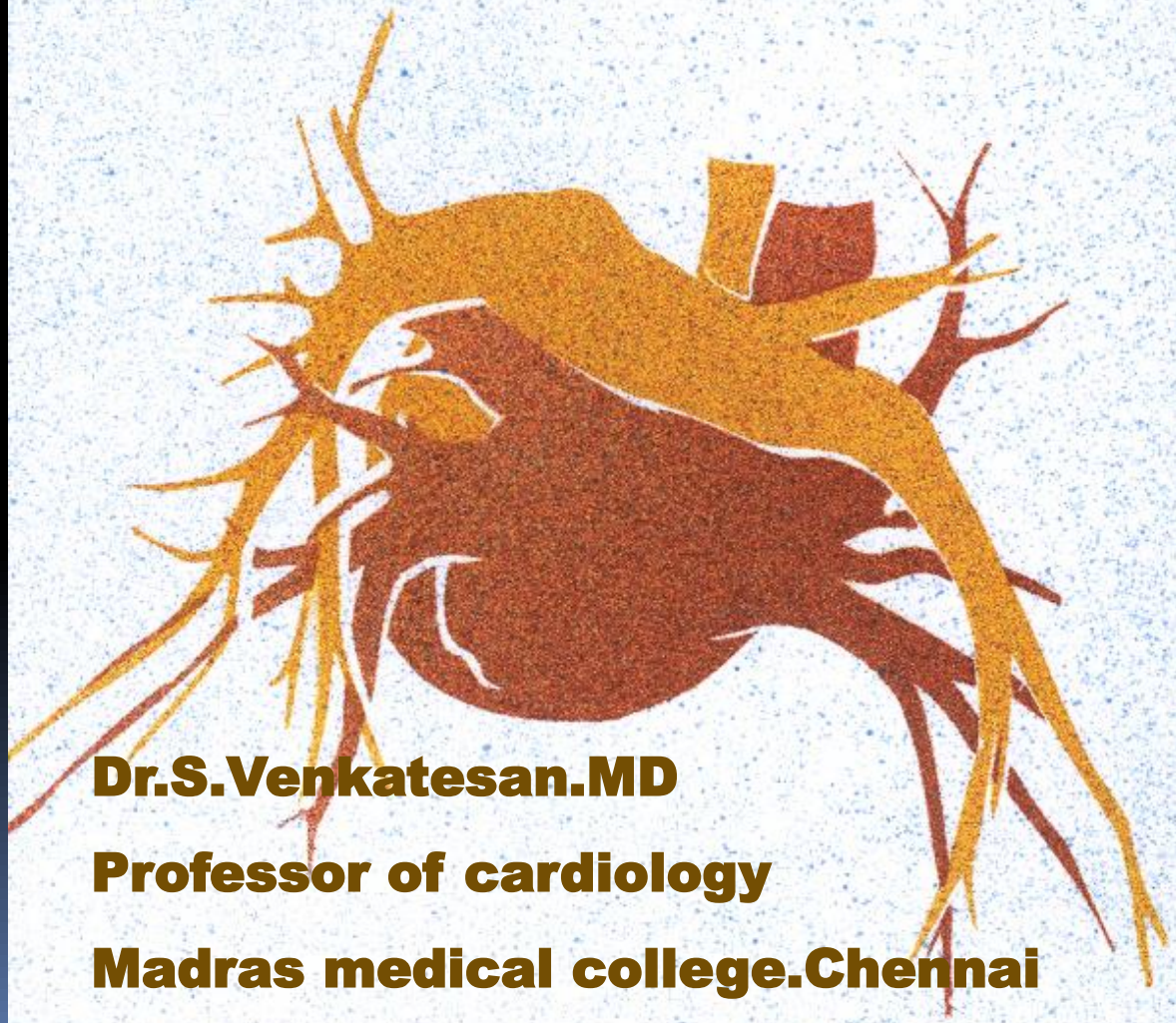
Atrial fibrillation : An Appraisal



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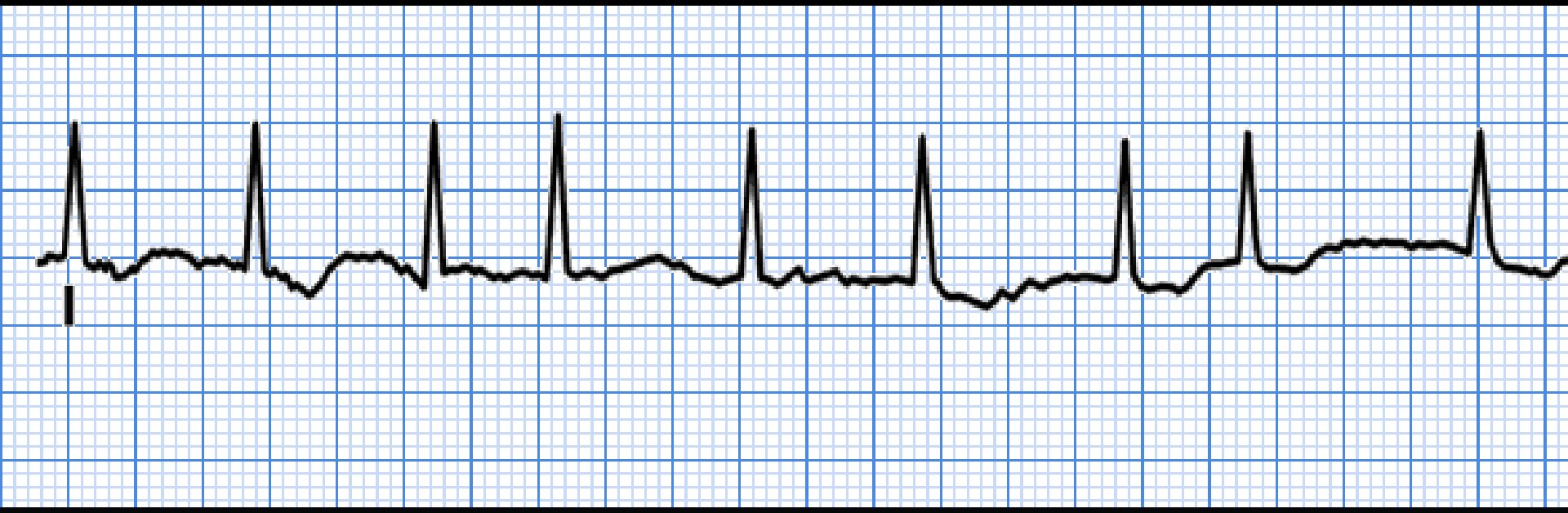
Madras medical college.Chennai



Commonest cardiac rhythm disorder

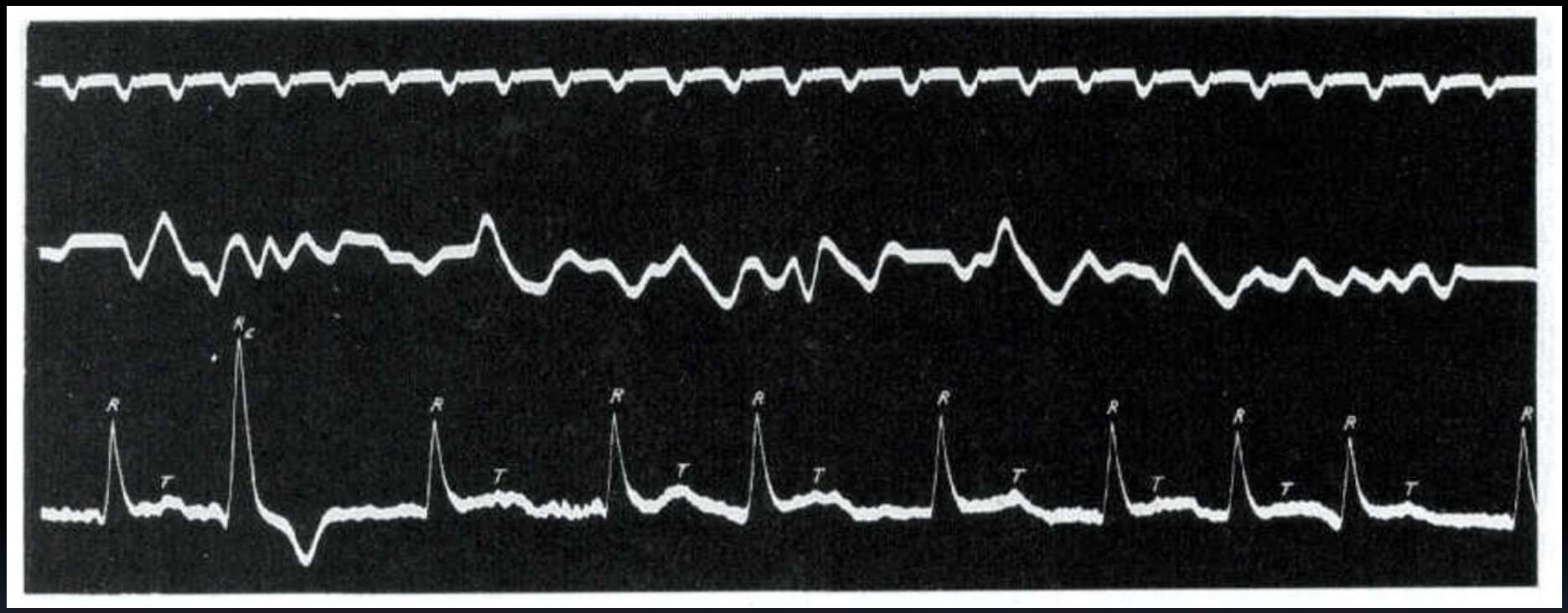
Ataxia of the pulse

Delirium cordis

1696 and 2598 BC

Bouilland J. Traite clinique des maladies du coeur. Paris: JB Bailliere; 1835:141-2.

Herring(1908), MacKenzie's, Lewis

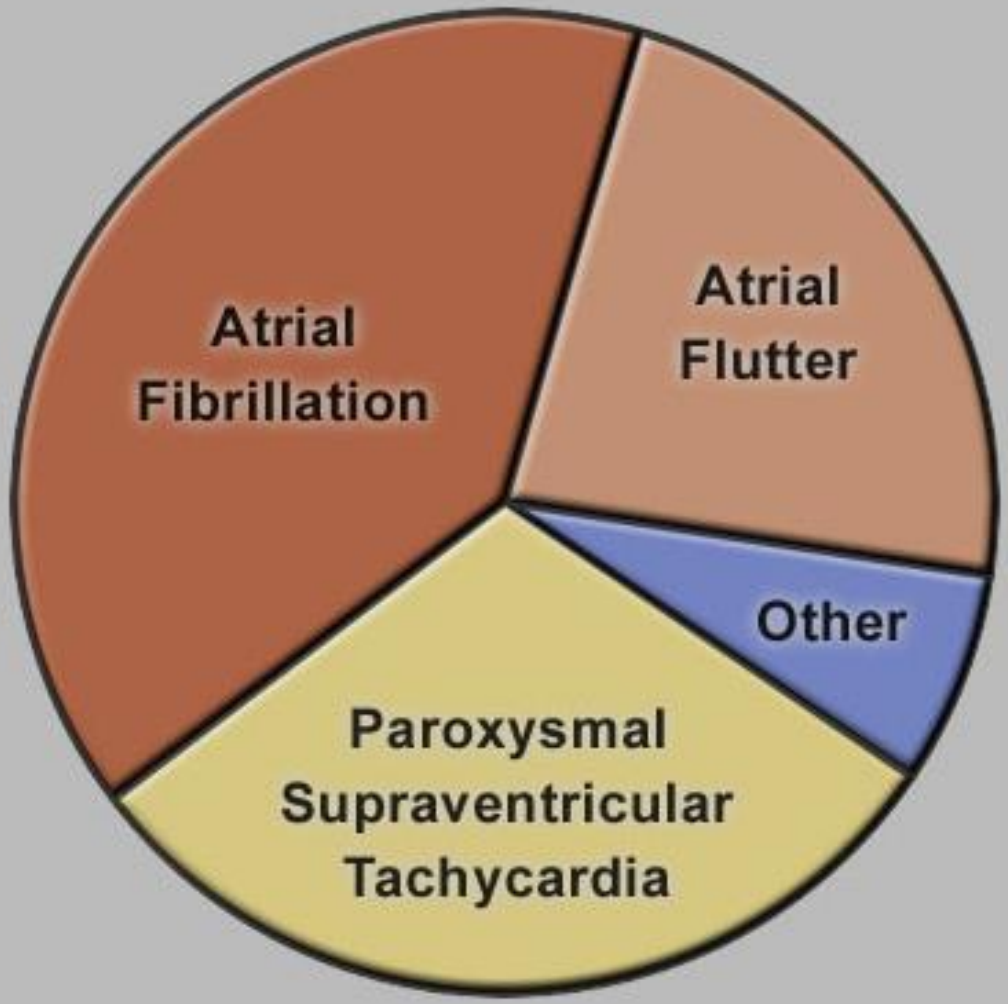


Hering HE. Das Elektrocardiogramm des Irregularis perpetuus. Deutsches Archiv fur Klinische Medizin. 1908; 94:205-8.

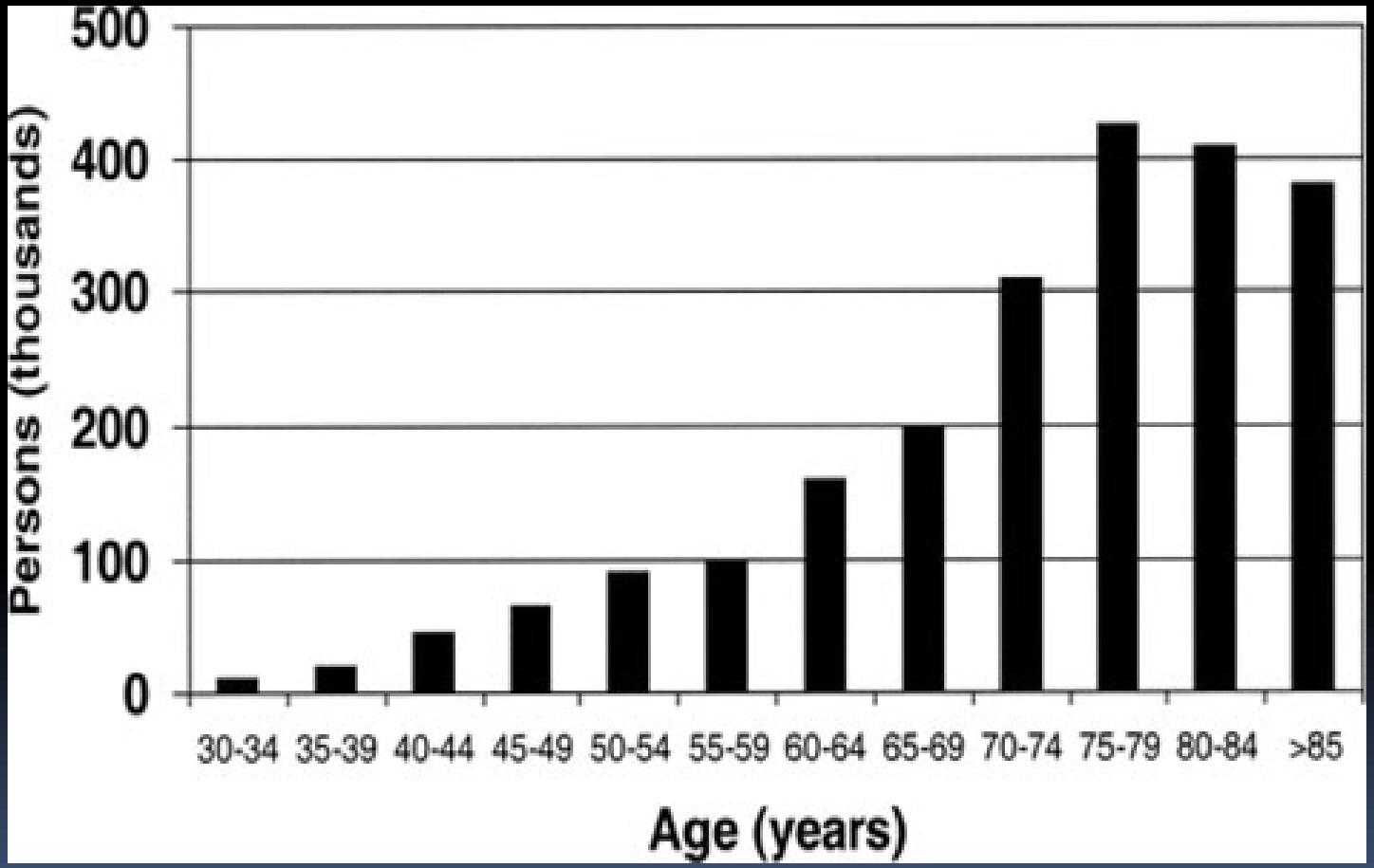
Scheme

- Clinical cardiology
- ECG
- Hemodynamics
- Electrophysiology
- Echocardiography
- Management strategies

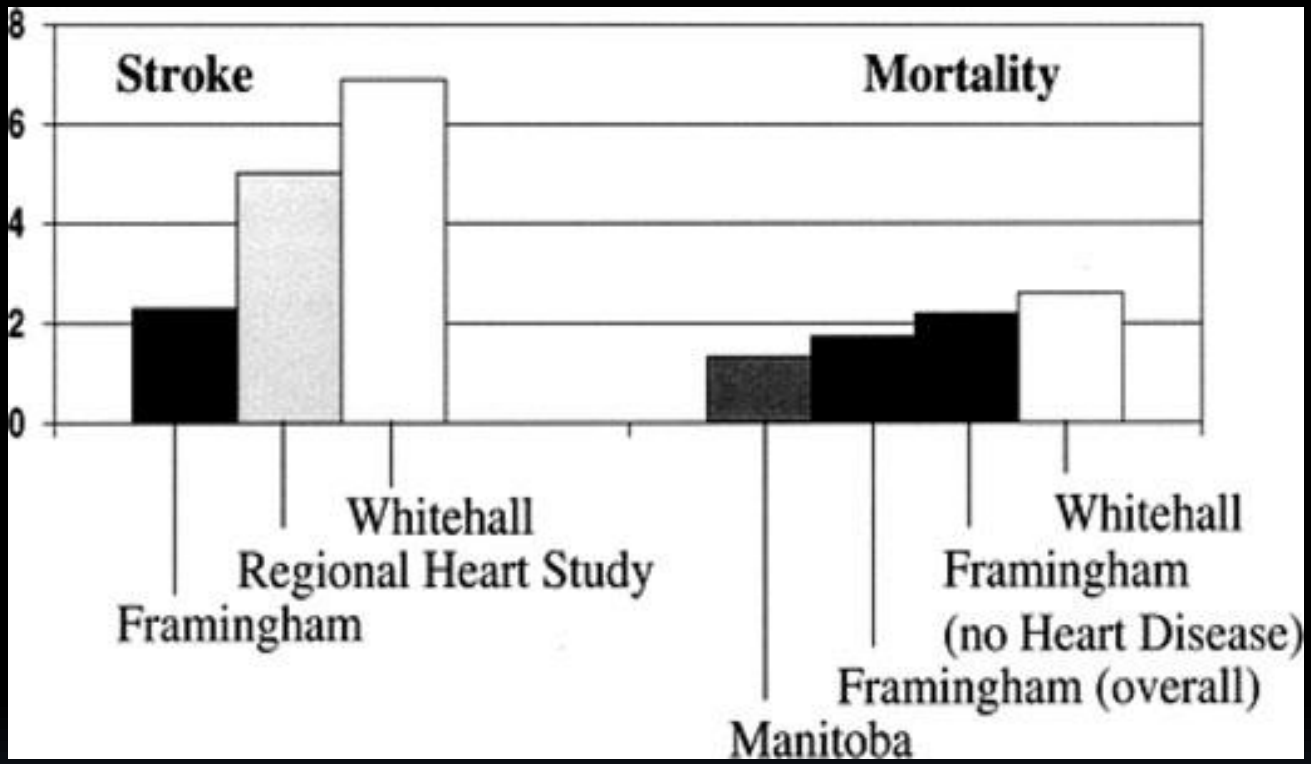
Supraventricular Arrhythmias



Predominantly an arrhythmia of elderly

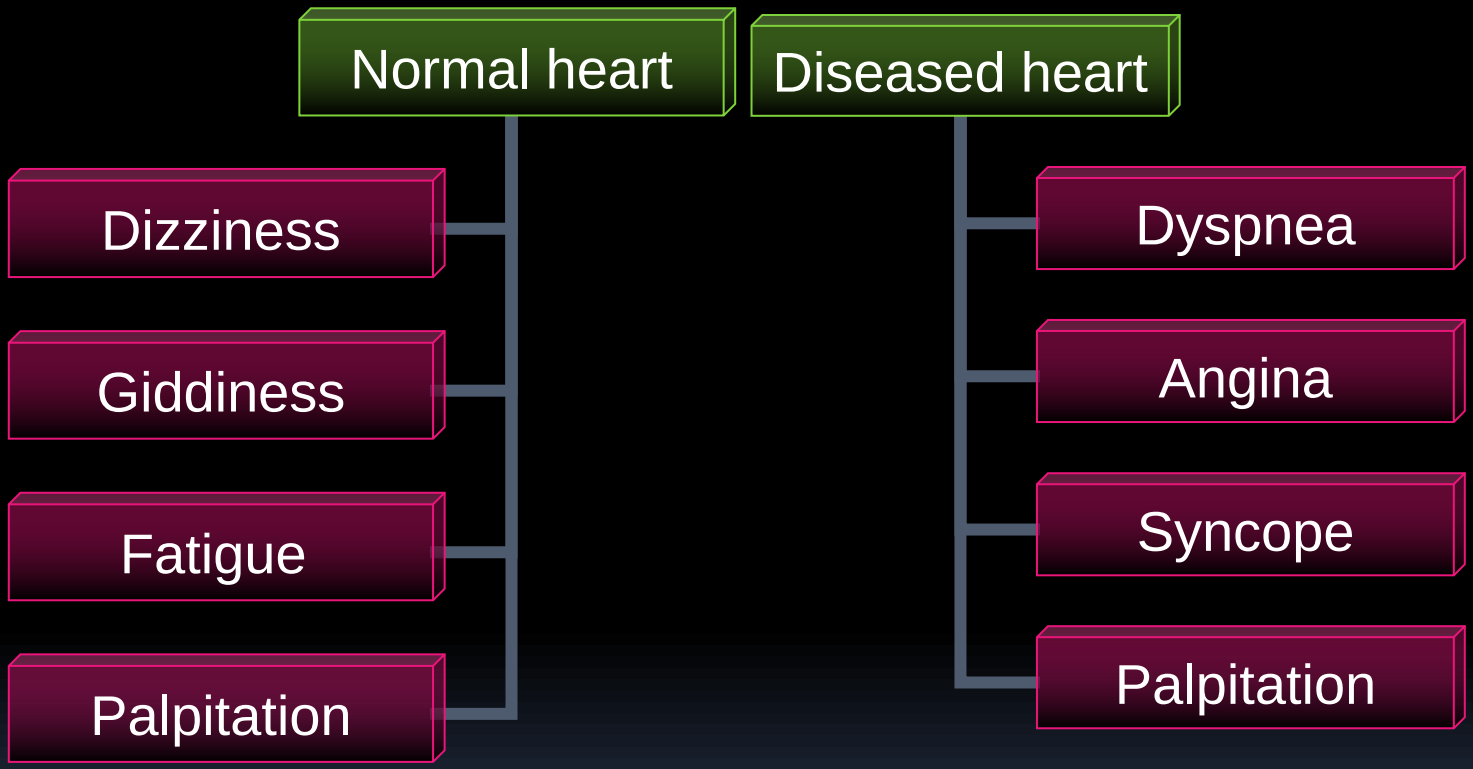


Carries both mortality and morbidity



Natural history of atrial fibrillation: incidence, risk factors, and prognosis in the Manitoba follow-up study. Am J Med 1995;98:476–84).

What are the usual symptoms of AF ?



Symptoms are more common in elderly

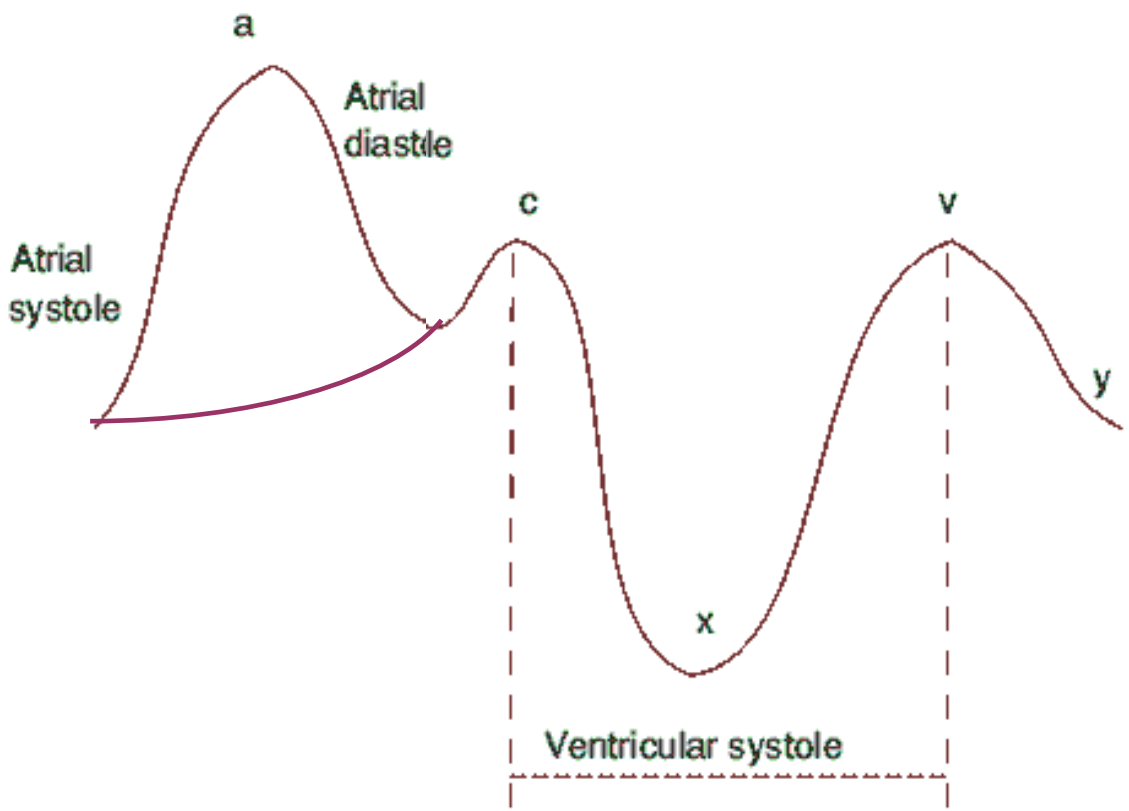
Heart Failure may be precipitated

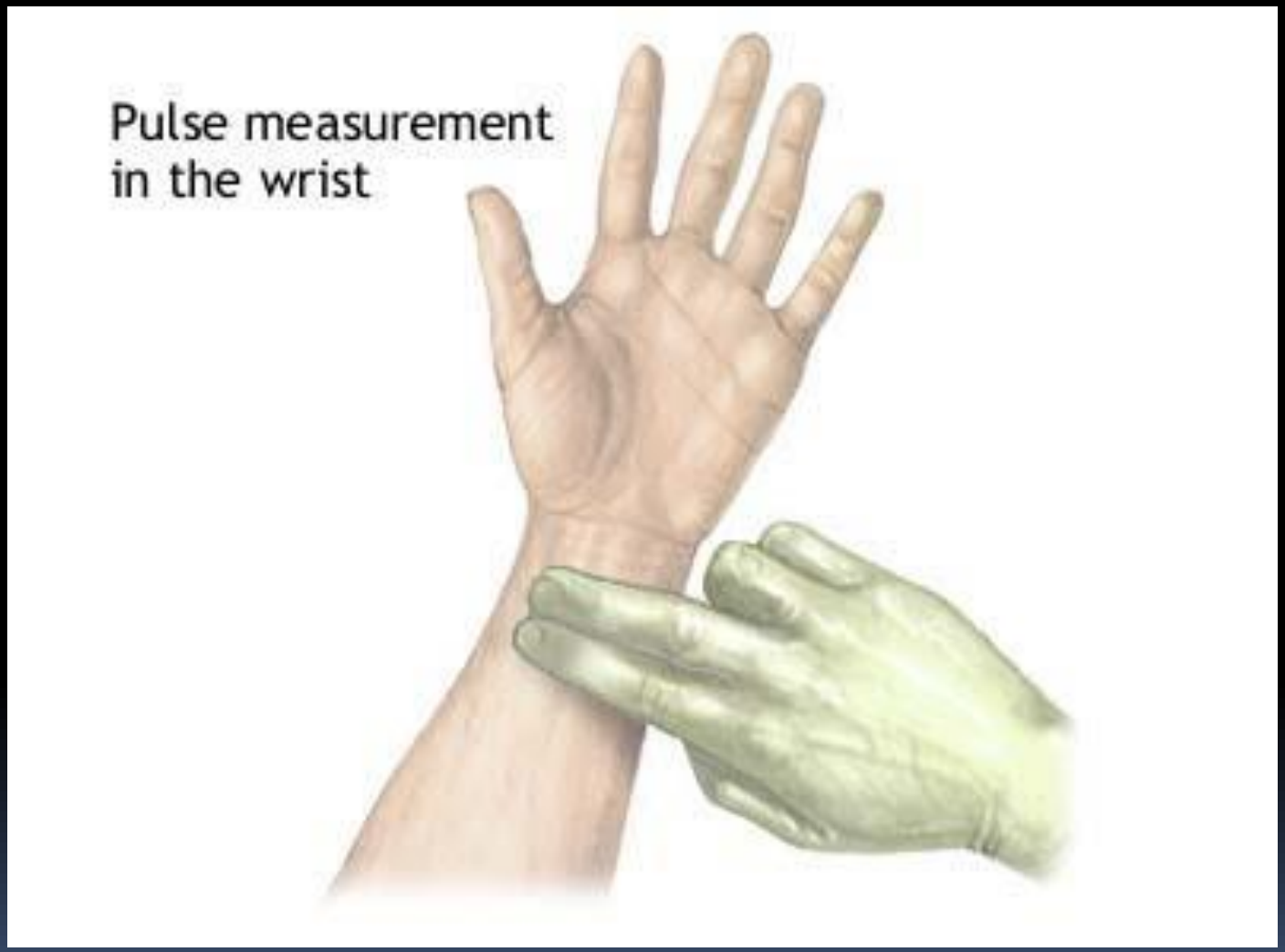
First episode may be a thrombo-embolism

The physical examination in AF

- Irregular pulse
- Pulse deficit
- Absent a wave in JVP
- Variable first heart sound
- Absence of a fourth sound

JVP in AF




Pulse measurement
in the wrist

- Irregular pulse

  (How will you differentiate multiple VPDs from AF ?)

- Pulse deficit

  (What is the mechanism?)

Atrial fibrillation

Chaotic atrial activity

Atrial rate 350-600 . Ventricular rate 100-160/mt.

P wave disappear , replaced by f waves (Fine /Coarse)

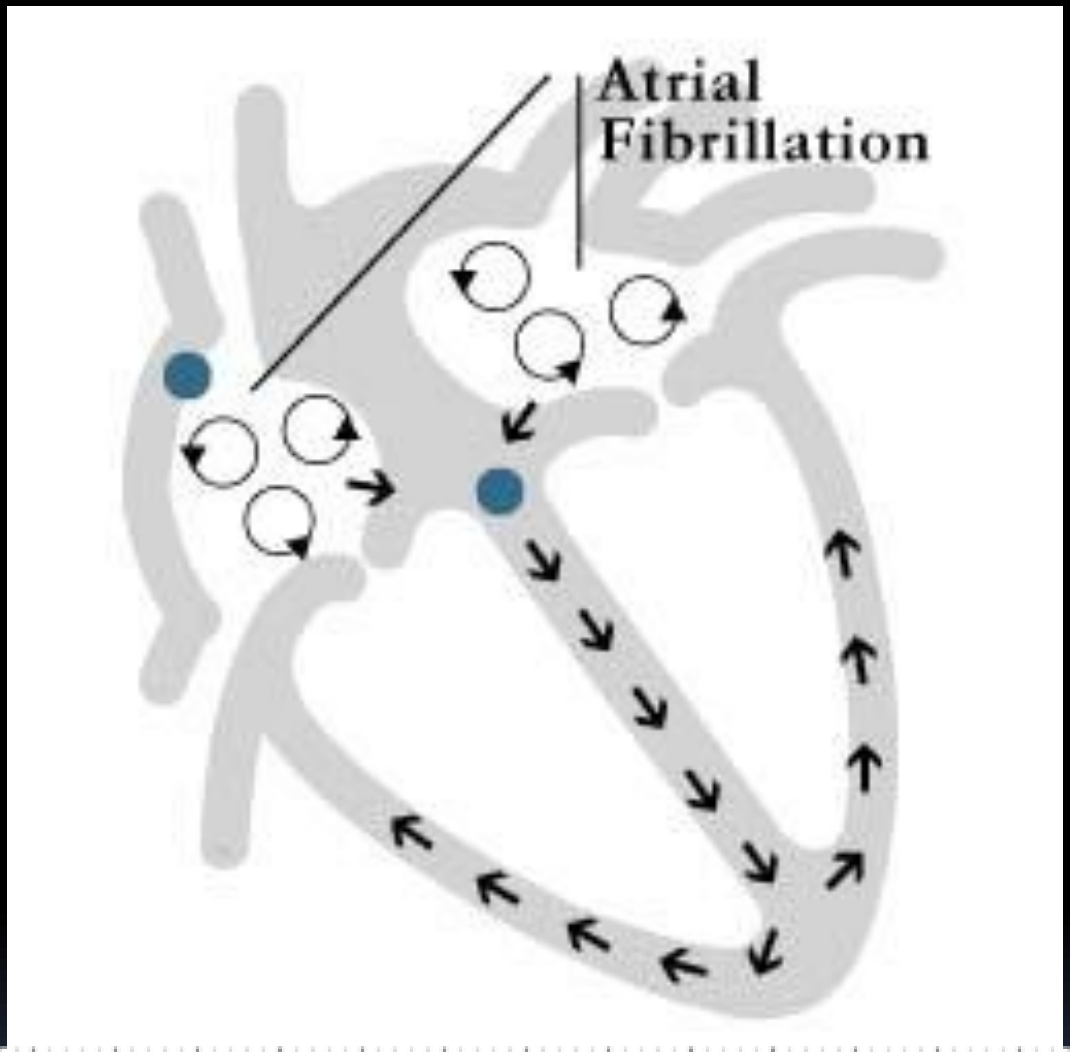
Why ventricular rate is irregularly irregular?

