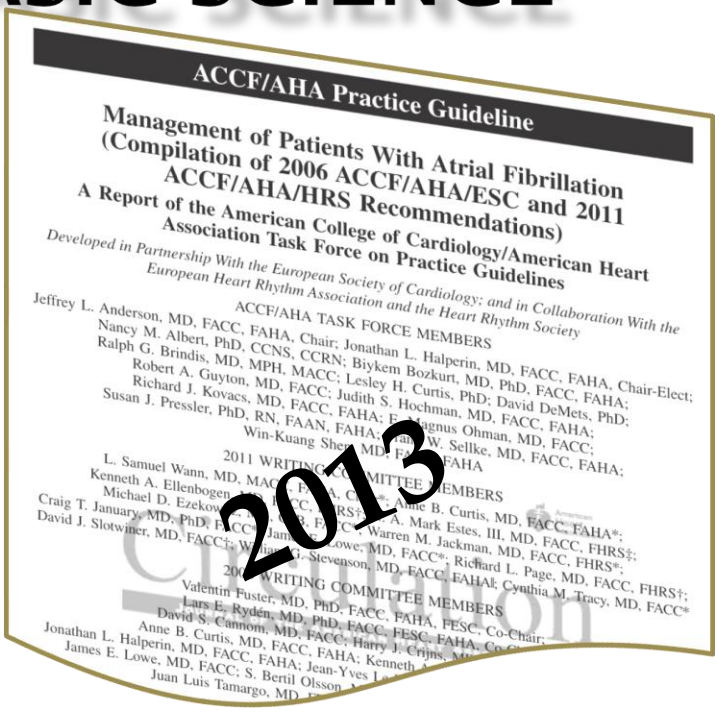
ATRIAL FIBRILLATION: BASIC SCIENCE TO CLINICAL PRACTICE



Focus: May 7, 2013 ACC/AHA guidelines

American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: Atrial fibrillation

Anderson J et al Circulation. 2013;127:May 7, 2013

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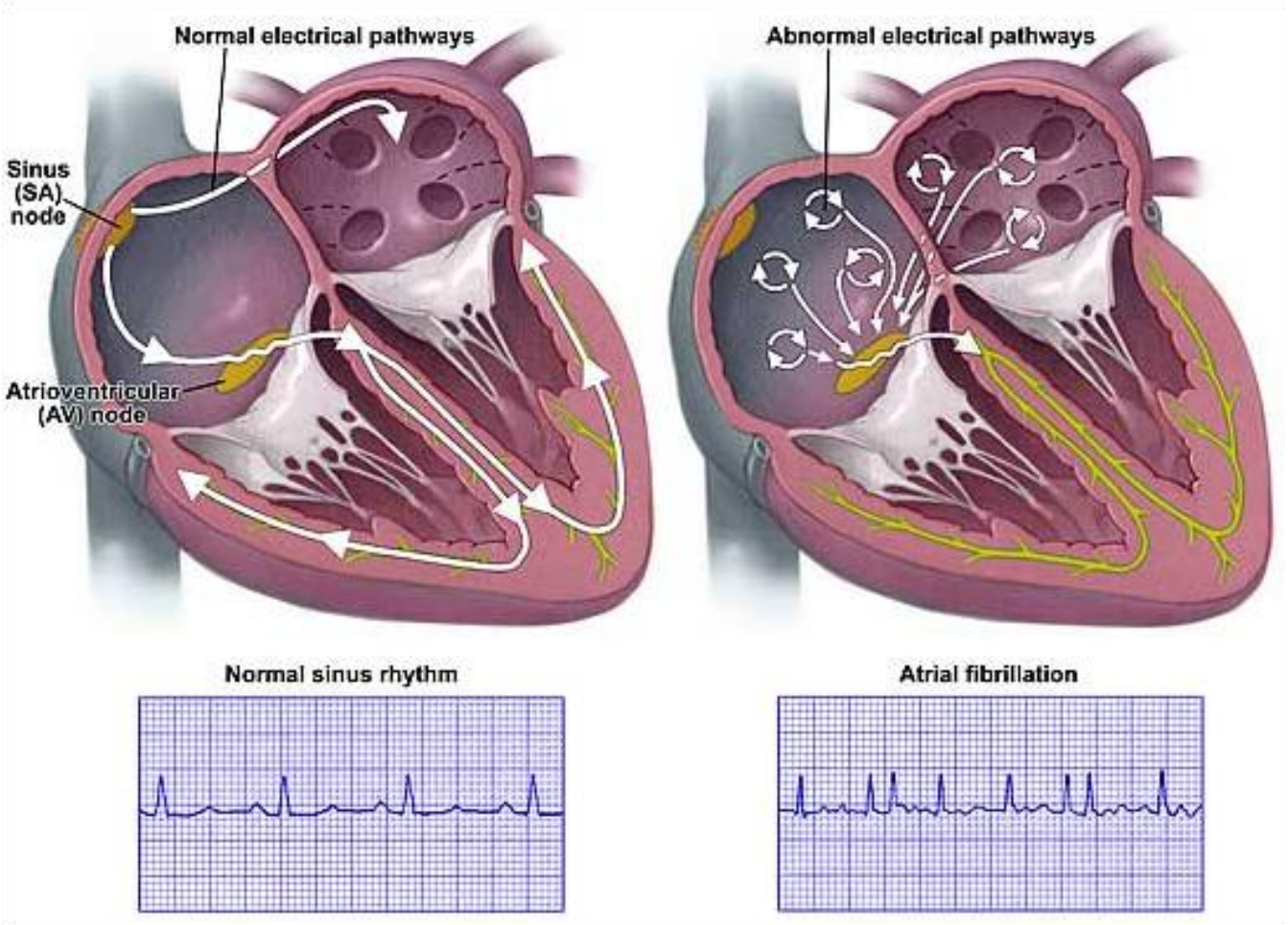
Single most common SVT

