Anti-arrhythmic drugs:
Practical Points for Primary Care

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Objectives

At the end of this presentation, the participant will be able to:

- Identify arrhythmias that can be treated pharmacologically and those that require urgent/emergent intervention.
- Differentiate between treatment and control of these arrhythmias.
- Identify common antiarrhythmic, rate controlling and risk reduction drugs and their initial doses and special considerations
- Be familiar with related necessary diagnostic monitoring (labs, EKG)
- Identify the goals of drug therapy, rate vs. rhythm control, effects and evaluation of patients' response, including management of adverse reactions and need for discontinuation.
- Give rationale for selecting a drug of choice, including evidence based guidelines and contraindications for specific antiarrhythmic drugs.
- Describe initial dosage, including age specific, renal and hepatic considerations
- Discuss the results of relevant or current clinical trials: ATHENA, DIONYSOS, DAPHNE.

Rhythm ID

- **Supraventricular tachycardia:**

  -atrial fibrillation (AF)

  -atrial flutter (AFL)

  -multifocal atrial tachycardia (MAT)

  -atrial tachycardia (AT)

  -sinus tachycardia (ST)

  -AV nodal reentrant tachycardia (AVNRT)

  -AV reentrant tachycardia (AVRT)

- **Ventricular arrhythmias**

  -ventricular tachycardia (VT)

  -ventricular fibrillation (VF)

What am I looking at?

- Be sure your EKG is as clear as possible
- Be sure your EKG is as current as possible (do one in the office)
- Get as much info from the patient as possible:
  - Symptoms
  - Onset
  - Duration
  - Provoking/relieving factors

What am I looking at?

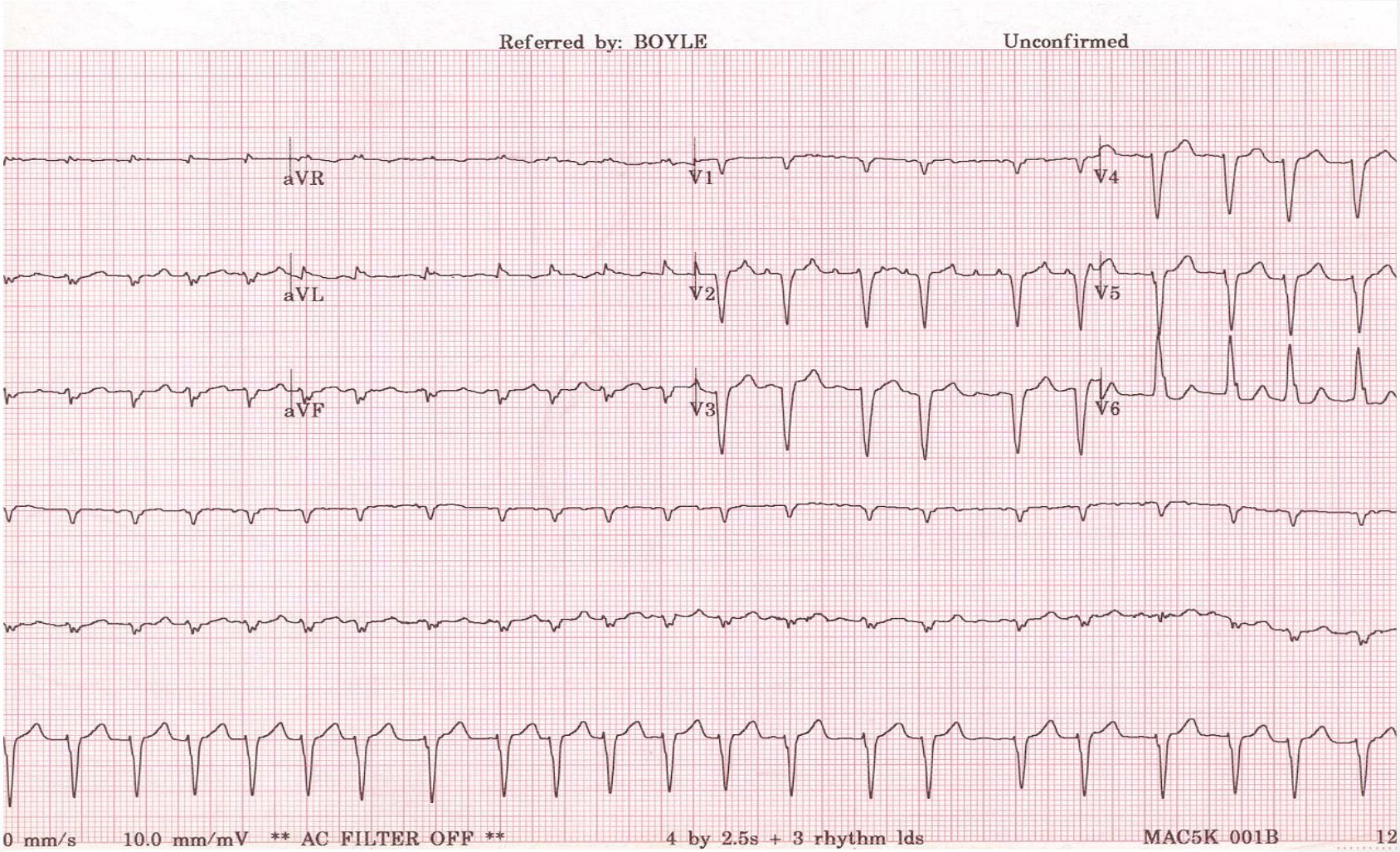
Remember your basic EKG:

- Regular?
- Rate?
- Is there a P wave for every QRS?
- QRS narrow or wide?

