ATRIAL FIBRILLATION: REVISITING CONTROVERSIES IN AN ERA OF INNOVATION

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DISCLOSURES

- I have no financial relationships with industry
- I have no other disclosures

OBJECTIVES

- Identify the patient groups in which data is lacking regarding medical management of atrial fibrillation
- Clarify the guideline recommendation regarding medical management of atrial fibrillation
- Describe the current mechanical management options for atrial fibrillation and proper patient selection

Clinical Case 1

An 82 year old female patient presents for follow up of her hypertension and diabetes. She claims to feel fine and remains independent and active. On examination she is found to be in atrial fibrillation with a rate of 115-125bpm. BP is 145/90. Lungs are clear and she has no edema. Medications are diltiazem CD 240mg, HCTZ 12.5 mg, and metformen 500mg BID.

What is the most appropriate approach to her management?

Clinical Case 2

A76 year old male with history of MI four years ago presents with palpitations and fatigue. He had a drug eluting stent placed in his right coronary artery at time of the MI. Subsequently he developed atrial fibrillation and underwent an ablation two years ago. He is again in atrial fibrillation with rate of 135 and BP of 120/60. Medications are metoprolol XL 50mg daily, apixaban 5mg BID, clopidogrel 75mg daily and ASA 81mg daily.

What are the guideline directed recommendations for his management?

The Growing Problem

- Incidence of Atrial Fibrillation is increasing due to population health
- Prevalence is rapidly rising as population ages
  - 50% of afib cases occur in the 6% population >75
  - Incidence in population 80-85 is 23%
  - Lifetime risk in persons over 40 is 26%
- Rapidly becoming one of the top 3 cardiac diagnoses

Current Controversies in Atrial Fibrillation

1. Detection
2. Rate vs Rhythm Control
3. Appropriate Antiarrhythmic Therapy
4. Anticoagulation
5. Ablation
6. Left Atrial Appendage Closure Devices

Classification

- Paroxysmal
  - Self terminating or converted within 7 days of onset
- Persistent
  - Lasting 7 days or more requiring conversion
- Recurrent
  - Either of above can recur
- Permanent
  - Lasting one year or more, or failed attempts at conversion

1. Detection

- Symptomatic arrhythmia presenting to hospital or clinic

- Asymptomatic detection on routine examination

- Identification via monitoring

- Identification via pacemaker interrogation

1. Detection Controversy

- What should be done with what is found?
  - Symptomatic: guideline therapy
  - Asymptomatic persistent: guideline therapy
  - Asymptomatic permanent: guideline therapy
  - Asymptomatic paroxysmal: Uncertain

1. Detection Controversy

- TransCanadian Study (2014)
  - 572 post CVA pts
  - Randomized ½ to Holter Monitor, ½ to 30 day monitor
  - Pafib detected 3.2% in HM and 16% with long term
  - No correlation between afib detection and timing of CVA or recurrent events