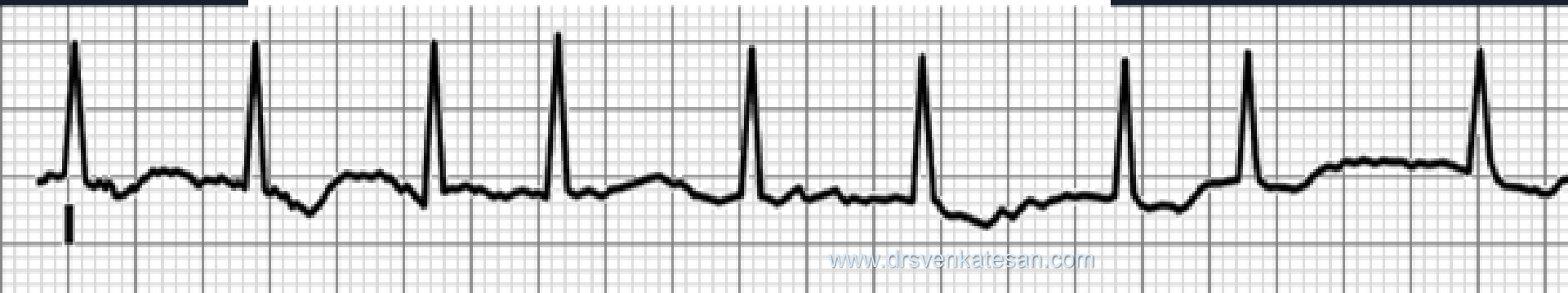
Not all impulses are conducted

Most are filtered

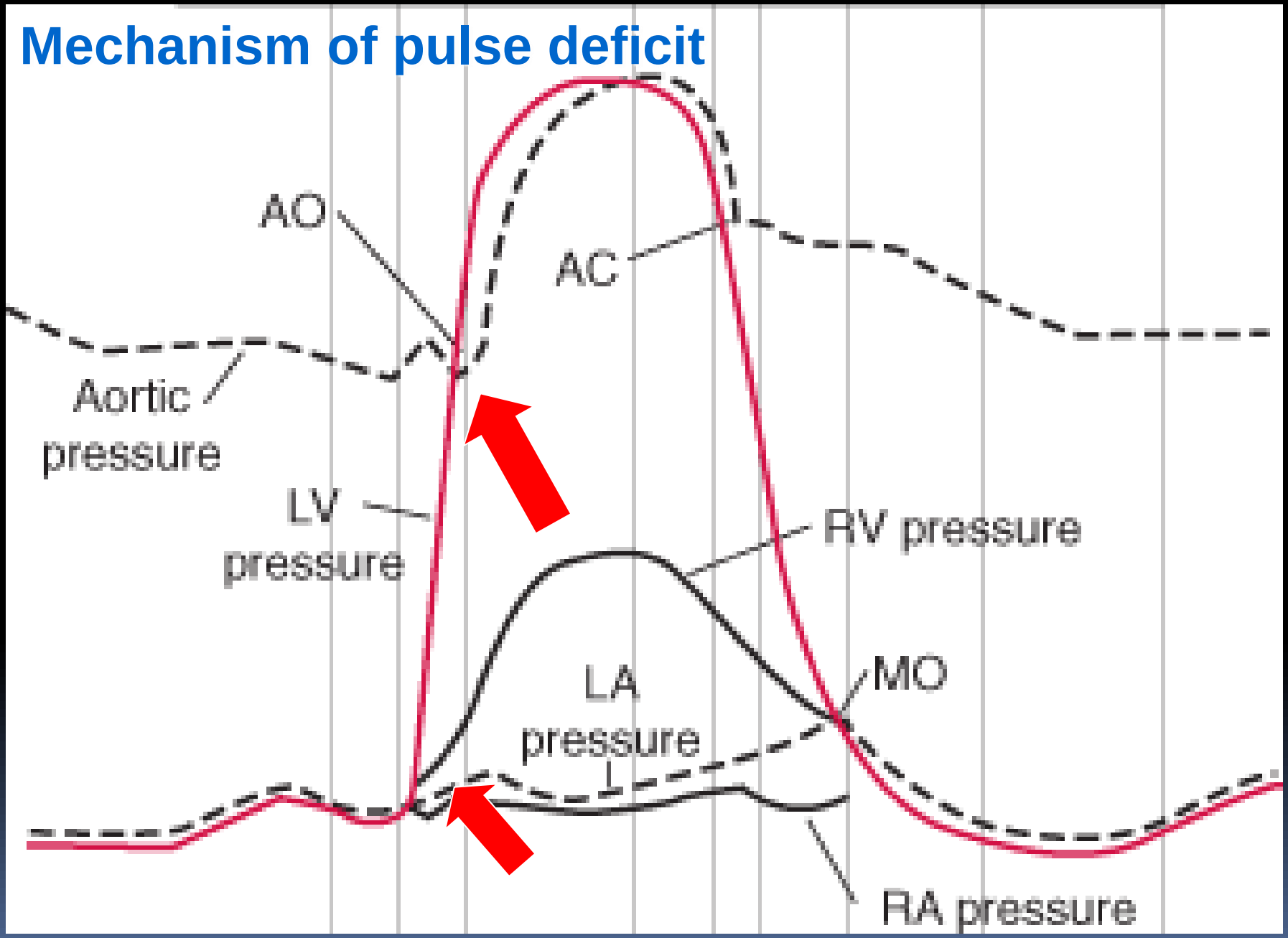
AV node refractory period

Concealed conduction in AV node determine the Ventricular response





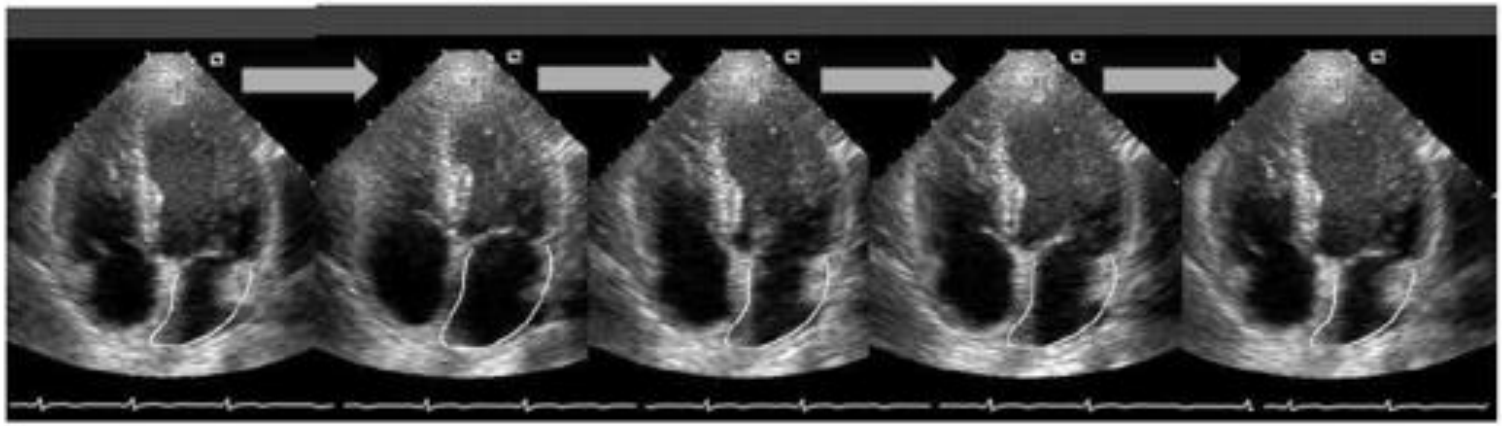
Mechanism of pulse deficit



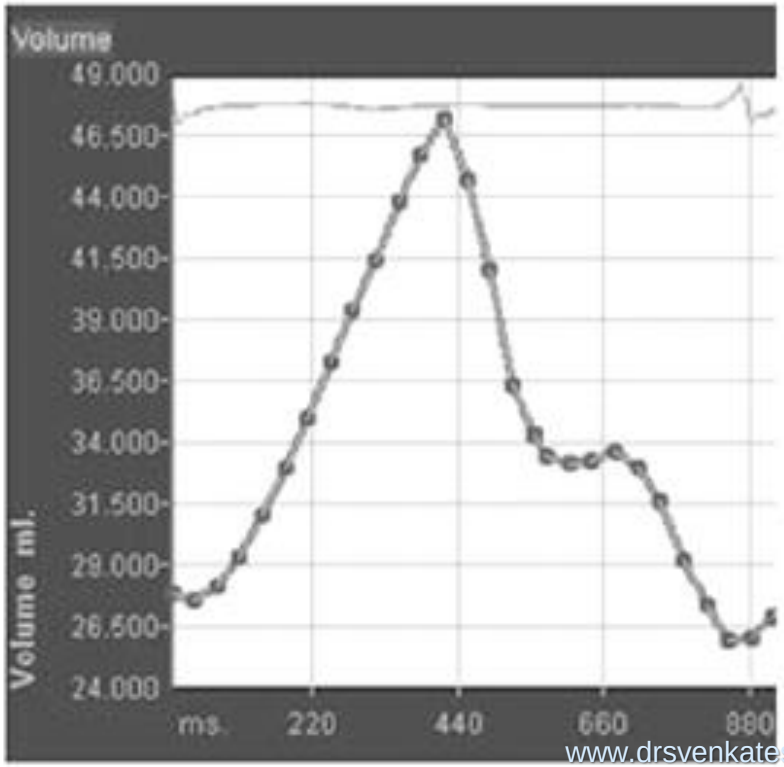
Determinants of Hemodynamic stability

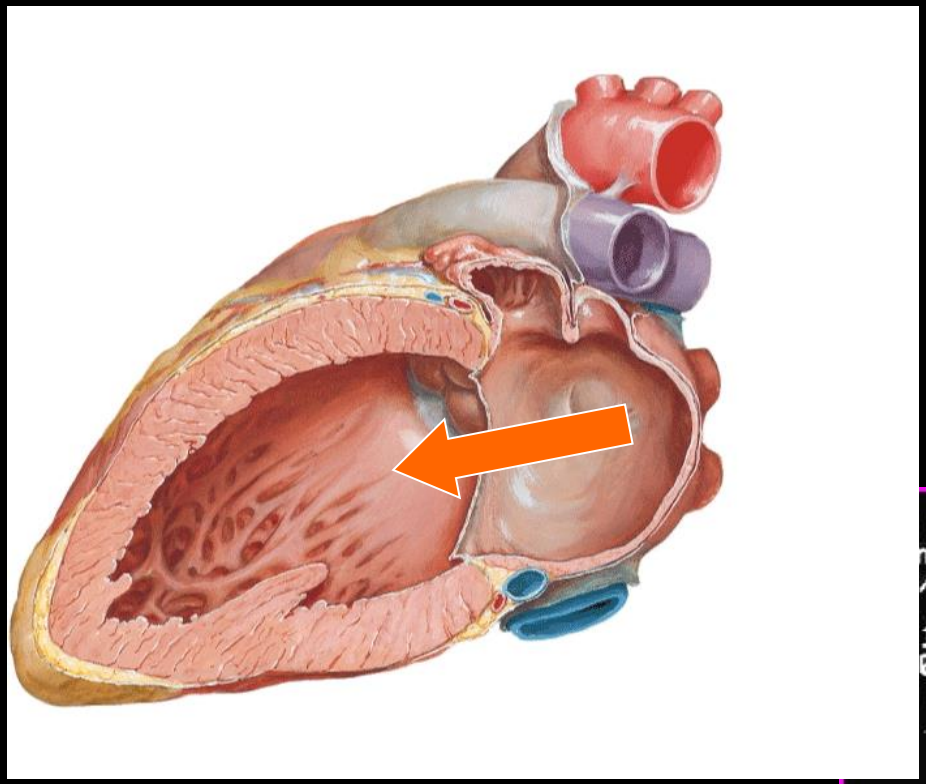
- Age
- Ventricular rate
- LV function
- Valve function

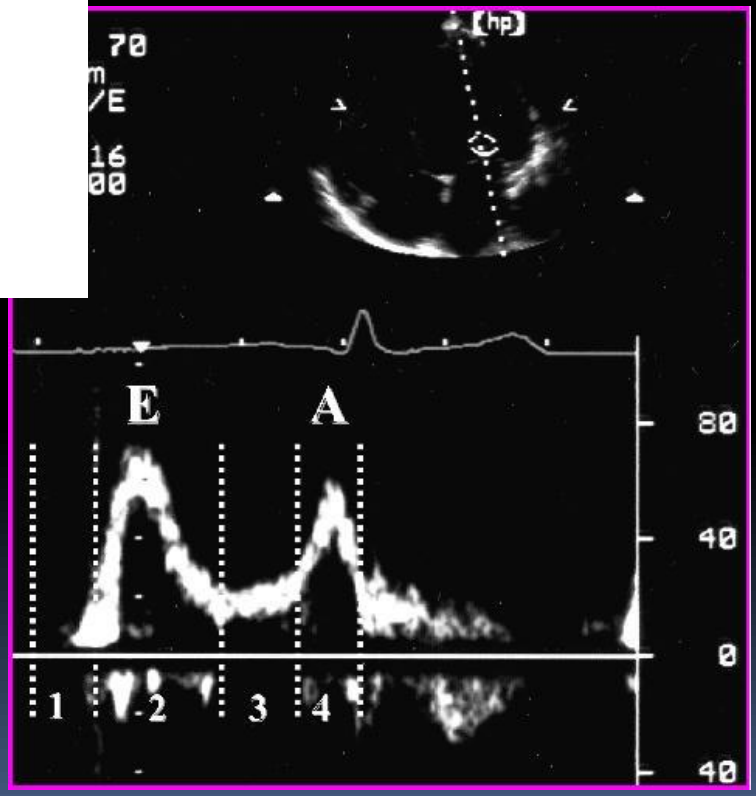
Left atrial function



Time-Left Atrial Volume Curve



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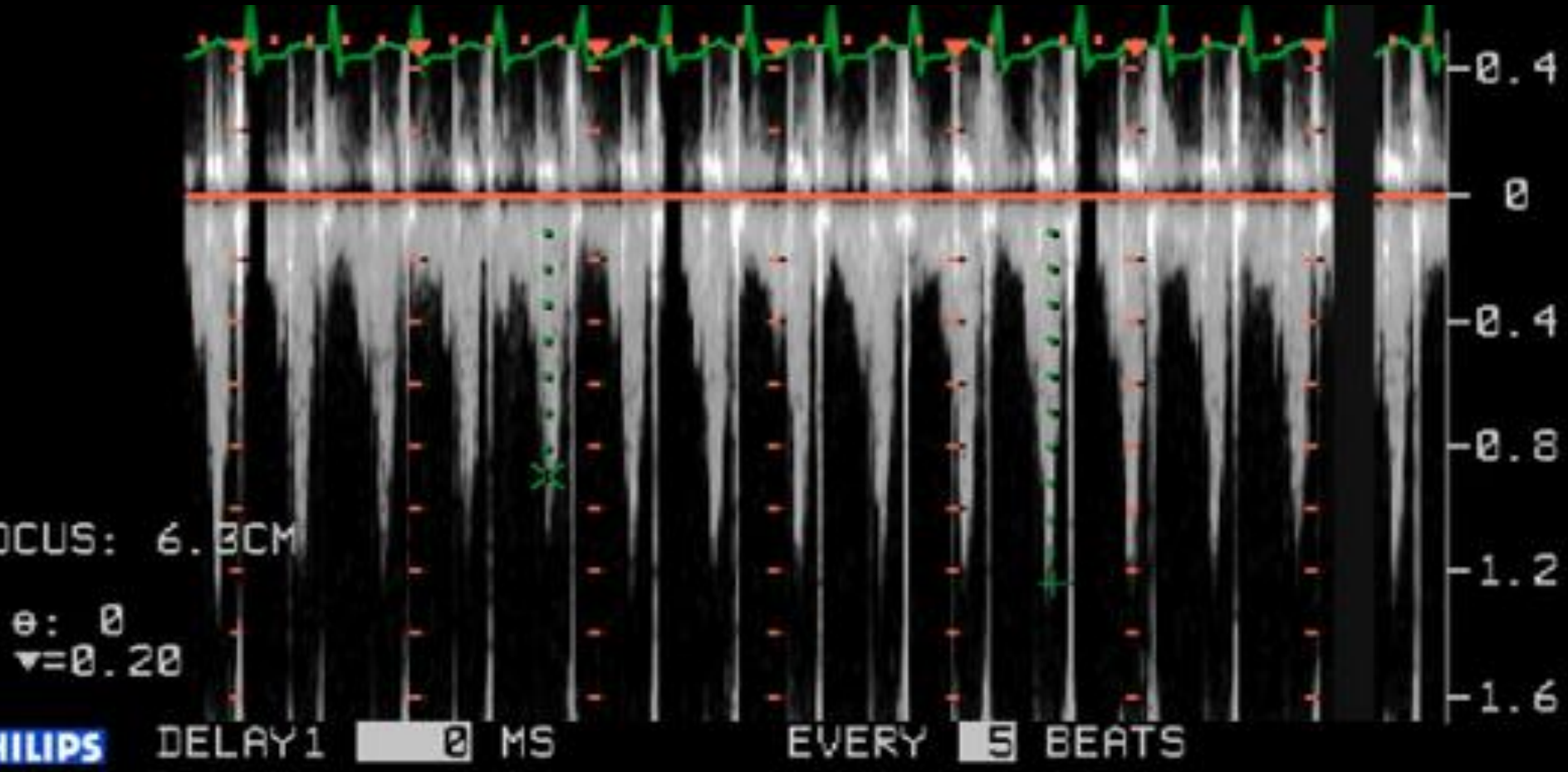
Effect of tachycardia on transmitral flow



How AF is tolerated well in some ?

- **The 25 % loss of atrial contribution is compensated by improved LV function.**

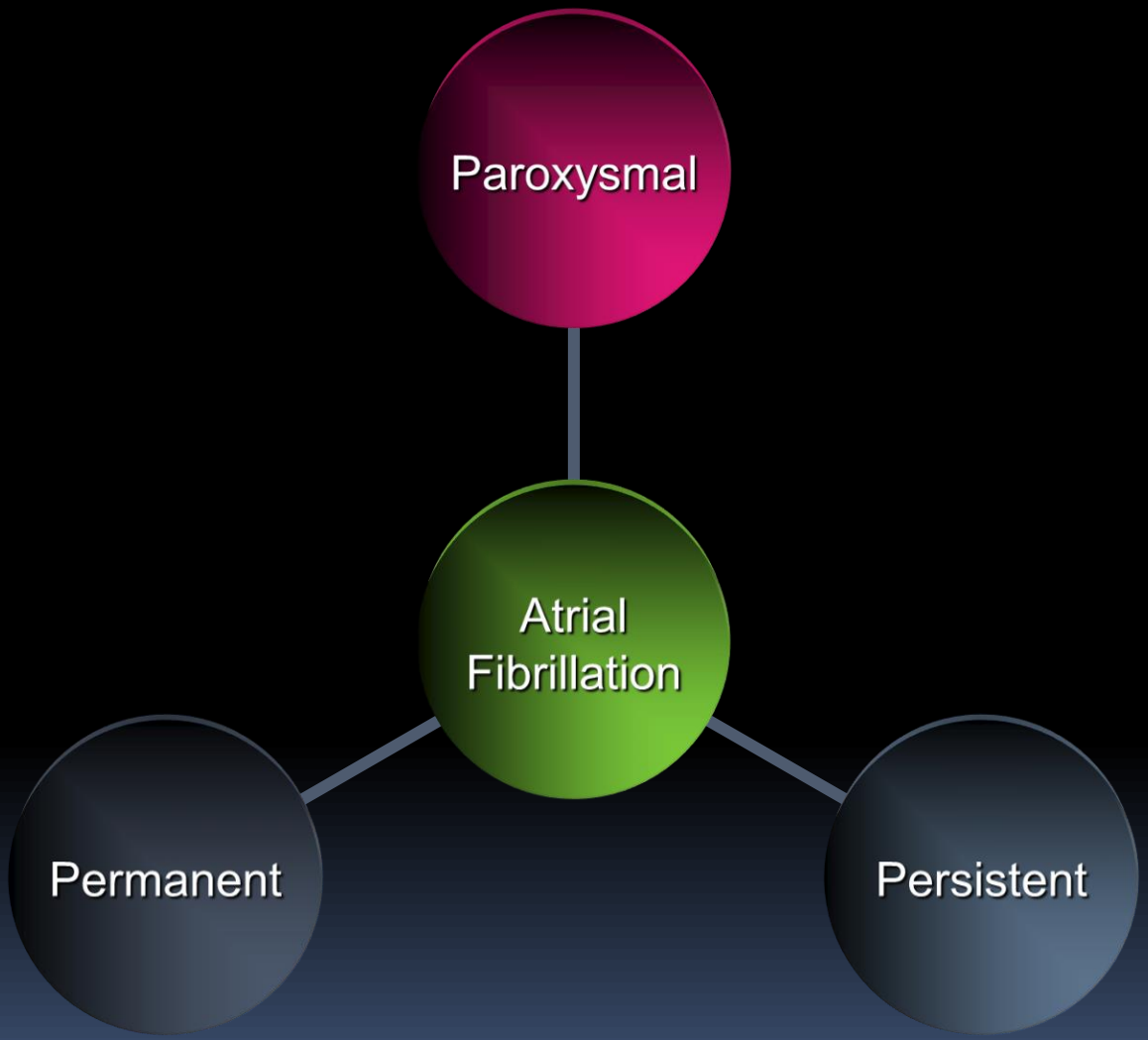
(LV a part of mitral apparatus self augments it's own filling)

- **If there is a decline in LV function these patients get symptoms.**

Classification of AF

- Etiological –Primary /secondary
- Valvular/Nonvalvular
- Chronological
- Hemodynamic
- ECG (Fine vs coarse)
- Vagal /Adrenergic
- Lone AF

Chronological

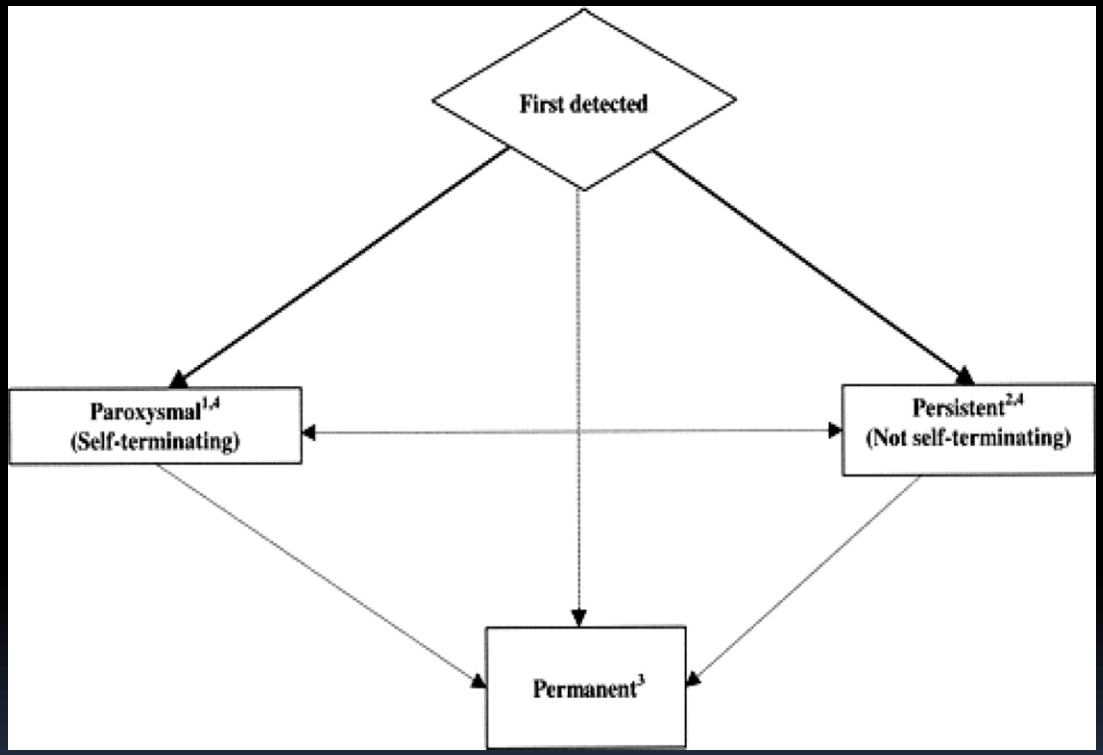


AF –Clinical classification

(Simplified by ACC/AHA/ESC consensus)

< 7 days, Most

< 24 h



> 7 days

> I year

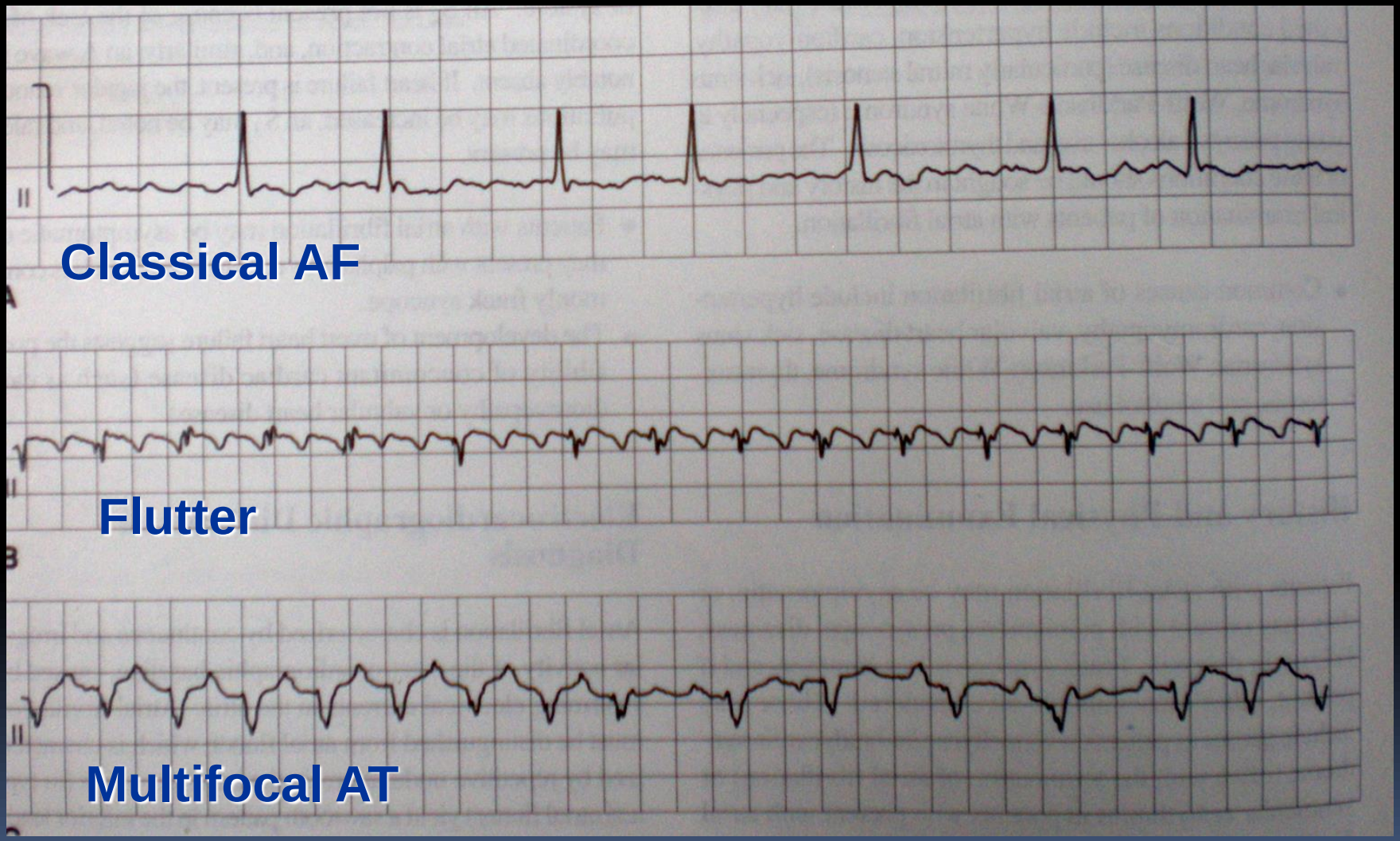
All grades are not mutually exclusive

Lone AF

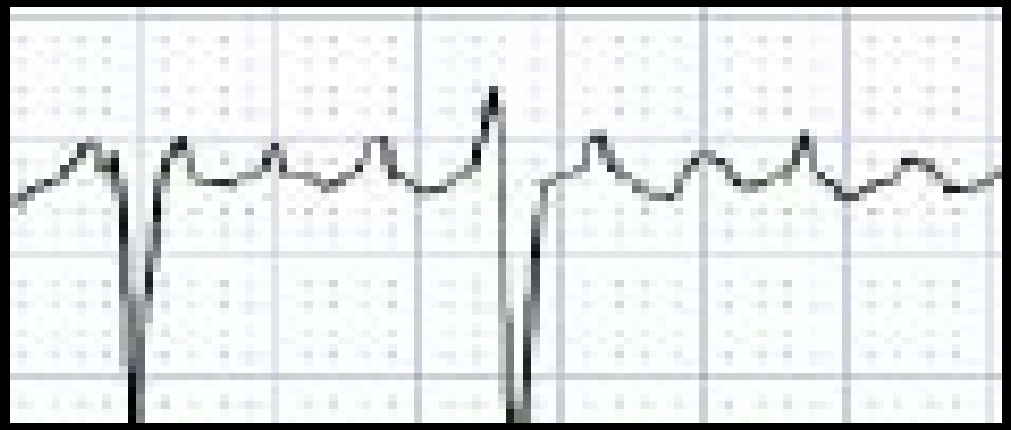
- Less than 60 years
- No clinical or ECG evidence of COPD
- No hypertension
- They have a favorable outcome
- Thrombo embolism and mortality low

ECG features

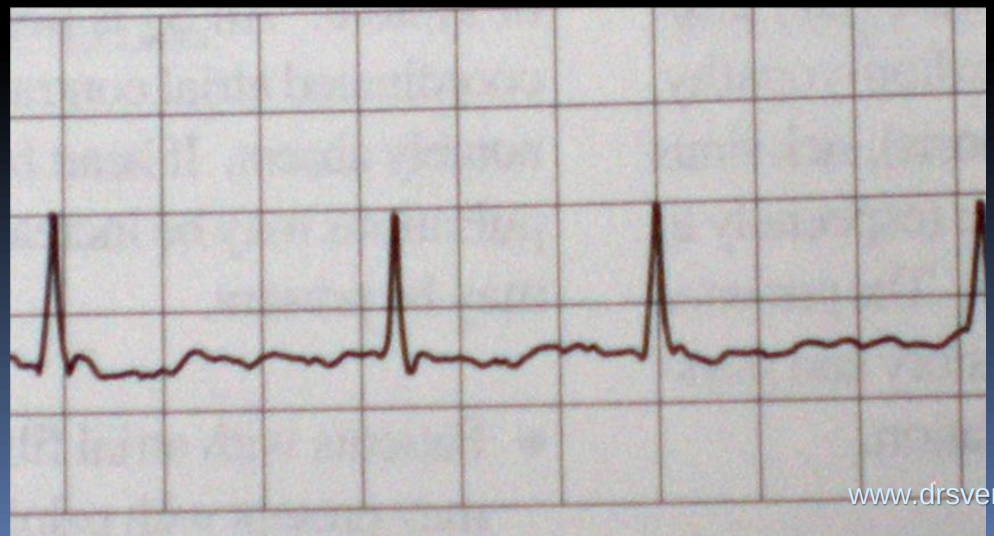
Atrial fibrillation differential diagnosis



Coarse verses fine AF



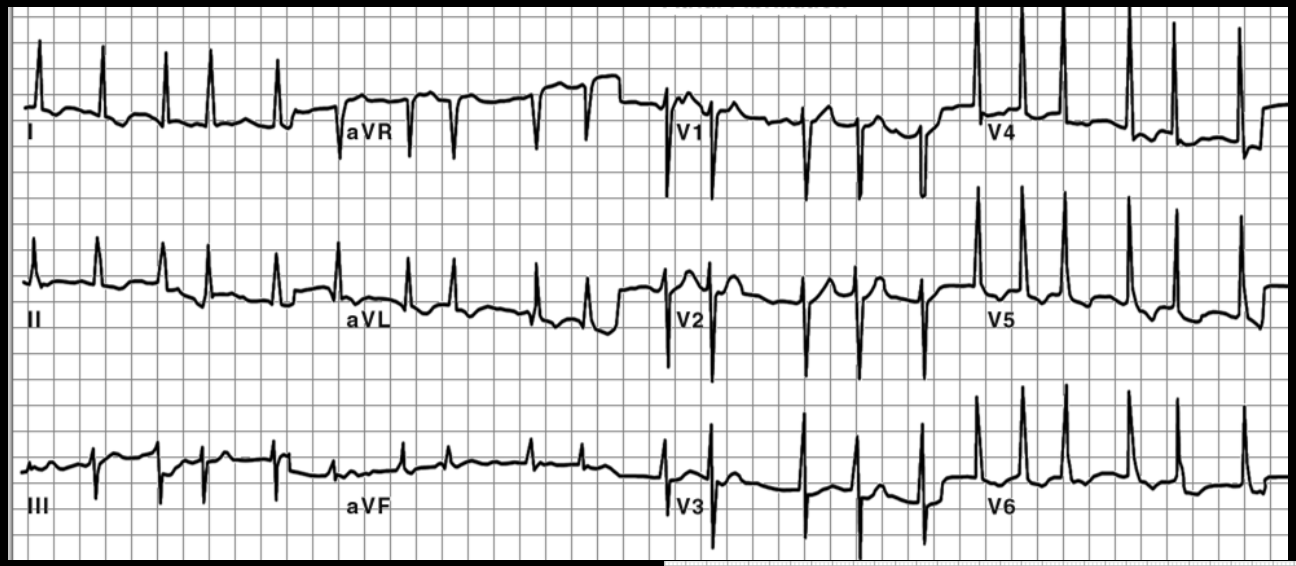
F waves > 0.5mm

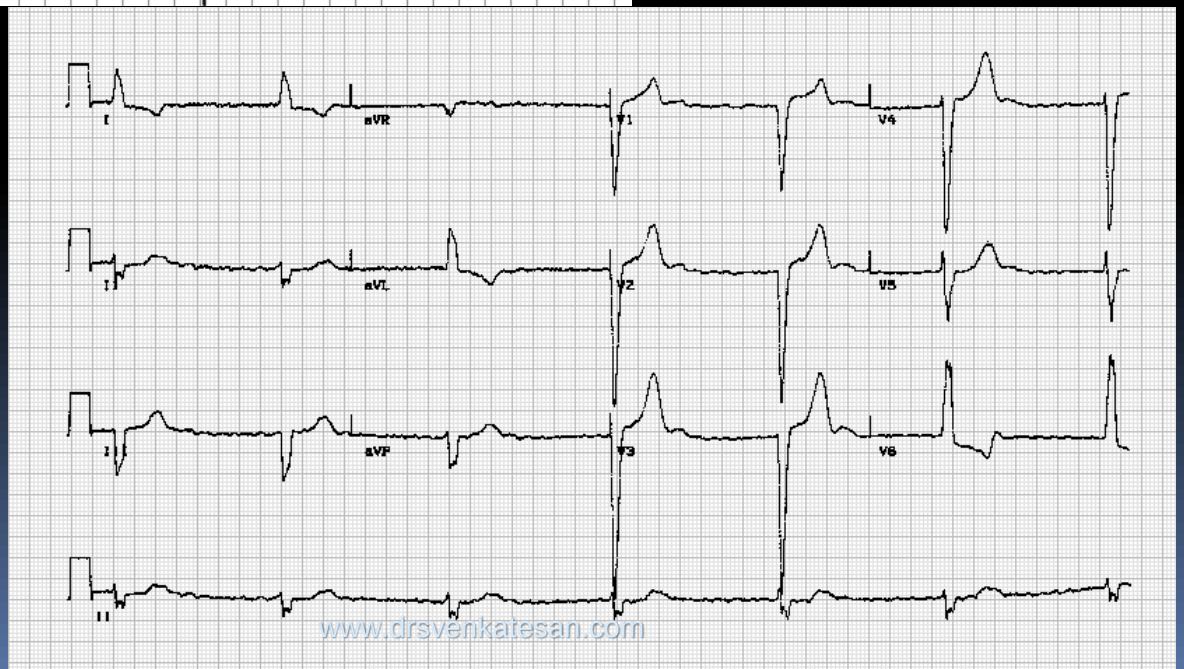


When does ventricular response become regular in AF ?

