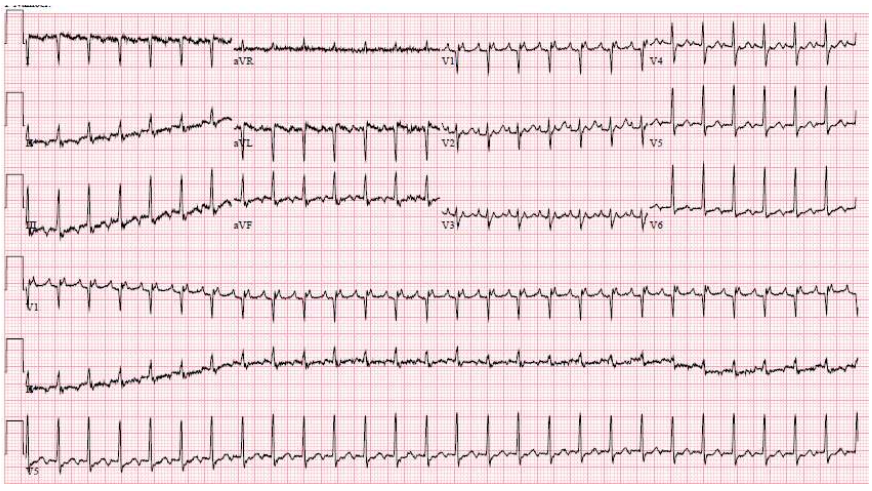
Comprehensive metabolic panel notable for creatinine 3 mg/dL (442 umol/L), potassium 3 mmol/L and magnesium 1 mmol/L

Thyroid stimulating hormone normal

Blood counts normal

Transthoracic echocardiogram shows normal biventricular function without significant valvular abnormalities

Case 2 continued



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Question*

What would be your next management steps for his atrial flutter?

A. Increase metoprolol to 100 q6h
B. Continue metoprolol add diltiazem
C. Continue metoprolol and load with digoxin
D. Continue metoprolol and start amiodarone
E. Schedule TEE and cardioversion

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Rate Control Agents

	Advantages	Disadvantages	Practical Tips

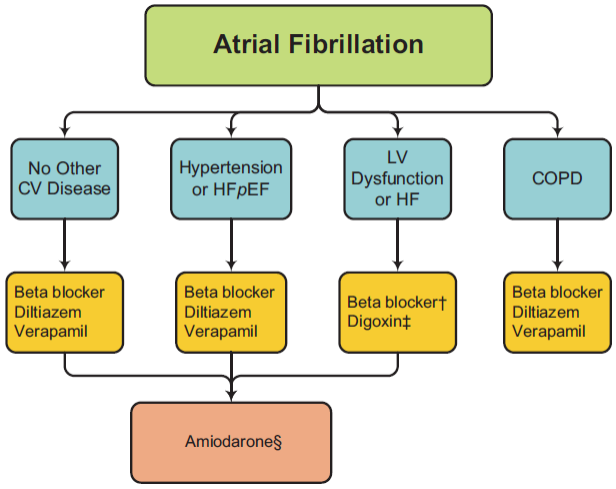
Beta-Blockers	• Most effective
	• Safe with LV dysfunction
		• Bolus IV for metoprolol
		• Esmolol available as continuous infusion
		• Bronchospasm possible
			• Always load with oral after IV
			• Cardioselective safe in COPD
			  • Cardioselective: bisoprolol >> atenolol > metoprolol
			  • Carvedilol: non-cardioselective

Non-dihydropyridine Calcium Channel Blockers	• No issues with bronchospasm • Diltiazem available as continuous infusion	• Avoid with LV dysfunction	• Always load with oral after IV • Verapamil sometimes more effective than diltiazem

Rate Control Agents

	Advantages	Disadvantages	Practical Tips
Digoxin	• No negative inotropic effect	• Slows resting ventricular response but not with exercise • Narrow therapeutic window • Slow onset	• Replace K/Mg first • Level < 1, check after a few doses • Avoid in elderly and CKD • Should not be used as monotherapy
Amiodarone	• Continuous infusion • Minimal negative inotropic effect	• Thromboembolism with pharmacologic conversion • Long-term toxicity • Thrombophlebitis	• Reserve only for those who cannot tolerate above therapies • Load slowly • Transition to oral as soon as possible

Rate Control Agents



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2014 ACC/AHA/HRS Guidelines. January et al. JACC 2014.