1. Detection Controversy

- ASSERT Trial (2017)
  - 256 pts at high risk for afib, over age 65
  - Long term monitors placed
  - Afib defined as >5 mins duration
  - Detected in 34%
  - 4 pts had CVA during study
  - No CVA pt had afib
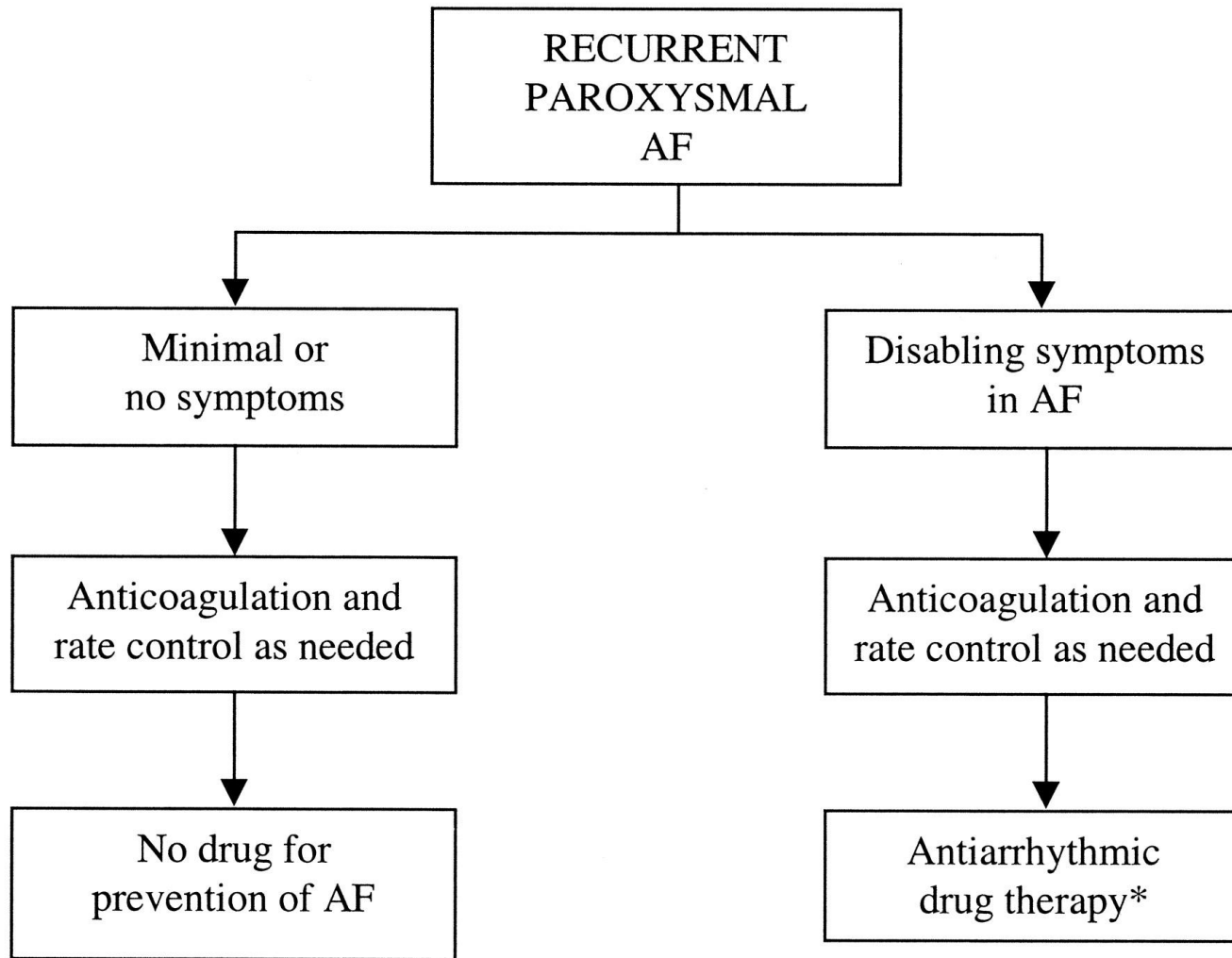
2. Rate vs Rhythm Control

- ACC/AHA/ASE Guidelines
  - Define separate algorithms for the classes of afib
  - Identify the most appropriate antiarrhythmics
  - Discuss anticoagulation strategy
  - Describe interventional therapeutic strategy