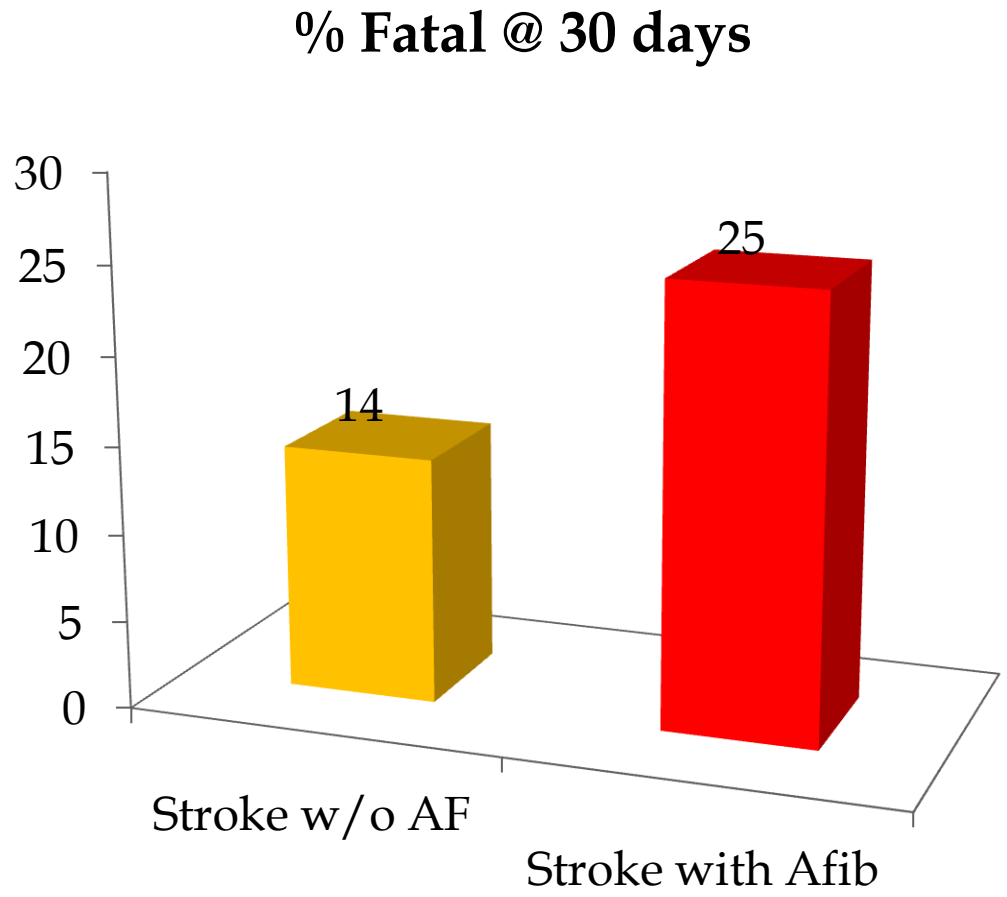
Affects 1 in 25 adults 60 years or older and nearly 1 in 10 adults 80 years or older



Introduction

Twice as many strokes with atrial fibrillation

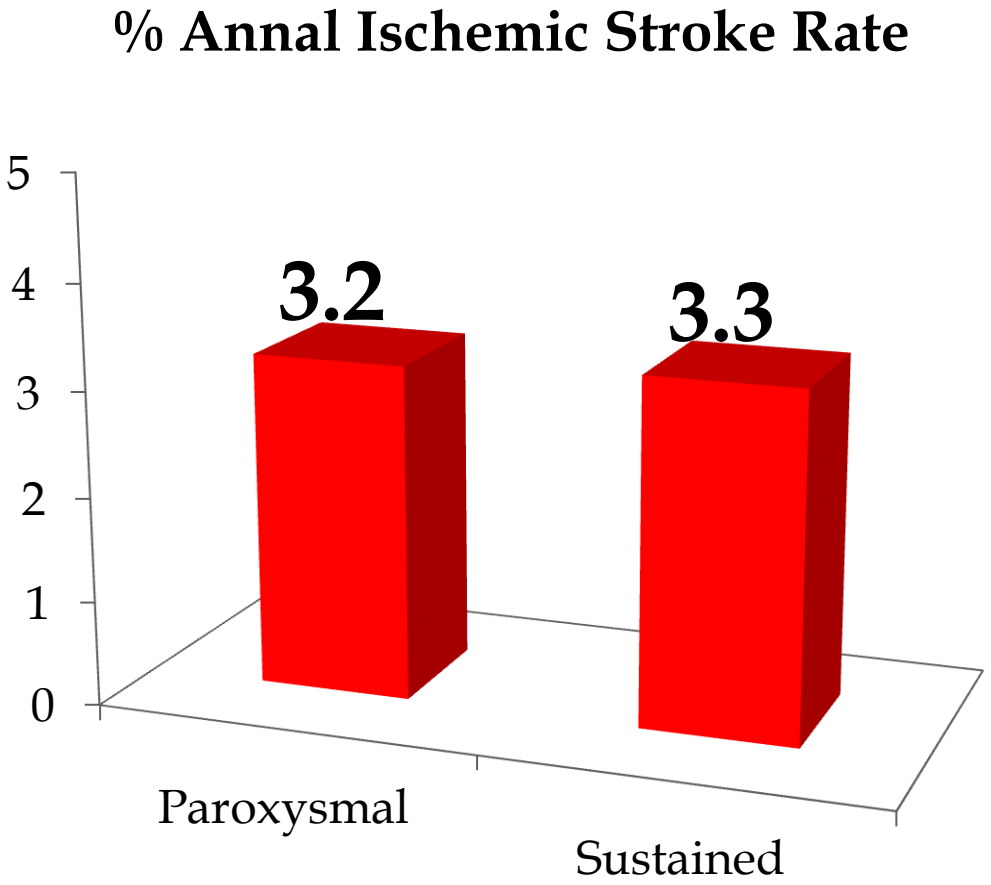
- Framingham
- 40 year f/u
- N=5070
  - 398 non afib strokes
  - 103 afib strokes



Stroke. 1996;27:1760-1764

Equal Risk of Stroke from Paroxysmal Afib or Sustained Afib

- SPAF 1-3
- 1987-1997
- 325 mg ASA vs ASA with warfarin
- N=1552 sustained
- N=460 intermittent (paroxymal)