Case 2 continued

- Metoprolol 50 q6h continued
- Magnesium/Potassium repleted
- Fluid resuscitated
- Diltiazem added with conversion to Afib and improvement in HR
- With hydration, renal function normalizes and he spontaneously converts back to sinus rhythm

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Tips for Rate Control in the Inpatient Setting

- **Treat the underlying illness and be patient!**
- **Replenish electrolytes**
- **Optimize fluid status**
- **Use BB and/or CCB as first line therapy**
- **Fine to combine BB and CCB**
- **Digoxin can be added as 2nd/3rd line therapy**
- **Amiodarone can be considered in hemodynamically unstable patient (not due to Afib)**
- **Resting HR of ~110 bpm reasonable target**

Case 2 continued

- Given how poorly he feels in Afib, he would like to pursue a rhythm control strategy but is not interested in additional medications
- As he awaits outpatient follow-up with electrophysiology, he would like to know what he can do to prevent Afib recurrence

Question*

Which of the following recommendations is most likely to lead to reduction in Afib?

A. Reduction in alcohol intake
B. Cessation of coffee intake
C. Increasing her exercise
D. Stopping exercise altogether

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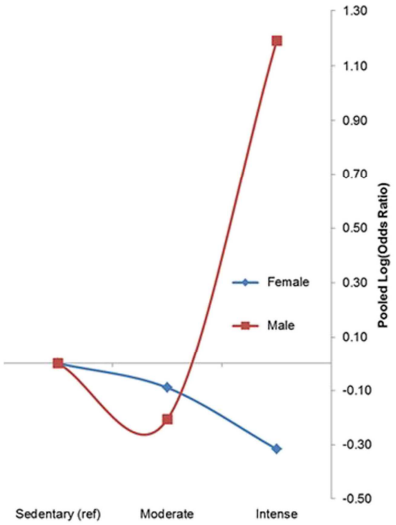
AFib and Exercise: A Complex Relationship



- U-shape association in men
- Endurance athletics in men associated with AF
- In women, exercise protective

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Mohanty et al. J Cardiovasc Electrophysiol. 2016.

AFib and Exercise: A Complex Relationship

- U-shape association in men

Endurance athletics associated with AF in men though moderate exercise beneficial!

Exercise protective in women!

- In women, exercise protective

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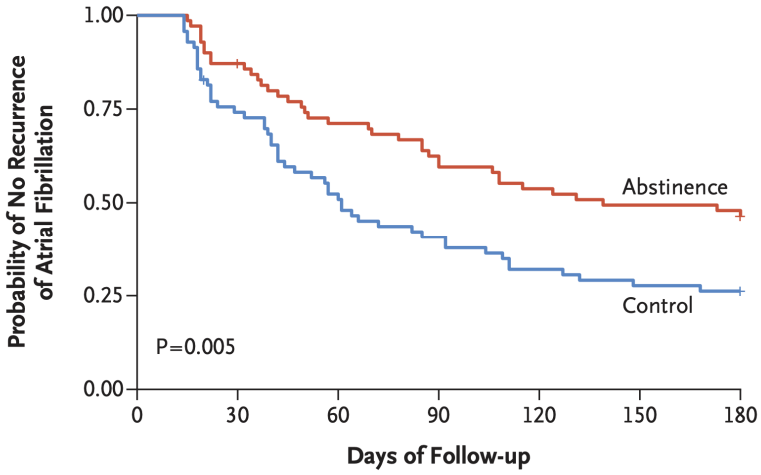
Mohanty et al. J Cardiovasc Electrophysiol. 2016.