Pharmacological management of patients with newly discovered AF. AF indicates atrial fibrillation; HF, heart failure.
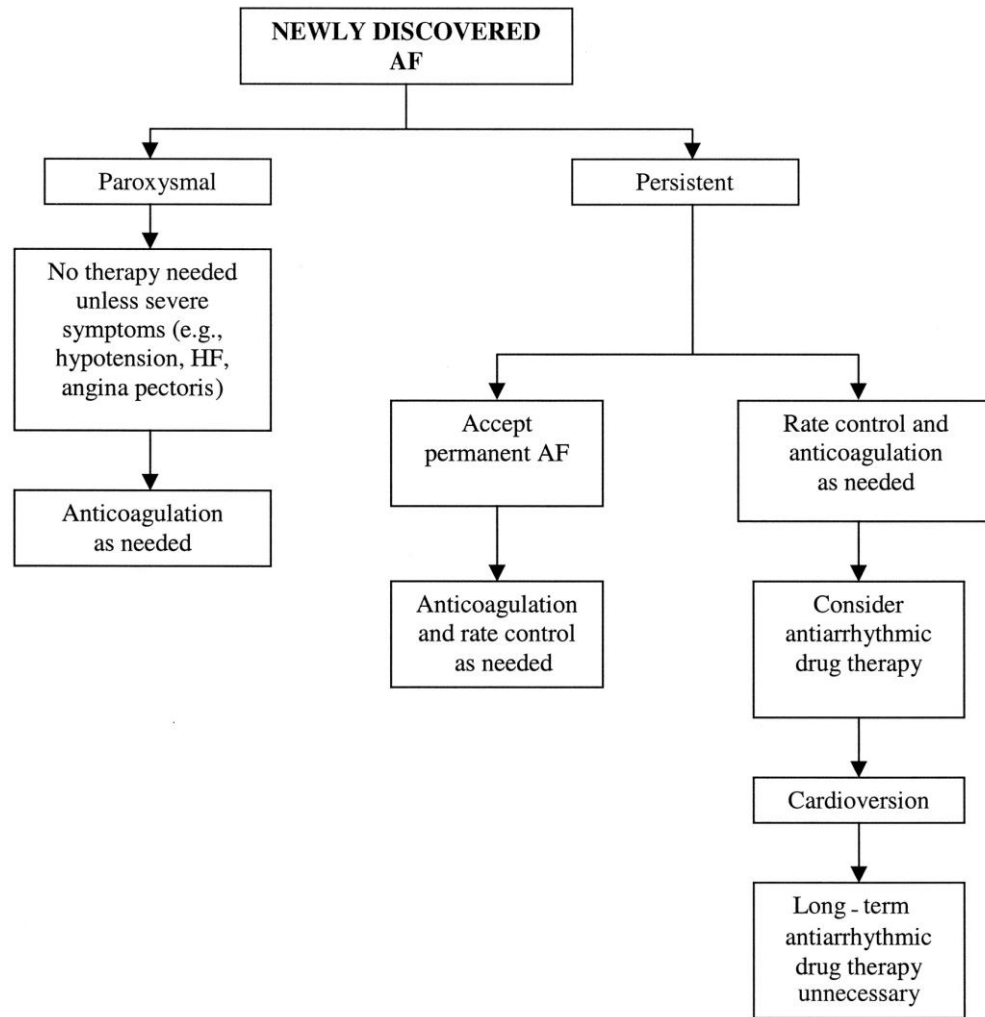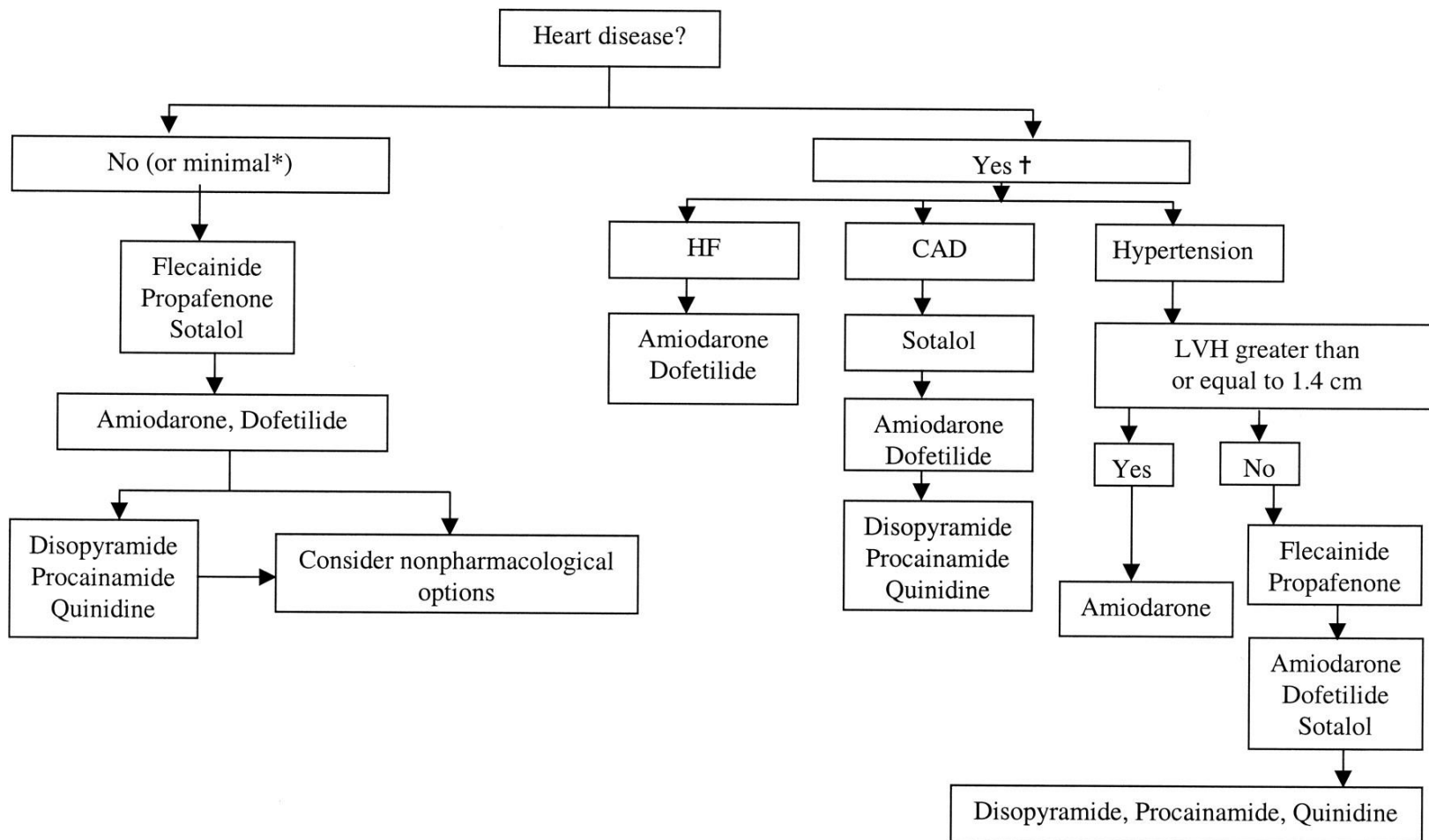