Hart JACC 2000;35:183

2050 estimated: 15 million atrial fibrillation patients

- **Etiologies**
  - **Remodeling**
    - **Electrical and structural**
  - **Metabolic**
  - **Aging**
  - **Genetics**
  - **Environmental**
- **High risk groups**
  - **Hypertension**
  - **CHF**
  - **Ischemic heart disease**
  - **Post cardiac surgery**

Atrial fibrillation patient with MS

Circulation 2006;114:119–25
JAMA 2001;285:2370–5

Atrial fibrillation prevalence will increase 2.5 fold in next 50 years

Cross sectional study age 20>Health Maintenance organization California

N=17974

Table 2. Projected Age and Sex Distribution of Adults With Atrial Fibrillation in the United States Between 2000 and 2050*

	Year		
	2000	2025	2050
Women	48.6	46.3	47.4
Age group, y			
<65	18.0	15.5	11.5
65-79	45.3	48.7	35.9
≥80	36.7	35.8	52.6

*Data are presented as percentage.

AnTicoagulation and Risk Factors In Atrial Fibrillation (ATRIA) Study

JAMA. 2001;285:2370-2375

Genetic associations with atrial fibrillation

- Framingham heart study
  - 1.8 X increase (1 parent with Afib)
    - JAMA 2004;291:2851–5
  - 3.2 X increase (parent <75)
- Iceland study (N=5000—population cohort)
  - 1.77 X increase (1 parent with Afib)
    - Eur Heart J 2006;27:708 –12

Chromosome 4q25 SNPs	AF by Age 50 Years	No AF by Age 50 Years
Absent	0	13
Present	21	8*

*$p = 1.21 \times 10^{-5}$ comparing the presence of both common and rare variants in 11 kindreds with familial AF.

AF = atrial fibrillation; SNP = single-nucleotide polymorphism.

Modifier Genes for Familial AF JACC Vol. xx, No. x, 2012

Classification of Atrial Fibrillation

- **Paroxysmal (ie, self-terminating)**
  - Terminate spontaneously in less than seven days, usually less than 24 hours
- **Persistent AF**
  - Fails to self-terminate within seven days
- **Permanent AF**
  - Lasts for more than one year
- **Lone AF**
  - Paroxysmal, persistent, or permanent AF in individuals without structural heart disease.
  - Lone AF has primarily been applied to patients <60 years of age but older patients also may be at low risk

This classification applies to episodes of AF that last more than 30 seconds and that are unrelated to a reversible cause.

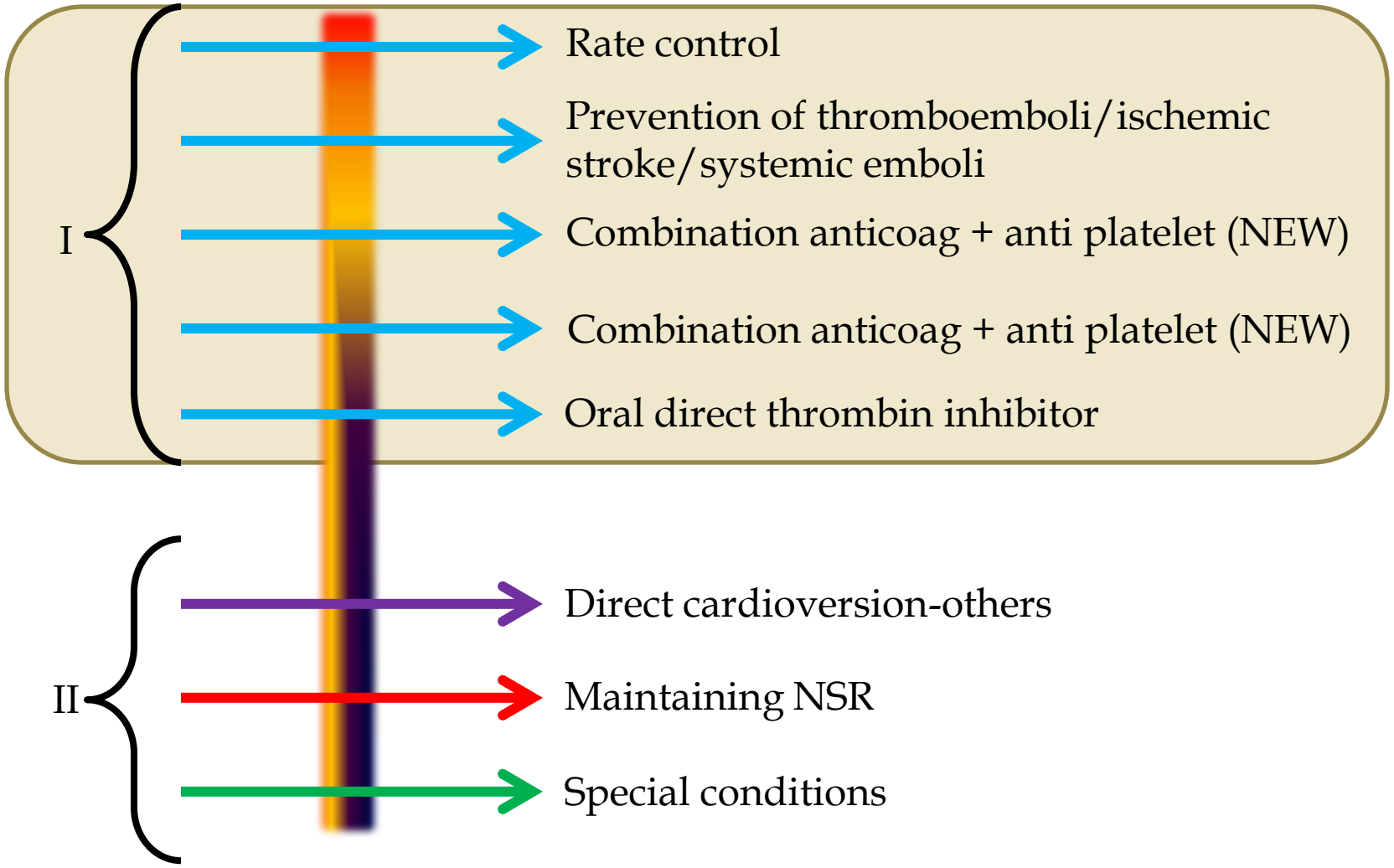
Echocardiogram can be very helpful

- Echo
  - TTE/TEE-chamber size, function
    - Valvular, LVH, pericardial, peak RV pressure
    - Atrial thrombi-low sensitivity
      - 4 weeks of anticoagulation prior to cardioversion