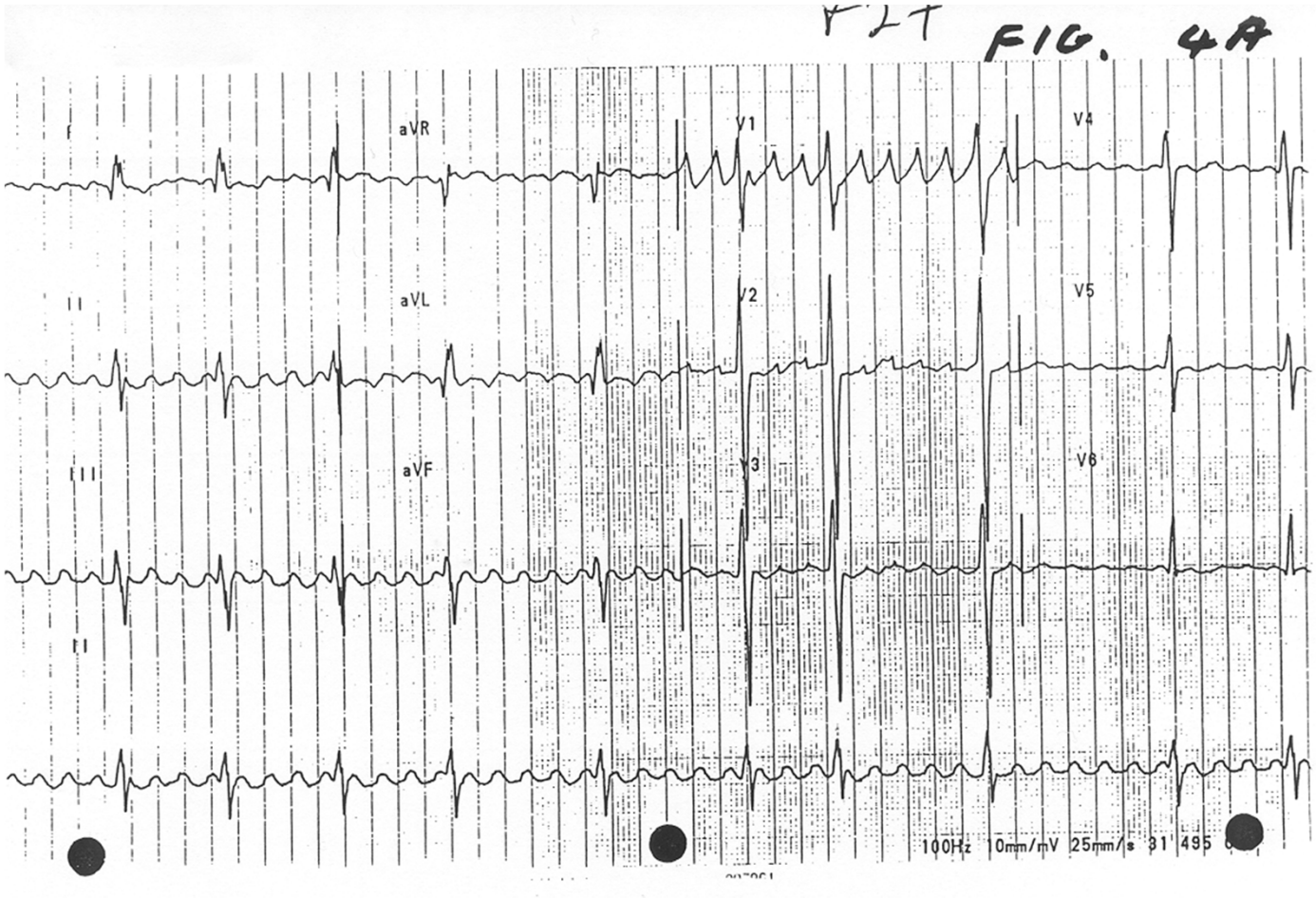
Clinical Manifestations of Arrhythmias

- Palpitations
- Dizziness or lightheadedness
- Loss of consciousness
- Dyspnea
- Weakness
- Asymptomatic