Committee Members et al. Circulation. 2001;104:2118-2150

# Pharmacological management of patients with recurrent paroxysmal AF.

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                    ┌─────────────────┐
                    │    RECURRENT    │
                    │   PAROXYSMAL    │
                    │       AF        │
                    └─────────────────┘
              ┌──────────────┴──────────────┐
              ▼                              ▼
    ┌──────────────────┐         ┌──────────────────┐
    │   Minimal or     │         │ Disabling symptoms│
    │   no symptoms    │         │      in AF        │
    └──────────────────┘         └──────────────────┘
              │                              │
              ▼                              ▼
    ┌──────────────────┐         ┌──────────────────┐
    │ Anticoagulation and│       │ Anticoagulation and│
    │ rate control as needed│    │ rate control as needed│
    └──────────────────┘         └──────────────────┘
              │                              │
              ▼                              ▼
    ┌──────────────────┐         ┌──────────────────┐
    │   No drug for    │         │   Antiarrhythmic │
    │  prevention of AF │        │   drug therapy*  │
    └──────────────────┘         └──────────────────┘
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Committee Members et al. Circulation. 2001;104:2118-2150

Antiarrhythmic drug therapy to maintain sinus rhythm in patients with recurrent paroxysmal or persistent atrial fibrillation.

Committee Members et al. Circulation. 2001;104:2118-2150

American Heart Association.