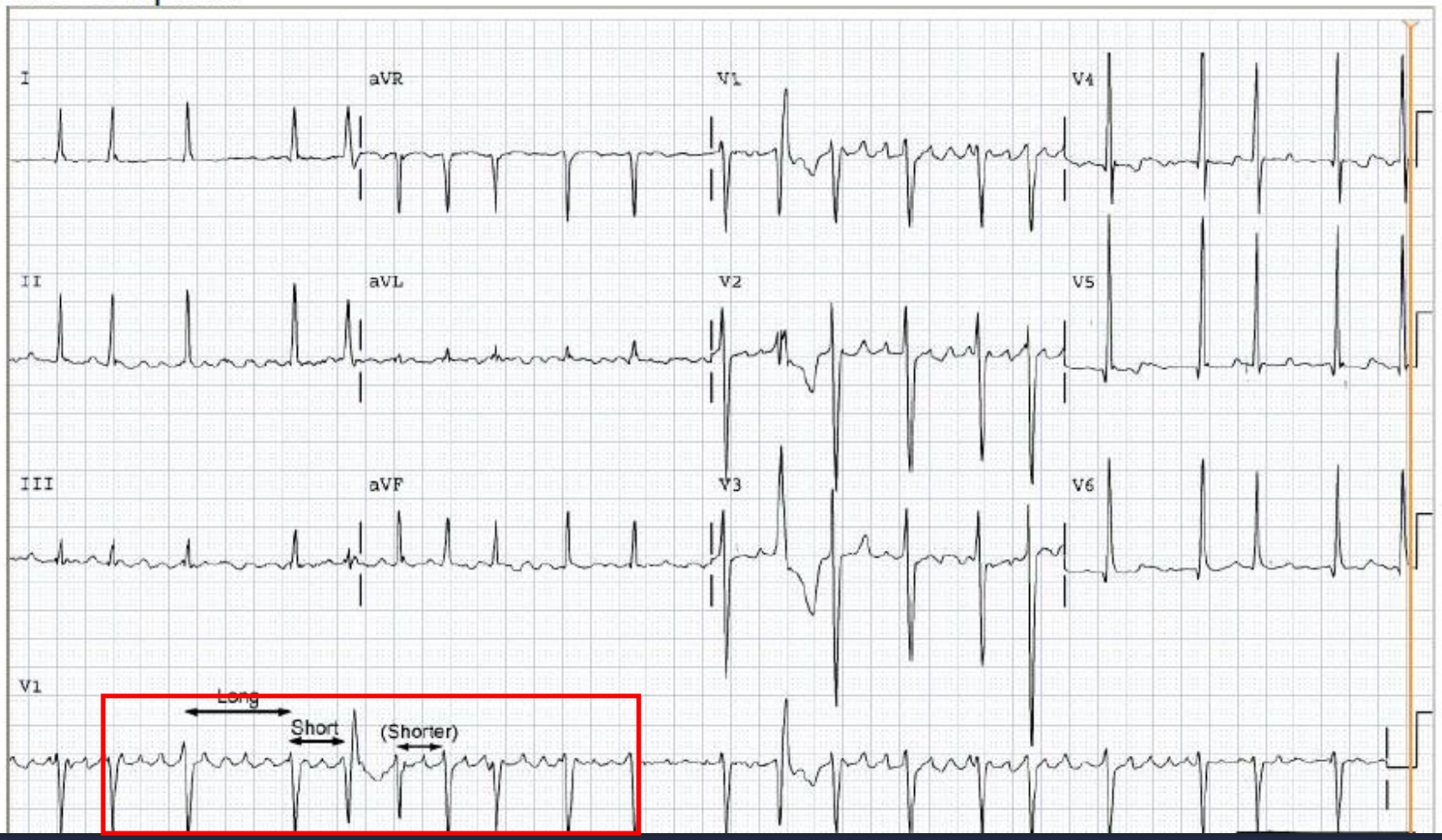
- At very rapid rates or very slow rates
- Conversion to Atrial flutter
- If CHB develop

Atrial fibrillation with CHB

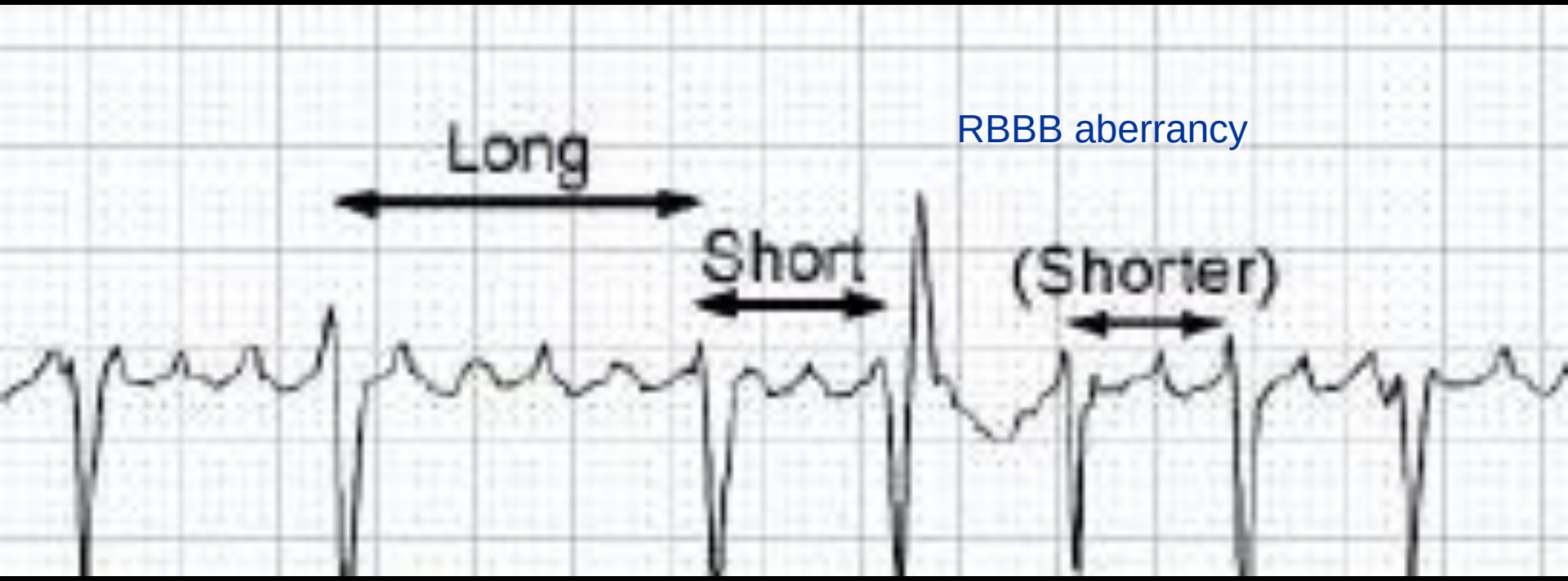




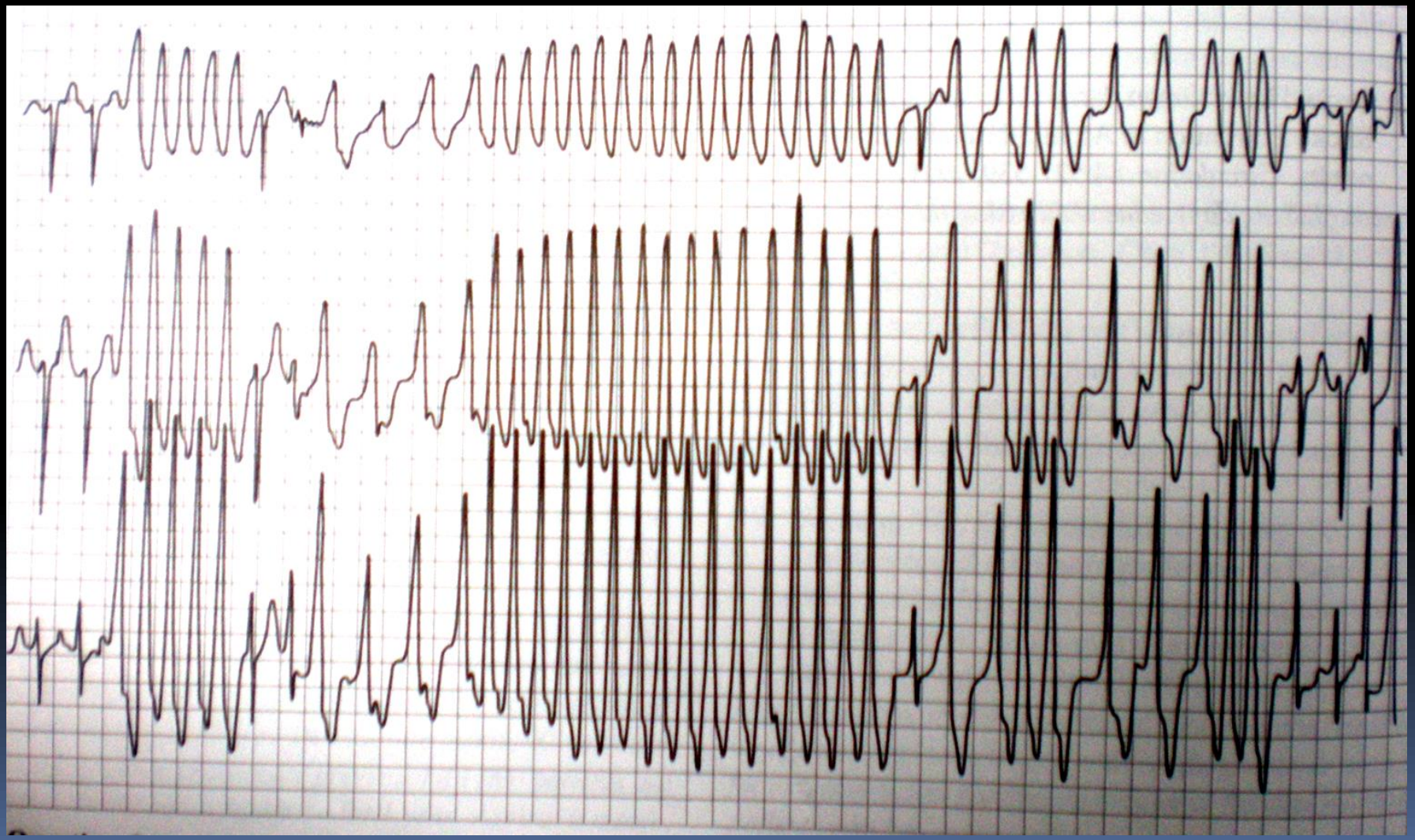
Ashman phenomenon



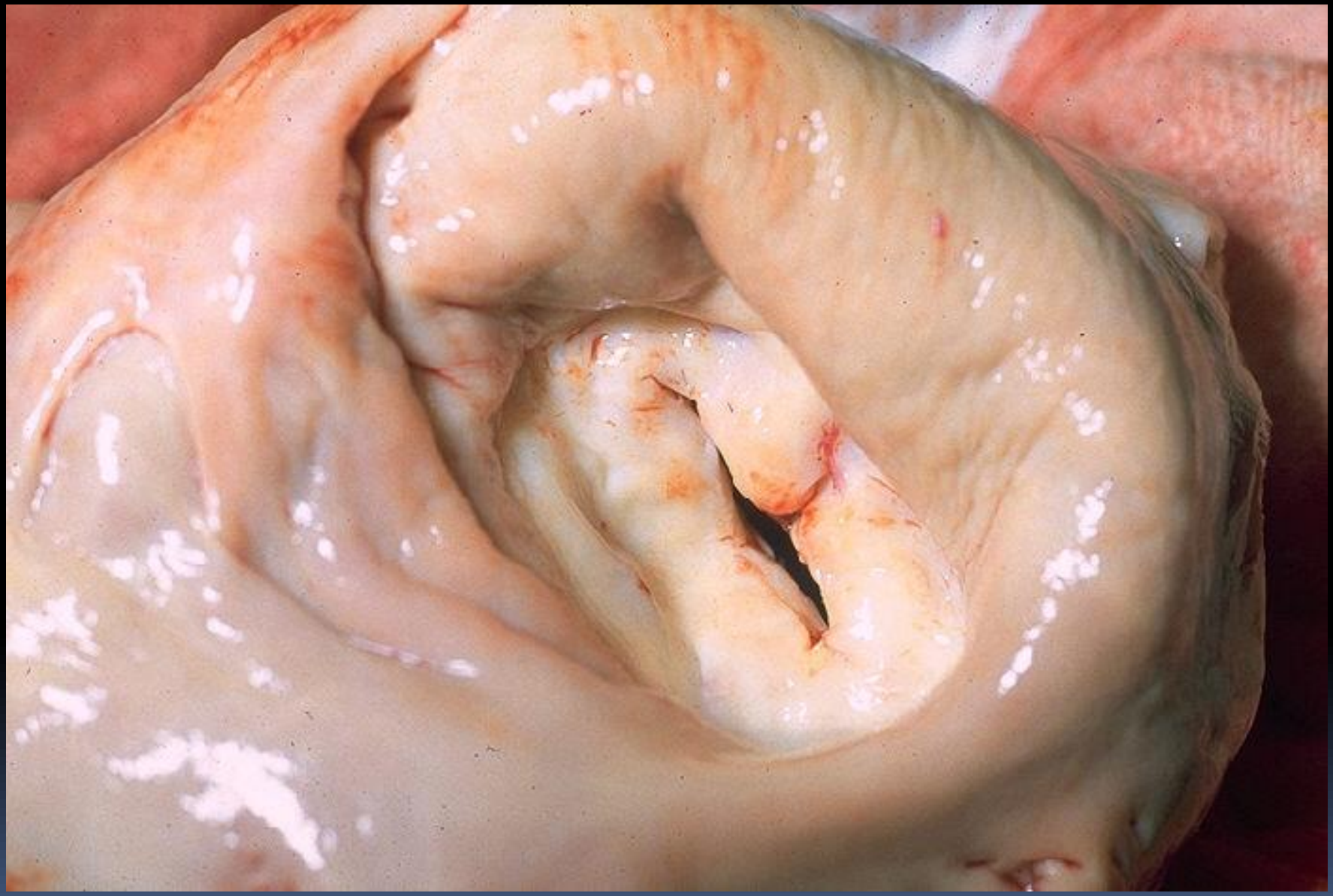
RBBB aberrancy



WPW and Atrial fibrillation



Pathology in AF

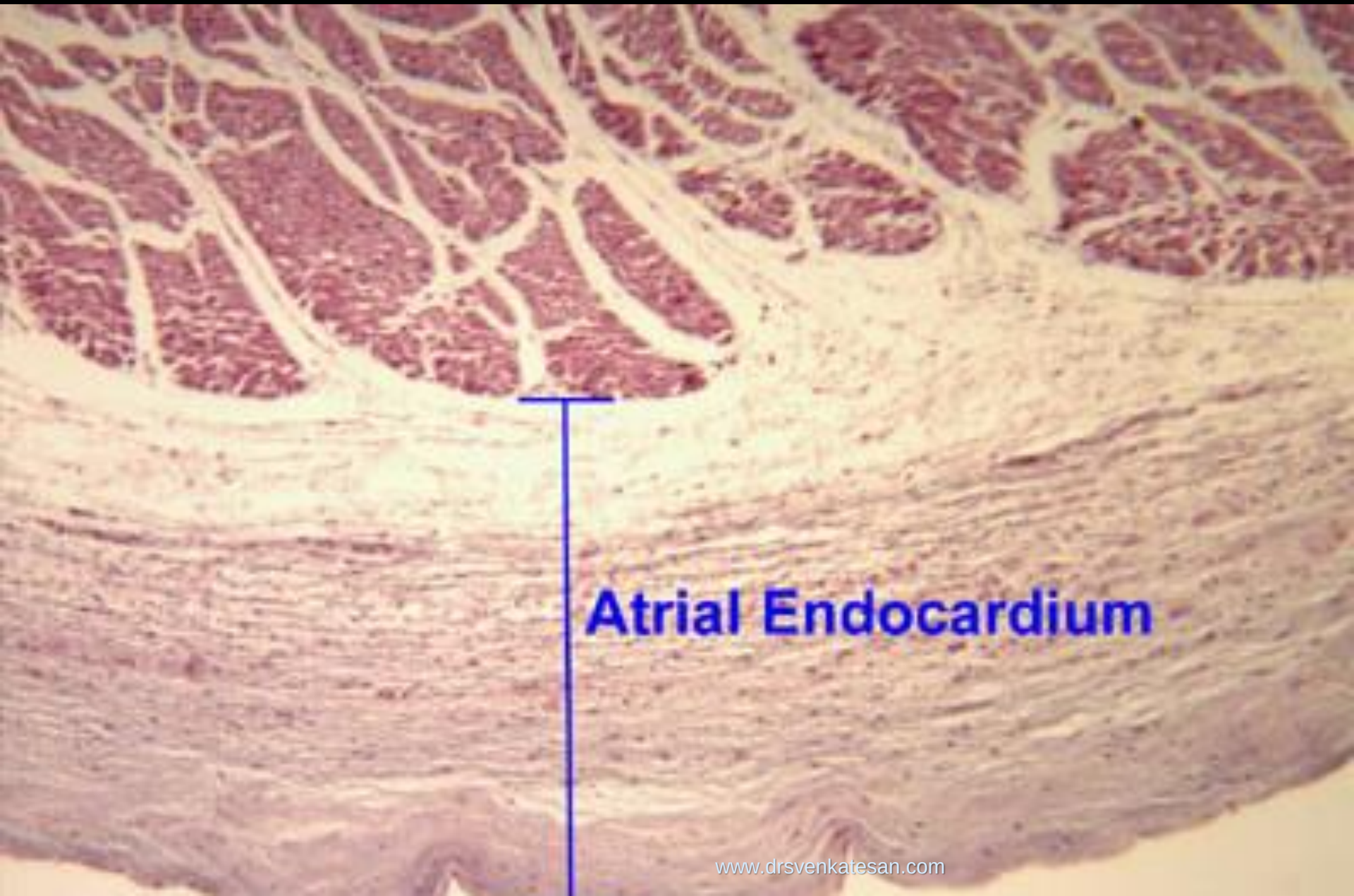


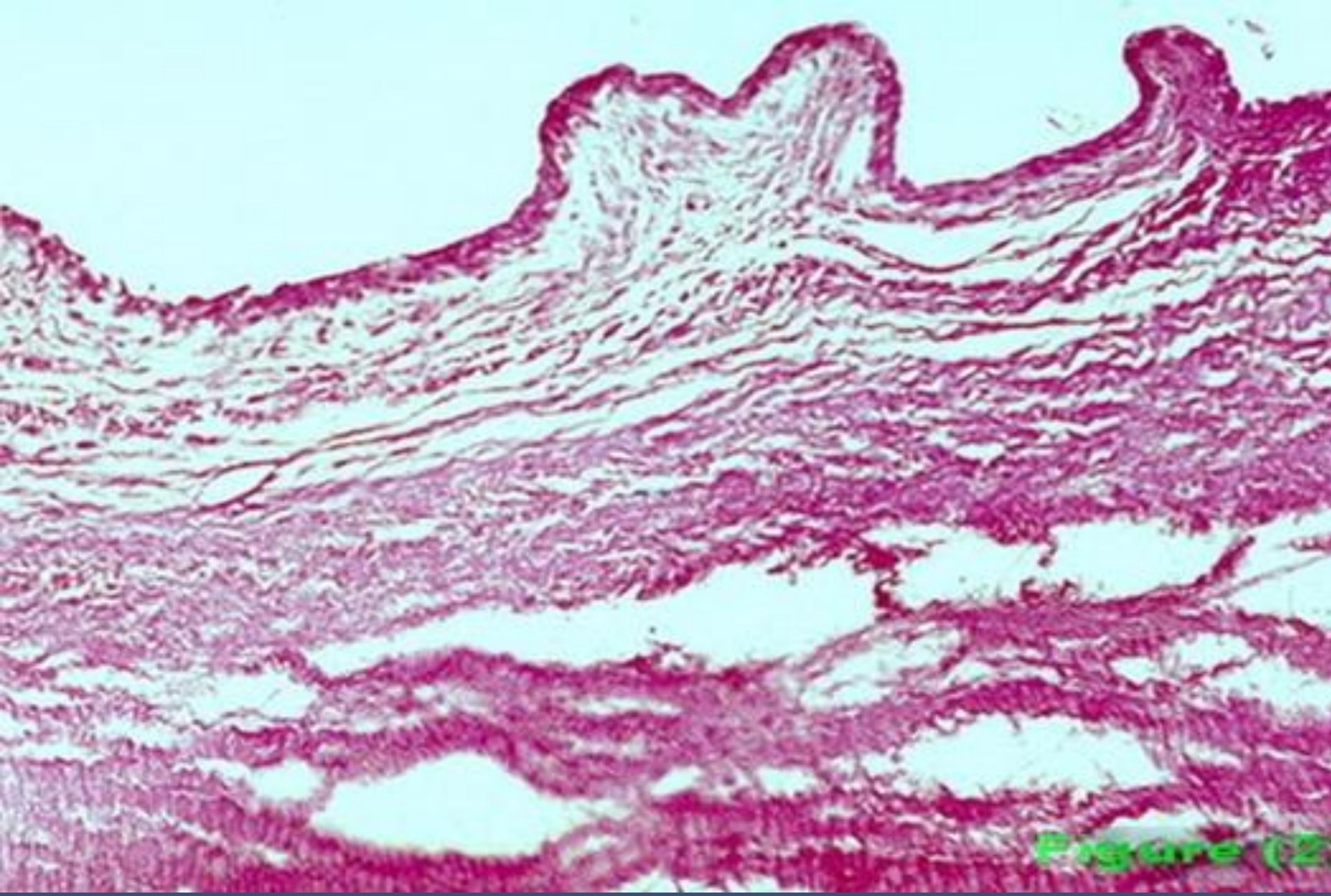
Gross pathology

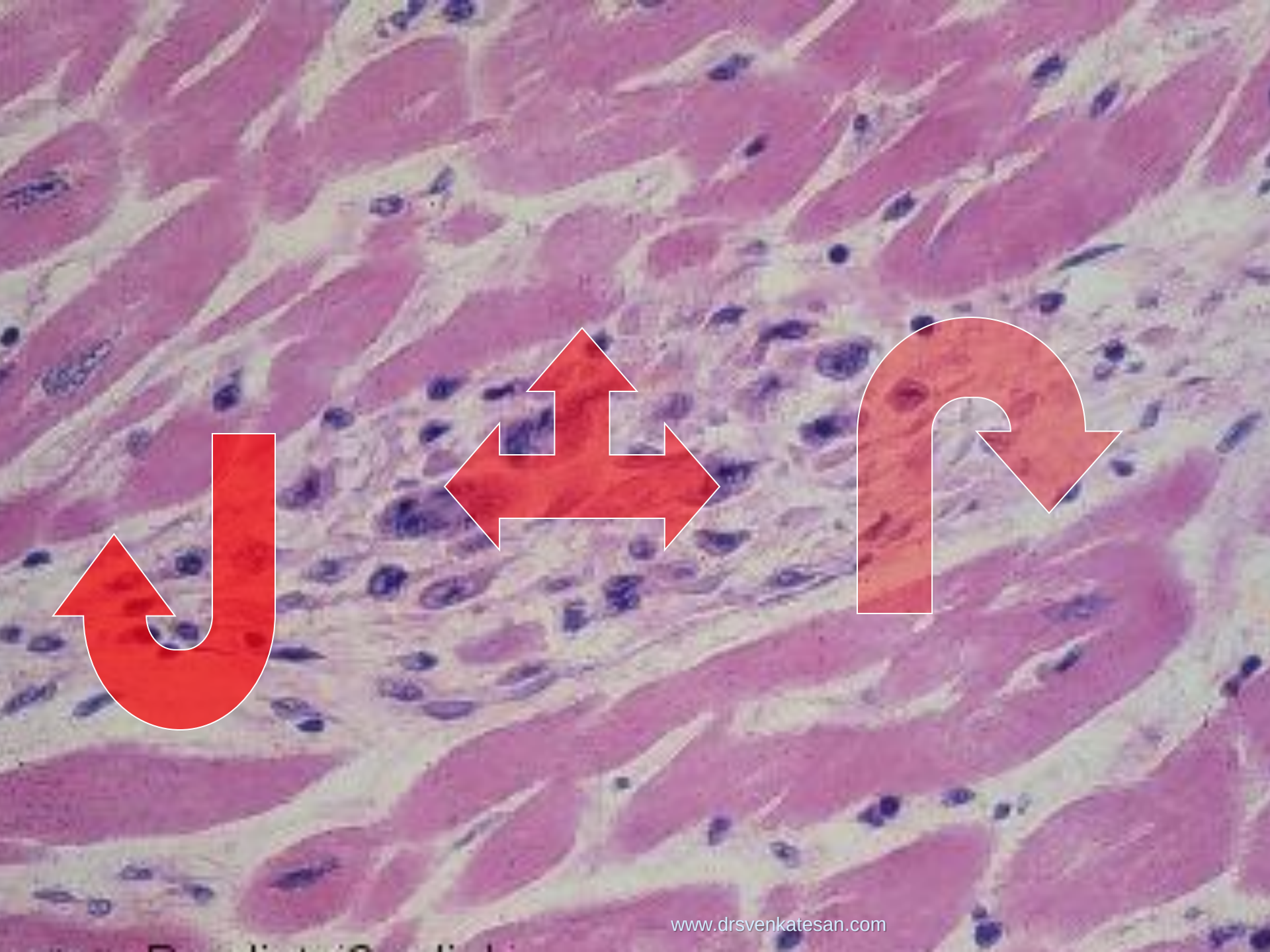
Atrial fibrosis
Loss of atrial muscle mass.
(Accounts for non homogeneity of conduction)

The sinoatrial (SA) and AV node involvement
(accounts for the sick sinus syndrome and AV block)

Normal atrial wall

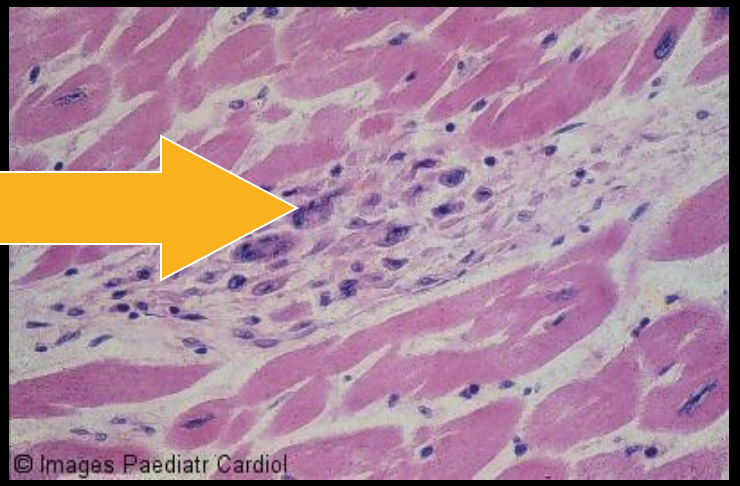






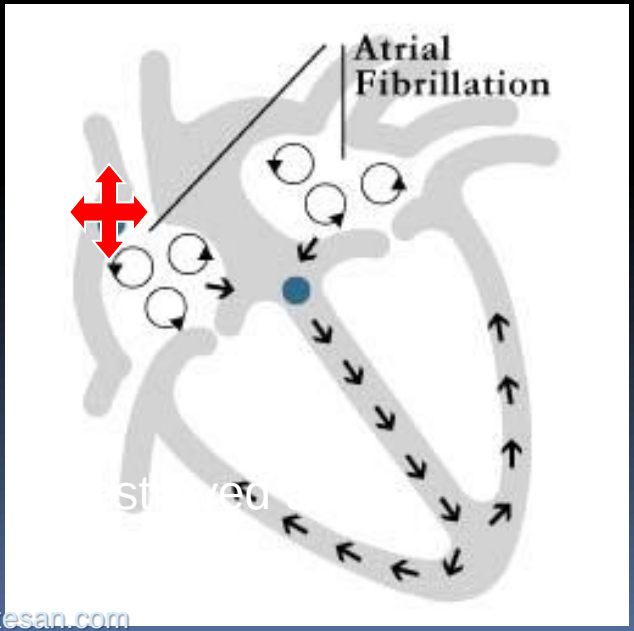
Link between SND and AF

Atrial interstitial fibrosis



Unidirectional or multidirectional block

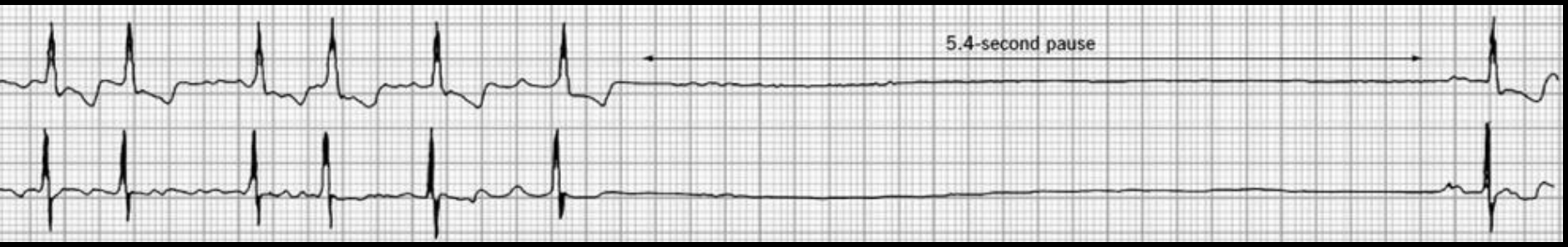
SA node also involved in fibrosis



One proposal suggests In every chronic AF SA node
AF is default irregular escape rhythm from atria

AF as a part of SND

Tachy brady syndrome

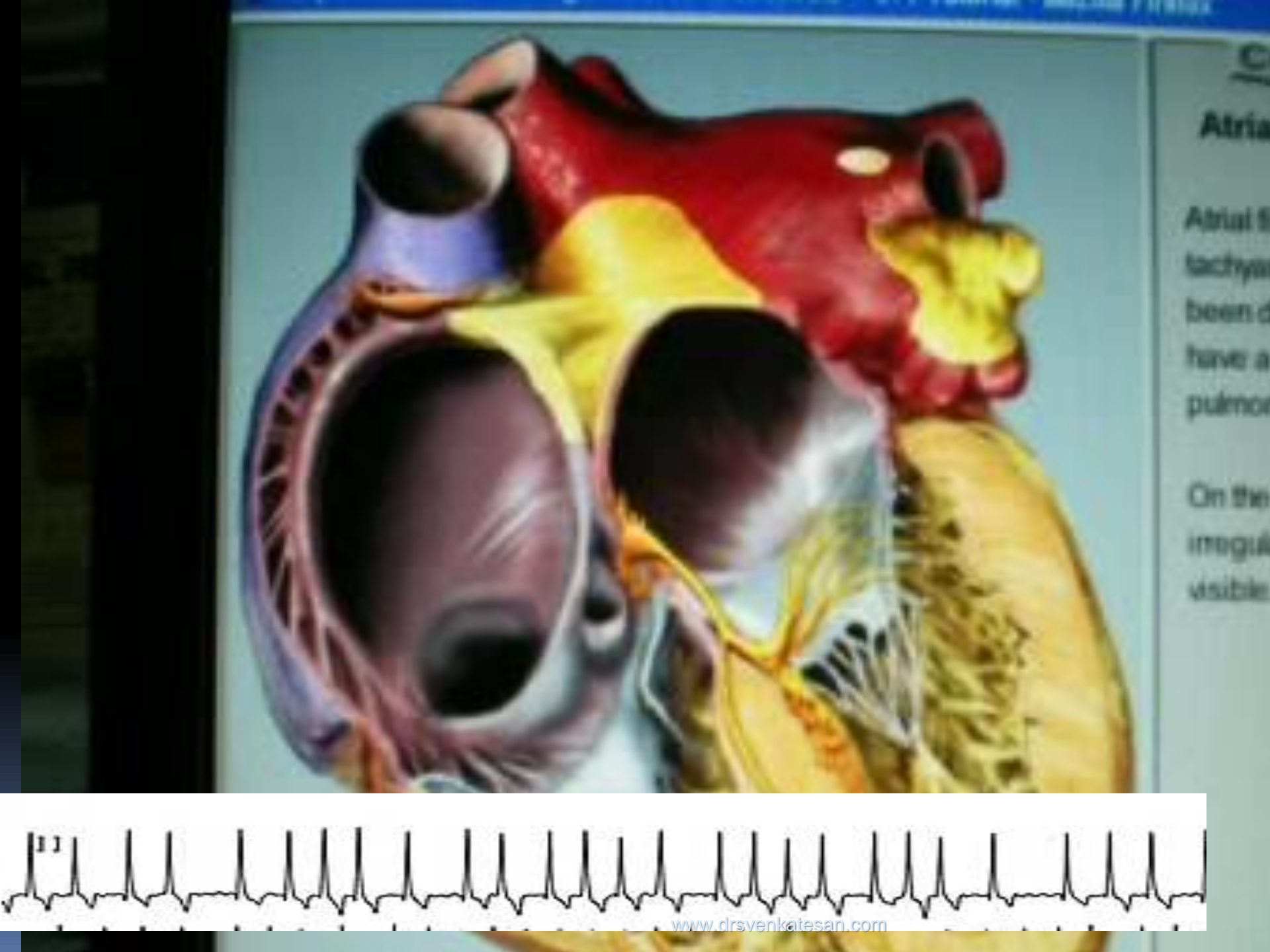


Mechanism & Electrophysiology

Atrial fibrillation what initiates ?