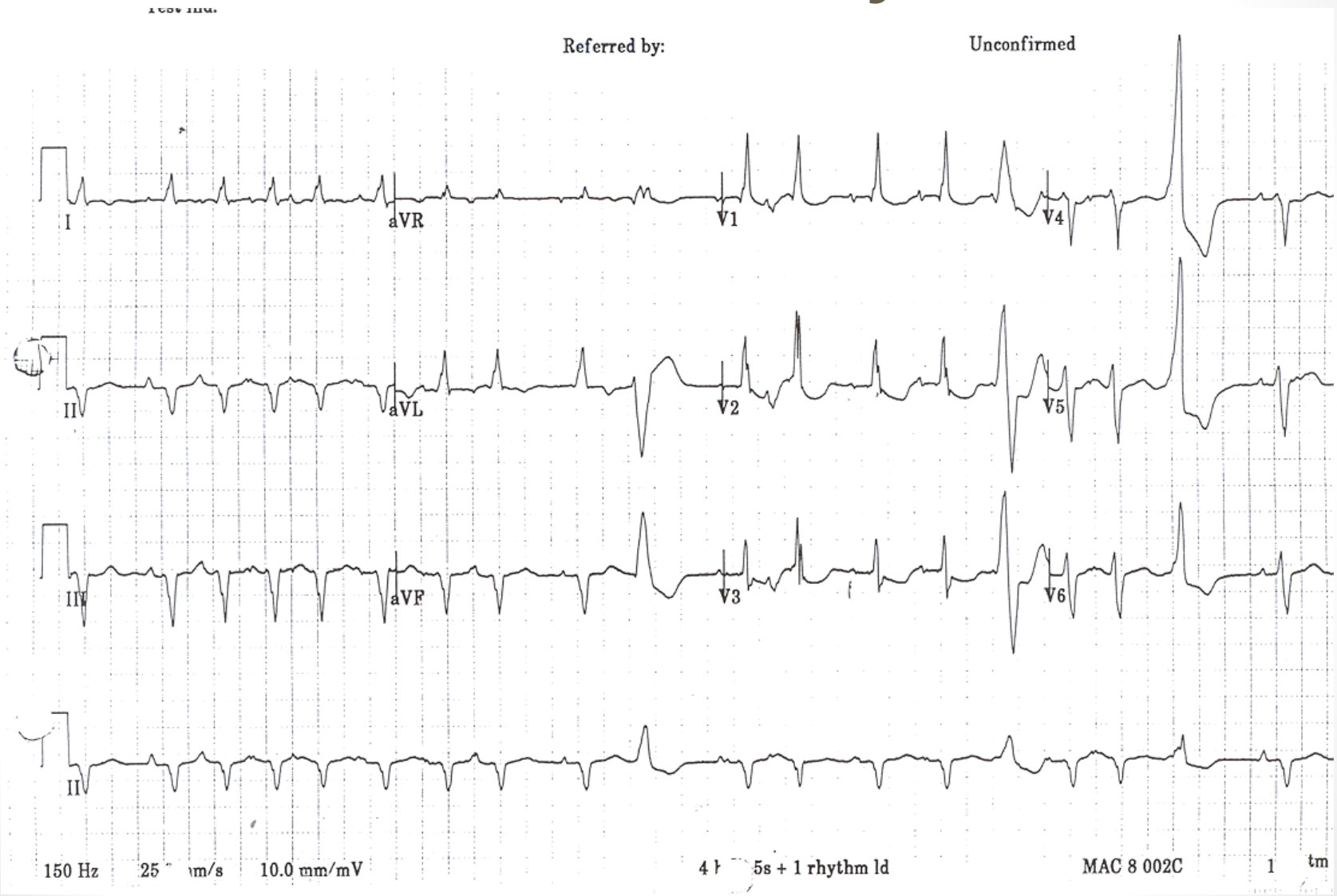
Atrial fibrillation



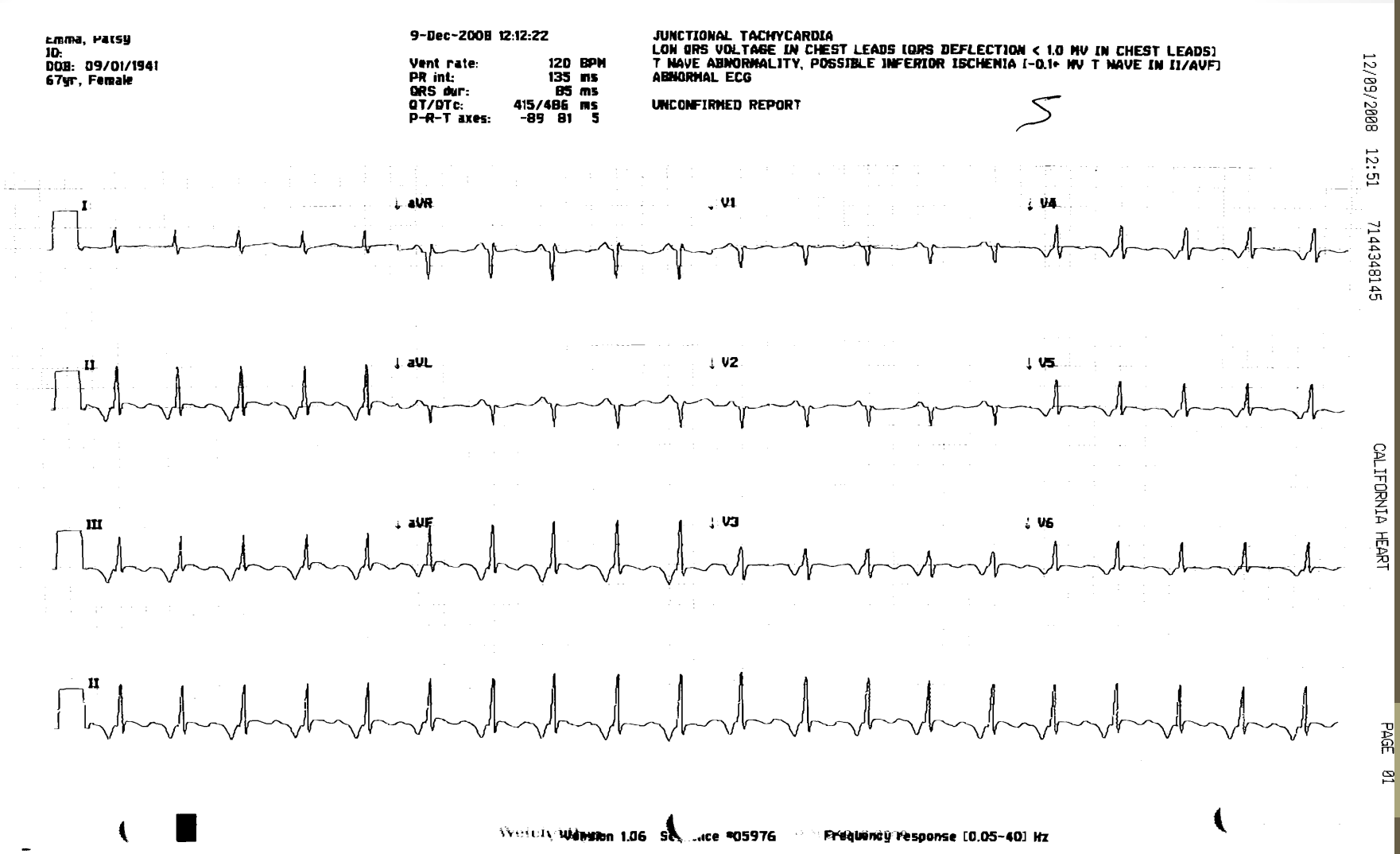