Summary highlights

- History/Physical
  - Symptoms/pattern-onset
  - 90% of episodes not recognized by patient
  - 90% of patients have recurrence
  - 48 hours of Afib frequently unrecognized by patients
  - 40% of patients in NSR think they have afib (prior history)
- History, physical examination, and specific laboratory and cardiologic testing are all part of the evaluation of the patient with AF (Guidelines

Heart rhythm 2012;9:632 guidelines



New guidelines for atrial fibrillation treatment

Circulation. 2013;127:May 7, 2013

Rate control

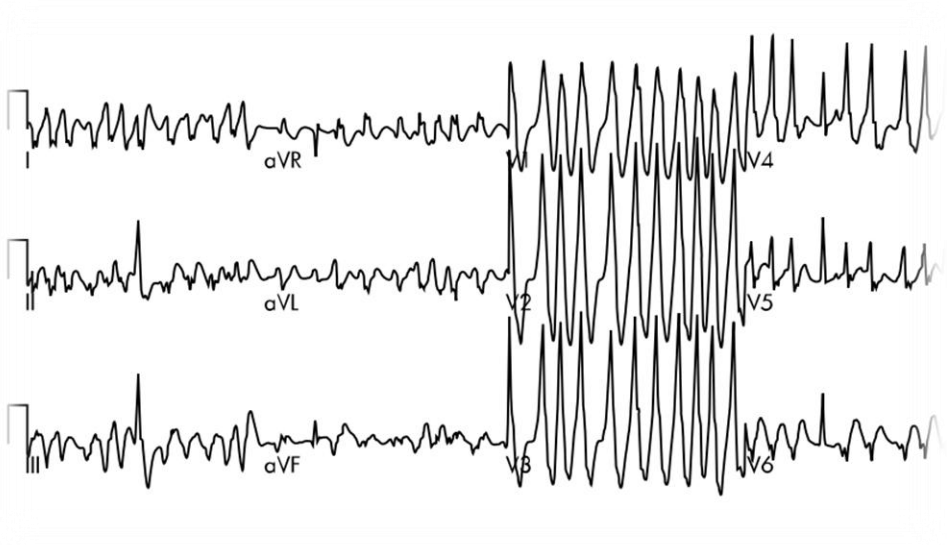
Accessory pathway-EP consult

- **Heart rate at rest (Class I)**
  - **Beta blocker / nondihydropyridine CCB**
    - **Esmolol, metoprolol**
    - **Verapamil, diltiazem (less negative inotrope)**
    - **Heart failure patient**
      - **Digoxin/amiodarone**
  - **Ablation AV node / EP (Class II) if not tolerate drugs**
  - **IV procainamide, disopyramide, ibutilide, or amiodarone may be considered for <u>hemodynamically stable patients</u> with AF involving conduction over an <u>accessory pathway</u>**

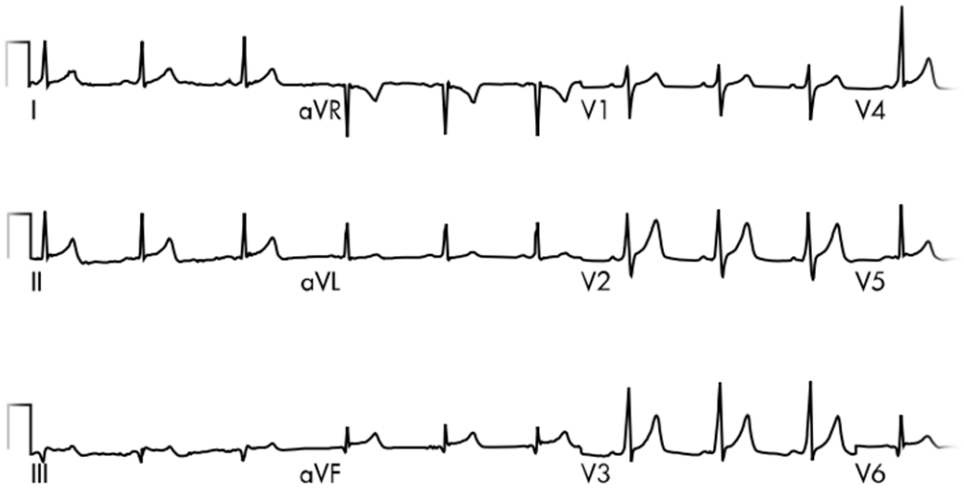
Resting heart rate 110 bpm in patients with persistent AF who have stable ventricular function (LV ejection fraction >0.40)

Circulation. 2013;127:May 7, 2013

37 y/o women with occasional lightheadness



After D/C cardioversion



Preventing Thromboembolism Class I

- **Selection of the antithrombotic agent should be based upon the absolute risks of stroke and bleeding and the relative risk and benefit for a given patient**
  - **High risk of stroke= chronic oral anticoagulant therapy with a vitamin k antagonist (INR 2-3)**

Highest risk groups → **Prior embolization**
Rheumatic mitral stenosis

>1 moderate risk →
Age >75 y
HT
LV systolic dysfucntion (EF <35%)
Diabetes mellitus

Circulation. 2013;127:May 7, 2013

Preventing Thromboembolism Class I

- Aspirin, 81–325 mg daily, is recommended as an alternative to vitamin k antagonists in low-risk patients or contraindication to Coumadin
- Mechanical heart valves (INR >2.5)
- Antithrombotic therapy is recommended for patients with atrial flutter as for those with AF.