ETOH Reduction Lowers Risk of Recurrent AF!



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Voskoboinik et al. NEJM 2020.

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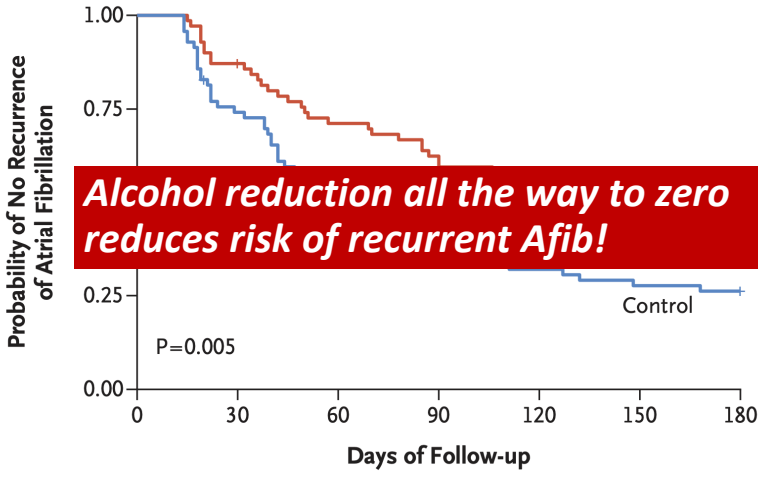

Alcohol reduction all the way to zero reduces risk of recurrent Afib!

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Voskoboinik et al. NEJM 2020.

Caffeine does NOT increase risk of AFib

- Majority of studies have NOT shown a relationship between regular caffeine intake and Afib
- < 300 mg MAY be protective

Beverage	Amount of Caffeine, mg
Can of Coca Cola	32
Cup of Lipton green tea	35
Cup of Lipton black tea	55
Starbucks Café Latte - short	75
Espresso shot	106
Starbucks Café Latte - grande	150
Monster Energy drink	160
Wired X344 Energy drink	344
Fixx Energy drink	500

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Voskoboinik et al. JACC EP 2016.

Take-Home Points

- Extreme endurance exercise may increase risk of AF in men but moderate amounts beneficial
- Exercise protective in women
- Caffeine use is not associated with risk of Afib
- Alcohol use strongly associated with risk of AF and recurrence and abstinence is strongly recommended

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Case 3

History of the Present Illness:

68 year old man with esophageal strictures status post multiple esophageal dilations with a history of hypertension presents with multiple embolic strokes and is found to have newly diagnosed atrial fibrillation. He has good functional capacity and has no anginal symptoms. He has been cleared by neurology to start anticoagulation and is currently on apixaban 5 mg twice daily and metoprolol 50 mg twice daily.

Case 3

Exam:

HR 86, BP 130/70, Right sided facial droop but remainder of neurologic exam normal, JVP 6 cm H2O, irregularly irregular, no murmurs, no S3/S4, extremities warm and no edema

TTE: LVEF 30-35% with global hypokinesis, no significant valvular abnormalities, LVEF significantly changed from 1 year prior

Question*

What is the next best management step?

A. Ischemic Testing with angiography
B. Ischemic evaluation with stress testing
C. No further testing, continuation of metoprolol and apixaban
D. Transesophageal echocardiography and cardioversion
E. Cardiac CT and cardioversion

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Contraindications to TEE

- TEE is an invasive procedure
- Absolute contraindications:
  - Neutropenia
  - Esophagitis
  - Recent esophageal surgery
  - Recent radiation with ongoing dysphagia
- Relative Contraindications
  - Varices
  - Thrombocytopenia (< 50K)
  - Unevaluated dysphagia
  - Esophageal strictures

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Cardiac CT effective at ruling out LAA Thrombus

- Cardiac CT much less invasive
- Requires contrast
- Cardiac CT very accurate
  - Sensitivity 98%
  - Specificity 100%
- Need specialized imaging techniques (late imaging)

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Yu et al. JAHA 2021.