Atrial flutter



Multifocal atrial tachycardia



Atrial tachycardia



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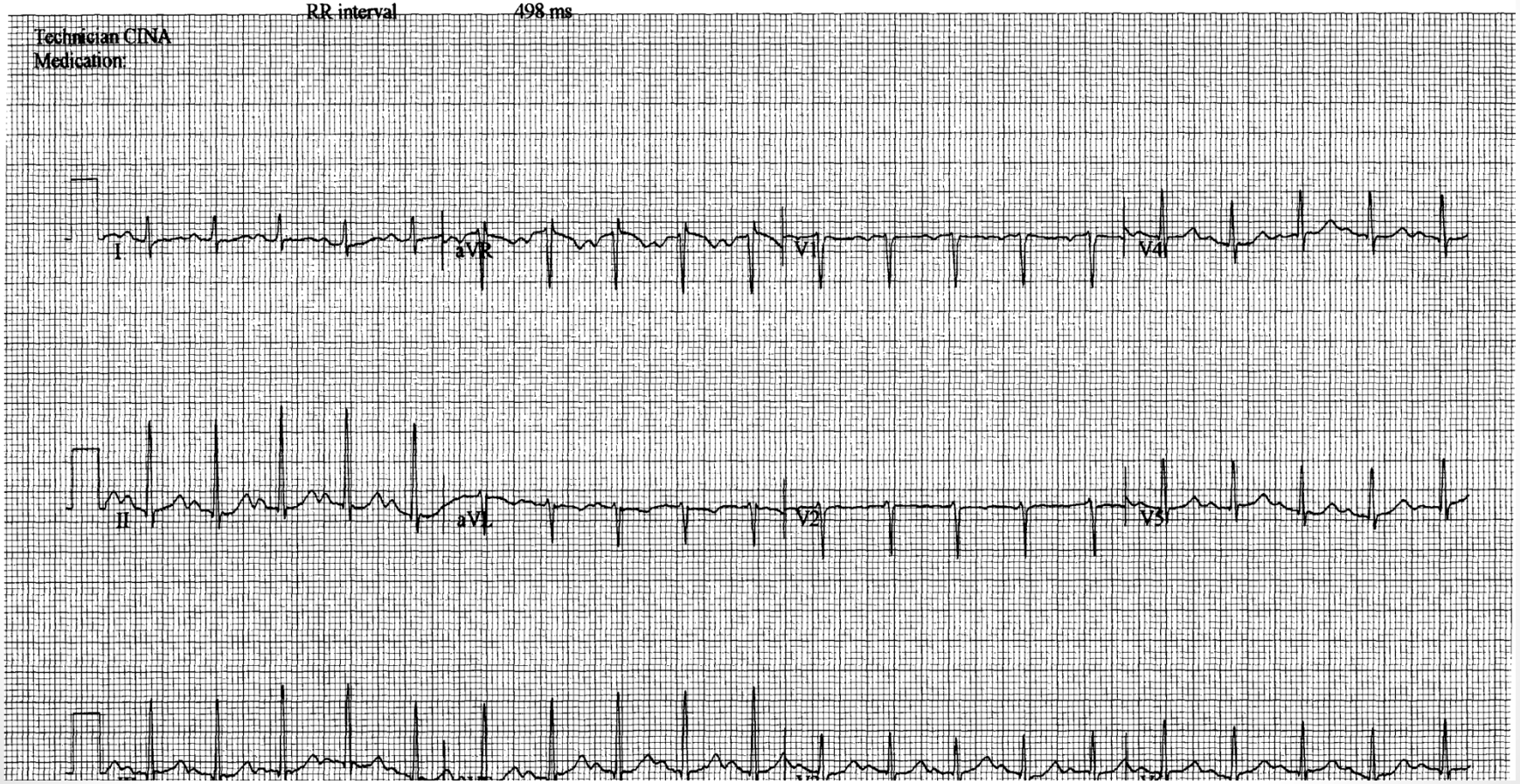
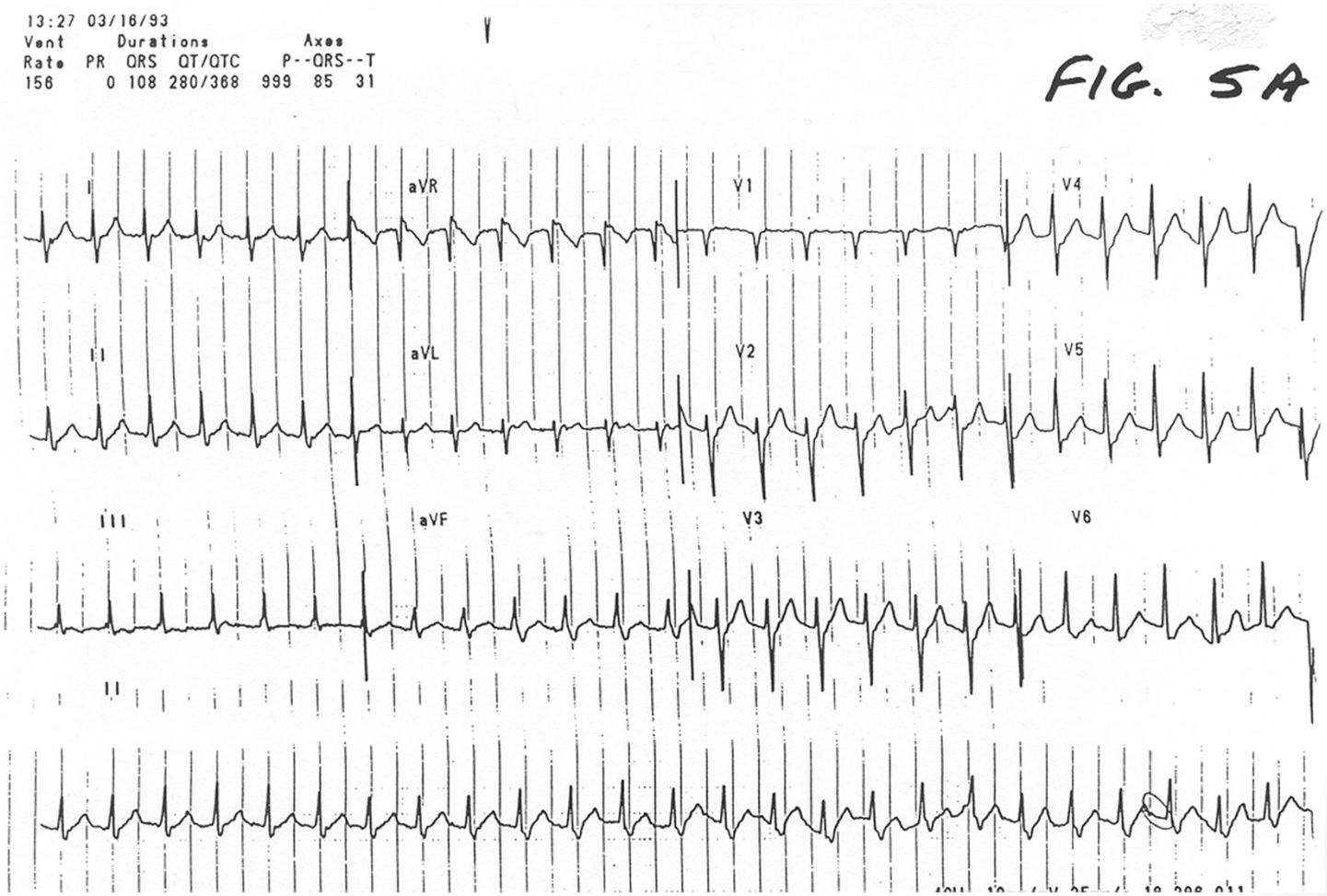
Sinus tachycardia