It is reasonable to interrupt anticoagulation for up to 1 week without substituting heparin for surgical or diagnostic procedures that carry a risk of bleeding.

Circulation. 2013;127:May 7, 2013

Percutaneous coronary intervention or revascularization surgery patients with AF

Low-dose aspirin (less than 100 mg per d) and/or clopidogrel (75 mg per d) may be given concurrently with anticoagulation to prevent myocardial ischemic events

Class IIb

Circulation. 2013;127:May 7, 2013

STENTS and atrial fibrillation PCI patients

Clopidogrel should be given for a minimum of
1 mo after implantation of a bare metal stent

3 mo for a sirolimus-eluting stent

6 mo for a paclitaxel-eluting stent

12 mo or longer in selected patients, following which warfarin may be continued as monotherapy in the absence of a subsequent coronary event.

When warfarin is given in combination with clopidogrel or low-dose aspirin, the dose intensity must be carefully regulated.

Class IIb

Circulation. 2013;127:May 7, 2013

Class III

Long-term anticoagulation with a vitamin k antagonist is not recommended for primary prevention of stroke in patients below the age of 60 y without heart disease

Circulation. 2013;127:May 7, 2013

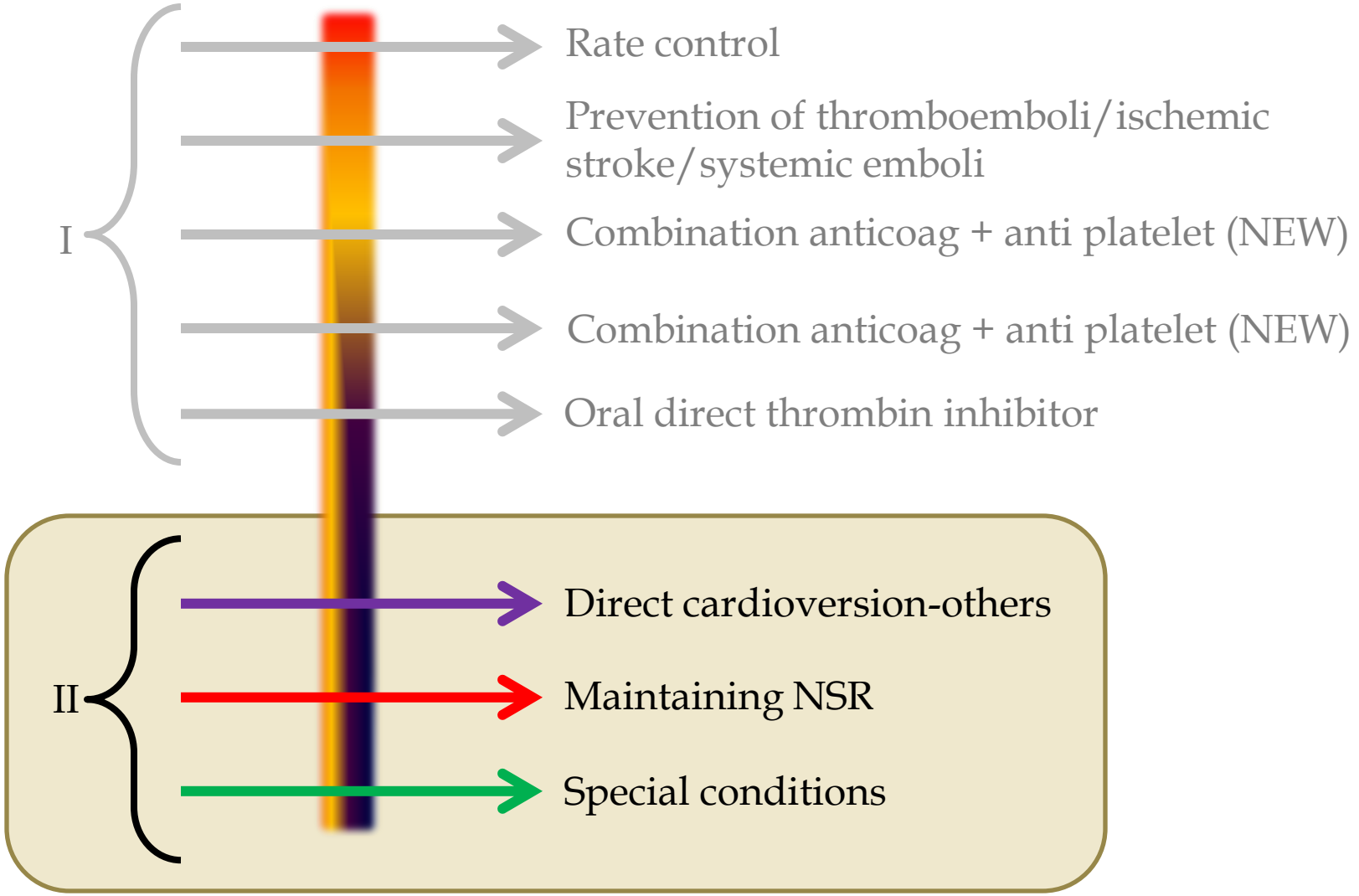
Oral Direct Thrombin Inhibitor Anticoagulant Agents—Class I

- **Dabigatran is useful as an alternative to warfarin for the prevention of stroke and systemic thromboembolism**
  - **Who do not have a prosthetic heart valve**
  - **Hemodynamically significant valve disease**
  - **Severe renal failure (creatinine clearance 15 mL/min)**
  - **Advanced liver disease (impaired baseline clotting function).**

(Level of Evidence: B)

FDA has ***approved*** rivaroxaban / apixaban to prevent stroke in patients with ***atrial fibrillation***

Circulation. 2013;127:May 7, 2013



New guidelines for atrial fibrillation treatment

Circulation. 2013;127:May 7, 2013

Cardioversion of AF

- **Class I**
  - **1. Administration of flecainide, dofetilide, propafenone, or ibutilide is recommended for pharmacological cardioversion of AF. (Level of Evidence: A)**

"We prefer direct current (DC) to pharmacologic cardioversion for most patients"….Uptodate 7 EP physicians