Cardiac CT effective at ruling out LAA Thrombus

- Cardiac CT much less invasive
- Requires contrast
- Cardiac CT very accurate
  - Sensitivity 98%

Cardiac CT good option to rule out LAA thrombus prior to DCCV!

- imaging)

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Yu et al. JAHA 2021.

Benefits of Rhythm Control

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., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*

- 1) LVEF ≤ 35% 2) NYHA Class II-IV 3) ICD in place
- Optimal medical therapy (OMT) versus OMT + catheter ablation

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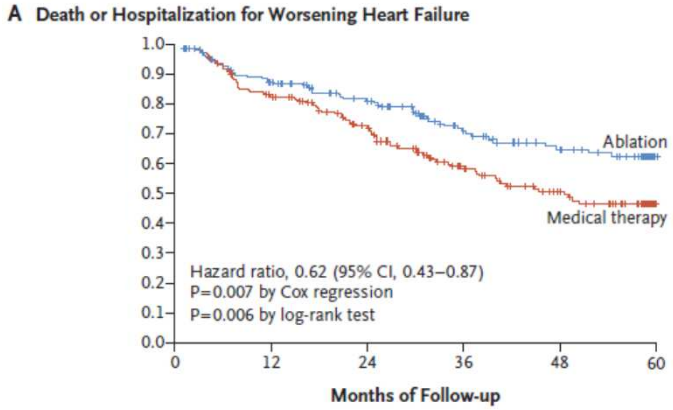
Benefits of Catheter Ablation in Low EF



Catheter ablation in patients with symptomatic HFrEF improves outcomes

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Marrouche et al. NEJM 2018.

Benefits of Early Rhythm Control

- East AFNET 4 Trial – NEJM 2020
- 2800 patients at 135 centers with:
  - AF 1 < year
  - Randomized to rhythm control versus usual care (rhythm control only for symptoms)
  - 5 year follow-up
  - Composite outcome of death from CV cause, stroke or CV hospitalization
  - Average CHA_2DS_2-Vasc = 3
  - 28% with NYHA Class II symptoms OR LVEF < 50%

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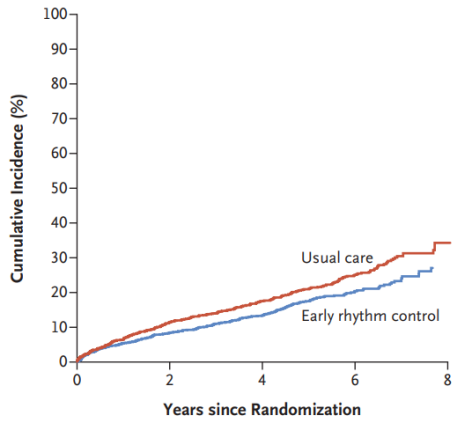
Benefits of Early Rhythm Control



Decreased primary endpoint but increased risk of adverse event!

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Kirchof et al. NEJM 2020.

When to consider rhythm control!

- Strongly consider rhythm control strategy in patients with low LVEF and new onset AF
- In patients with symptomatic heart failure on optimal medical therapy with high burden of AF → catheter ablation reasonable
- Catheter ablation is probably more effective than oral antiarrhythmic therapy
- Not quite ready for primetime as a one-size fits all but threshold for ablation getting lower

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Case 3 continued

- The patient was successfully cardioverted
- Repeat TTE 3 months later showed resolution of LV function
- Not interested in rhythm control
- He remained on metoprolol and apixaban with outstanding compliance.
- 1 year later, develops a lower GI bleed without clear identifiable source requiring hospitalization and multiple transfusion.