- APDs
- Short runs of ectopic AT
- Multifocal AT
- Pre AF
- Flutter fibrillation
- Fibrillation

May appear without any preceding arrhythmia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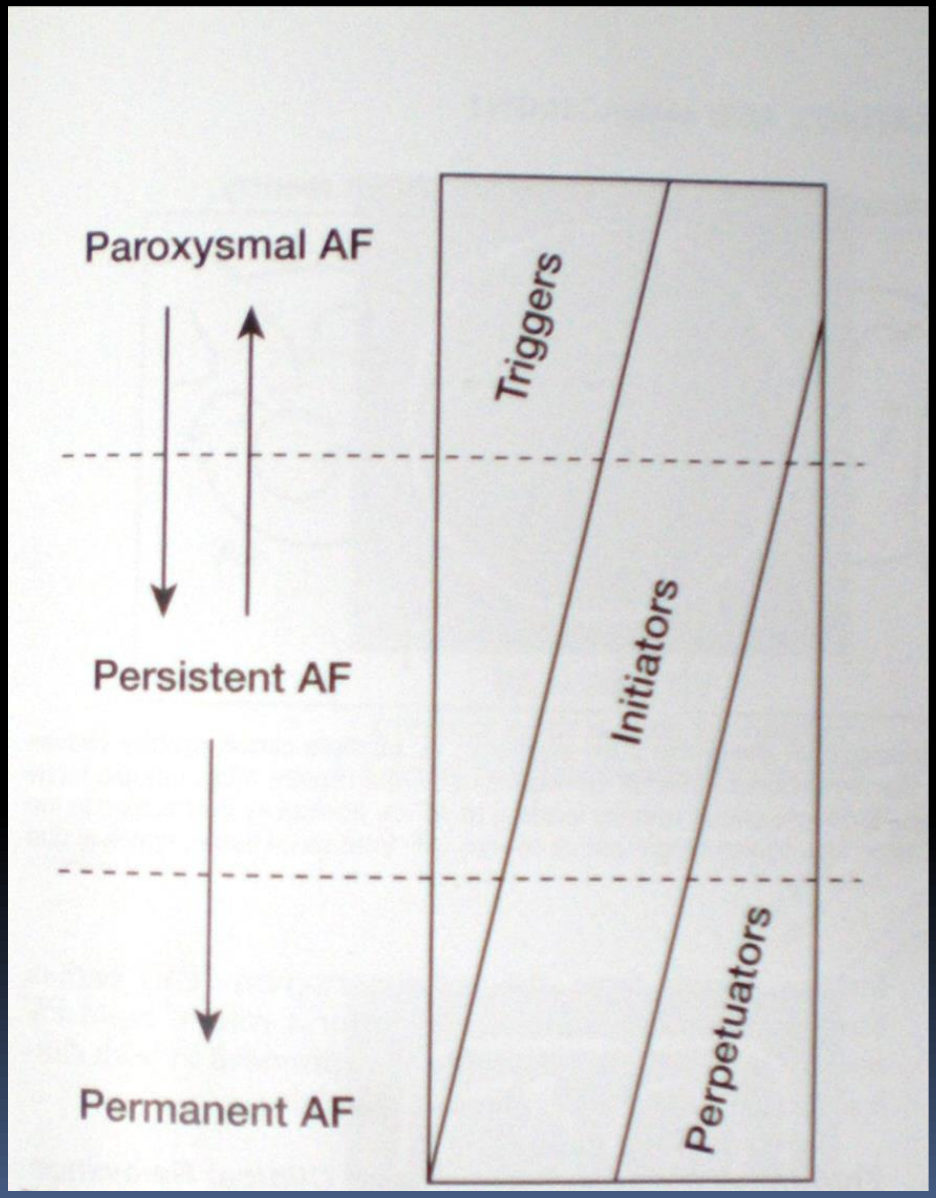


Triggers

Atrial ectopics

Myocardial ischemia

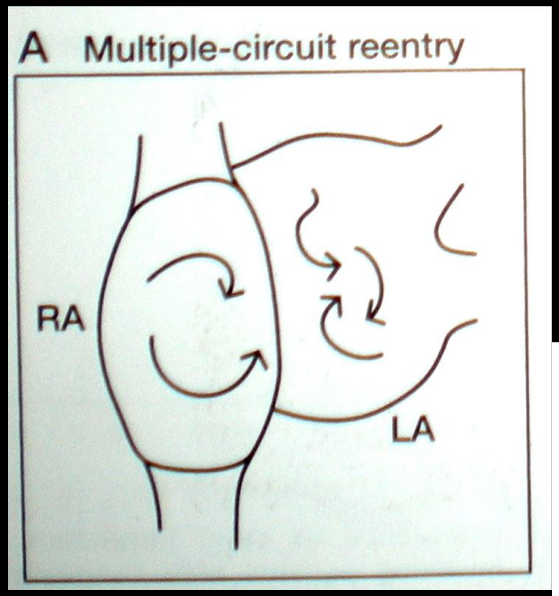
Acidosis

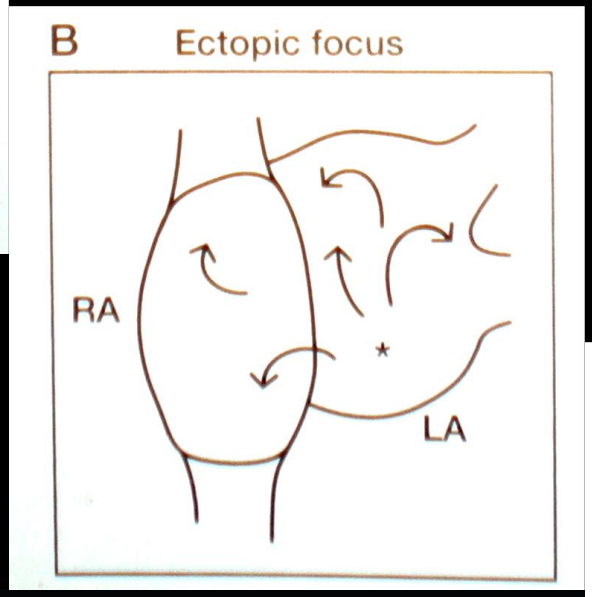
Hypoxia

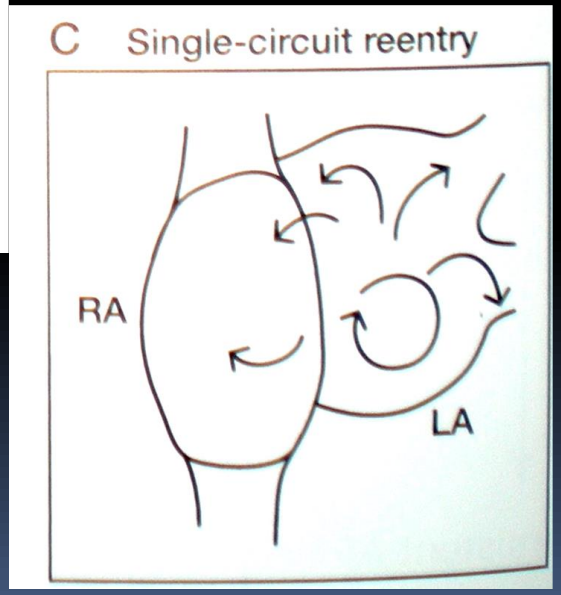
Perpetuators

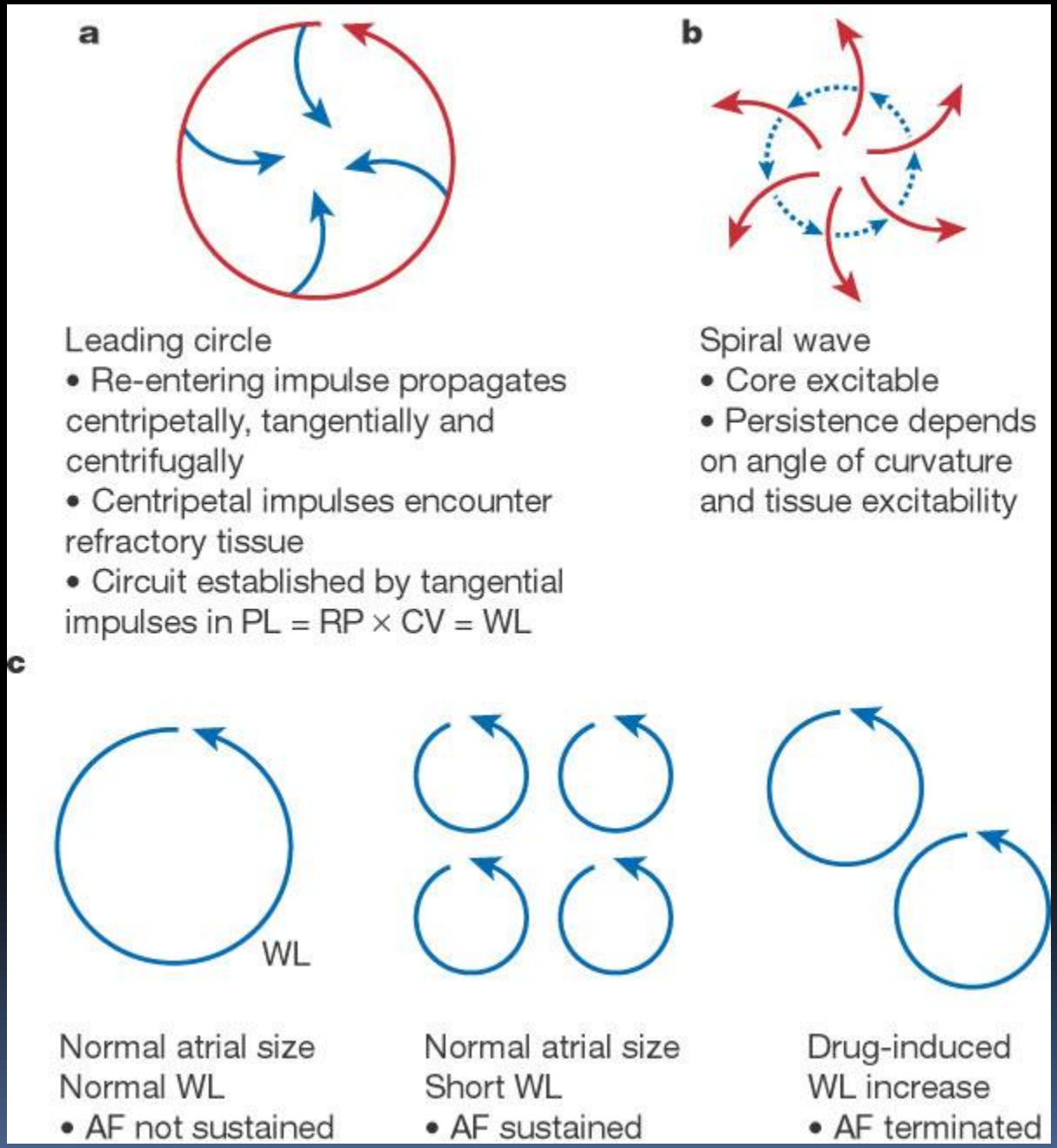
Anatomical remodeling

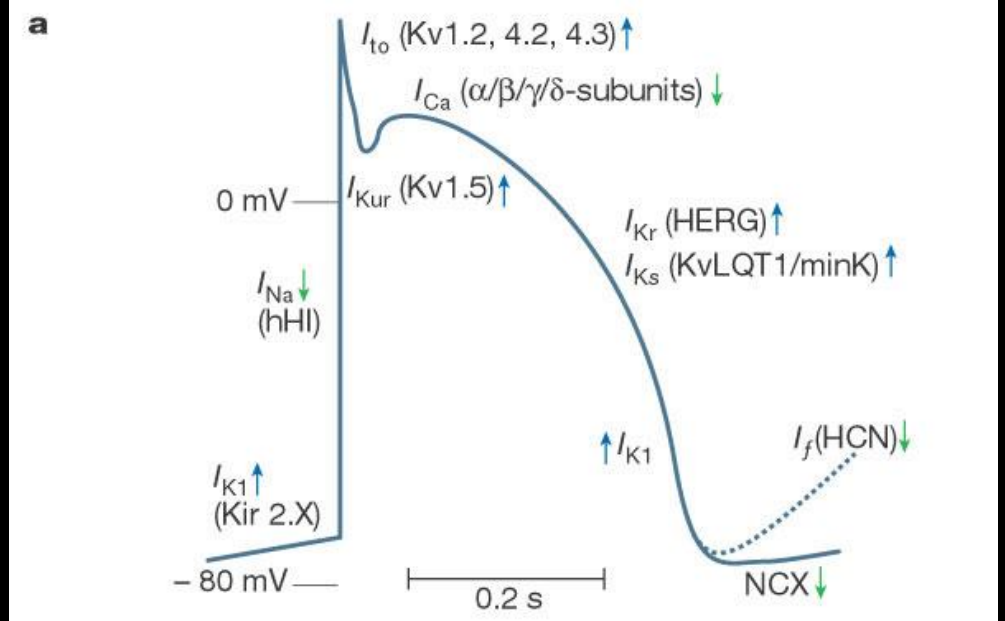
Atrial fibrosis

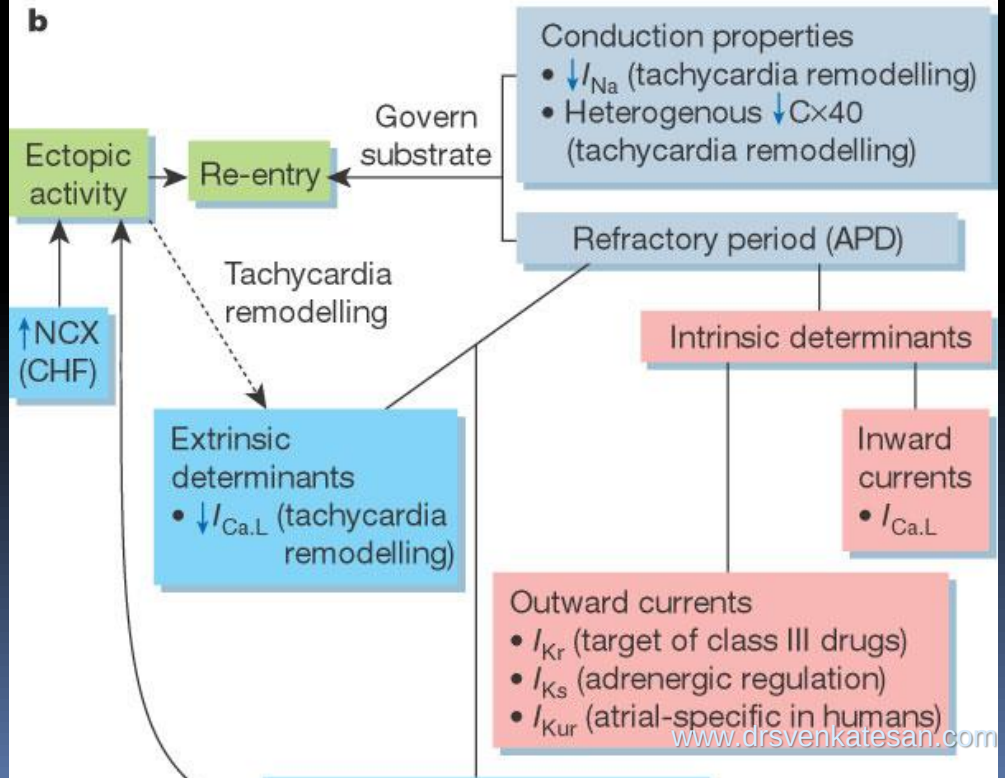

A Multiple-circuit reentry
RA
LA


B Ectopic focus
RA
LA

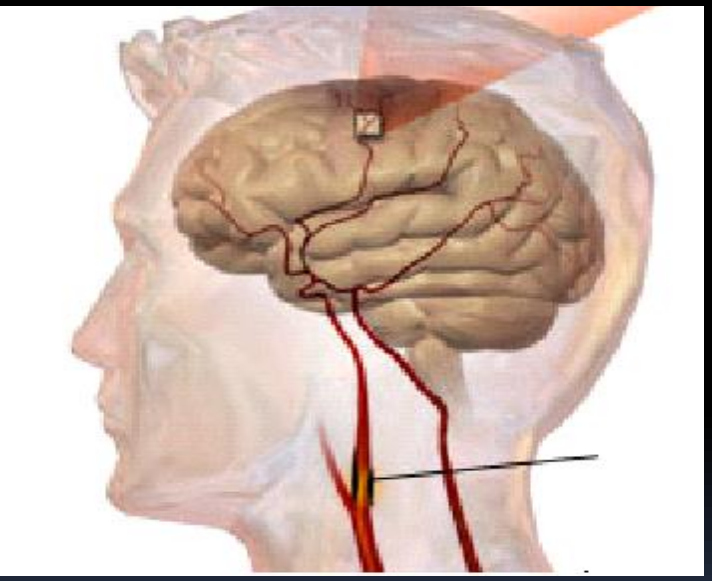

C Single-circuit reentry
RA
LA

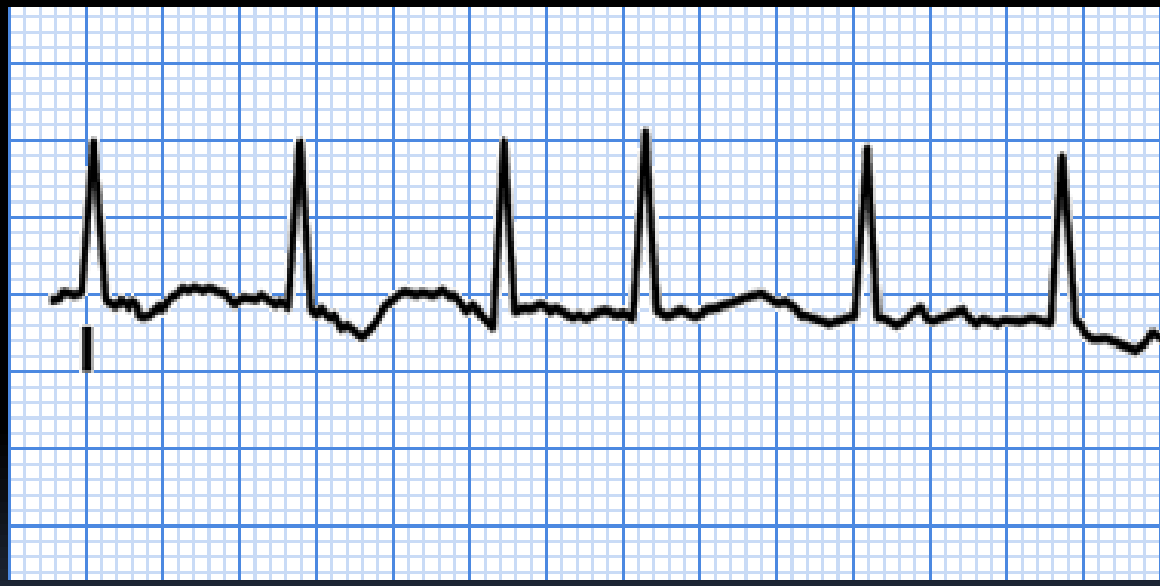

a
b
Leading circle
• Re-entering impulse propagates centripetally, tangentially and centrifugally
• Centripetal impulses encounter refractory tissue
• Circuit established by tangential impulses in PL = RP × CV = WL
Spiral wave
• Core excitable
• Persistence depends on angle of curvature and tissue excitability
c
WL
Normal atrial size
Normal WL
• AF not sustained
Normal atrial size
Short WL
• AF sustained
Drug-induced
WL increase
• AF terminated





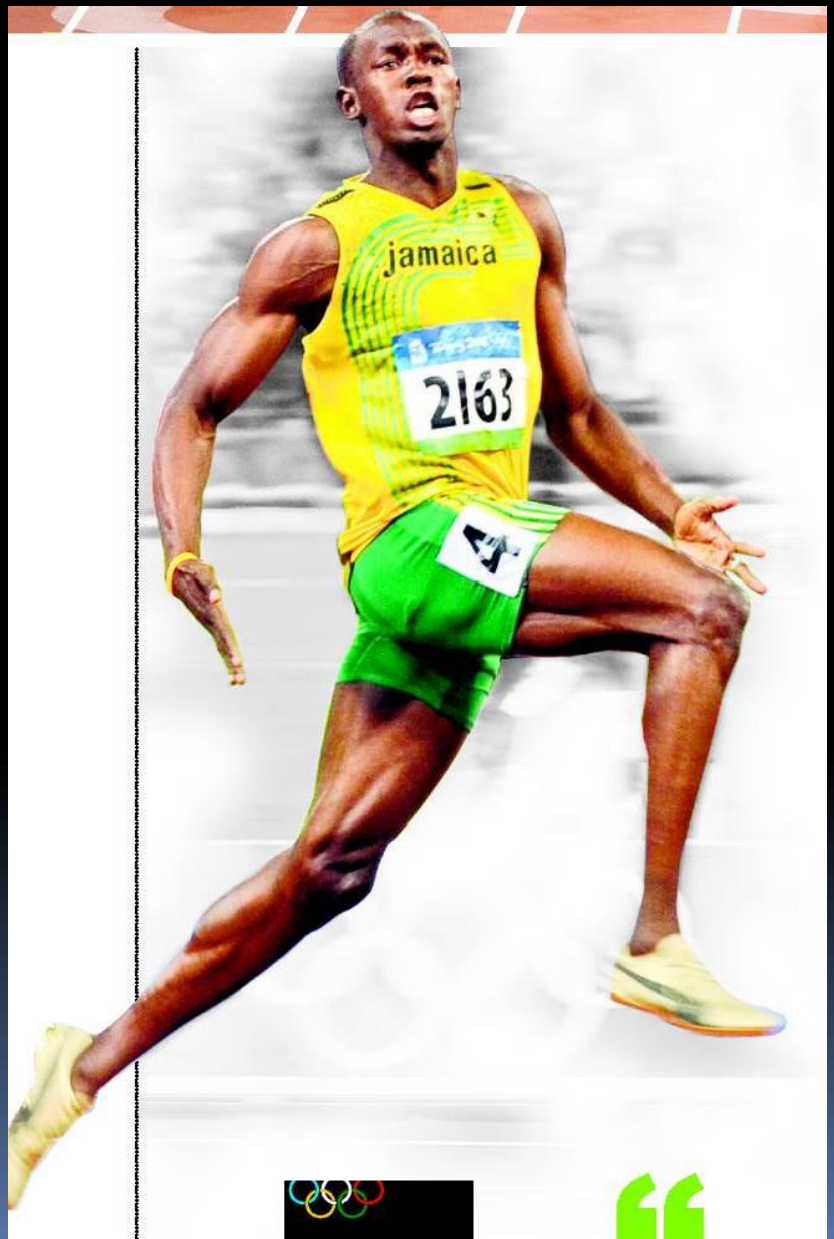
Autonomic modulation of Atrial fibrillation





Vagal / Adrenergic

Athlete's heart

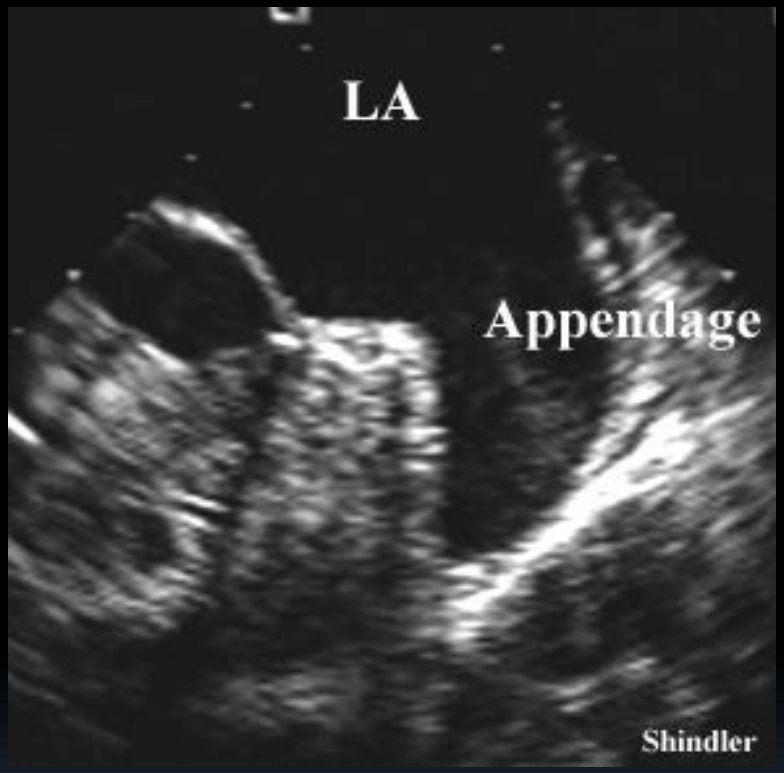


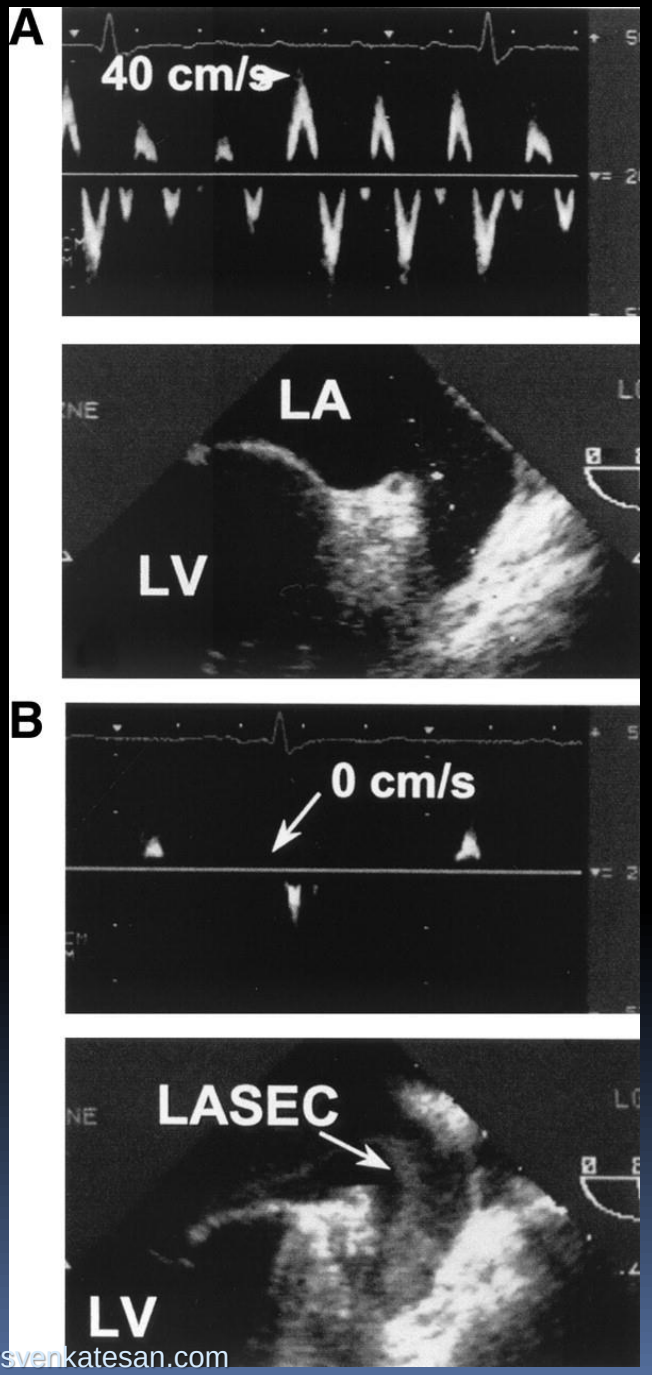
Endurance athletes

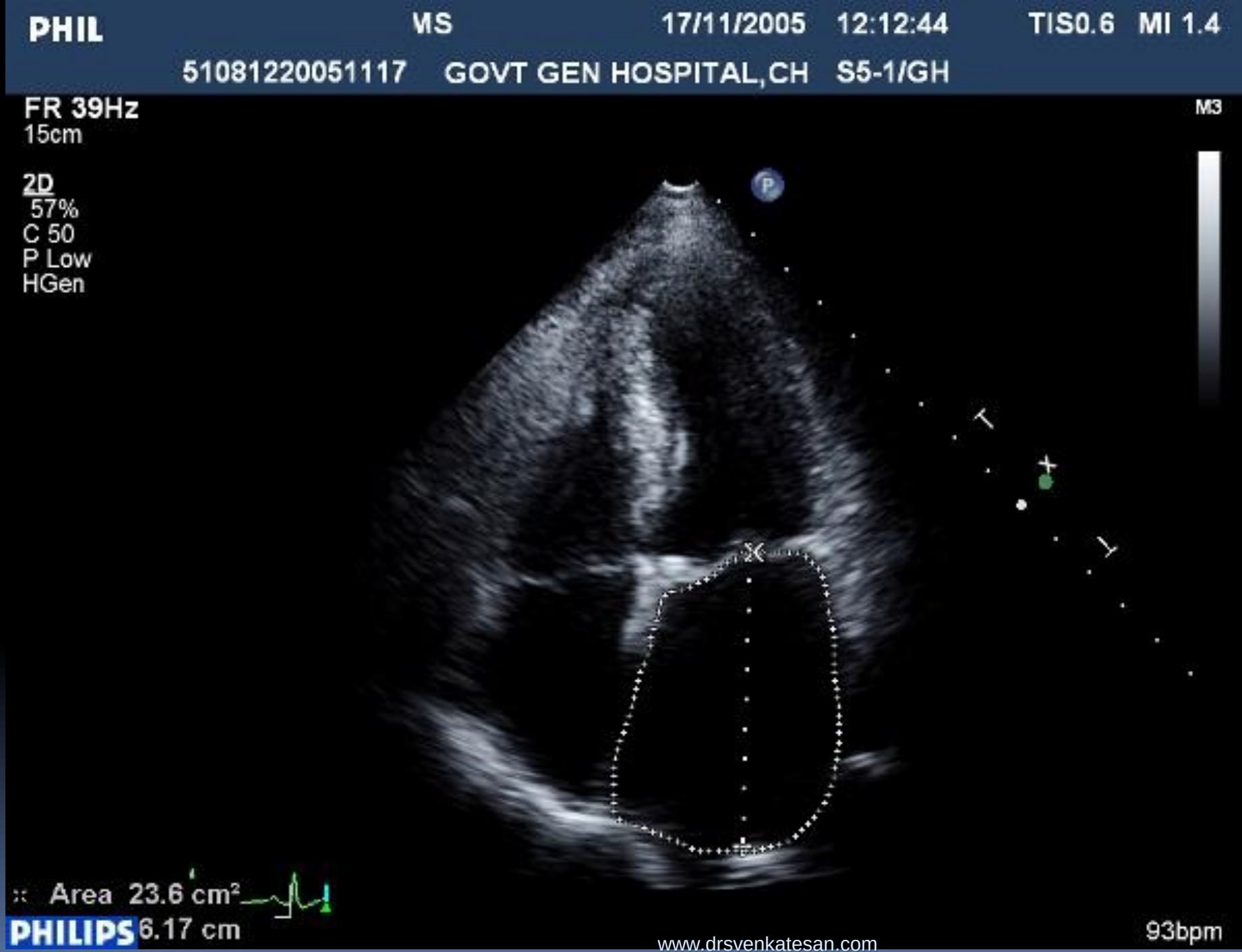
- Dilated atria /LVH
- High vagal tone
- Surges of catecholamines
- Precipitate re-entrant rhythms
- Paroxysmal AF

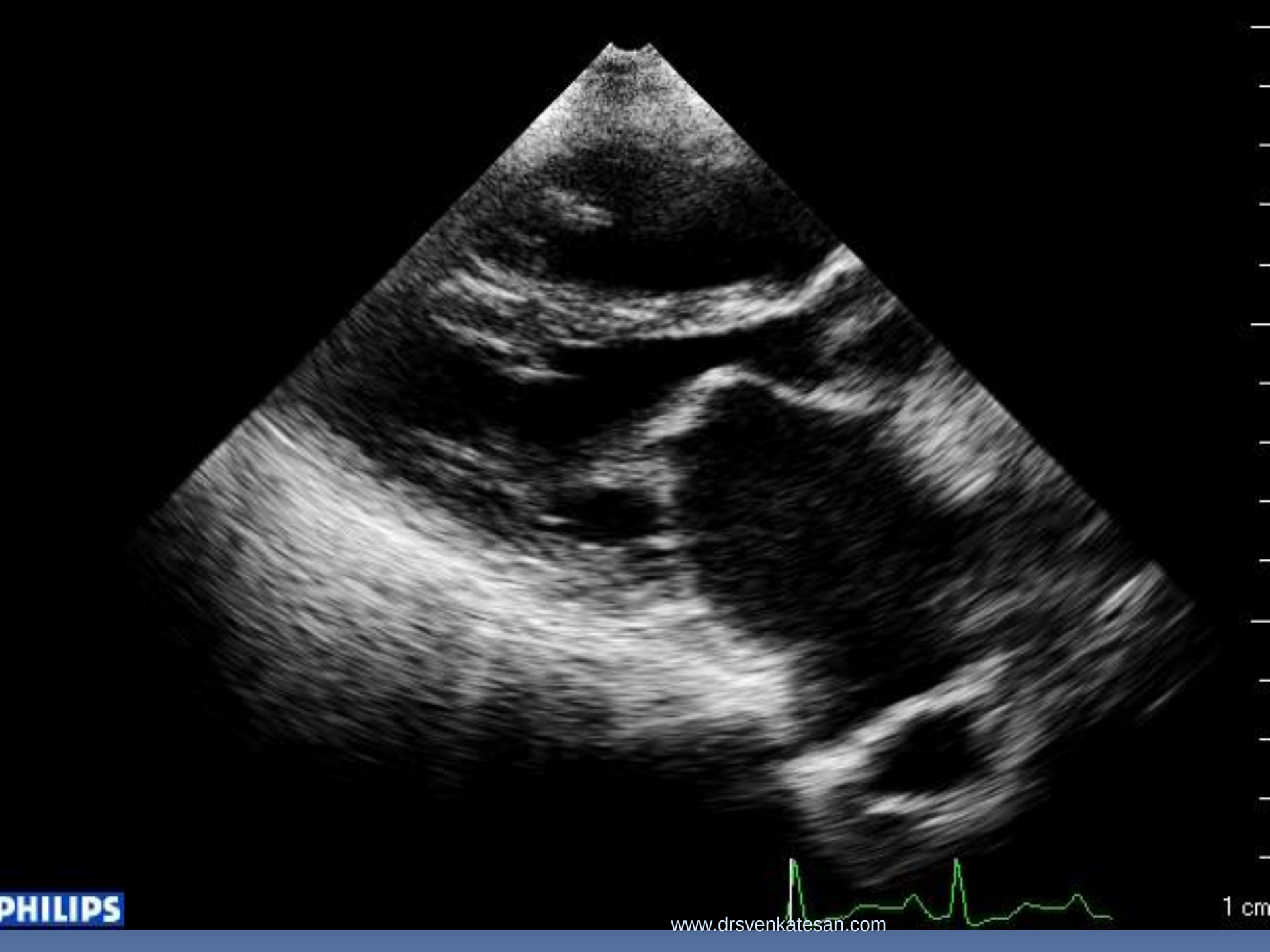
Atrial fibrillation effect on left atrial hemodynamics