Pharmacological conversion of (recent-onset) AF (European Society of Cardiology)

Drug	Dose	Risk
Amiodarone	5 mg/kg IV over 1 hour	Phlebitis, hypotension. Will slow the ventricular rate. Delayed AF conversion to sinus rhythm
Flecainide	2 mg/kg IV over 10 minutes, or 200 to 300 mg orally	Not suitable for patients with marked structural heart disease; may prolong QRS duration, and hence the QT interval; and may inadvertently increase the ventricular rate due to conversion to atrial flutter and 1:1 conduction to the ventricles.
Ibutilide	1 mg IV over 10 minutes	Can cause prolongation of the QT interval and torsades de pointes; watch for abnormal T-U waves or QT prolongation. Will slow the ventricular rate
Propafenone	2 mg/kg IV over 10 minutes, or 450 to 600 mg orally	Not suitable for patients with marked structural heart disease; may prolong QRS duration; will slightly slow the ventricular rate, but may inadvertently increase the ventricular rate due to conversion to atrial flutter and 1:1 conduction to the ventricles

Eur Heart J 2010; 31:2369

Cardioversion of AF….Class II

- Before antiarrhythmic medication is initiated, a beta blocker or nondihydropyridine calcium channel antagonist should be given to prevent rapid AV conduction in the event atrial flutter occurs

- Amiodarone reasonable option
- A single oral bolus dose of propafenone or flecainide (pill-in-the-pocket) can be administered to terminate persistent AF outside the hospital once treatment has proved safe in hospital for selected patients without sinus or AV node dysfunction, bundle-branch block, QT-interval prolongation, the brugada syndrome, or structural heart disease.

Circulation. 2013;127:May 7, 2013

Quinidine, procainamide, disopyramide, and dofetilide should not be started out of hospital for conversion of AF to sinus rhythm.

Class III

Circulation. 2013;127:May 7, 2013

Dronedarone for the Prevention of Recurrent AF…Class II

- **Dronedarone is reasonable to decrease the need for hospitalization for cardiovascular events in patients with paroxysmal AF or after conversion of persistent AF.**
- **Dronedarone can be initiated during outpatient therapy.**

Class III: Harm

Dronedarone should not be administered to patients with class IV heart failure or patients who have had an episode of decompensated heart failure in the past 4 weeks, especially if they have depressed left ventricular function (left ventricular ejection fraction <35%)

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Direct-Current Cardioversion of AF and Flutter….Class I

- AF with ongoing myocardial ischemia, symptomatic hypotension, angina, or HF, immediate r-wave synchronized direct-current cardioversion is recommended.
- AF involving preexcitation when very rapid tachycardia or hemodynamic instability

- Frequent repetition of direct-current cardioversion is not recommended for patients who have relatively short periods of sinus rhythm between relapses of AF…..Class III

Pharmacological Enhancement of Direct-Current Cardioversion..

Class IIa

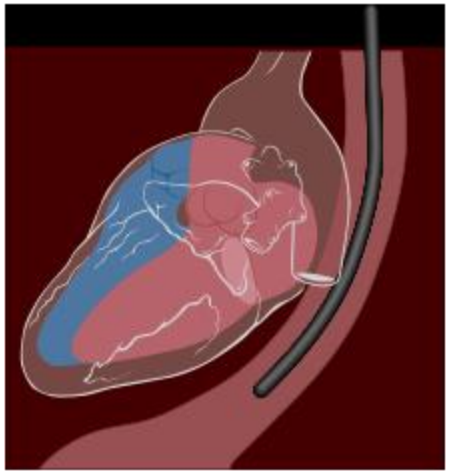
- Pretreatment with amiodarone, flecainide, ibutilide, propafenone, or sotalol

Prevention of Thromboembolism in Patients With AF Undergoing Cardioversion

Class I

- AF of 48-hour duration or longer, or when the duration of AF is unknown, anticoagulation (INR 2.0 to 3.0) is recommended for at least 3 wk prior to and 4 wk after cardioversion, regardless of the method (electrical or pharmacological) used to restore sinus rhythm. (Level of Evidence: B)

Class II b



As an **alternative to anticoagulation prior to cardioversion of AF**, it is reasonable to perform transesophageal echocardiogram in search of thrombus in the left atrium or left atrium appendage. (Level of Evidence: B)

No identifiable thrombus, cardioversion is reasonable immediately after anticoagulation with unfractionated heparin (eg, initiate by intravenous bolus injection and an infusion continued at a dose adjusted to prolong the activated partial thromboplastin time to 1.5 to 2 times the control value **until oral anticoagulation has been established with a vitamin k antagonist (eg, warfarin), as evidenced by an INR equal to or greater than 2.0.) (Level of Evidence: B).**

Transesophageal echocardiography can detect thrombi in both the left atrium and left atrial appendage--specificity varying from 93% to 100%

Its not zero

Table 3. Summary of Studies of Transesophageal Echocardiography (TEE)-Guided Approach to Cardioversion of Atrial Fibrillation, Including the Incidence of Thrombus by TEE and Recorded Embolic Events

Study	Reference Number	n	Atrial Thrombi	Embolic Events
Orsinelli (1993)	103	39	9 (23%)	1 (2.56%)
Stoddard (1995)	113	206	37 (18%)	0
Klein (1997)	4	126	7 (13%)	0
Weigner (1998)	114	466	64 (13.9%)	1 (0.21%)
Grimm (1998)	115	417	28 (7%)	0
Corrado (1999)	116	123	11 (9%)	0
ACUTE (2000)	16	619	79 (13.6%)	5 (0.81%)
Total		1,996	235 (11.8%)	7 (0.35%)

ACUTE = Assessment of Cardioversion Using Transesophageal Echocardiography.