Question*

What is the next best management step?

A. Transition from apixaban to rivaroxaban
B. Transition from apixaban to aspirin 81 mg daily
C. Transition from apixaban to dose adjusted warfarin for INR 2-3
D. Cessation of anticoagulation
E. Cessation of anticoagulation and referral for LAA occlusion

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Percutaneous LAA occlusion

- Non-inferior to warfarin
- LAA occlusion is FDA approved for
  - CHA_2DS_2-Vasc ≥ 2
  - *Appropriate* rationale for forgoing anticoagulation
  - Candidate for 6 weeks of anticoagulation
- Can consider if patient cannot tolerate AC at all but ideally on short-term anticoagulation to prevent device thrombosis

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https://www.bostonscientific.com/en-EU/products/laac-system/watchman-flx.html
https://www.structuralheartsolutions.com/us/structural-heart-products-solutions/laa-amplatzer-amulet-occluder/overview/

Practical Application of LAA closure

- Consider referral in patients with :
  - CHA_2DS_2-Vasc ≥ 2
  - Cannot tolerate anticoagulation
- Benefit is not immediate and rarely done acutely
- Procedural complication rate with newest generation device 0.5% in experienced hands

Case 4

History of the Present Illness

A 67 year-old man with a history of hypertension (well-controlled on lisinopril and amlodipine) and diabetes presents for an elective knee replacement. On POD 3, he is noted to have an irregular pulse though asymptomatic. 12-lead ECG shows sinus rhythm. Over the next 24 hours, he is placed on telemetry and is noted to have paroxysmal atrial fibrillation with 3 episodes of atrial fibrillation lasting 30-60 minutes.

Exam and Workup

Pulse is 86 and blood pressure 130/72 and is otherwise unremarkable. ECG and transthoracic echocardiogram are also unremarkable except for a mildly dilated left atrium.

Question*

What is the next best management step

A. Initiate beta-blocker
B. Initiate beta-blocker and aspirin
C. Discharge home without any changes
D. Initiate beta-blocker and anticoagulation

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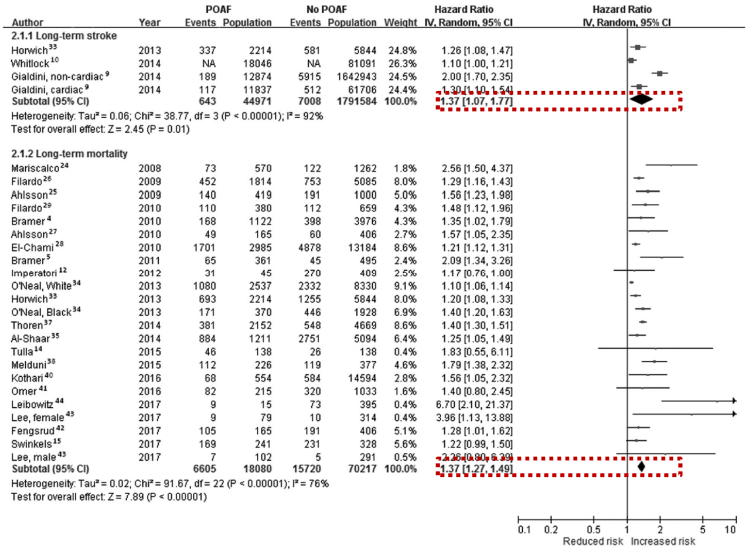
What is the risk of post-operative Afib?