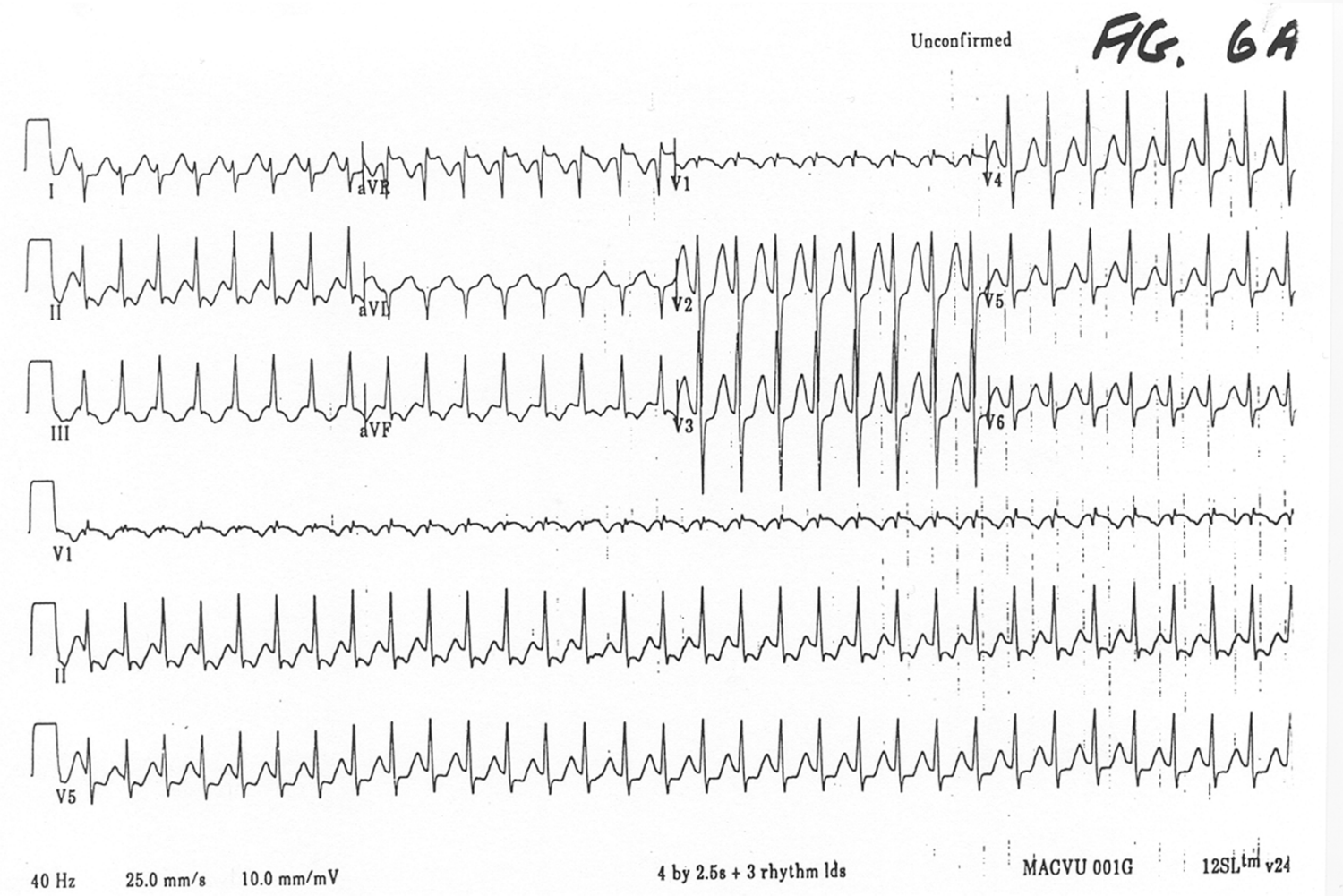
Vent. Rate	120 bpm	Sinus tachycardia
PR interval	162 ms	Otherwise normal ECG
QRS duration	86 ms	
QT/QTc	320/452 ms	
P-R-T axes	50/85/79	
P duration	86 ms	
RR interval	498 ms	