J Am Coll Cardiol 2001;37:691–704

Thrombus resolution in 40-90% by 17 weeks

Table 5. Previous Studies Documenting Resolution of Atrial Thrombus by Serial Transesophageal Echocardiography

Study (Reference no.)	n	Frequency of Thrombus	Anticoagulation Duration	Atrial Thrombus Resolved on Second TEE
Stoddard 1995 (106)	21	NA	5 to 17 weeks	9/21 (43%)
Collins 1995 (120)	18	NA	4 weeks (median)	16/18 (89%)
Tsai 1997 (121)	8	10%	NA	6/8 (75%)
Klein 1997 (4)	7	13%	6 weeks	3/7 (43%)
Jaber 2000 (122)	164	NA	6.7 weeks (mean)	131/164 (80%)
Corrado 1999 (116)	11	11%	4 weeks (median)	9/11 (82%)

NA = not available; TEE = transesophageal echocardiography.

J Am Coll Cardiol 2001;37:691–704

Table 1. Reported Incidences of Embolic Events After Electrical and Chemical Cardioversion From Atrial Fibrillation

Study	Reference Number	n	AC Rx	Percent Embolism
Electrical cardioversion				
Lown (1963)	44	50	Some	1.7
Killip (1963)	45	62	In 45%	0.0
Morris (1964)	48	70	In 6%	3.4
Oram (1964)	49	100	Some	1.9
Hurst (1964)	50	121	No	1.3
Morris (1966)	51	108	Some	2.5
Korsgren (1965)	52	138	Yes	0.0
Halmos (1966)	53	175	No	0.4
Selzer (1966)	54	189	No	2.1
Lown (1967)	55	350	In 29%	0.9
Resnekov (1967)	56	204	Some	0.6
Hall (1968)	57	142	In 39%	0.8
Radford (1968)	58	156	In 17%	0.0
Aberg (1968)	59	207	Most	0.7
Bjerkelund (1969)	60	437	Yes	1.1
McCarthy (1969)	61	149	Some	1.6
Henry (1976)	62	37	Some	5.6
Roy (1986)	63	152	In 72%	1.3
Arnold (1992)	64	454	Most	1.3
				1.4 ± 1.3*

J Am Coll Cardiol 2001;37:691–704

Table 1. Reported Incidences of Embolic Events After Electrical and Chemical Cardioversion From Atrial Fibrillation

Study	Reference Number	n	AC Rx	Percent Embolism
Chemical cardioversion				
Sokolow (1956)	42	177	Some	1.3
Goldman (1960)	43	400	No	1.5
Freeman (1963)	46	100	Yes	0.0
Rokseth (1963)	47	274	Yes	1.6
Carlsson (1996)	65	1,152	Some	0.26
Mitchell (1997)	66	110	Some	2.7
				1.2 ± 1.0*

5.6% risk of stroke in the week after cardioversion in non-anticoagulated patients

Cardioversion increases or concentrates the embolic risk of AF by perhaps **50-fold** during the week after the procedure.