Author	Year	POAF Events	POAF Population	No POAF Events	No POAF Population	Weight	Hazard Ratio IV, Random, 95% CI
2.1.1 Long-term stroke							
Horwich[33]	2013	337	2214	581	5844	24.8%	1.26 [1.08, 1.47]
Whitlock[10]	2014	NA	18046	NA	81091	26.3%	1.10 [1.00, 1.21]
Gialdini, non-cardiac[9]	2014	189	12874	5915	1642943	24.5%	2.00 [1.70, 2.35]
Gialdini, cardiac[9]	2014	117	11837	512	61706	24.4%	1.30 [1.10, 1.54]
Subtotal (95% CI)		643	44971	7008	1791584	100.0%	**1.37 [1.07, 1.77]**
Heterogeneity: Tau² = 0.06; Chi² = 38.77, df = 3 (P < 0.00001); I² = 92%							
Test for overall effect: Z = 2.45 (P = 0.01)							
2.1.2 Long-term mortality							
Mariscalco[24]	2008	73	570	122	1262	1.8%	2.56 [1.50, 4.37]
Filardo[26]	2009	452	1814	753	5085	8.0%	1.29 [1.16, 1.43]
Ahlsson[25]	2009	140	419	191	1000	5.0%	1.56 [1.23, 1.98]
Filardo[29]	2010	110	380	112	659	4.3%	1.48 [1.12, 1.96]
Bramer[4]	2010	168	1122	398	3976	4.3%	1.35 [1.02, 1.79]
Ahlsson[27]	2010	49	165	60	406	2.7%	1.57 [1.05, 2.35]
El-Chami[28]	2010	1701	2985	4878	13184	8.6%	1.21 [1.12, 1.31]
Bramer[5]	2011	65	361	45	495	2.4%	2.09 [1.34, 3.26]
Imperatori[12]	2012	31	45	270	409	2.5%	1.17 [0.76, 1.00]
O'Neal, White[34]	2013	1080	2537	2332	8330	9.1%	1.10 [1.06, 1.14]
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O'Neal, Black[34]	2013	171	370	446	1928	6.9%	1.40 [1.20, 1.63]
Thoren[37]	2014	381	2152	548	4669	8.6%	1.40 [1.30, 1.51]
Al-Shaar[35]	2014	884	1211	2751	5094	6.4%	1.25 [1.05, 1.49]
Tulla[14]	2015	46	138	26	138	0.4%	1.83 [0.55, 6.11]
Melduni[38]	2015	112	226	119	377	4.6%	1.79 [1.38, 2.32]
Kothari[40]	2016	68	554	584	14594	2.8%	1.56 [1.05, 2.32]
Omer[41]	2016	82	215	320	1033	1.6%	1.40 [0.80, 2.45]
Leibowitz[44]	2017	9	15	73	395	0.4%	6.70 [2.10, 21.37]
Lee, female[45]	2017	9	79	10	314	0.4%	3.96 [1.13, 13.88]
Fengsrud[42]	2017	105	165	191	406	5.1%	1.28 [1.01, 1.62]
Swinkels[15]	2017	169	241	231	328	5.6%	1.22 [0.99, 1.50]
Lee, male[43]	2017	7	102	5	291	0.5%	2.26 [0.80, 6.39]
Subtotal (95% CI)		6605	18080	15720	70217	100.0%	**1.37 [1.27, 1.49]**
Heterogeneity: Tau² = 0.02; Chi² = 91.67, df = 22 (P < 0.00001); I² = 76%							
Test for overall effect: Z = 7.89 (P < 0.00001)							