Pharmacological management of patients with recurrent persistent or permanent AF.
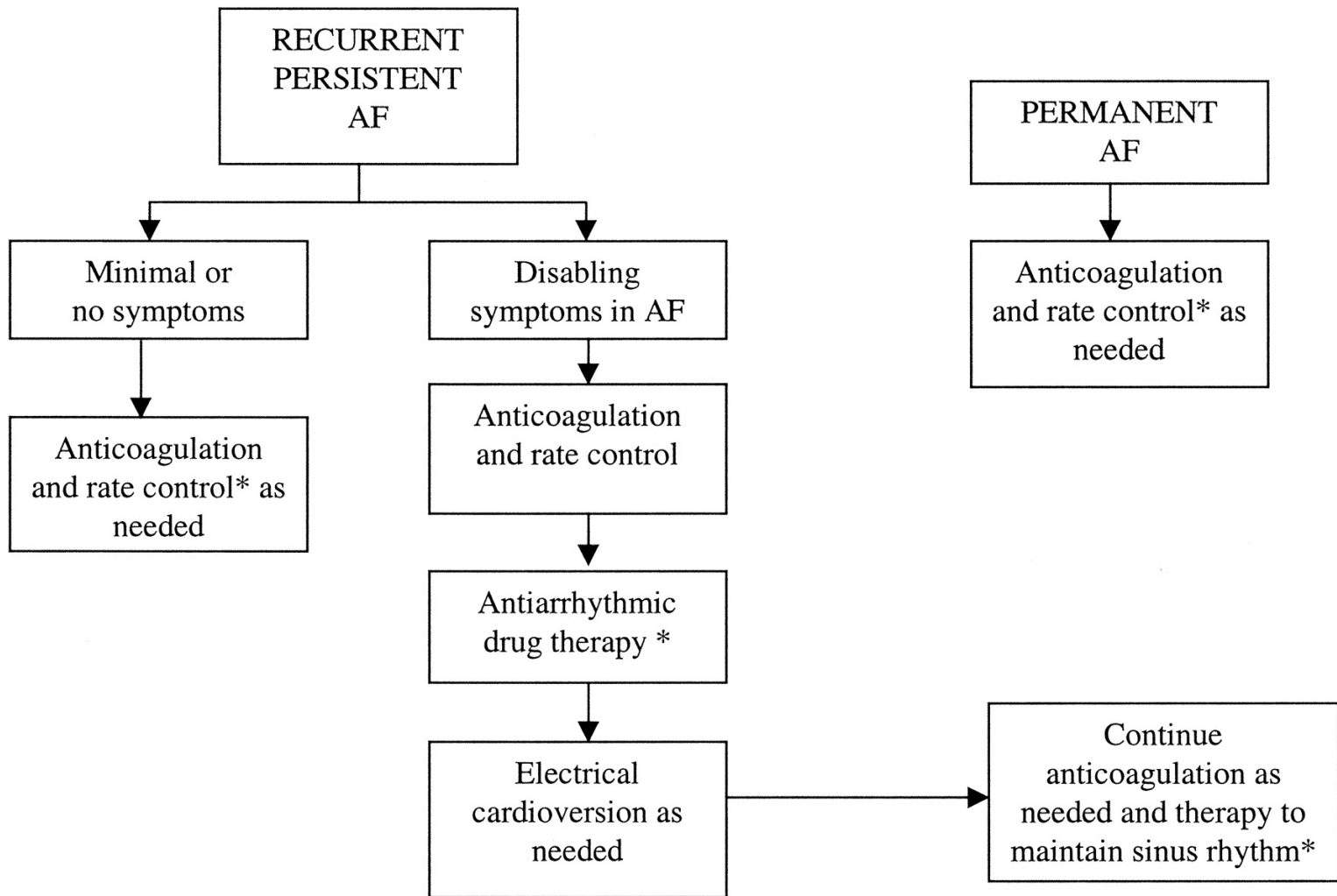
Committee Members et al. Circulation. 2001;104:2118-2150

2. Rate vs Rhythm Controversy

- AFFIRM Trial (NEJM 2002)
  - 4000 pts with at least one episode of afib
  - Average age 69
  - Endpoint was <u>mortality</u>
  - Randomized to rate vs rhythm control
  - Results demonstrated no difference in mortality
  - Trend for more morbidity and complications with rhythm control arm

2. Rate vs Rhythm Controversy

- Problem with AFFIRM
  - Only primary endpoint was mortality
  - Not applicable to pts under 65
  - Most patients were asymptomatic or only mildly symptomatic with afib episodes

2. Rate vs Rhythm Controversy

- RACE Trial (JACC 2003)
- 512 pts in afib on entry.
- Randomized ½ to rate control, ½ to cardioversion and rhythm control, 3years
- Primary endpoints: mortality, CVA, bleeding, drug toxicity
- 44 events in rate control arm
- 60 events in the rhythm control arm (ns)

3. Appropriate Antiarrhythmic Use

□ Amiodarone often over-utilized

    □ PRO:

        ■ Ease of IV or PO administration

        ■ Broad population application: Ischemia, LV dysfunction, normal hearts

        ■ Effectiveness

    □ CON:

        ■ Difficult pharmacokinetics

        ■ Toxicities severe and long term

        ■ Requires long term monitoring

3. Appropriate Antiarrhythmic Use

- Class 1 Agents
  - Flecainide and Propafenone
    - Indicated for chronic use or Intermittent for rare Pafib
    - Contraindicated in ischemia or LV dysfunction
    - Caution with Wide QRS
  - Procainamide and Disopyramide
    - Weak agents, rarely used
    - Contraindicated in ischemia or LV dysfunction
    - Contraindicated in Wide QRS

3. Appropriate Antiarrhythmic Use

□ Sotolol

- Indicated in normal heart or with ischemia
- Contraindicated in CHF, marked LVH, AV block or Widened QRS

3. Appropriate Antiarrhythmic Use

- Newer agents often have smaller population indication
  - Dofetilide
    - Indicated in normal heart
    - Contraindicated in CHF or ischemia
    - Required hospitalization for initiation
  - Dronedarone
    - Indicated in normal heart
    - Contraindicated in CHF, ischemia or Wide QRS

4. Anticoagulation

- CHA2DS2-Vasc Score: Risk of Stroke
  - CHF   1
  - Hypertension   1
  - Age 60-74   1
  - Age 75>   2
  - Diabetes   1
  - Stroke/TIA   2
  - Female gender 1
  - Vascular disease   1

4. Anticoagulation

- HAS BLED Score: Risk of Bleeding
  - Hypertension   1
  - Abnormal LFT   1
  - Stroke   1
  - Bleeding   1
  - Labile INR   1
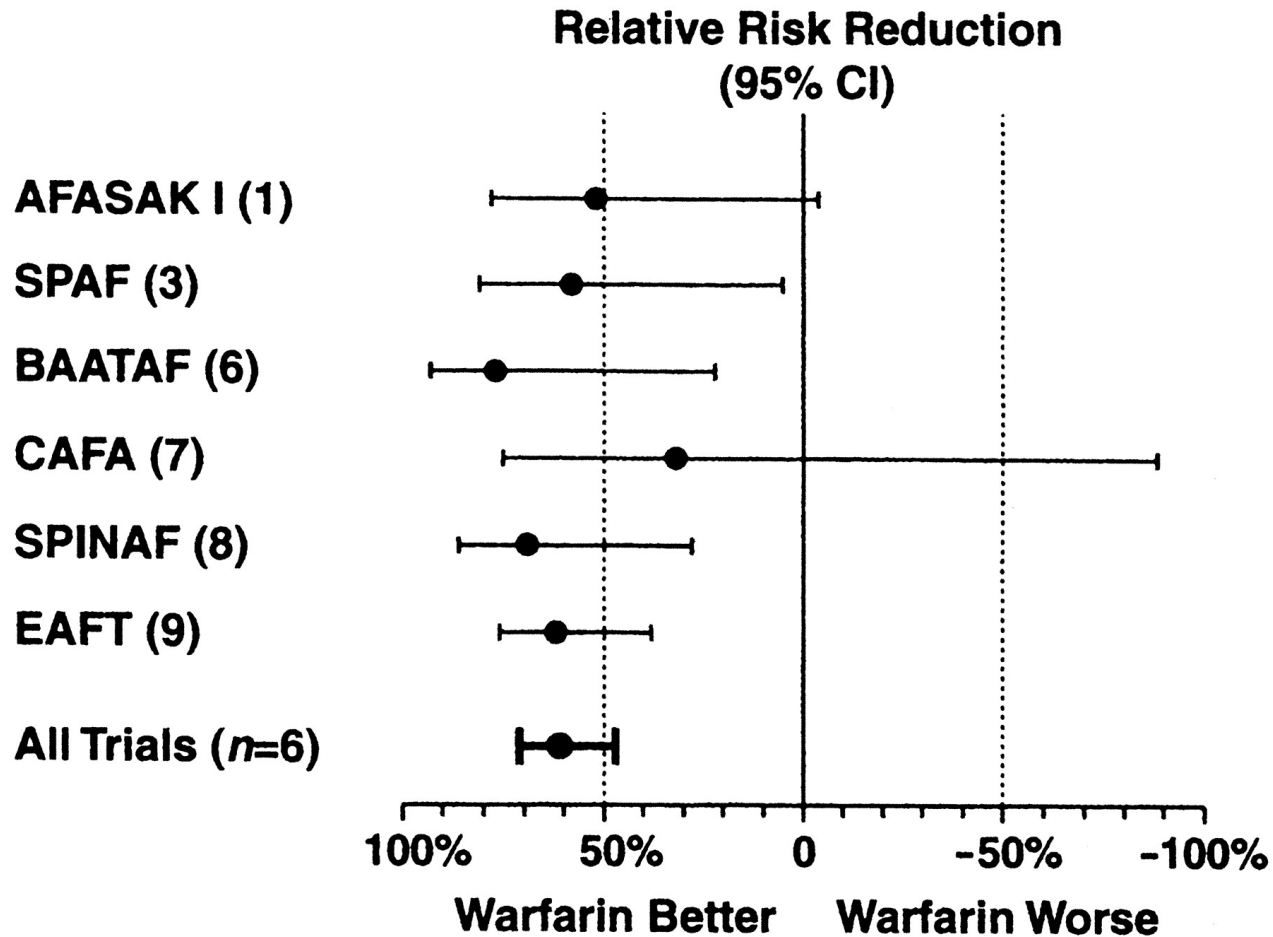 - Elderly (>65)   1
  - Diabetes   1