LAA appendage velocity








PHILIPS
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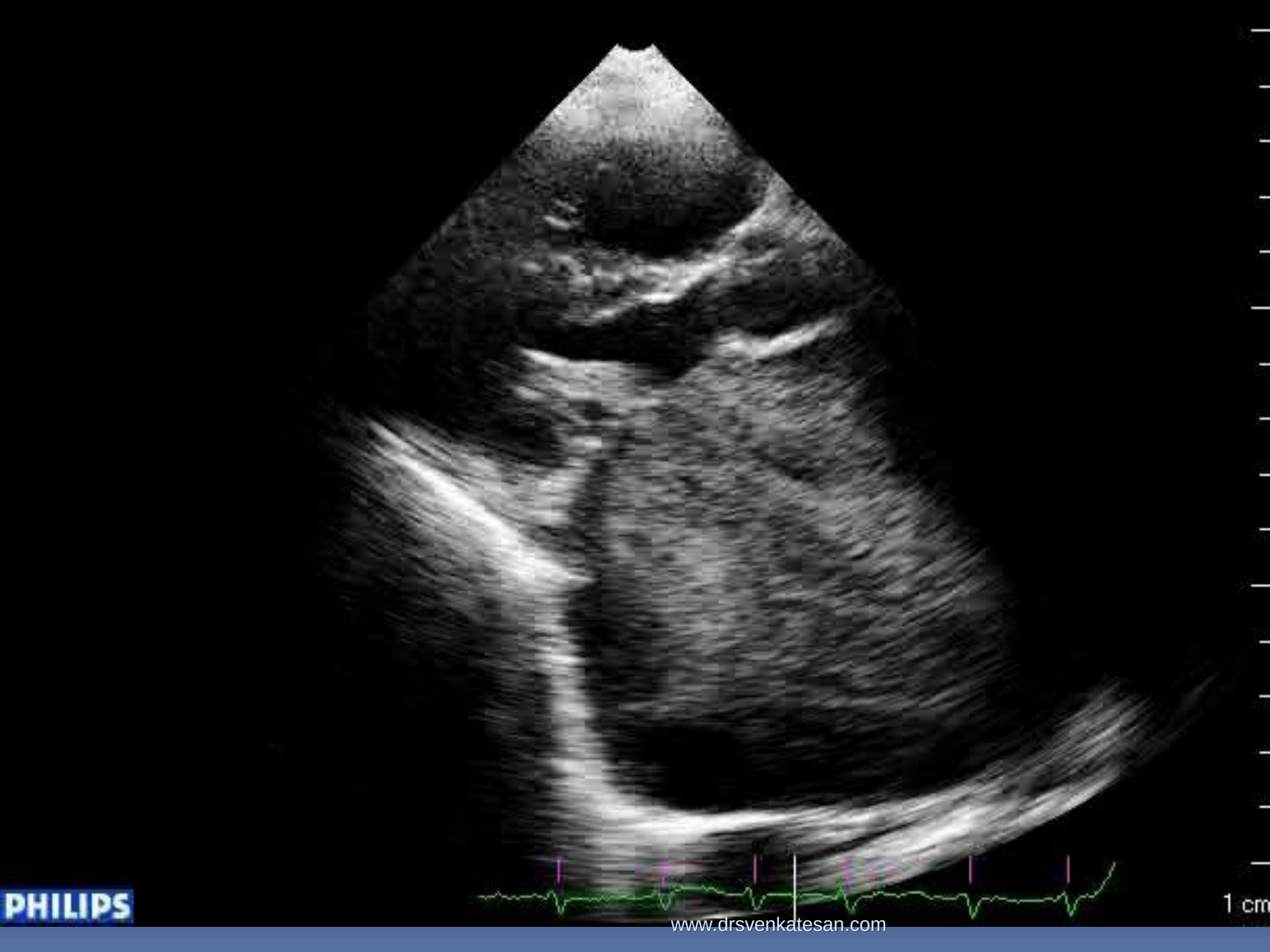
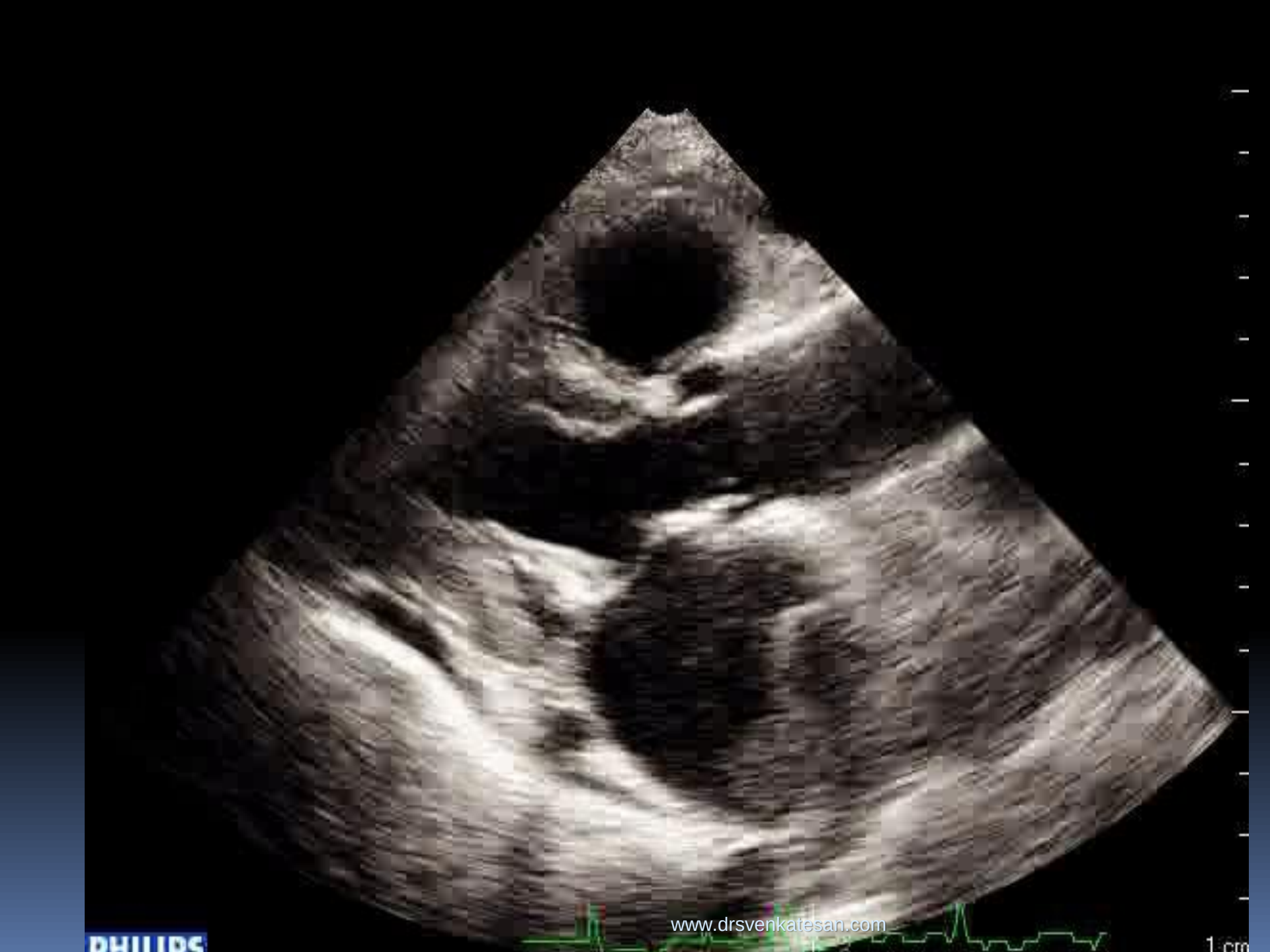

PHILIPS
1 cm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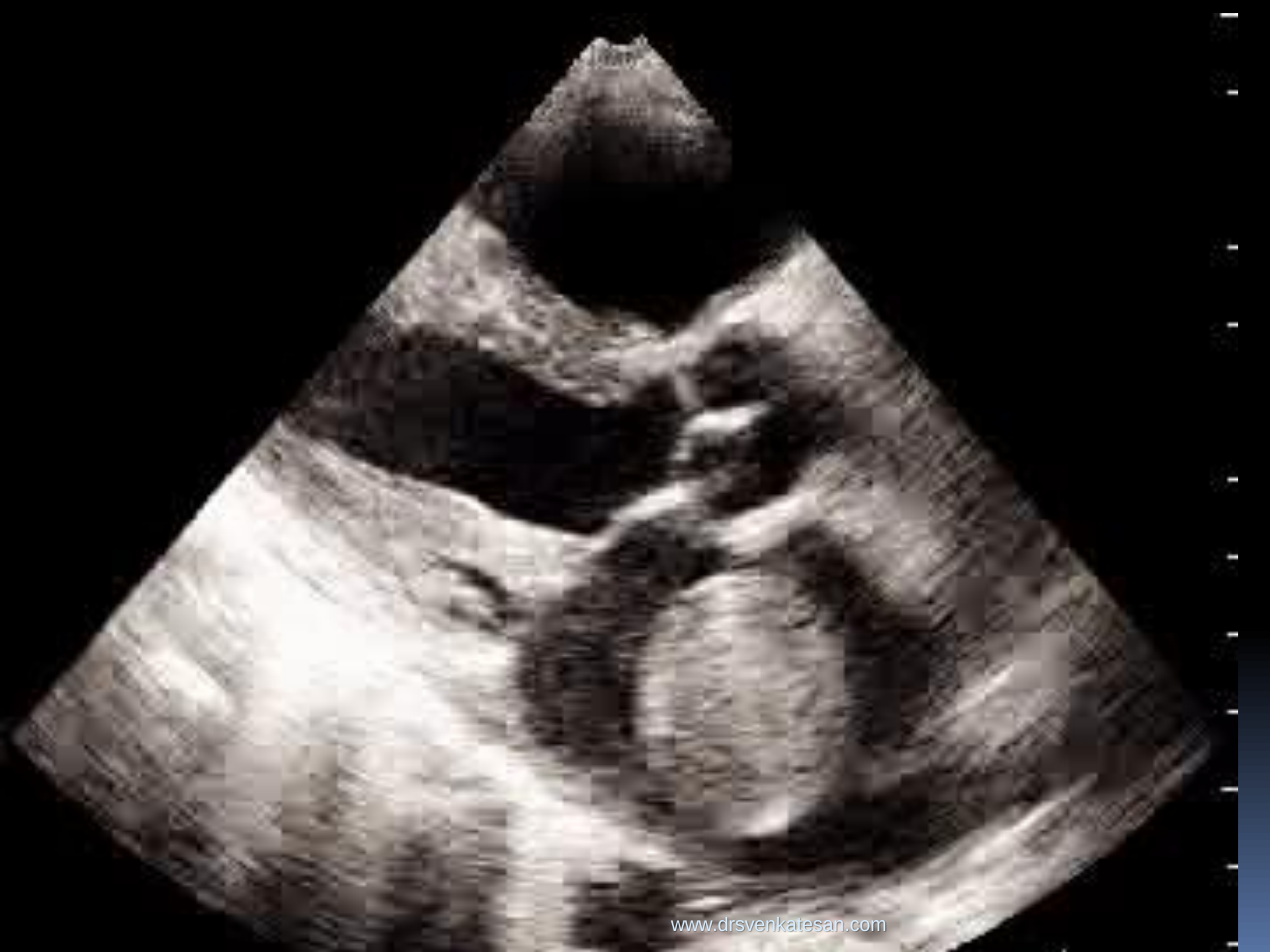
www.drsvenkatesan.com
1 cm


www.drsvenkatesan.com

Management of Atrial fibrillation

Diagnostic work up

- History ,(Alcohol, Thyroid)
- Clinical examination
- ECG
- X-ray
- Echocardiography-TTE, TTE
- Thyroid profile
- Holter

Western

- Elderly
- HT
- CAD
- COPD
- Valvular

Indian

- Valvular
- CAD
- HT
- Elderly

Acute management

- Cardiac
- Non cardiac

Emergency management of AF

Cardiac

ACS – STEMI
SHT
DCM
HOCM
Pericarditis

Non cardiac

COPD
Pneumonia
Thyrotoxicosis
Electrolytes
Peri operative
Hypoxia

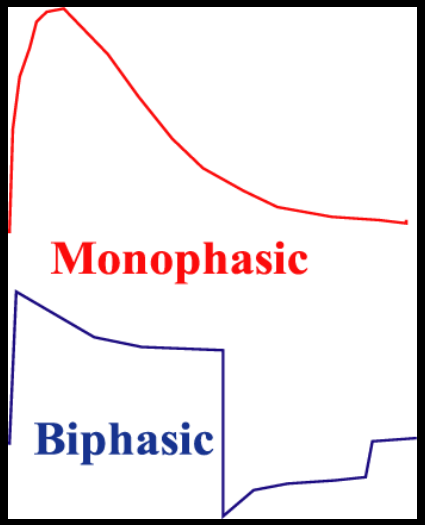
AF in Acute myocardial infarction

- DC shock
- IV Amiodarone
- IV Beta blocker

(With Unfractioned heparin)

- Very transient AFs left alone.

DC Cardioversion



200-300J

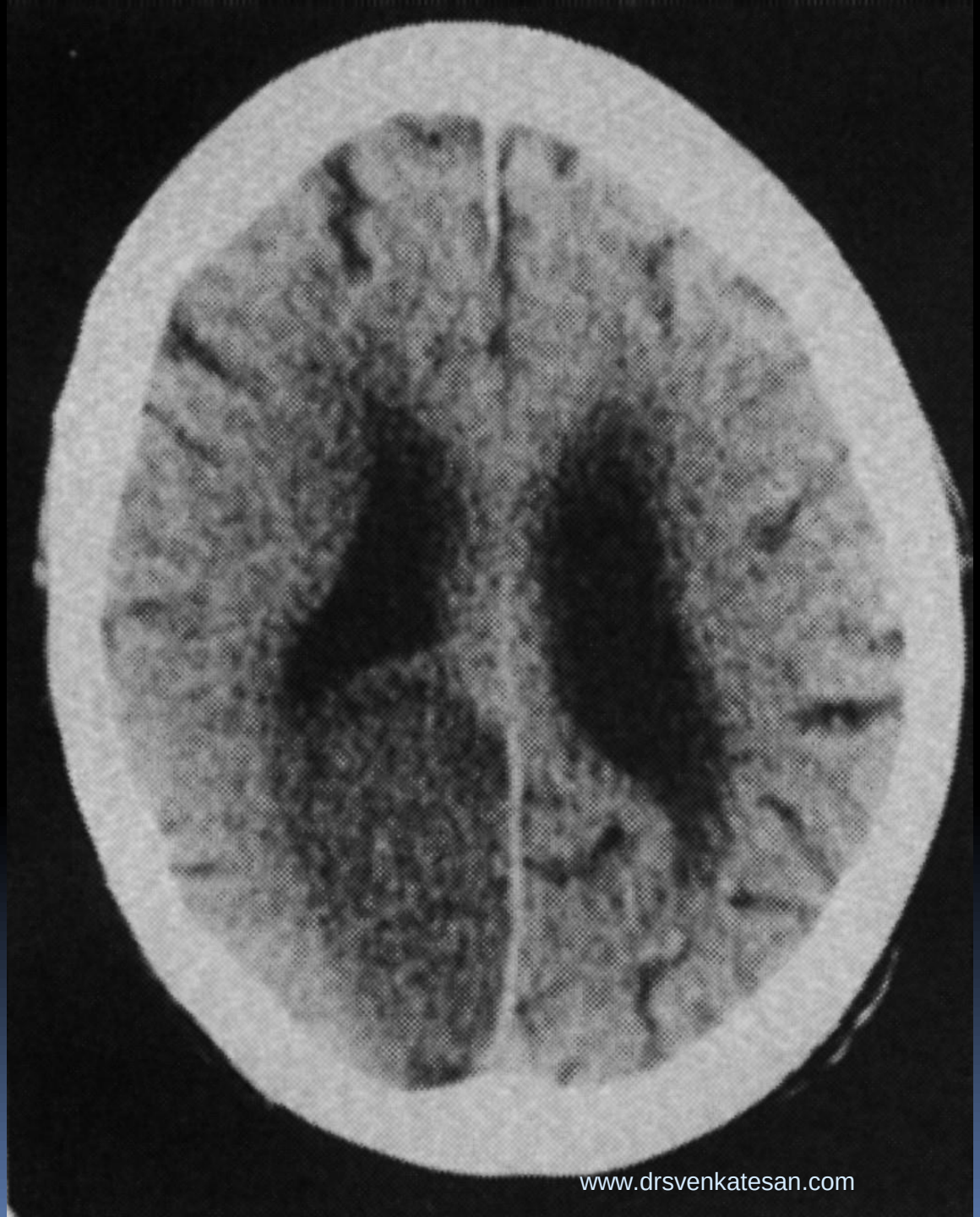
biphasic 100J

Table 2: Ventricular rate control in acute AF

Drug	Loading dose	Intravenous maintenance dose
Metoprolol	5 mg IV over 2–4 min; may be repeated every 5 min until 15 mg total	5–10 mg IV every 6 h
Esmolol	0.5 mg/kg per min IV over 2–4 min	0.05–0.2 mg/kg per min IV infusion
Diltiazem	20–25 mg IV over 20 min	5–15 mg/h IV
Verapamil	5–15 mg IV	0.05–0.2 mg/min IV
Digoxin	1 mg IV or PO in divided doses over 24 h	0.125–0.5 mg/d*

Note: IV = intravenously or intravenous, PO = orally.
*Adjust based on body size and renal function.

Cardioversion : Both pharmacological And DC shock has a unique risk



Cardioversion rules

48 hour

3 week

4 week

Pre treatment anti coagulation may be skipped if TEE done

Why this rule is important ?

Peri- cardioversion stroke
risk 1-5%

Rule 1 : It takes minimal 48h for LA clot to form after onset of AF.

Rule 2 : It needs three weeks of intense anticoagulation to effectively prevent new LA clot & possibly dissolve preexisting clot.

Rule 3 : It takes 4 weeks for the mechanical function of LA to resume

Acute AF protocol

	Stable	Unstable
AF less than 48h	No Cardioversion	Cardiovert without A.G
AF >48h or duration unknown	AG. Pre 3 weeks Post 4 weeks	Heparin bolus &Infusion Follow with AG 4 Weeks.

The other option would be a Emergency TEE and cardiovert without precardioversion AG but should recevive post DC AG for 4 weeks.

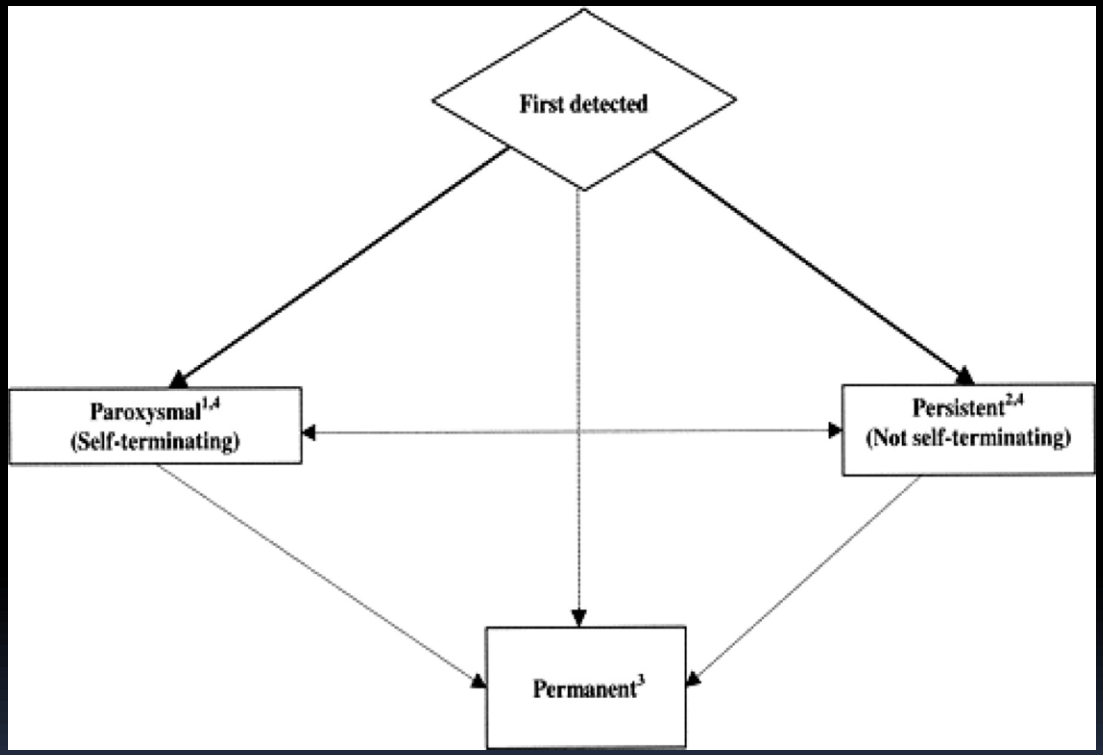
Approach to chronic atrial fibrillation

AF –Clinical classification

(Simplified by ACC/AHA/ESC consensus)

< 7 days, Most

< 24 h



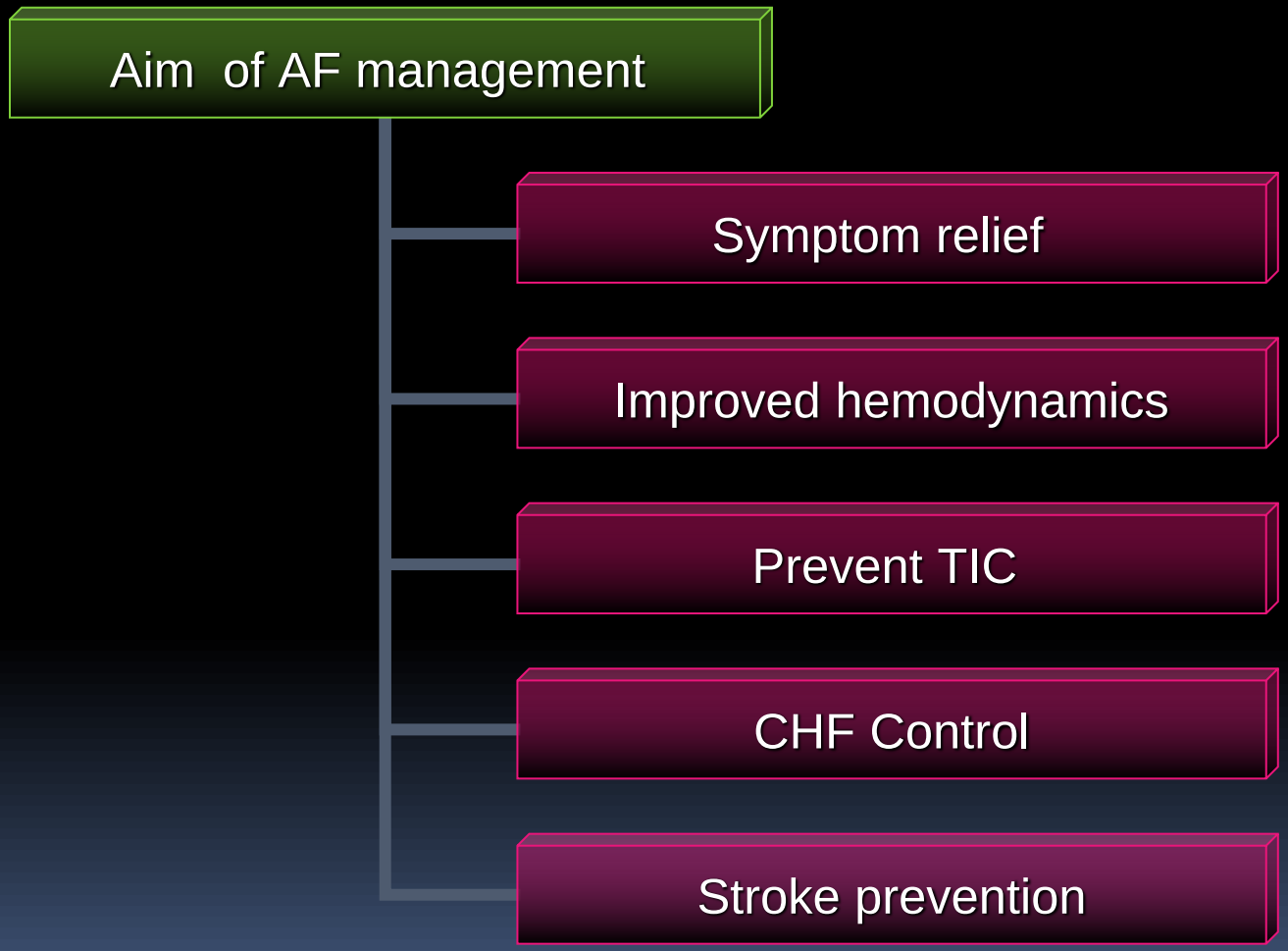
> 7 days

> I year

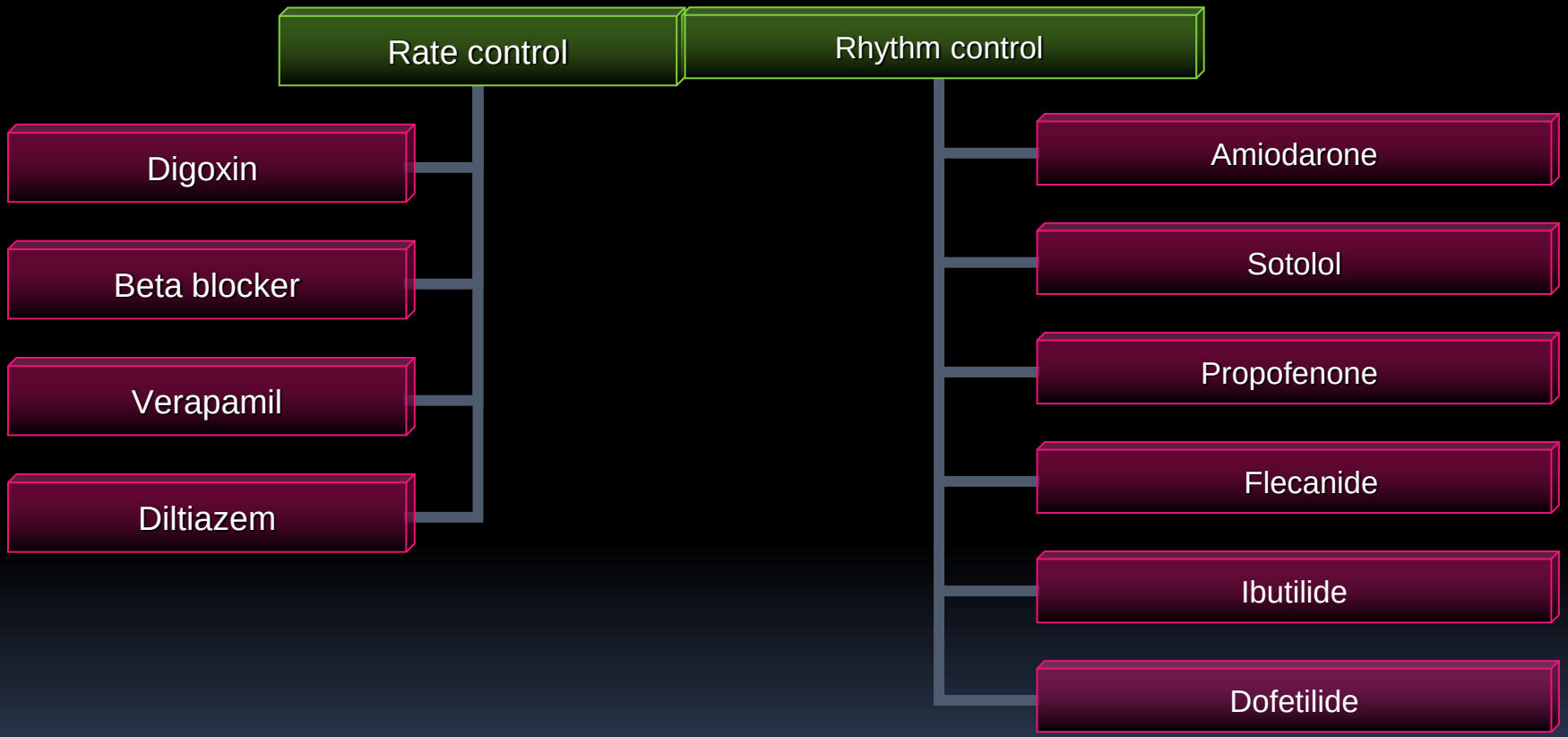
All grades are not mutually exclusive

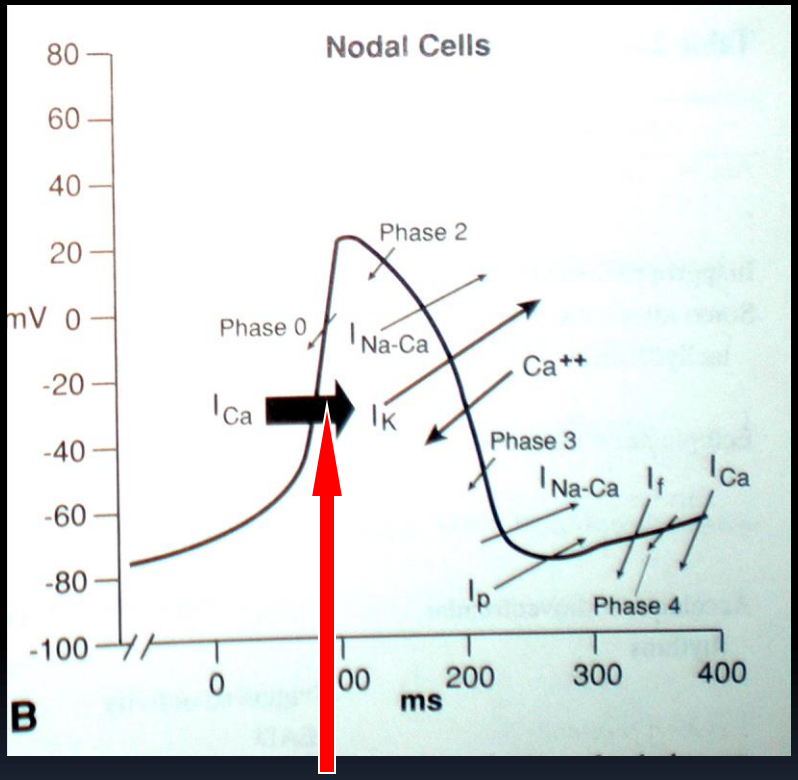
AF management

- Underlying problem
- Rate control
- Rhythm control
- Stroke prevention

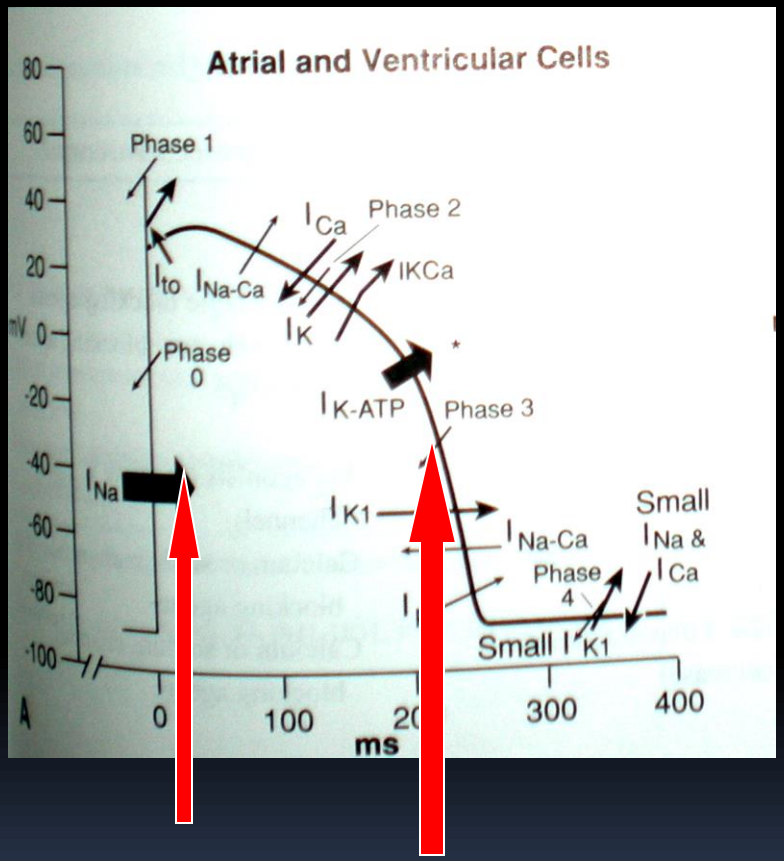

Aim of AF management
Symptom relief
Improved hemodynamics
Prevent TIC
CHF Control
Stroke prevention

Atrial fibrillation





Rate controlling drugs



Rhythm controlling drugs

Table 3: Antiarrhythmic pharmacological therapy for acute AF

Drug	Route	Dosage	Potential adverse effects
Amiodarone (class III)	PO/IV	0.8–1.2 g/d IV or PO (in divided doses) until a total of 10 g, then 200–400 mg/d	Bradycardia, hypotension, ↑QT, TdP (rare), GI intolerance, phlebitis with IV formulation
Dofetilide (class III)	PO	According to creatinine clearance (mL/min): < 20 –contraindicated 20–40 – 125 μg bid 40–60 – 250 μg bid > 60 – 500 μg bid	↑QT, TdP
Flecainide (class IC)	PO	100–300 mg/d in divided doses	Hypotension, rapidly conducting atrial flutter
Ibutilide (class III)	IV	1 mg over 10 min, repeat once	↑QT, TdP
Procainamide (class IA)	IV	12 mg/kg at 20 mg/min, then 2 mg/min	↑QT, TdP, hypotension
Propafenone (class IC)	PO	450–600 mg/d in divided doses	Hypotension, rapidly conducting atrial flutter

Note: bid = twice daily, ↑QT = QT interval prolongation, TdP = torsades de pointes, GI = gastrointestinal.

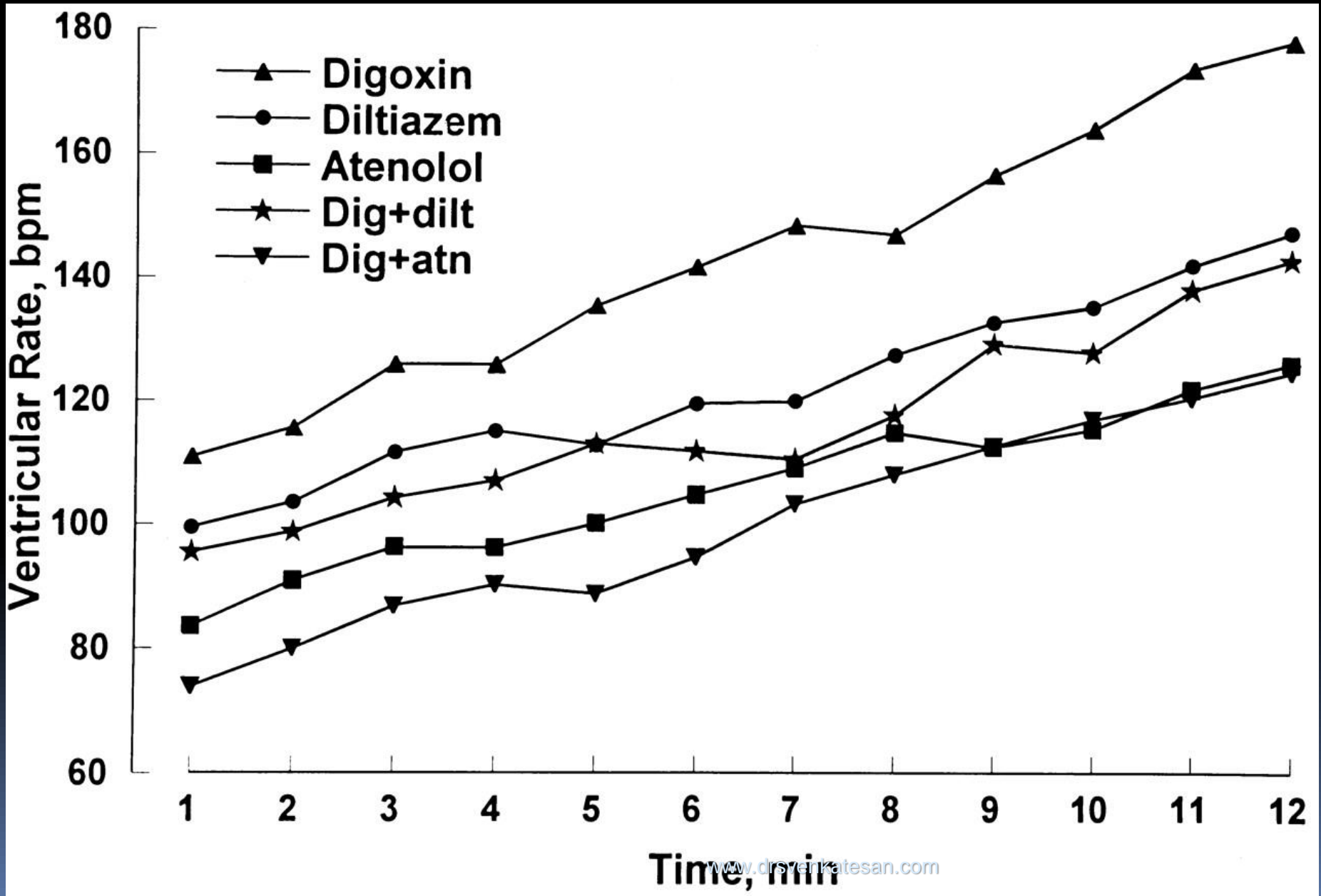
How to control VR most effectively in chronic AF ?