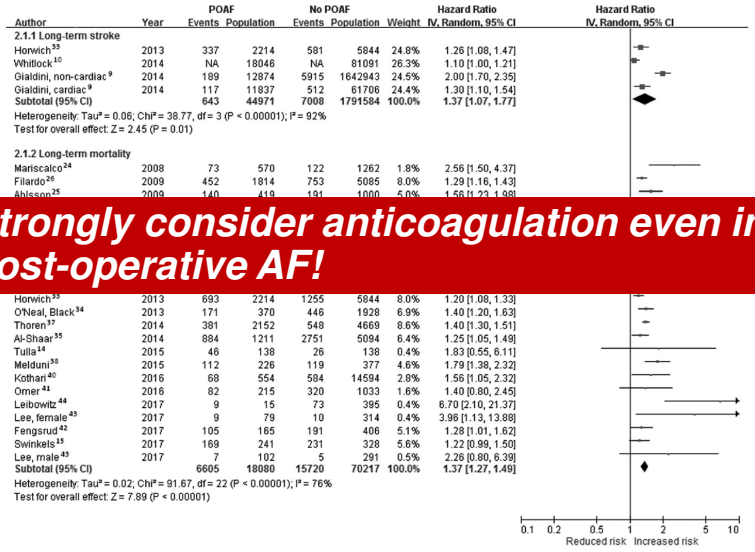
Hazard Ratio IV, Random, 95% CI

0.1 0.2 0.5 1 2 5 10

Reduced risk Increased risk

Lin et al. Stroke. 2019.

What is the risk of post-operative Afib?



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Hazard Ratio IV, Random, 95% CI

0.1 0.2 0.5 1 2 5 10

Reduced risk Increased risk

Strongly consider anticoagulation even in post-operative AF!

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Lin et al. Stroke. 2019.

Management of Post-Operative Afib

Take Home Points

- Risk of stroke is increased even in isolated post-operative AFib
- Strongly consider anticoagulation based on the CHA_2DS_2-Vasc score regardless of duration and post-operative status

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January et al. JACC 2014.

Case 4 continued

Given his CHA_2DS_2-Vasc of 3 and given that it seemingly occurred while asymptomatic and as his clinical illness was improving, the decision was made to start him on rivaroxaban.

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Case 5

A 74 year old man with a long-standing history of atrial fibrillation presents with acute decompensated heart failure. He has undergone 4 prior atrial fibrillation ablations that have failed. He is currently being managed on amiodarone 200 mg daily, metoprolol 200 mg daily, verapamil 360 mg daily and digoxin 0.125 mg daily. On exam, he is normotensive and hypoxic. On auscultation, he is irregularly irregular without murmurs, jugular venous pressure is elevated, crackles are present bilaterally, lower extremity edema is present but they are warm. ECG shows atrial fibrillation with ventricular rates in the 140s. TTE shows a reduction in LV function with massive biatrial enlargement despite a recent negative ischemic evaluation. Thyroid function testing is normal.

Question*

What is the next best step?

A. IV furosemide, continue all of his remaining medications
B. IV furosemide, continue all of his remaining medications except his calcium-channel blocker
C. Cardioversion
D. EP consult for AV junctional ablation and pacemaker

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Case 5 continued

IV diuresis is implemented effectively. His verapamil is stopped. Overnight, his ventricular rates improve but he is noted to have a 4 second pause when he converts from afib to sinus while asleep. Once awake, he returns to ventricular rates in the 140-150s.

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Question*

What is the next best management step

A. Cardioversion
B. EP request for repeat ablation
C. EP request for permanent pacemaker implantation
D. EP request for pacemaker implantation with AV junctional ablation

Indications for PPM in AFib

- High grade AV block in awake, symptom-free patients with AF and bradycardia with 1 or more pauses of at least 5 seconds or longer
- After catheter ablation of the AV junction
- Permanent AF and symptomatic bradycardia

Kusumoto et al. JACC 2019.
January et al. JACC 2008.

Take-Home Points

- Advanced age is not a contraindication to anticoagulation
- DOACs can be used safely in many patients with bioprosthetic valves
- Cardiac CT is a reasonable alternative to TEE to exclude LAA thrombus
- Consider rhythm control strategy in patients with HFrEF on GDMT with high burden of Afib AND in new onset Afib
- Alcohol but not caffeine cessation prevents recurrent Afib
- LAA occlusion should be considered in those who cannot tolerate anticoagulation
- CHA_2DS_2-Vasc is the most important consideration
- PPM therapy should only be considered in patients with concomitant significant bradyarrhythmias or those undergoing AV junctional ablation

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