4. Anticoagulation

CHA2DS2-Vasc Stroke Risk%	
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	12.5
9	15.2

HAS BLED Bleeding Risk%	
1	1.13
2	1.88
3	3.74
4	8.70
5	12.50

Antithrombotic therapy for prevention of stroke (ischemic and hemorrhagic) in patients with nonvalvular AF: adjusted-dose warfarin compared with placebo.



Adjusted-Dose Warfarin Compared with Placebo

Relative Risk Reduction (95% CI)

AFASAK I (1)
SPAF (3)
BAATAF (6)
CAFA (7)
SPINAF (8)
EAFT (9)
All Trials (*n*=6)

100%   50%   0   −50%   −100%
Warfarin Better   Warfarin Worse

American Heart Association.

Antithrombotic therapy for prevention of stroke (ischemic and hemorrhagic) in patients with nonvalvular AF: warfarin compared with aspirin and aspirin compared with placebo.
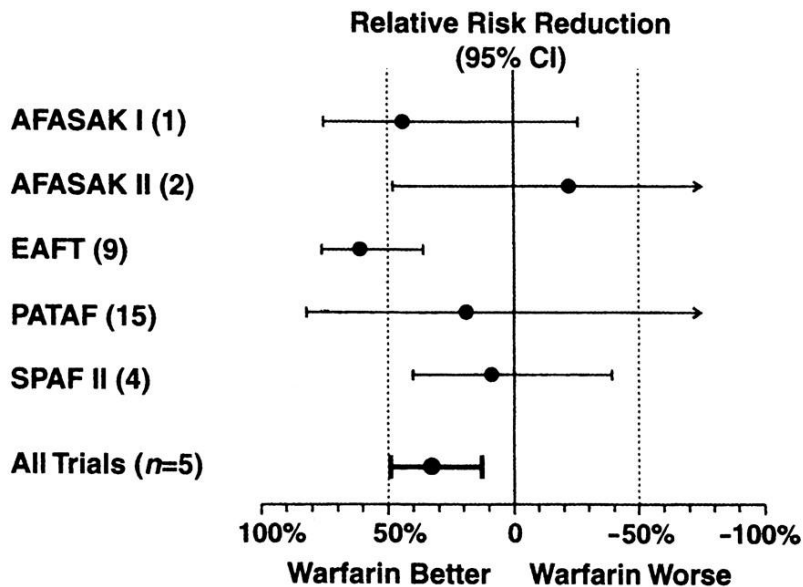
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Association®
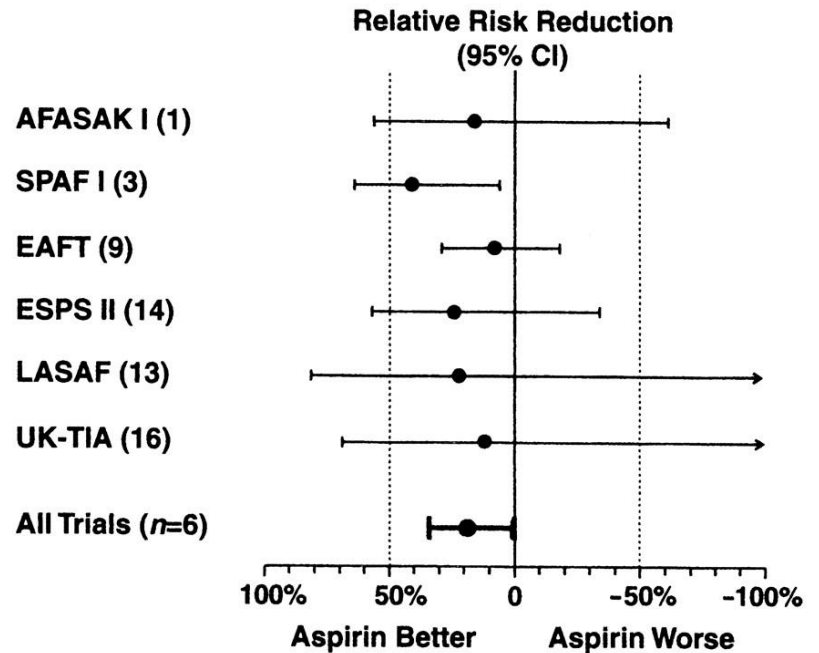
4. Anticoagulation