J Am Coll Cardiol 2001;37:691–704

Maintenance of Sinus Rhythm

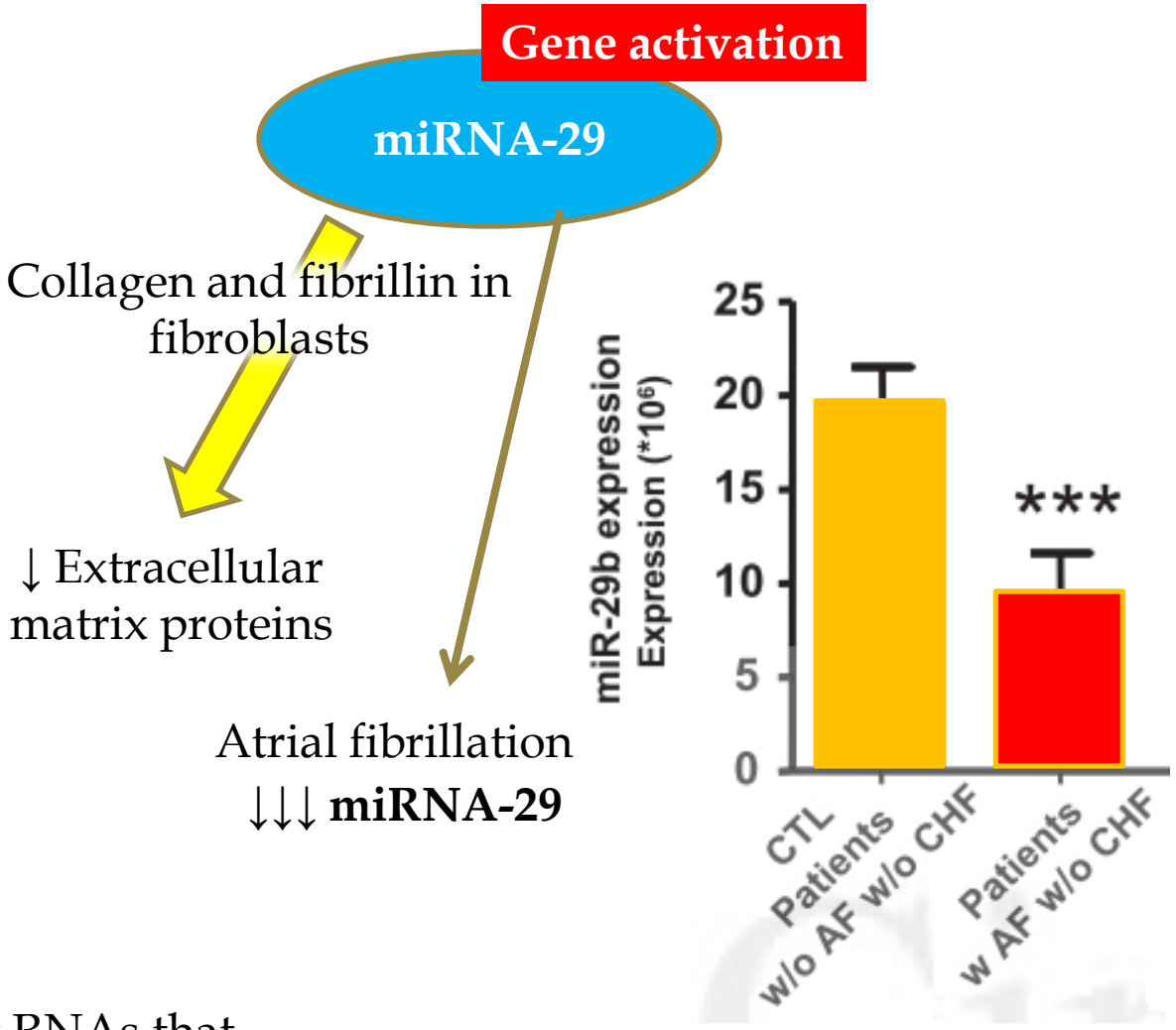
Class I

- Before initiating antiarrhythmic drug therapy, treatment of precipitating or reversible causes of AF is recommended.
- 2011 Updated Recommendation: Catheter ablation performed in experienced centers§ is useful in maintaining sinus rhythm in selected patients with significantly symptomatic, paroxysmal AF who have failed treatment with an antiarrhythmic drug and have normal or mildly dilated left atria, normal or mildly reduced LV function, and no severe pulmonary disease

Circulation. 2013;127:May 7, 2013

Future considerations

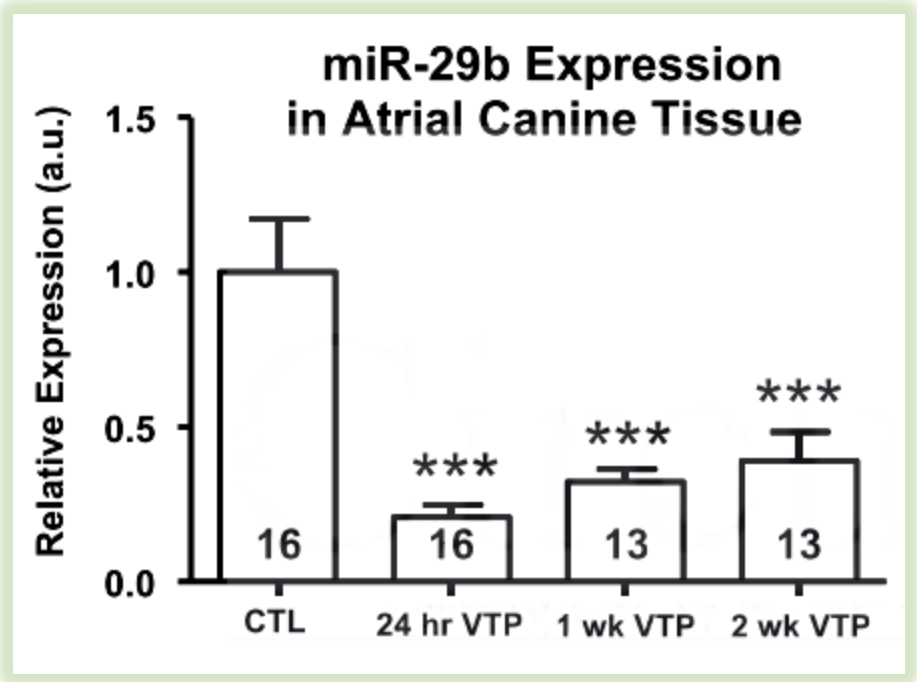
- **New developments in molecular biology**
  - **Protonomics / microRNA technology**

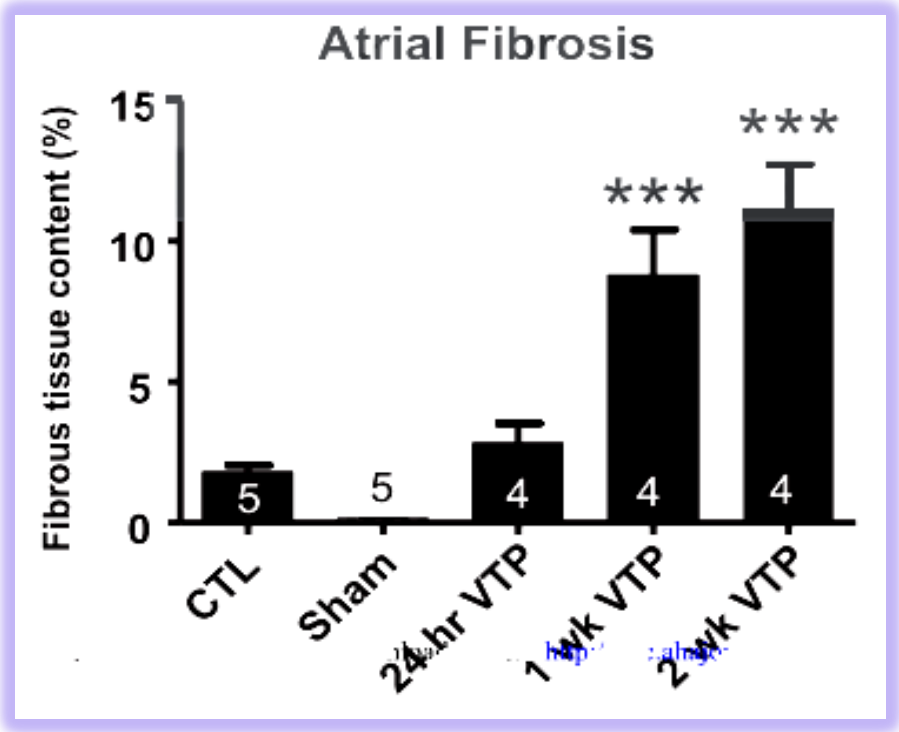


MicroRNAs (miRs) non-coding RNAs that block mRNA-translation and/or promote mRNA-breakdown of target-genes.

DOI: 10.1161/CIRCULATIONAHA.112.001207

Atrial fibrillation – reduces miRNA 29b with associated increased atrial fibrosis





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VTP-ventircular tachy pacing

5 take home points

- Afib increases risk for embolization
- Anticoagulation 1 month before and 1 month after cardioversion
- Warfarin INR 2-3
  - Can add ASA / antiplatelet agents carefully
- Anti-arrhythmics – aminodarone
- Afib ablation – Class I in good centers, appropriate cases
- Future of research - impressive

Thank you