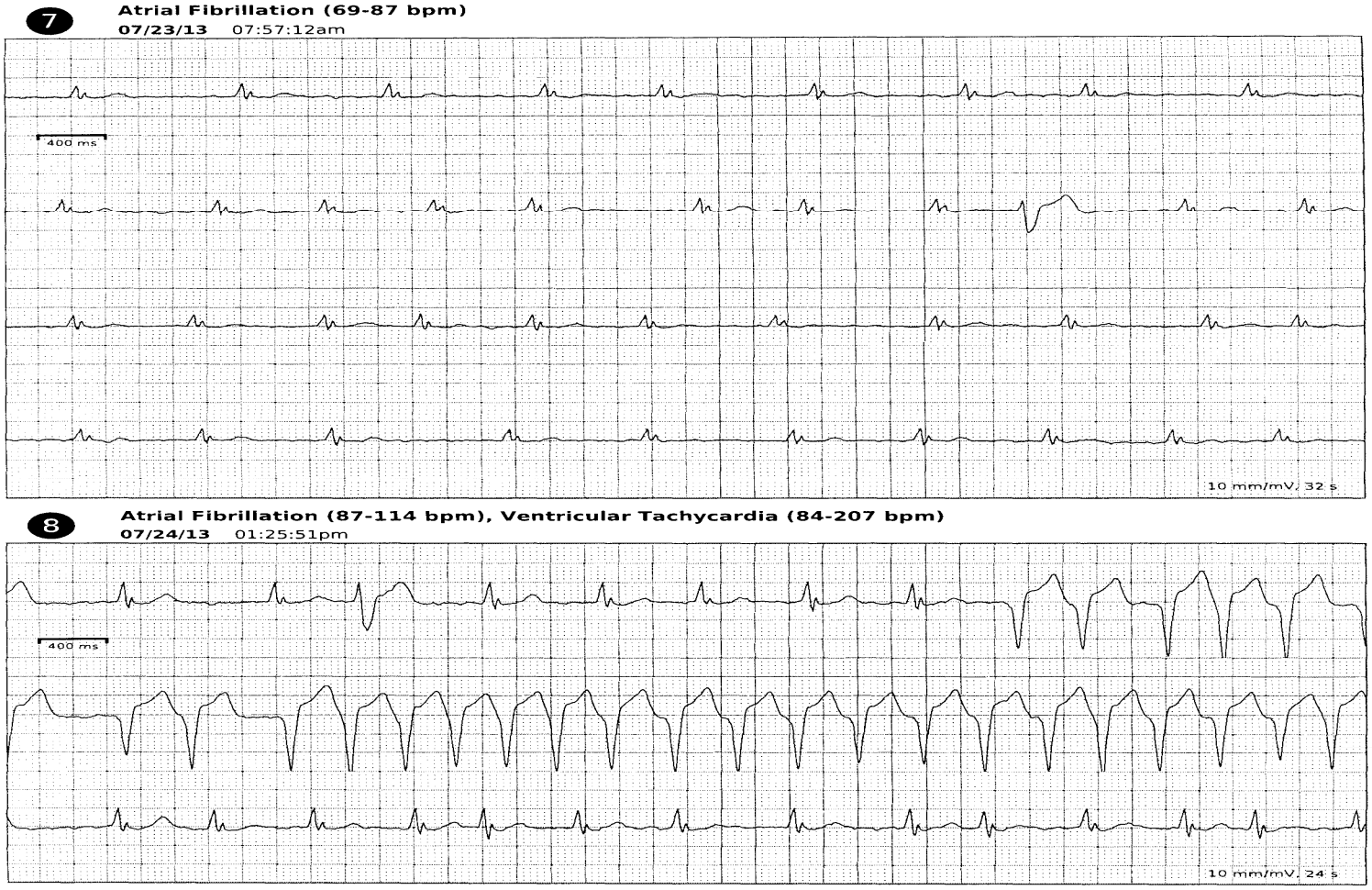
AV nodal reentrant tachycardia



AV reentrant tachycardia



Ventricular tachycardia



Patient: **Houghtaling, David** ID: **7666961** S/N: **Z320813972** © 2013 iRhythm Technologies, Inc. Page 16 of 19

Ventricular Tachycardia

- Will most likely be identified on event monitor, not EKG
- Refer to cardiology:

  -needs ischemia/cardiomyopathy work-up

  -management of symptoms (if any)

  -suppression drugs vs. ablation

Initial Treatment of most SVT

Determine whether or not it needs immediate attention

-Symptoms and/or poor rate control=yes

-Asymptomatic and rate controlled=no

…excepting atrial fibrillation of course.

Initial Treatment of Most SVT

Presently occurring in the office with symptoms:

- unstable goes to ER
- vagal maneuvers
- fails to terminate then rate control with beta blockers, verapamil, diltiazem and refer to cardiology

Vagal maneuvers

- Bear down
- Cough
- Ice water
- Or carotid massage

Long term Treatment

- Vagal maneuvers-enough
- Frequent recurrence, unable to terminate with vagal maneuvers-antiarrhythmic meds
- Meds fail or patient refuses meds-ablation

Treatment vs. Control

Both result in increased cardiac output.