- Introduction of Newer Oral Anticoagulants (NOAC) have changed the course of therapy
  - All have demonstrated less CNS bleeding risk
  - All non-inferior or superior to warfarin in effectiveness
  - Not indicated for valvular atrial fibrillation, described as Mitral Stenosis <u>ONLY</u>
  - Not indicated if patient has mechanical heart valve

4. Anticoagulation Controversy

- The effectiveness/safety studies of NOACs did not include significant number of patients over 80

- Very little safety/effectiveness data on subgroup of end stage renal disease/dialysis patients

- No compelling data supporting use of warfarin in dialysis patients, regardless of the guidelines

4. Anticoagulation Controversy

- Very little prospective safety data on triple therapy (ASA, P2Y3 inhibitor, NOAC) in patients with stents and atrial fibrillation

- Many varied schemes have been offered to deal with this, and no consensus

  - Current expert opinion is to continue triple therapy for 3 months, then stop ASA

  - Current expert opinion suggests use of clopidogrel with triple therapy

5. Ablation

- Class Ia Recommendation: Ablation is indicated for symptomatic patients with paroxysmal atrial fibrillation who have failed at least one attempt at cardioversion and antiarrhythmic maintenance

5. Ablation

- Class IIa Recommendation: May be considered first line therapy for symptomatic patients with paroxysmal or persistent atrial fibrillation, or after failed attempt at cardioversion and antiarrhythmic

- Class IIb Recommendation: May be considered first line therapy for persistent afib, or for permanent afib after failed attempt at cardioversion and antiarrhythmic

5. Ablation

- Class III Recommendation (Harm): Not indicated for purposes of discontinuing anticoagulation

5. Ablation Controversy

- Initial effectiveness 60-80%.

- Success varies widely based on technique and operator experience

- Most effective for paroxysmal afib, but utilized widely

- May result in aflutter

- Second or third procedure may be undertaken to achieve best success

6. Left Atrial Appendage Closure Devices

- Currently one device approved and a second is in process

Left Atrial Appendage Closure Device

6. Left Atrial Appendage Closure Devices

- Indication: For patients with CHA2DS2-Vasc score of 3 or more who are not candidates for long term anticoagulation
- Must be able to tolerate short term anticoagulation post procedure

6. Left Atrial Appendage Occlusion Devices: Controversy

- Use in patients who prefer not to have anticoagulation
- Use in patients with paroxysmal atrial fibrillation
- Evidence of potential for device thrombosis now emerging
- Extending use to valvular atrial fibrillation

Clinical Case 1

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