Farshi et all *JACC* 1999; 33:304-10

- Digoxin
- Diltiazem
- Atenolol
- Digoxin + Diltiazem
- Digoxin + Atenolol

Combination therapy of Digoxin and Atenolol was superior, Digoxin as a single agent proved less effective. 12 patients with AF duration of at least one year duration who were randomly assigned to cross control study Ramin Farshi,, California, JACC

Ventricular rate control



Ventricular rate control – Issues

Digoxin –Primarily acts by vagolytic .

(Little effect in exercise as already vagal withdrawl)

Associated SND may be unmasked

Amiodarone should not be used as rate control agent

Rate control difficult in paroxysmal AF

Choice of drugs for rate control

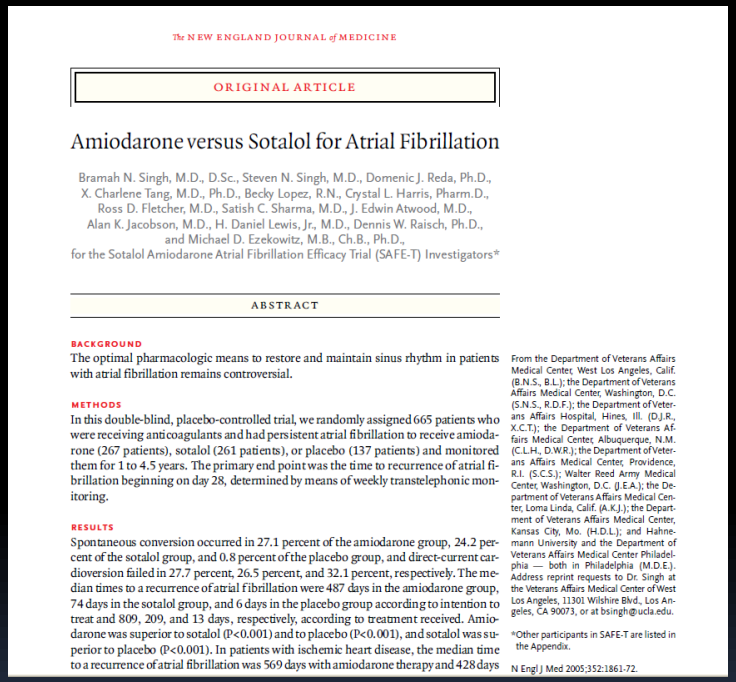
Atenolol

Verapamil

Diltiazem

Which drug for rhythm control?

- Amiodarone
- Sotolol
- Propofenone
- Dofitilide



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Amiodarone versus Sotalol for Atrial Fibrillation

Bramah N. Singh, M.D., D.Sc., Steven N. Singh, M.D., Domenic J. Reda, Ph.D., X. Charlene Tang, M.D., Ph.D., Becky Lopez, R.N., Crystal L. Harris, Pharm.D., Ross D. Fletcher, M.D., Satish C. Sharma, M.D., J. Edwin Atwood, M.D., Alan K. Jacobson, M.D., H. Daniel Lewis, Jr., M.D., Dennis W. Raisch, Ph.D., and Michael D. Ezekowitz, M.B., Ch.B., Ph.D., for the Sotalol Amiodarone Atrial Fibrillation Efficacy Trial (SAFE-T) Investigators*

ABSTRACT

BACKGROUND
The optimal pharmacologic means to restore and maintain sinus rhythm in patients with atrial fibrillation remains controversial.

METHODS
In this double-blind, placebo-controlled trial, we randomly assigned 665 patients who were receiving anticoagulants and had persistent atrial fibrillation to receive amiodarone (267 patients), sotalol (261 patients), or placebo (137 patients) and monitored them for 1 to 4.5 years. The primary end point was the time to recurrence of atrial fibrillation beginning on day 28, determined by means of weekly transtelephonic monitoring.

RESULTS
Spontaneous conversion occurred in 27.1 percent of the amiodarone group, 24.2 percent of the sotalol group, and 0.8 percent of the placebo group, and direct-current cardioversion failed in 27.7 percent, 26.5 percent, and 32.1 percent, respectively. The median times to a recurrence of atrial fibrillation were 487 days in the amiodarone group, 74 days in the sotalol group, and 6 days in the placebo group according to intention to treat and 809, 209, and 13 days, respectively, according to treatment received. Amiodarone was superior to sotalol ($P<0.001$) and to placebo ($P<0.001$), and sotalol was superior to placebo ($P<0.001$). In patients with ischemic heart disease, the median time to a recurrence of atrial fibrillation was 569 days with amiodarone therapy and 428 days

From the Department of Veterans Affairs Medical Center, West Los Angeles, Calif. (B.N.S., B.L.); the Department of Veterans Affairs Medical Center, Washington, D.C. (S.N.S., R.D.F.); the Department of Veterans Affairs Hospital, Hines, Ill. (D.J.R., X.C.T.); the Department of Veterans Affairs Medical Center, Albuquerque, N.M. (C.L.H., D.W.R.); the Department of Veterans Affairs Medical Center, Providence, R.I. (S.C.S.); Walter Reed Army Medical Center, Washington, D.C. (J.E.A.); the Department of Veterans Affairs Medical Center, Loma Linda, Calif. (A.K.J.); the Department of Veterans Affairs Medical Center, Kansas City, Mo. (H.D.L.); and Hahnemann University and the Department of Veterans Affairs Medical Center Philadelphia — both in Philadelphia (M.D.E.). Address reprint requests to Dr. Singh at the Veterans Affairs Medical Center of West Los Angeles, 11301 Wilshire Blvd., Los Angeles, CA 90073, or at bsingh@ucla.edu.

*Other participants in SAFE-T are listed in the Appendix.

N Engl J Med 2005;352:1861-72.

Newer drugs for rhythm control

Table 3: Antiarrhythmic pharmacological therapy for acute AF

Drug	Route	Dosage	Potential adverse effects
Amiodarone (class III)	PO/IV	0.8–1.2 g/d IV or PO (in divided doses) until a total of 10 g, then 200–400 mg/d	Bradycardia, hypotension, ↑QT, TdP (rare), GI intolerance, phlebitis with IV formulation
Dofetilide (class III)	PO	According to creatinine clearance (mL/min): < 20 –contraindicated 20–40 – 125 μg bid 40–60 – 250 μg bid > 60 – 500 μg bid	↑QT, TdP
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Propafenone (class IC)	PO	450–600 mg/d in divided doses	Hypotension, rapidly conducting atrial flutter

Note: bid = twice daily, ↑QT = QT interval prolongation, TdP = torsades de pointes, GI = gastrointestinal.

What is pharmacoogical cardioversion in semiurgent situation

Also called "Pill-In-The-Pocket" treatment a cure for A-Fib

A. Flecainide (Tambocor) 100mg up to three times at 20 minute intervals to stop or shorten an A-Fib

B. Propofenone (Rythmol) 300 mg and Propronalol 20 mg, every three hours three doses.

Rate control –Other options

(Ablate and Pace)

Patients who remain symptomatic despite drugs, or those who cannot tolerate may undergo AV node ablation with pacemaker

If AF is paroxysmal DDD(R) / VVI(R) pacemaker suffices.

When do you say rate is adequately controlled ?

60 - 80 at rest

90- 110 at moderate exercise

When do you say rhythm is controlled ?

- Not clearly defined (unlike rate control)
- Sustained sinus rhythm
- Occasional paroxysmal AF could be allowed.
- AF arrhythmia burden < 50% by event monitors proposed

So we have two options in the management of AF

Rate control & Rhythm control

which one to choose ?

Who generated this controversy ?

Should we necessarily answer this question

This question does not arise in all patients with AF

Applicable only in Chronic recurrent AF after correcting the primary condition

The logic is restoration of SR is restoring physiology & it should be better

But small observational studies suggested reverting to SR was difficult in many times and also the morbidity continued to occur even with rhythm control .

So between 2000 -2004 number of clinical trials were performed to answer this question

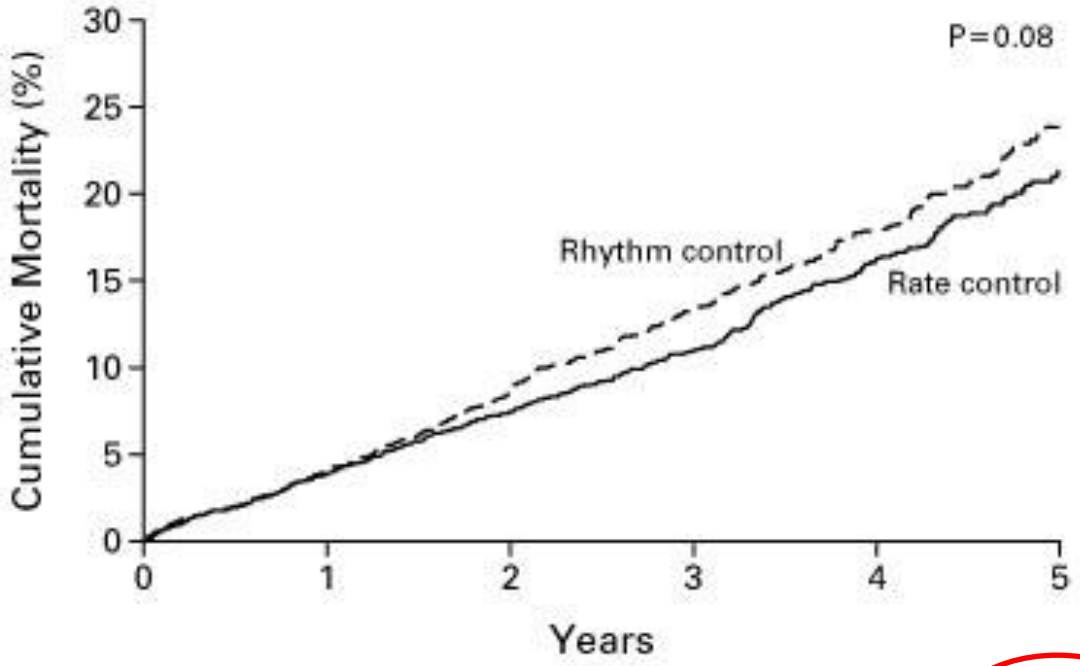
The studies that changed fundamental principle of AF management

- AFFIRM
- RACE
- PIAF
- STAF
- HOT CAFE

AFFIRM

- A total of 4060 patients .
- Chronic recurrent AF
- 60 % HT, 30%CAD
- Follow up 5 years
- Rate control vs Rhythm

AFFIRM



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

Adverse outcomes in AFFIRM

End point	Rate group No. (%)	Rhythm group No. (%)	p
Death	310 (25.9)	356 (26.7)	0.08
Death, disabling stroke, anoxic encephalopathy, major bleeding, cardiac arrest	416 (32.7)	445 (32.0)	0.33
Hospitalization after baseline	1220 (73.0)	1374 (80.1)	<0.001

AFFIRM

The New England
Journal of Medicine

VOLUME 347 DECEMBER 5, 2002 NUMBER 23

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

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

ABSTRACT

Background There are two approaches to the treatment of atrial fibrillation: one is cardioversion and

ATRIAL fibrillation is the most common sustained cardiac arrhythmia, yet the optimal strategy for its management remains

Conclusions Management of atrial fibrillation with the rhythm-control strategy offers no survival advantage over the rate-control strategy, and there are potential advantages, such as a lower risk of adverse drug effects, with the rate-control strategy. Anticoagulation should be continued in this group of high-risk patients. (N Engl J Med 2002;347:1825-33.)

The New England Journal of Medicine

RACE

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

ISABELLE C. VAN GELDER, M.D., VINCENT E. HAGENS, M.D., HANS A. BOSKER, M.D., J. HERRE KINGMA, M.D., OTTO KAMP, M.D., TSJERK KINGMA, M.SC., SALAH A. SAID, M.D., JULIUS I. DARMANATA, M.D., ALPHONS J.M. TIMMERMANS, M.D., JAN G.P. TIJSSEN, PH.D., AND HARRY J.G.M. CRIJNS, M.D., FOR THE RATE CONTROL VERSUS ELECTRICAL CARDIOVERSION FOR PERSISTENT ATRIAL FIBRILLATION STUDY GROUP*

ABSTRACT

Background Maintenance of sinus rhythm is the main therapeutic goal in patients with atrial fibrillation. However, recurrences of atrial fibrillation and side effects of antiarrhythmic drugs offset the benefits of sinus rhythm. We hypothesized that ventricular rate control is not inferior to the maintenance of sinus rhythm for the treatment of atrial fibrillation.

Methods We randomly assigned 522 patients who had persistent atrial fibrillation after a previous elec-

ATRIAL fibrillation is not a benign condition.[1,2] For many clinicians, maintenance of sinus rhythm is the main therapeutic goal. In patients with persistent atrial fibrillation, repeated electrical cardioversion and prophylactic antiarrhythmic drugs are used to maintain sinus rhythm.[3] However, frequent recurrences of atrial fibrillation and adverse effects of drugs decrease the potential benefits of electrical cardioversion.[4-6] Also, the beneficial ef-

Conclusions Rate control is not inferior to rhythm control for the prevention of death and morbidity from cardiovascular causes and may be appropriate therapy in patients with a recurrence of persistent atrial fibrillation after electrical cardioversion. (N Engl J Med 2002;347:1834-40.)

	Rate control	Rhythm control
PIAF	BB,CC, Dig	
STAF	BB,CC, Dig.Ablate/Pace	CV, Class1 , Sotolol
RACE	BB,CC, Dig.	CV, Soltolol.CV Flecanide Amidodarone
AFFIRM	BB,CC,Dig	Amiodarone, disopyramide, flecainide, moricizine, procainamide, propafenone, quinidine, sotalol
HOT CAFE	BB,CC,Dig	Propafenone disopyramide sotalol Amiodarone

RACE trial

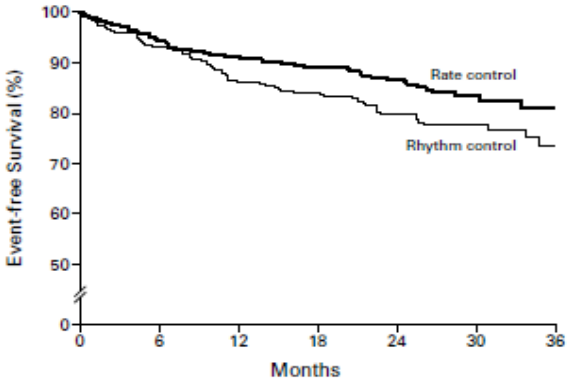


Figure 2. Kaplan–Meier Curves for Event-free Survival in the Rate-Control and Rhythm-Control Groups.

Table 2. Incidence of the Primary End Point and Its Components According to the Treatment Group.*

End Point	Rate Control (N=256)	Rhythm Control (N=266)	Absolute Difference (90% CI)†
	no. (%)		
Composite end point	44 (17.2)	60 (22.6)	−5.4 (−11.0 to 0.4)
Death from cardiovascular causes	18 (7.0)	18 (6.8)	0.2 (−3.4 to 3.9)
Heart failure	9 (3.5)	12 (4.5)	−1.0 (−3.8 to 1.8)
Thromboembolic complications	14 (5.5)	21 (7.9)	−2.4 (−6.0 to 1.2)
Bleeding	12 (4.7)	9 (3.4)	1.3 (−1.5 to 4.1)
Severe adverse effects of antiarrhythmic drugs	2 (0.8)	12 (4.5)	−3.7 (−6.0 to −1.4)
Implantation of a pacemaker	3 (1.2)	8 (3.0)	−1.8 (−3.9 to 0.2)

*Some patients had more than one end point.

†CI denotes confidence interval.

TABLE 2. INCIDENCE OF THE PRIMARY END POINT AND ITS COMPONENTS ACCORDING TO THE TREATMENT GROUP.*

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*Some patients had more than one end point.

†CI denotes confidence interval.

Rate Control vs Rhythm Control in Patients With Nonvalvular Persistent Atrial Fibrillation*

The Results of the Polish How to Treat Chronic Atrial Fibrillation (HOT CAFE) Study

Grzegorz Opolski, MD, PhD; Adam Torbicki, MD, PhD; Dariusz A. Kosior, MD, PhD; Marcin Szulc, MD, PhD; Beata Wożakowska-Kapłon, MD, PhD; Piotr Kołodziej, MD, PhD; and Piotr Achremczyk, MD, PhD; for the Investigators of the Polish HOT CAFE Trial

Study objectives: **The relative risks and benefits of strategies of rate control vs rhythm control in patients with atrial fibrillation (AF) remain to be fully explored.**
Design: **The How to Treat Chronic Atrial Fibrillation (HOT CAFE) Polish trial was designed to evaluate in a randomized, multicenter, and prospective manner the feasibility and long-term outcomes of rate control vs rhythm control strategies in patients with persistent AF.**
Patients: **Our study population comprised 205 patients (134 men and 71 women; mean [± SD] age, 60.8 ± 11.2 years) with a mean AF duration of 273.7 ± 112.4 days. The mean observation period was 1.7 ± 0.4 years. One hundred one patients were randomly assigned to the rate control group and received rate-slowing therapy guided by repeated 24-h Holter monitoring. Direct current cardioversion and atrioventricular junctional ablation with pacemaker placement were alternative nonpharmacologic strategies for patients with tachycardia that was resistant to medical therapy. One hundred four patients were randomized to sinus rhythm restoration and maintenance using serial cardioversion supported by a predefined stepwise antiarrhythmic drug**

Clinical research

Rate-control vs. rhythm-control in patients with atrial fibrillation: a meta-analysis

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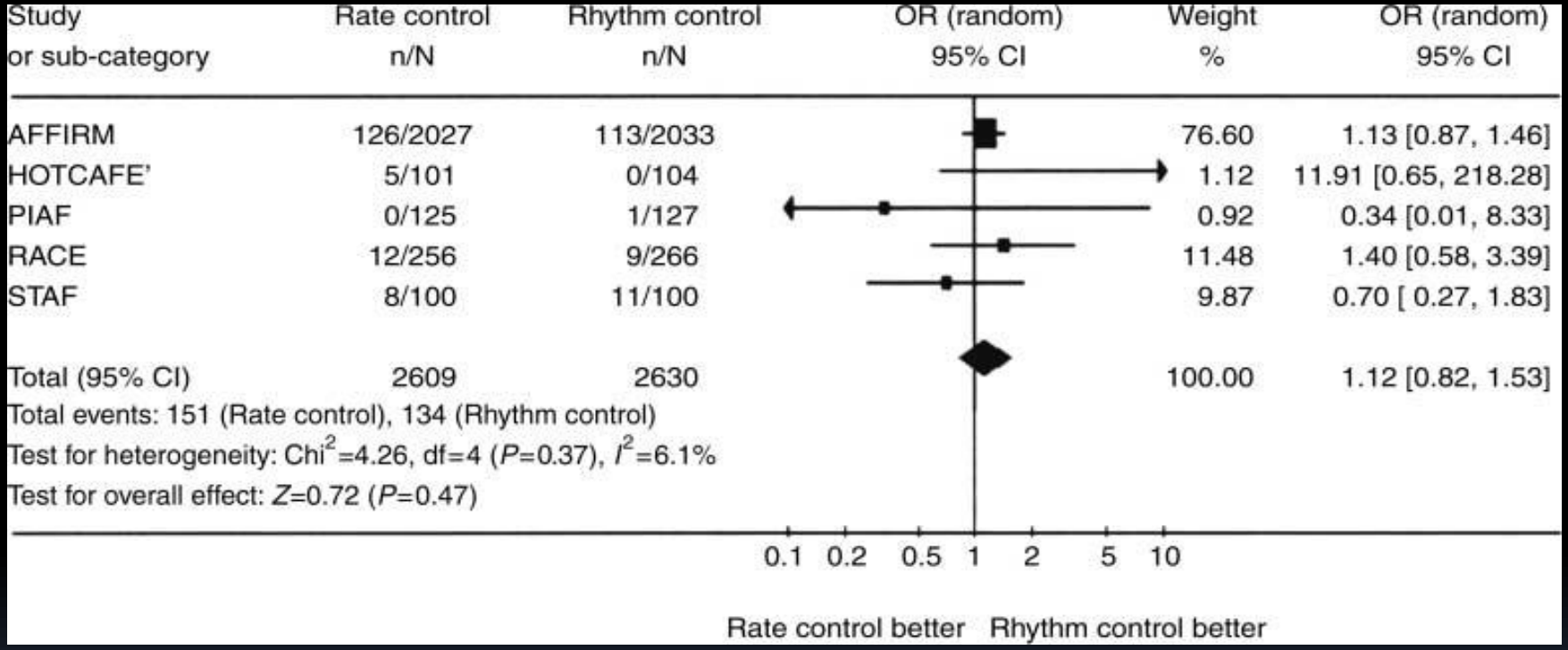
Received 18 November 2004; revised 16 December 2005; accepted 31 March 2005

KEYWORDS
Rate-control;
Rhythm-control;
Atrial fibrillation

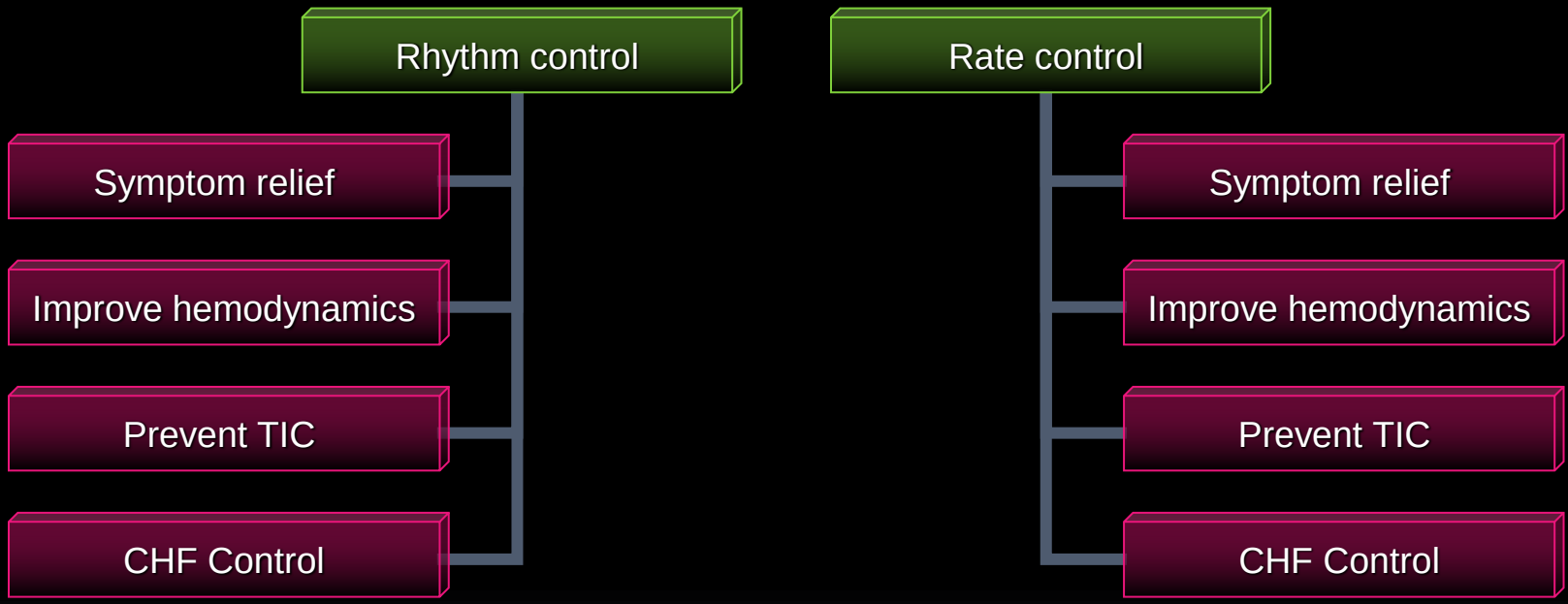
Aims To systematically assess the risk/benefit ratio of a rate-control strategy vs. a rhythm-control strategy in patients with first or recurrent atrial fibrillation (AF).
Methods and results We searched Medline, CENTRAL, and other sources up to September 2004 for randomized trials. Individual and pooled random-effect odd ratios (OR) and 95% confidence intervals (CI) [OR (95% CI)] were calculated for the combined endpoint of all cause death and thromboembolic stroke (CEP), major bleeds (intra and extracranial), and systemic embolism. Number needed to treat (NNT) to avoid one CEP and heterogeneity were also assessed. Five studies enrolling 5239 patients with AF compared rate-control vs. rhythm-control. Average follow-up ranged from 1 to 3.5 years. A rate-control strategy compared with a rhythm-control approach was associated with a significantly reduced risk of CEP [OR 0.84 (0.73, 0.98), $P = 0.02$], and with a trend towards a reduced risk of death [OR 0.87 (0.74, 1.02), $P = 0.09$] and thromboembolic stroke [OR 0.80 (0.6, 1.07), $P = 0.14$]. NNT to save one CEP was 50. There was no significant difference in the risk of major bleeds [OR 1.14 (0.9, 1.45), $P = 0.28$] and systemic embolism [OR 0.93 (0.43, 2.02), $P = 0.90$]. No significant heterogeneity was found in any of the analyses ($P > 0.1$).
Conclusion This meta-analysis of 5239 patients with AF indicates that an initial rate-control strategy compared with a rhythm-control one is associated with a better prognosis, thus representing the standard treatment against which to test new therapeutic approaches.



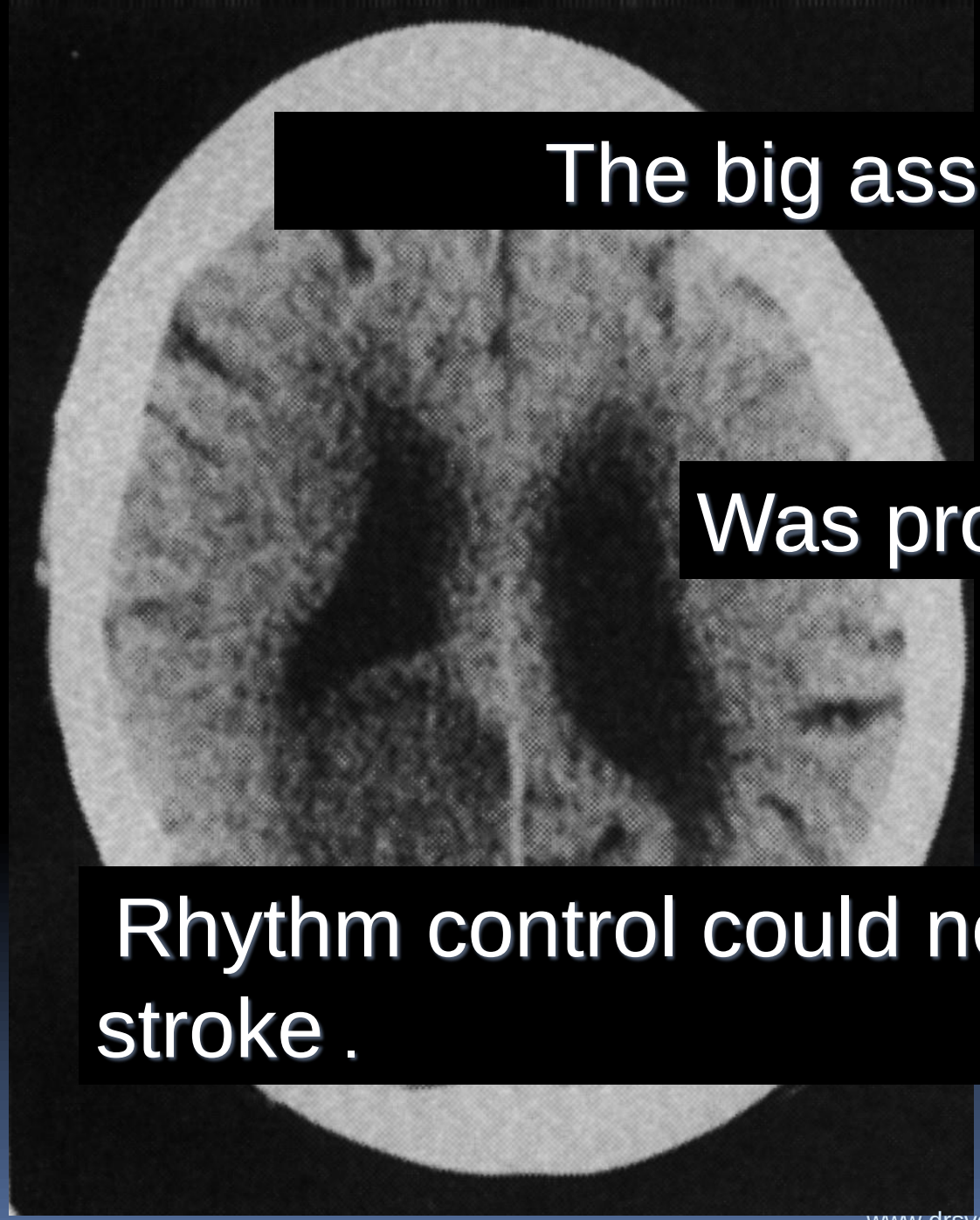
Why rhythm control faired poorly

- Rhythm control was never easy to achieve 39% in Race .Affirm 60%
- Class 3/ 1 A drugs are more harmful
- Controlling rate alone helps to prevent CHF/TIC

Rate control could achieve the the same as rhythm control



What about stroke ?



The big assumption !

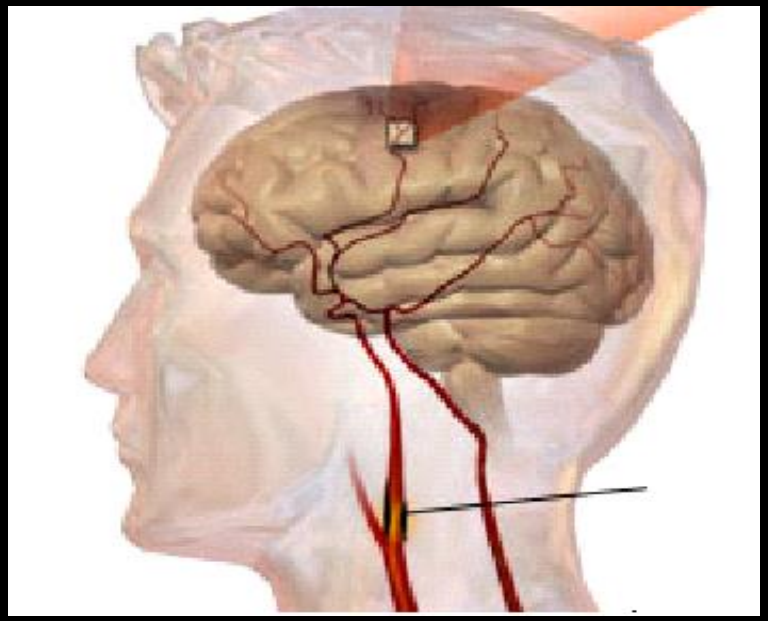
Was proved wrong

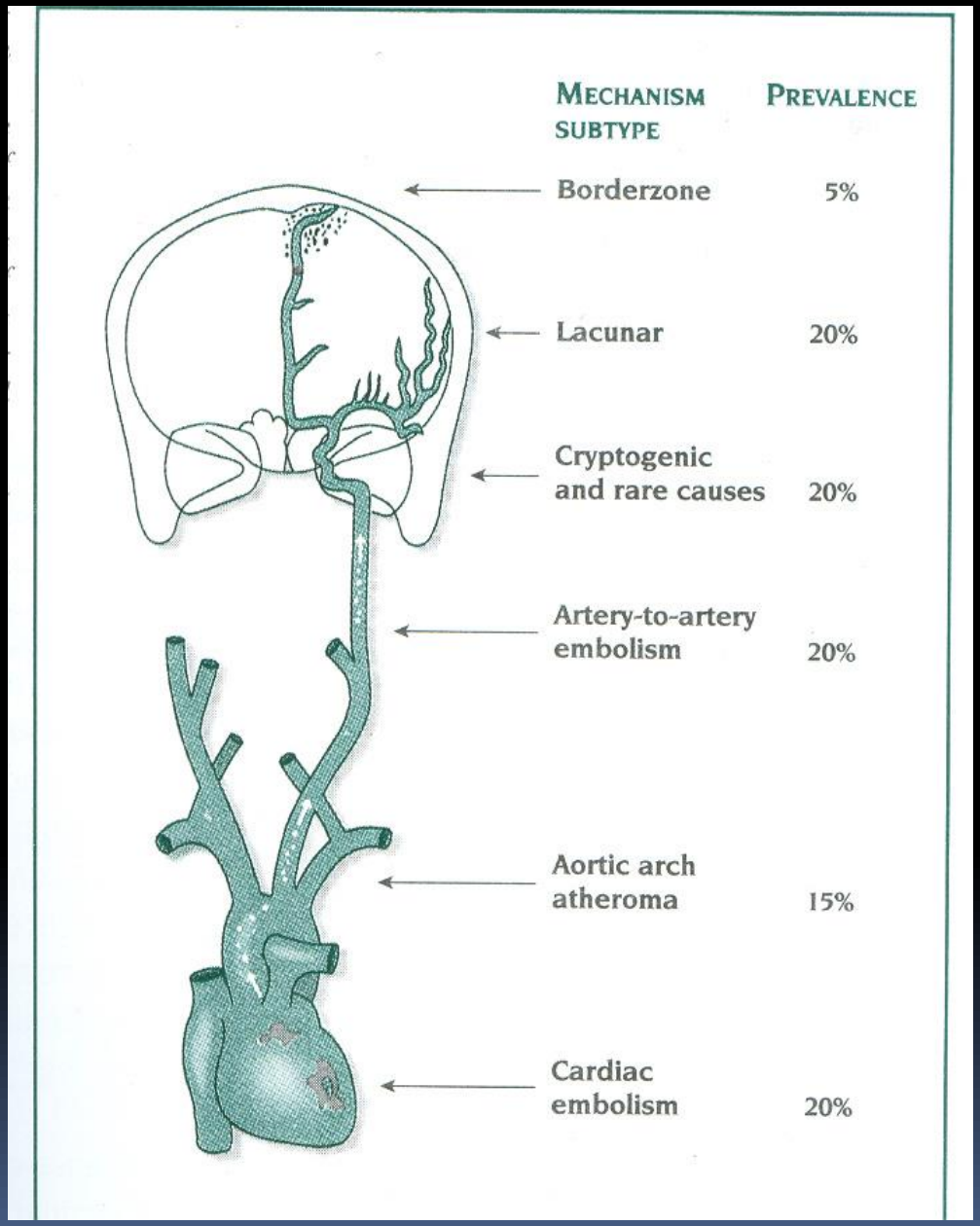
Rhythm control could not prevent stroke .

TABLE 2. Stroke Rates in the 4 Rate vs Rhythm Trials

Trial	n	Stroke Rate, Rate-Control Trials, %	Stroke Rate, Rhythm-Control Trials, %	RR (95% CI)	*P*
AFFIRM	4060	5.7	7.3	1.28 (0.95–1.72)	0.12
RACE	522	5.5	7.9	1.44 (0.75–2.78)	0.44
PIAF	252	0.8	0.8	1.02 (0.73–2.16)	0.49
STAF	266	1.0	3.0	3.01 (0.35–25.3)	0.52
Total	5100	5.0	6.5	1.28 (0.98–1.66)	0.08

Data are modified from references 12 through 15 and from Verheught et al, presented at the American College of Cardiology 52nd Annual Scientific Sessions, Chicago, Ill, March 30 to April 2, 2003.




MECHANISM
SUBTYPE
PREVALENCE
Borderzone
5%
Lacunar
20%
Cryptogenic
and rare causes
20%
Artery-to-artery
embolism
20%
Aortic arch
atheroma
15%
Cardiac
embolism
20%

When do you prefer what ?

CONTROVERSIES IN CARDIOVASCULAR MEDICINE

Is rate control or rhythm control preferable in patients with atrial fibrillation?

Rate Control Is Preferable to Rhythm Control in the Majority of Patients With Atrial Fibrillation

Rodney H. Falk, MD, FRCP

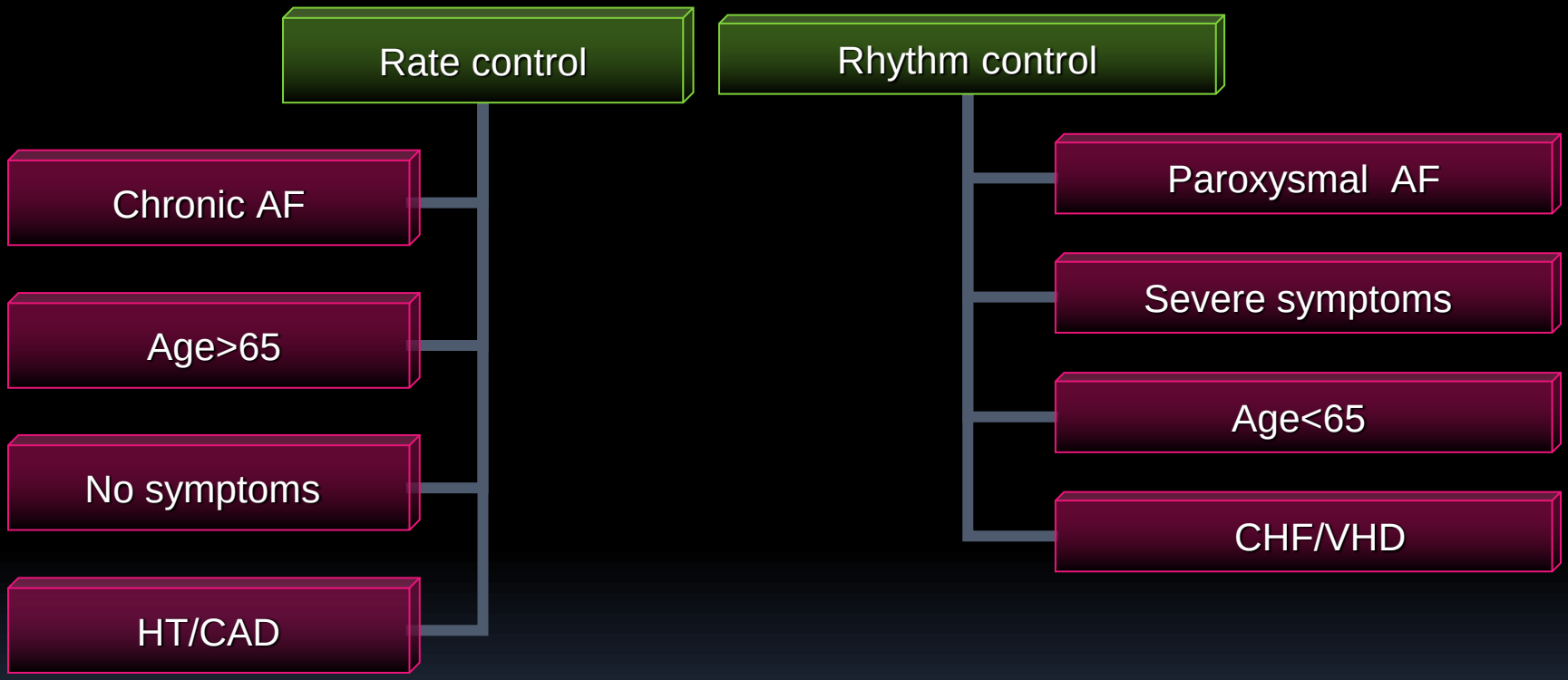
". . .but to his surprise — the more he looked — the more Piglet wasn't there."

A.A. Milne, *The House at Pooh Corner*

The management of patients with atrial fibrillation has been the subjects of intense investigation over the past 2 decades. In the 1980s and early 1990s, large clinical

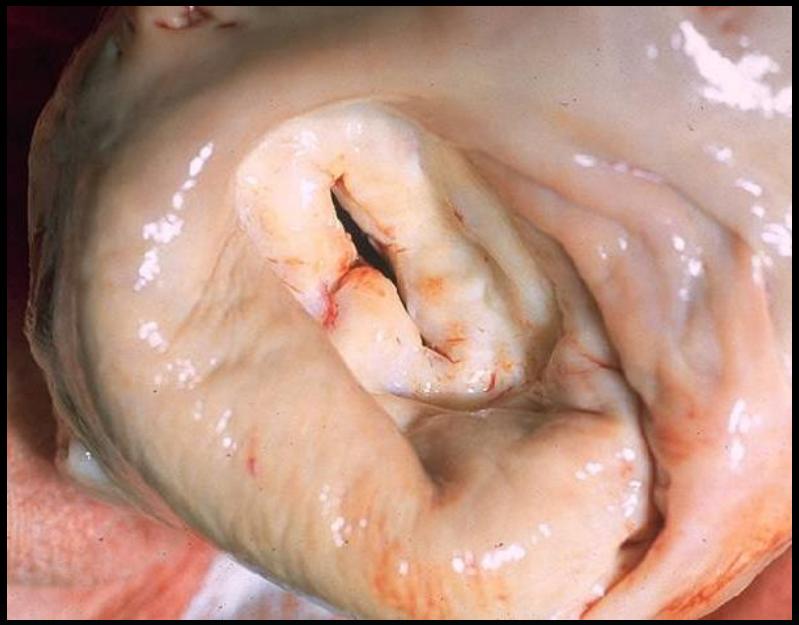
outcome after a strategy of restoration and maintenance of sinus rhythm.[12–15] Analysis of these trials demonstrated no benefit either in mortality or in a combined end point of mortality and morbidity. These results are generally interpreted as showing that either rate control or rhythm control is a suitable strategy in a patient with atrial fibrillation, and there has therefore been a rethinking of the appropriate

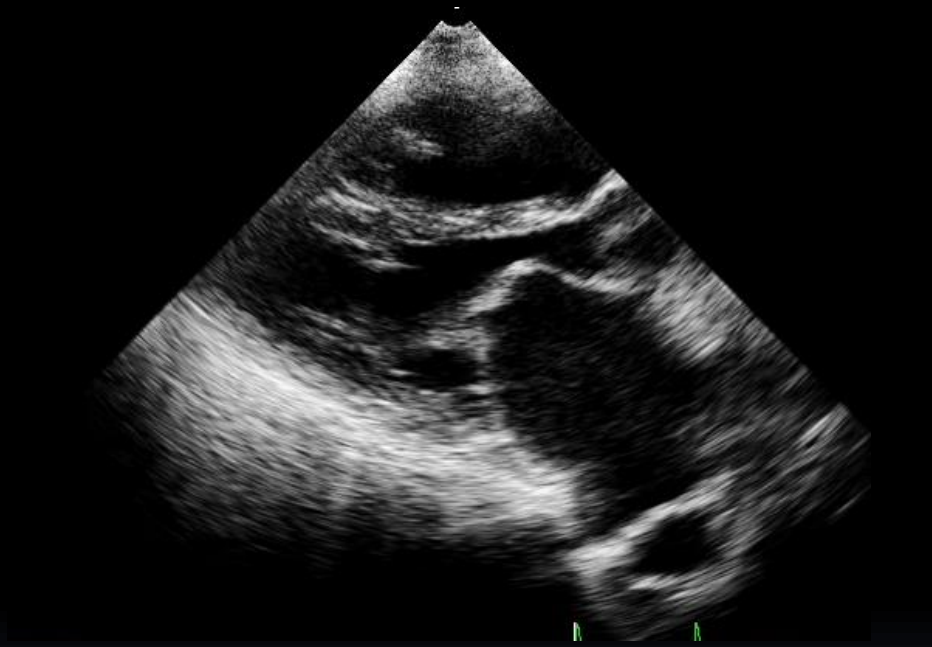
When do you prefer what ?



Atrial fibrillation In India how it is different ?

AF in RHD





The Control of Rate versus Rhythm in Rheumatic Atrial Fibrillation trial (CRRAFT)

- 47 patients
- Diltiazem SR 90mg twice daily (90 -130 beats)
- Amiodarone and or electrical conversion,
- Follow up 1 year.

Implications of CRAAFT study

- It was the only major study suggested rhythm control can be attempted in RHD
- Could be beneficial too !
- Correction of primary valve disease will ultimately determine the outcome

AF in special situations

AF in special situations

- Pregnancy
- WPW
- HOCM
- Athletes

Atrial fibrillation in Pregnancy

Mostly associated with RHD in India. (With or without Prosthetic valve)

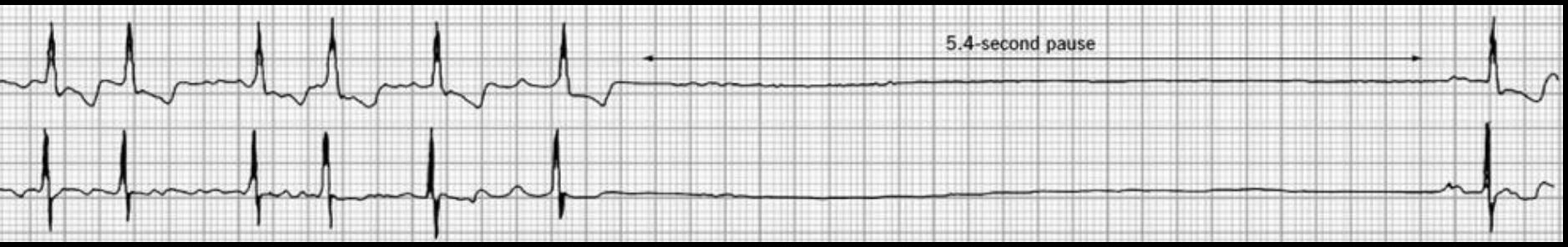
- Digoxin
- Beta blocker
- Verapamil

DC cardiversion rarely needed

Anitocoagulation in all with VHD/Aspirin for non Valvular AF

AF as a part of SND

Tachy brady syndrome



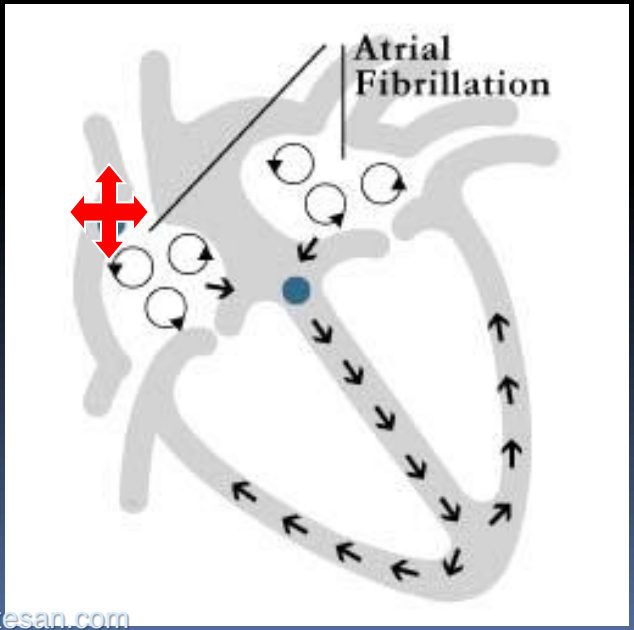
Link between SND and AF

Atrial interstitial fibrosis

Unidirectional or multidirectional block

SA node also involved in fibrosis

One proposal suggests In every chronic AF SA node is and AF is default irregular escape rhythm from atria

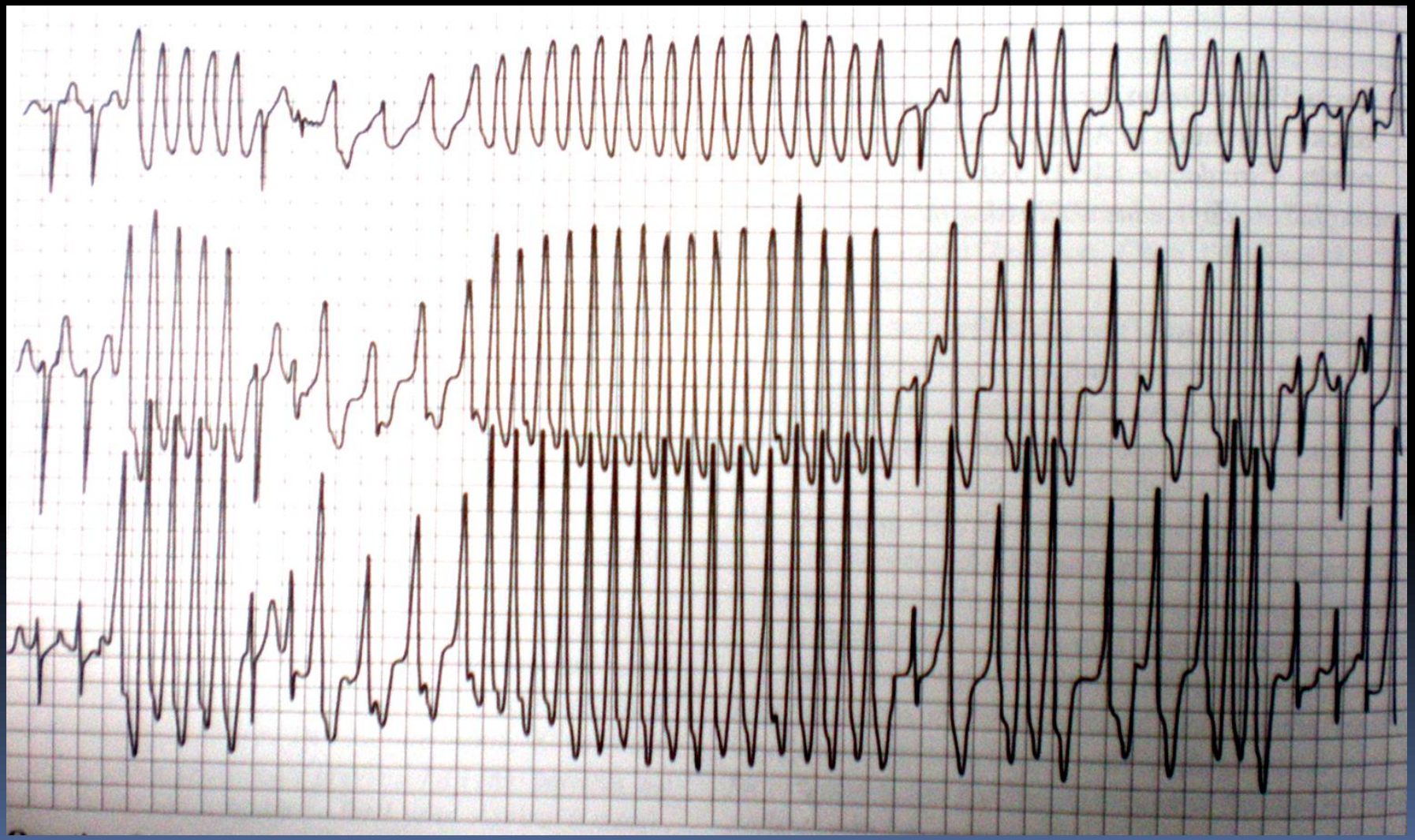


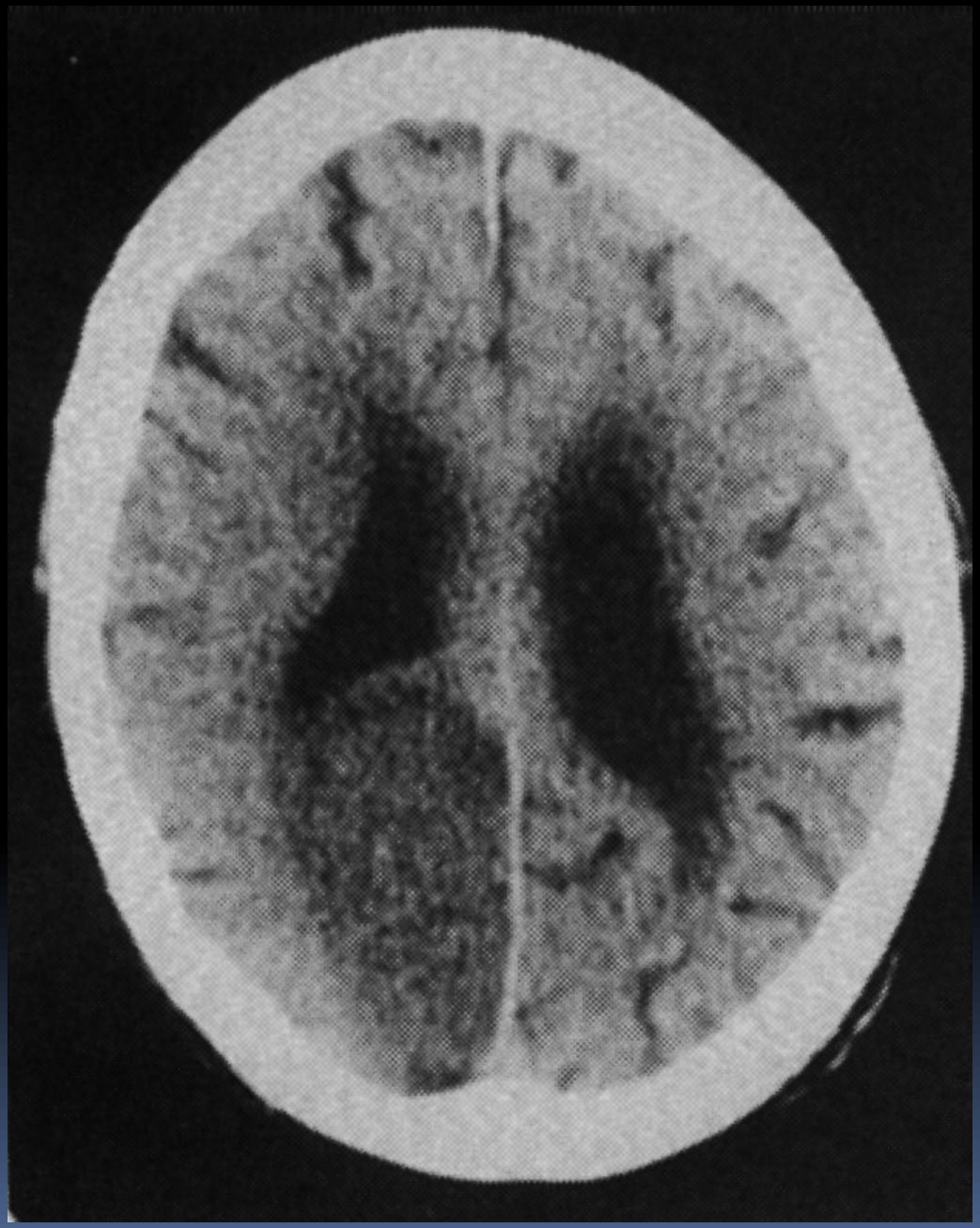
Post operative Atrial fibrillation

- Relatively common
- Elderly prone
- Mainly adrenergic
- Hypoxia related

Drug of first choice Bea blocker

WPW and Atrial fibrillation

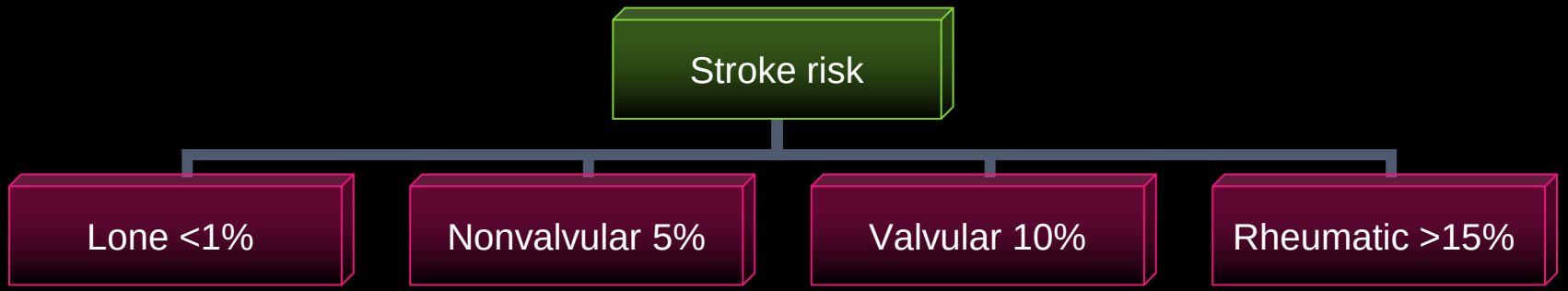




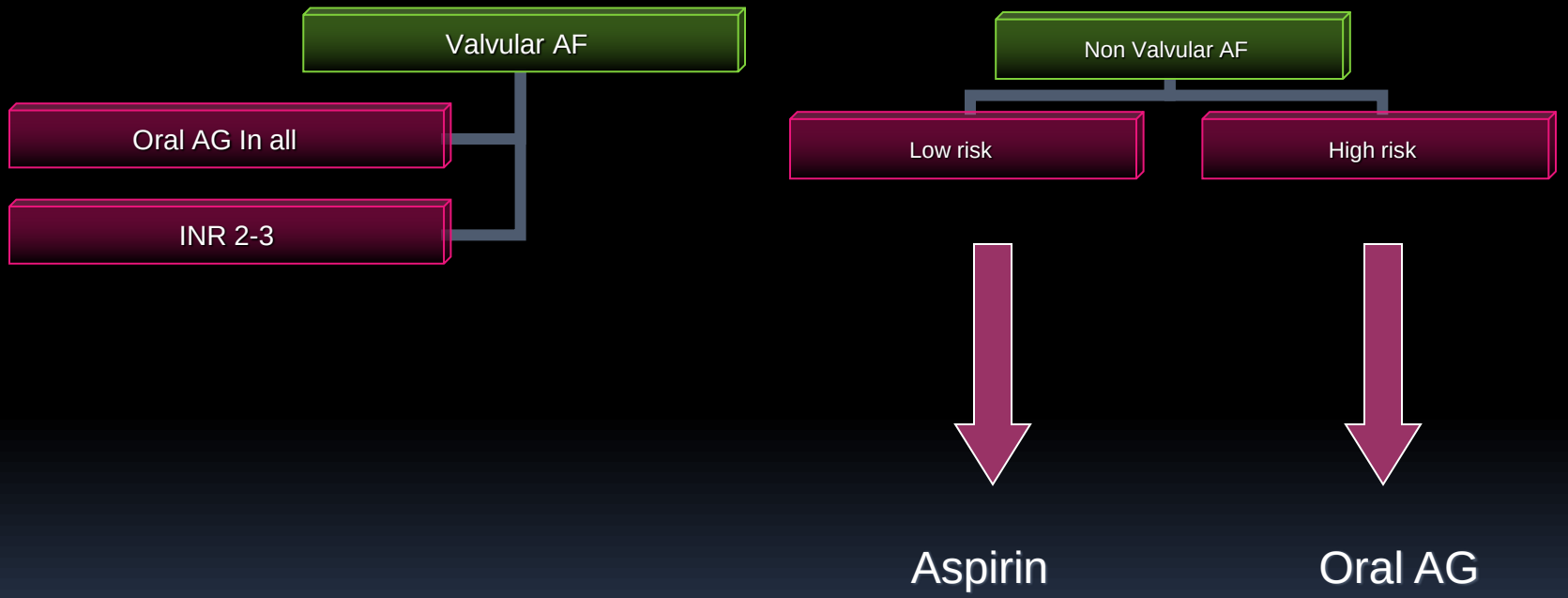
AG are given to

Reduce the risk of ischemic stroke from 6% to 1 %

INR 2-3


Stroke risk
Lone <1%
Nonvalvular 5%
Valvular 10%
Rheumatic >15%

Stroke anticoagulation - simplified approach



The CHADS/CHADS2 scoring table is shown below:[3]

C:	Congestive heart failure	= 1 point
H:	Hypertension (or treated hypertension)	= 1 point
A:	Age >75 years	= 1 point
D:	Diabetes	= 1 point
S:	Prior Transient ischemic attack or Stroke	= 2 points

Risk of stroke

According to the findings of the JAMA study, the risk of stroke as a percentage per year is:

Score	Annual Risk of Stroke	95% CIs from JAMA Study
0	1.9%	
1	2.8%	
2	4.0%	
3	5.9%	
4	8.5%	
5	12.5%	
6	18.2%	

Recommendations for anticoagulation [edit]

The following treatment strategies were recommended by the authors of the *JAMA* and *Circulation* articles:

Score	Risk	Anticoagulation Therapy	Considerations
0	Low	Aspirin	325 mg/day most likely to offer benefit, although lower doses may be similarly efficacious
1	Moderate	Aspirin or Warfarin	ASA daily or Raise INR to 2.0-3.0, depending on factors such as patient preference
2 or greater	Moderate or High	Warfarin	Raise INR to 2.0-3.0, unless contraindicated (e.g., history of falls, clinically significant GI bleeding, inability to obtain regular INR screening)

Table 3. Risk-Based Approach to Antithrombotic Therapy in Patients With Atrial Fibrillation[9]

Patient Features	Antithrombotic Therapy	Class of Recommendation
Age <60 y, no heart disease (lone AF)	Aspirin (81-325 mg/d) or no therapy	I
Age <60 y, heart disease but no risk factors*	Aspirin (81-325 mg/d)	I
Age 60-74 y, no risk factors*	Aspirin (81-325 mg/d)	I
Age 65-74 y with diabetes mellitus or CAD	Oral anticoagulation (INR 2.0-3.0)	I
Age ≥75 y, women	Oral anticoagulation (INR 2.0-3.0)	I
Age ≥75 y, men, no other risk factors	Oral anticoagulation (INR 2.0-3.0) or aspirin (81-325 mg/d)	I
Age ≥65, heart failure	Oral anticoagulation (INR 2.0-3.0)	I
LV EF <35% or fractional shortening <25%, and hypertension	Oral anticoagulation (INR 2.0-3.0)	I
Rheumatic heart disease (mitral stenosis)	Oral anticoagulation (INR 2.0-3.0)	I
Prosthetic heart valves	Oral anticoagulation (INR 2.0-3.0 or higher)	I
Prior thromboembolism	Oral anticoagulation (INR 2.0-3.0 or higher)	I
Persistent atrial thrombus on TEE	Oral anticoagulation (INR 2.0-3.0 or	IIA

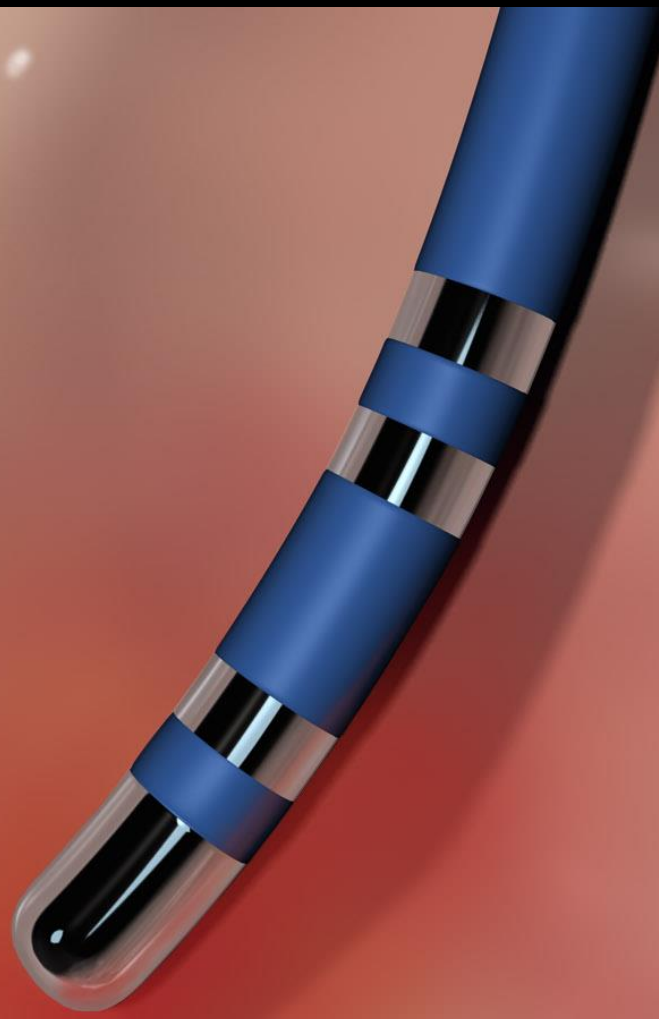
Acute stroke and the patient in AF how do you proceed ?

Don’t give Anticoagulants during stroke

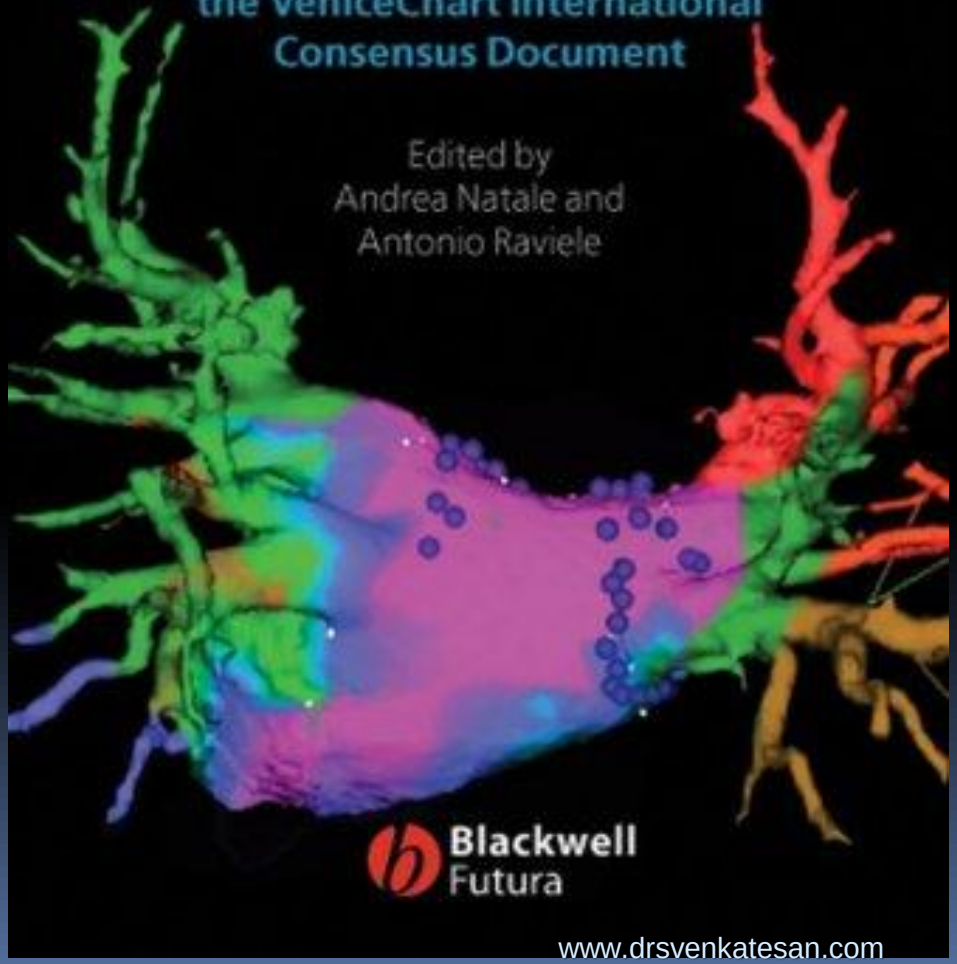
Risk of converting into hemorrhagic is high (It precludes AG use forever)

Emerging technologies

In atrial fibrillation



Atrial Fibrillation Ablation



The NEW ENGLAND JOURNAL of MEDICINE

Previous Volume 339:659-666 September 3, 1998 Number 10 Next

Spontaneous Initiation of Atrial Fibrillation by Ectopic Beats Originating in the Pulmonary Veins

Michel Haïssaguerre, M.D., Pierre Jaïs, M.D., Dipen C. Shah, M.D., Atsushi Takahashi, M.D., Mélèze Hocini, M.D., Gilles Quiniou, M.D., Stéphane Garrigue, M.D., Alain Le Mouroux, M.D., Philippe Le Métayer, M.D., and Jacques Clémenty, M.D.

ABSTRACT

Background Atrial fibrillation, the most common sustained cardiac arrhythmia and a major cause of stroke, results from simultaneous reentrant wavelets. Its spontaneous initiation has not been studied.

Methods We studied 45 patients with frequent episodes of atrial fibrillation (mean [±SD] duration, 344±326 minutes per 24 hours) refractory to drug therapy. The spontaneous initiation of atrial fibrillation was mapped with the use of multielectrode catheters designed to record the earliest electrical activity preceding the onset of atrial fibrillation and associated atrial ectopic beats. The accuracy of the mapping was confirmed by the abrupt disappearance of triggering atrial ectopic beats after ablation with local radio-frequency energy.

Results A single point of origin of atrial ectopic beats was identified in 29 patients, two points of origin were identified in 9 patients, and three or four points of origin were identified in 7 patients, for a total of 69 ectopic foci. Three foci were in the right atrium, 1 in the posterior left atrium, and 65 (94 percent) in the pulmonary veins (31 in the left superior, 17 in the right superior, 11 in the left inferior, and 6 in the right inferior pulmonary vein). The earliest activation was found to have occurred 2 to 4 cm inside the veins, marked by a local depolarization preceding the atrial ectopic beats on the surface electrocardiogram by 106±24 msec. Atrial fibrillation was initiated by a sudden burst of rapid depolarizations (340 per minute). A local depolarization could also be recognized during sinus rhythm and abolished by radio-frequency ablation. During a follow-up period of 8±6 months after ablation, 28 patients (62 percent) had no recurrence of atrial fibrillation.

Conclusions The pulmonary veins are an important source of ectopic beats, initiating frequent paroxysms of atrial fibrillation. These foci respond to treatment with radio-frequency

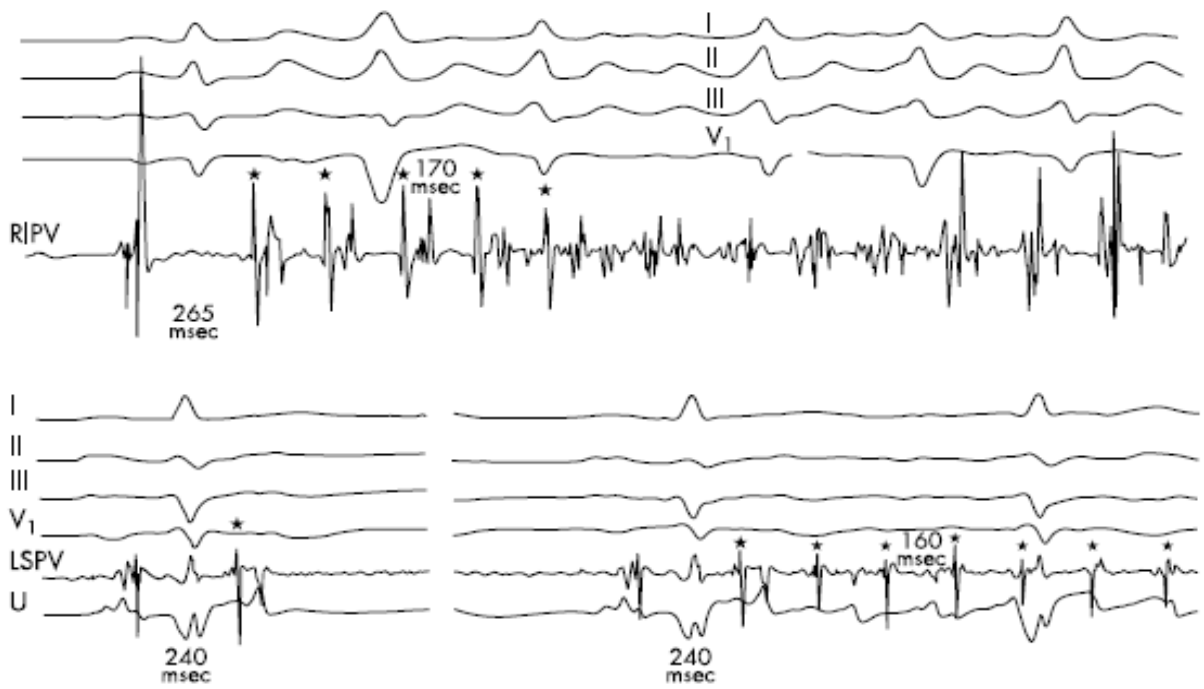
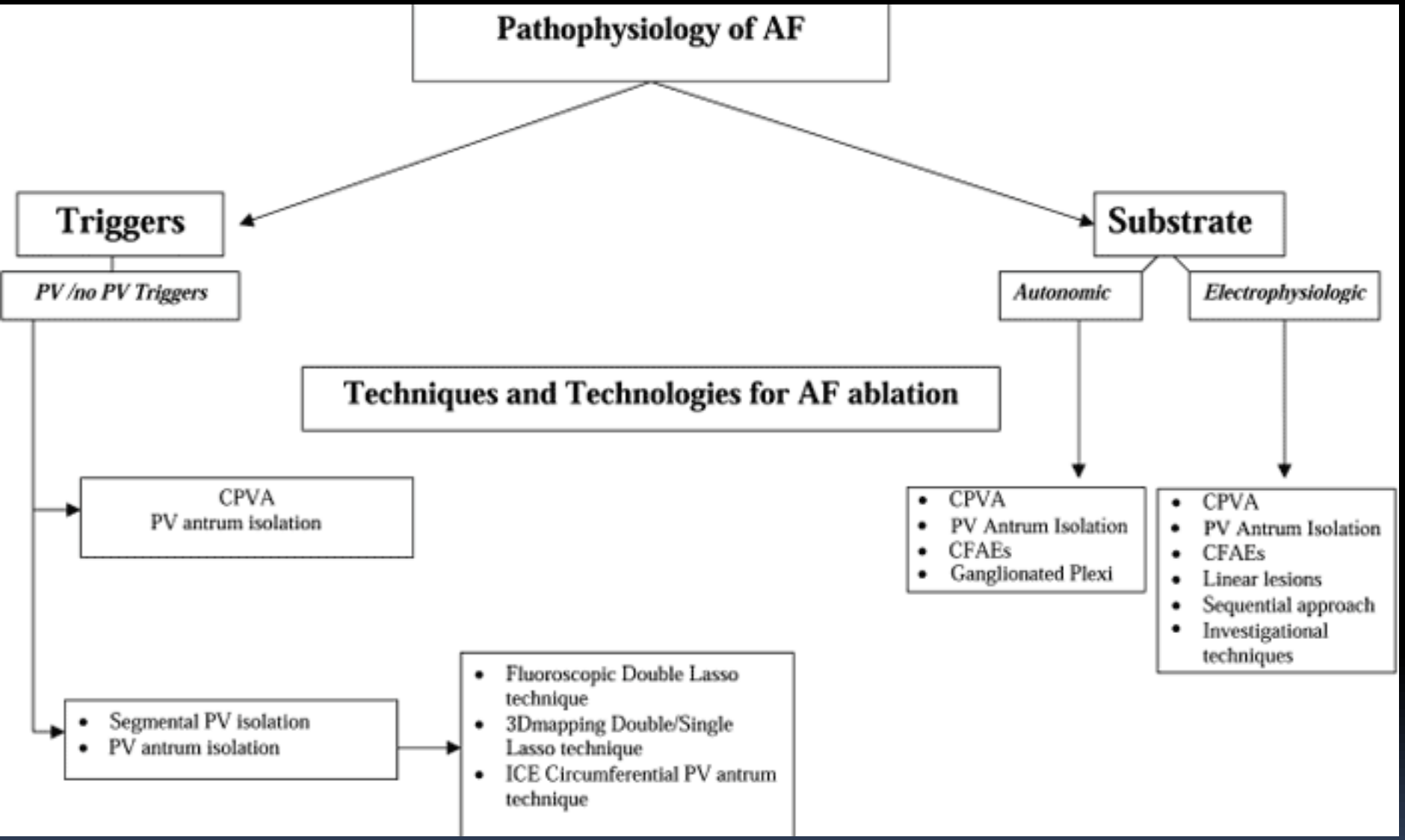
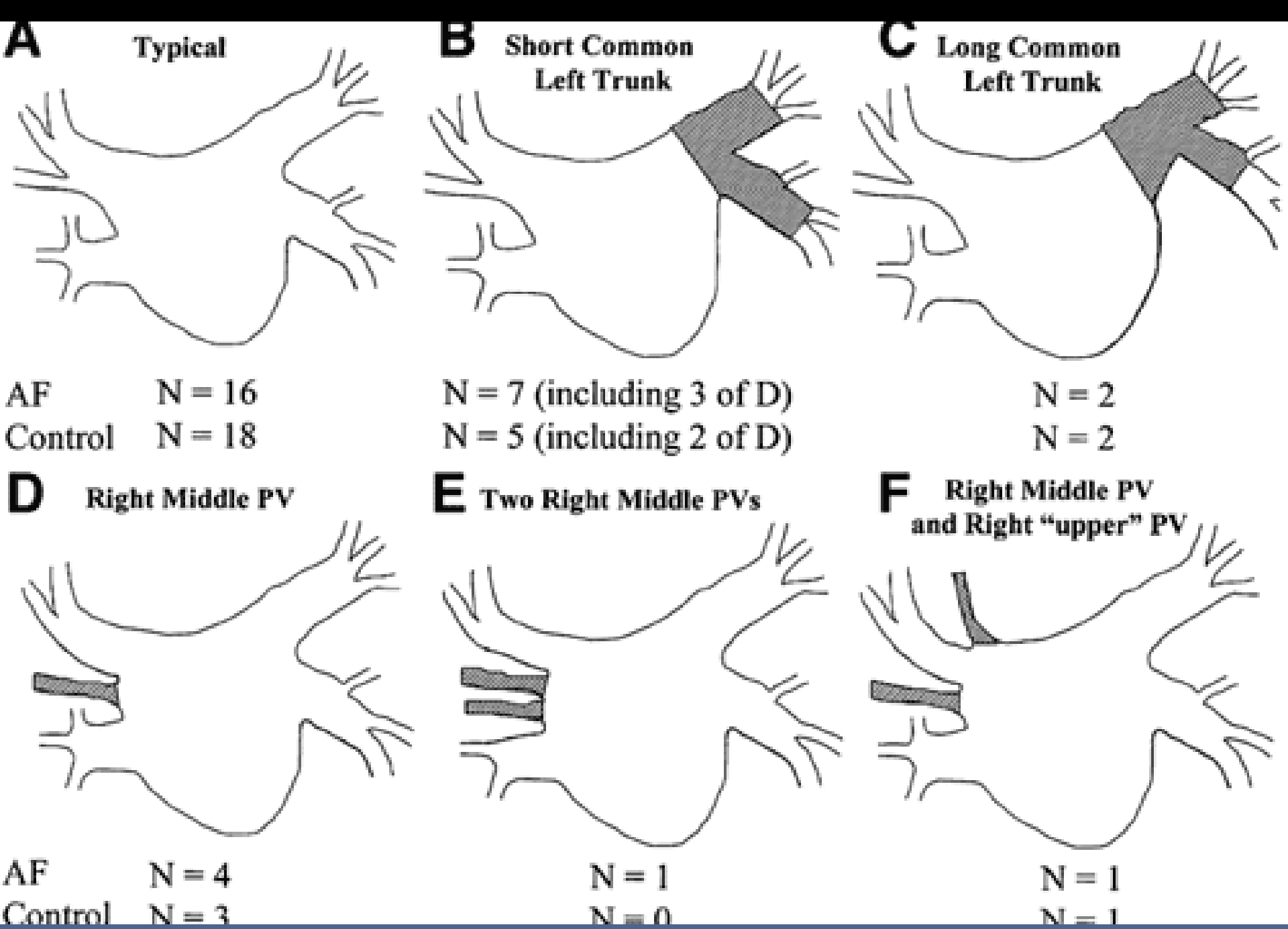
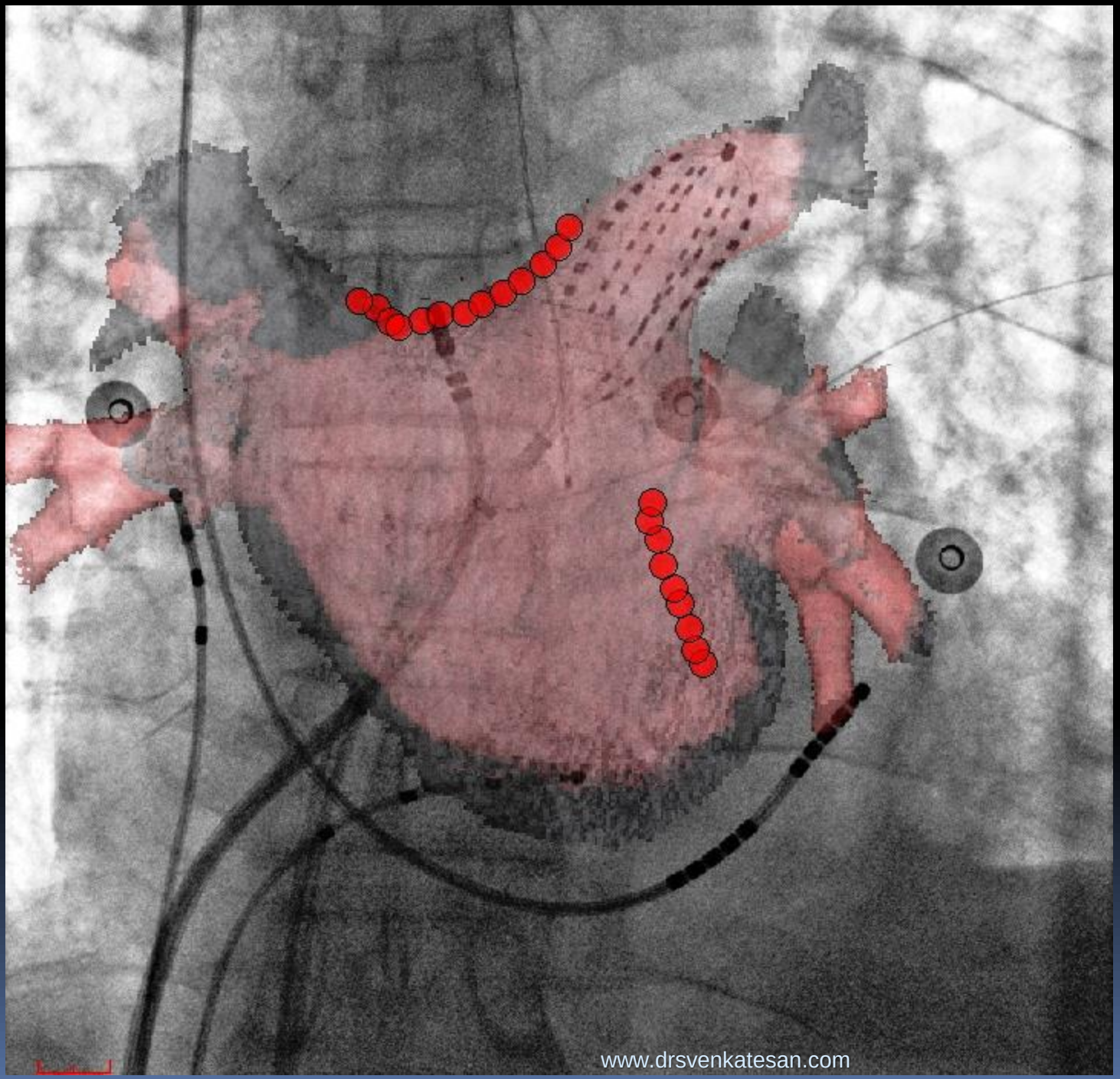
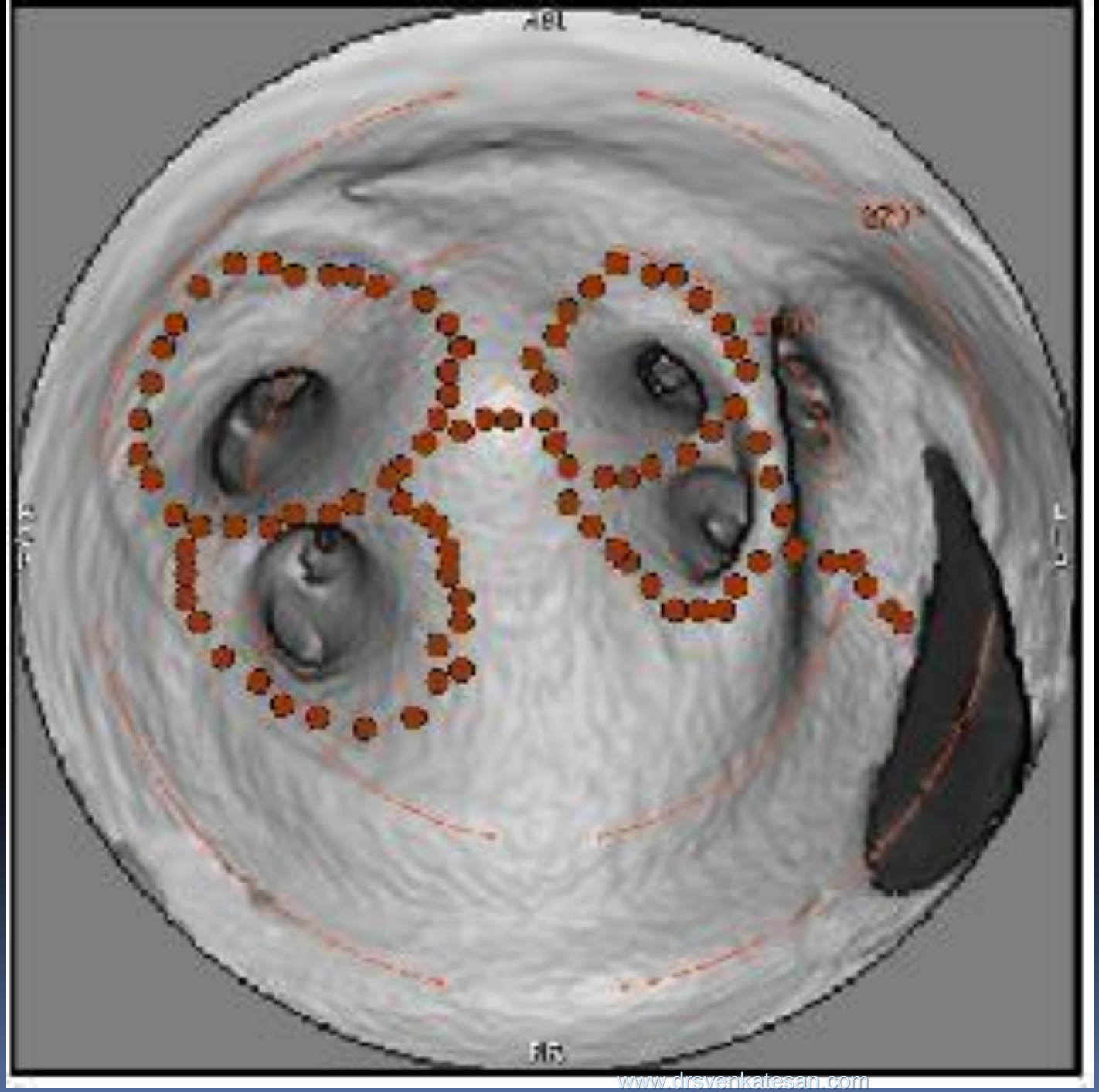


Figure 18.4 Two examples of the onset of atrial fibrillation from foci in a right inferior pulmonary vein (RIVP) and a left superior pulmonary vein (LSVP). In the upper panel, sinus rhythm is followed by a burst of five ectopic beats from the right inferior pulmonary vein, with coarse atrial fibrillation on the surface ECG. In the lower panel, two tracings with ectopic activity from the left superior pulmonary vein are shown. On the left an ectopic beat with a coupling interval of 240 ms does not induce atrial fibrillation. In the same patient (on the right), a train of spike discharges (asterisk) at a cycle length of 160 ms initiates atrial fibrillation. Reproduced from Haissaguerre *et al*,[3] with permission of the Massachusetts Medical Society.


Pathophysiology of AF
Triggers
Substrate
PV /no PV Triggers
Autonomic
Electrophysiologic
Techniques and Technologies for AF ablation
CPVA
PV antrum isolation
CPVA
PV Antrum Isolation
CFAEs
Ganglionated Plexi
CPVA
PV Antrum Isolation
CFAEs
Linear lesions
Sequential approach
Investigational techniques
Segmental PV isolation
PV antrum isolation
Fluoroscopic Double Lasso technique
3Dmapping Double/Single Lasso technique
ICE Circumferential PV antrum technique


A
Typical
B
Short Common
Left Trunk
C
Long Common
Left Trunk
AF N = 16
Control N = 18
N = 7 (including 3 of D)
N = 5 (including 2 of D)
N = 2
N = 2
D
Right Middle PV
E
Two Right Middle PVs
F
Right Middle PV
and Right "upper" PV
AF N = 4
Control N = 3
N = 1
N = 0
N = 1
N = 1


www.drsvenkatesan.com



Future directions

Defibrillator strategies

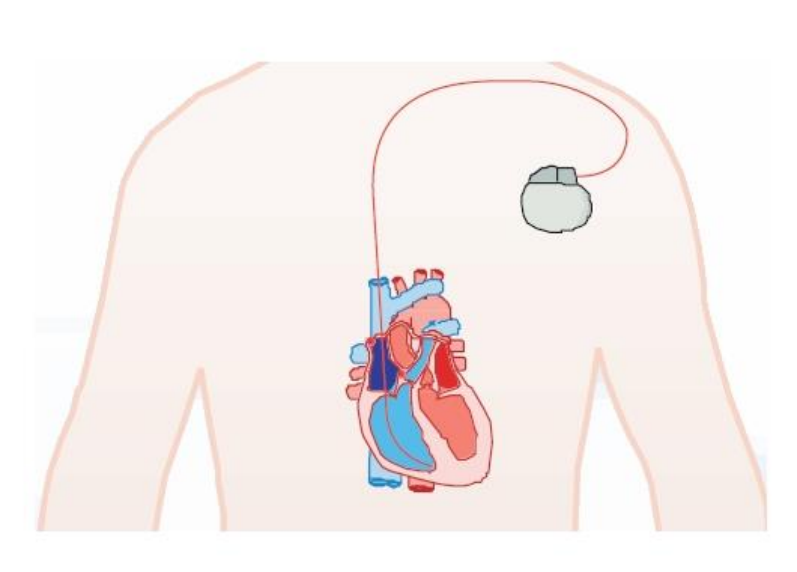
•The ICD can detect and treat AF early after initiation

• Combined atrial and ventricular ICDs are useful in selected patients, especially in those who need a ventricular ICD and also suffer from poorly tolerated AF.

• Stand alone atrial ICD will be available soon

Disadvantage: AF is not prevented. the shock is painful

Pacing strategies



Pacing strategies to prevent or terminate AF In several clinical situations atrial pacing has been shown to prevent the development of AF. In patients with sick sinus node disease, AAI pacing proved to be superior to VVI pacing in reducing the incidence of

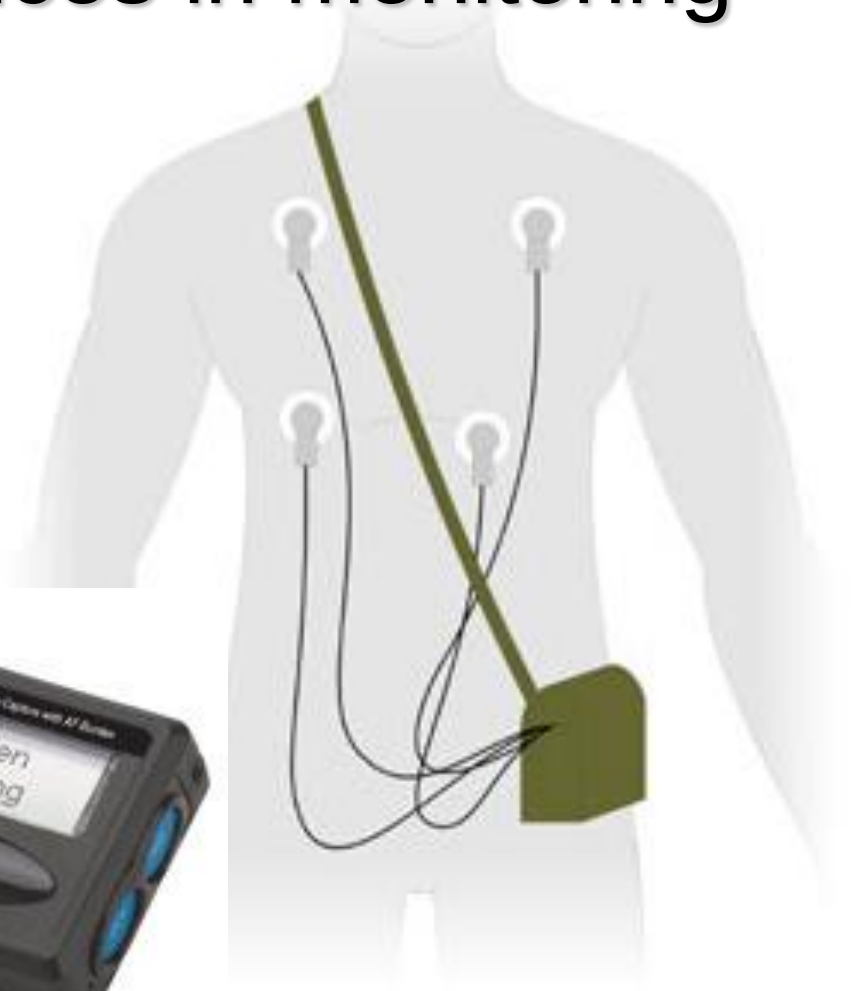
Surgical strategies

Maze

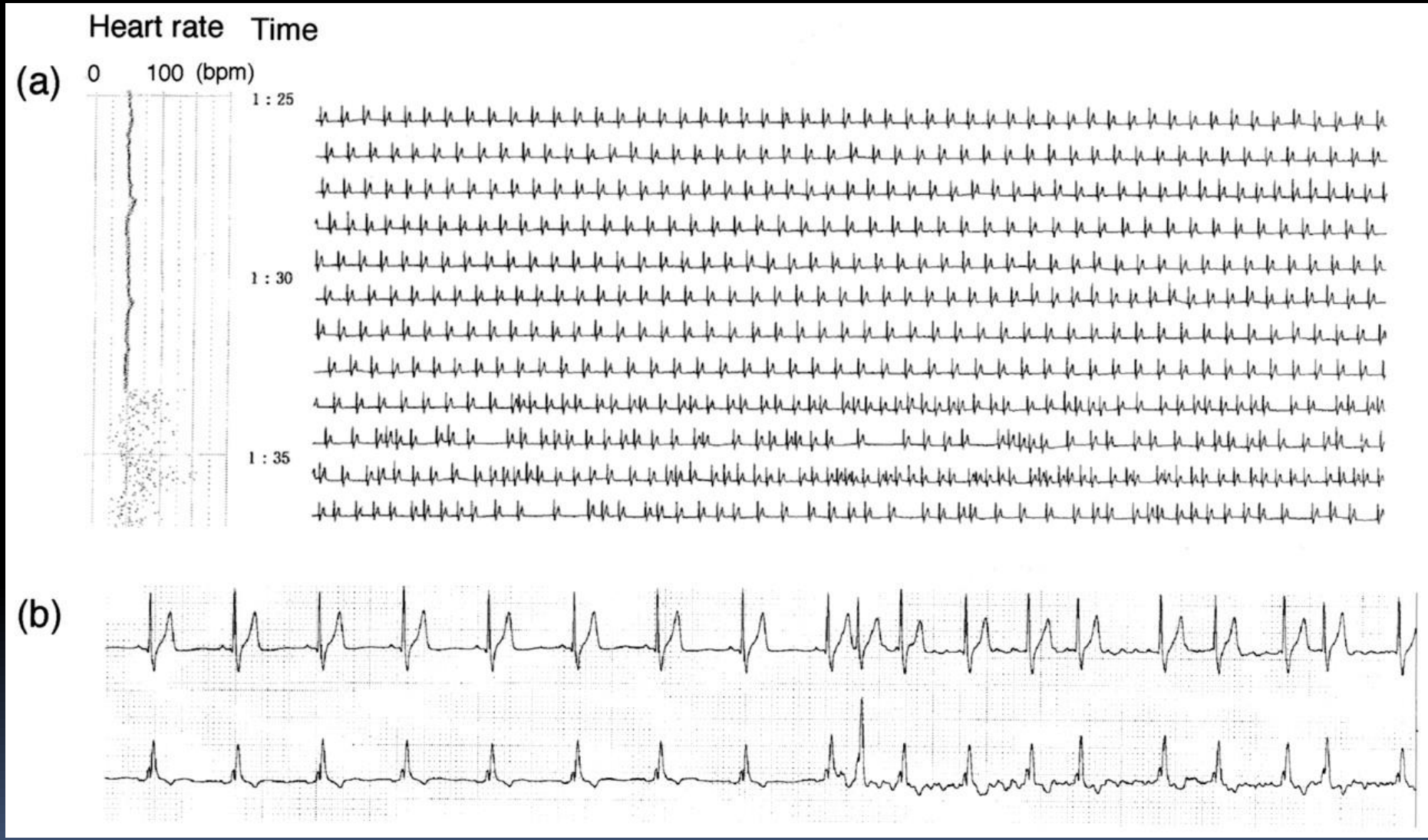
Corridor

During MVR

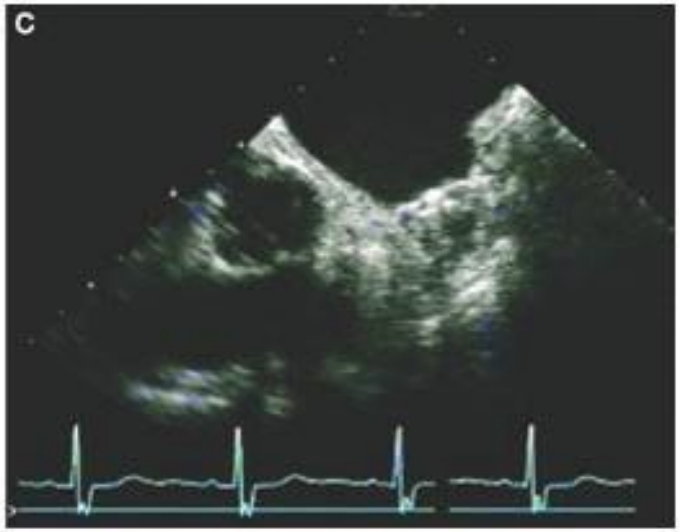
Advances in monitoring

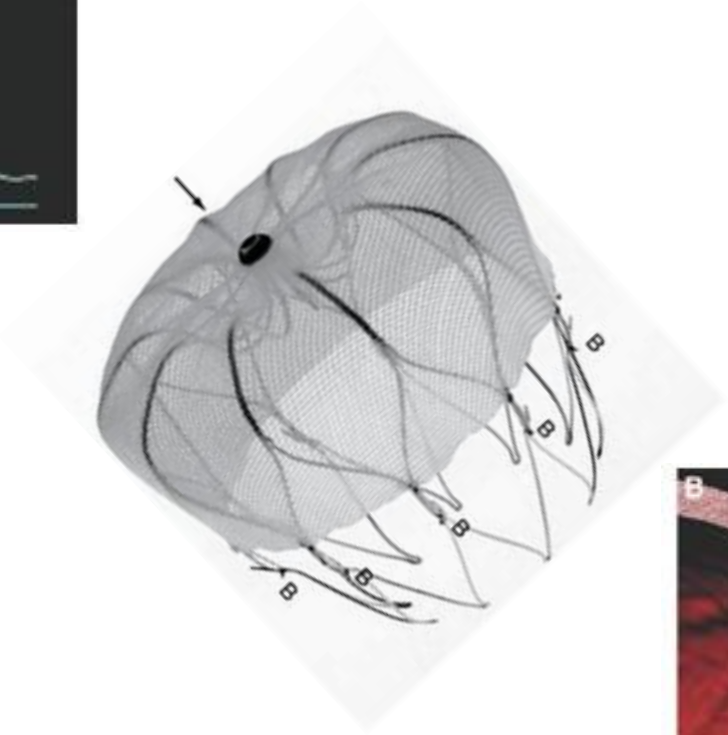


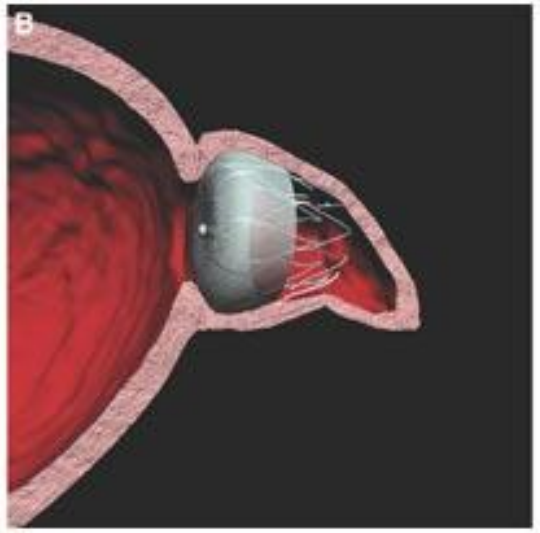
AF burden by advanced loop recorders


Heart rate
Time
(a)
0
100 (bpm)
1 : 25
1 : 30
1 : 35
(b)

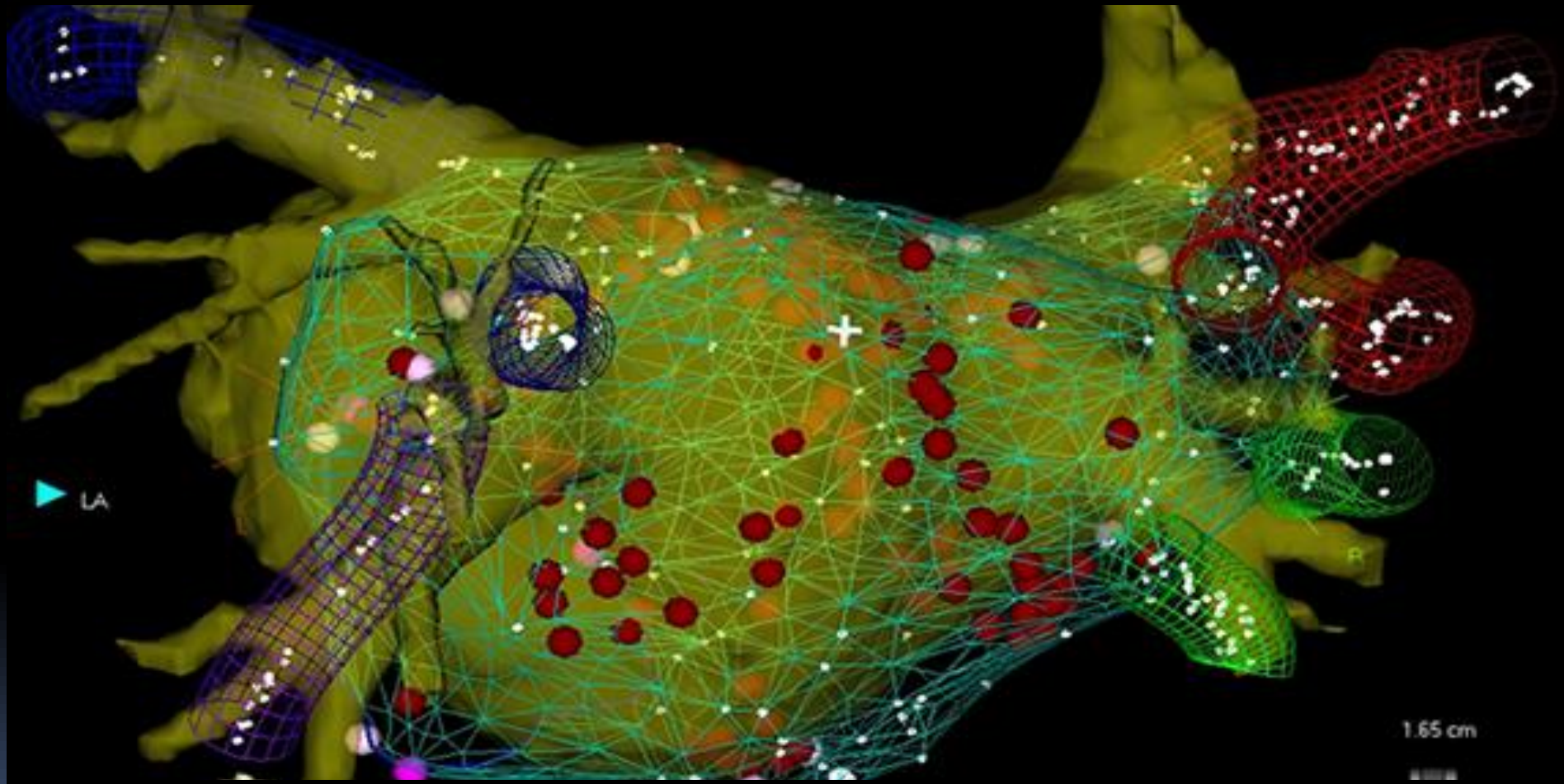
Left atrial appendage occlusion







Advances in science make AF look A complex problem ,



The essential principle in management remain simple !

Final messages

- AF is the most common cardiac arrhythmia.
- Occurs both in diseased heart as well as normal hearts.
- In India the ratio is very much tilted towards diseased heart.
- So correct the primary problem

- Some require emergency management.
- While few require no treatment
- Controlling the VR is the primary aim
- AG in all valvular & high risk nonvalvular
- Attempt rhythm control at least once If possible
- Do not worry too much if patient remains in AF but ensure rate control.

“The main purpose of science is to make things simple not to add complexity ”