- Treatment is aimed at eliminating the arrhythmia or reducing the frequency of its recurrence

  -may be vagal maneuvers, ablation or antiarrhythmic meds

- Control is aimed at managing HR, reducing symptoms and associated risks

  -may be antiarrhythmic meds, anticoagulation or ablate and pace therapy

(O'Brien, 2012)

Pregnancy

- SVT increases in frequency during pregnancy
- Most common is AVNRT
- Adenosine, digoxin, propranolol, procainamide and flecainide are considered safe, highest risk in first eight weeks
- Use of multiple drugs can lead to fetal bradycardia

(Perez-Silva, 2014)

And then there's AF…

- Now projected to occur in 1:4 persons over the age of 65
- Wide range of associated symptoms from none to chest pain and hypotension
- Treatment/control can be difficult due to vague symptoms
- Associated stroke risk in some

(Rienstra, 2012)

Atrial Fibrillation : Clinical Syndromes

- Paroxysmal Atrial Fibrillation (< 48 hours) ; spontaneously converts

- Persistent Atrial Fibrillation;
  requires cardioversion (chemical or electrical)

- Permanent (Chronic) Atrial Fibrillation (> 6 months)

Reasons for Restoring Sinus Rhythm in Patients with Atrial Fibrillation

- mortality double in those with AF
- appropriate/physiologic rate control
- regularization of heart rhythm
- improved hemodynamics
- maintenance of normal electrophysiology
- prevention of left atrial dilatation
- prevention of left ventricular dysfunction
- reduce thromboembolic complications (?)
- relief of symptoms (dyspnea, fatigue, palpitations)

(O'Brien, 2012, p. 120)

Drugs in Atrial Fibrillation

Eleven drugs available in US :

IA	IC	III
Quinidine	Flecainide	Sotalol
Procainamide	Propafenone	Amiodarone
Disopyramide		Ibutilide
		Dofetilide

II Propanolol

IV Diltiazem
Verapamil

OTHER: Digoxin

FDA Approved for Atrial Fibrillation: Quinidine, Flecainide,Propafenone, Ibutilide, Sotalol, Dofetilide, Dronedarone

(Lehne, 2007)

SVT Meds

- Beta blockers may prevent or at least reduce symptoms
- Class IV meds: verapamil, diltiazem
- Class IC meds: flecainide, per cardiology

AF Treatment

- Quinidine
- Disopyramide
- Propafenone
- Flecainide
- Dofetilide
- Sotalol
- Amiodarone (not FDA approved)
- Ibutilide
- Dronedarone

Quinidine

- Class IA, depresses action potential
- 300-600 mg Q8-12 hours, individualize dose
- Adverse effects: arrhythmia, AV block, GI, headache, hypotension, blurred vision
- Monitor: Cr,LFT, EKG

Disopyramide

- Class IA, depresses action potential
- 400-750 mg daily, divided doses
- Adverse effects: CHF, hypotension, syncope, constipation, dizziness, headache
- Monitor: both renal and hepatic function, may need dose adjustment, ECG

Flecainide

- Class IC, depresses action potential
- 50-300 mg daily, divided doses
- Side effects: arrhythmias, CHF, heart block, hematologic, dyspnea, headache, nausea, fatigue
- Monitor: Cr, electrolytes, ECG
- Allow cardiology to manage

Propafenone

- Class IC, depresses action potential
- 150-300 mg Q8 hrs
- Adverse effects: ventricular arrhythmias, CHF, AV block, dizziness, nausea, fatigue, headache
- Monitor:ECG

Dofetilide

- Class III, prolongs action potential
- 500 mg Q 12 hrs, adjust for QTc
- Adverse effects: QT prolongation, ventricular arrhythmias, torsade's, headache, dizziness, nausea
- Monitor: QT, renal and hepatic function, MUST be started in house by cardiology

Sotalol

- Class III, beta-1/beta-2 antagonist, prolongs action potential
- 80-160 Q 12 hrs
- Adverse effects: CHF, bradycardia, bronchospasm, dyspnea, fatigue, headache
- Monitor: renal function, adjust dose, EKG

Amiodarone

- Class III, prolongs action potential
- 200-600 mg daily
- Adverse effects: bradycardia, AV block, pulmonary tox, thyroid tox, pancreatitis, etc…
- Monitor: LFT, TFT, PFT, ECG

Control

- Beta blockers
- Calcium channel blockers
- Amiodarone
- Digoxin

Beta blockers

- Class II, beta-1 antagonist
- Atenolol: 50-100mg daily
- Metoprolol: 20-200 mg daily
- Bisoprolol: 2.5-20 mg
- Nebivolol: 2.5-40 mg daily

Side effects general to drug class: bradycardia, hypotension, fatigue, dizziness, bronchospasm

No lab monitoring

Calcium channel blockers

- Class IV, prolongs AV refractory period
- Verapamil: 80-120 mg TID to QID
- Diltiazem: 30-420 mg, varies due to different formulations

Side effects general to drug class: bradycardia, AV block, hypotension, constipation

Monitor: BUN/Cr, LFTs

Digoxin

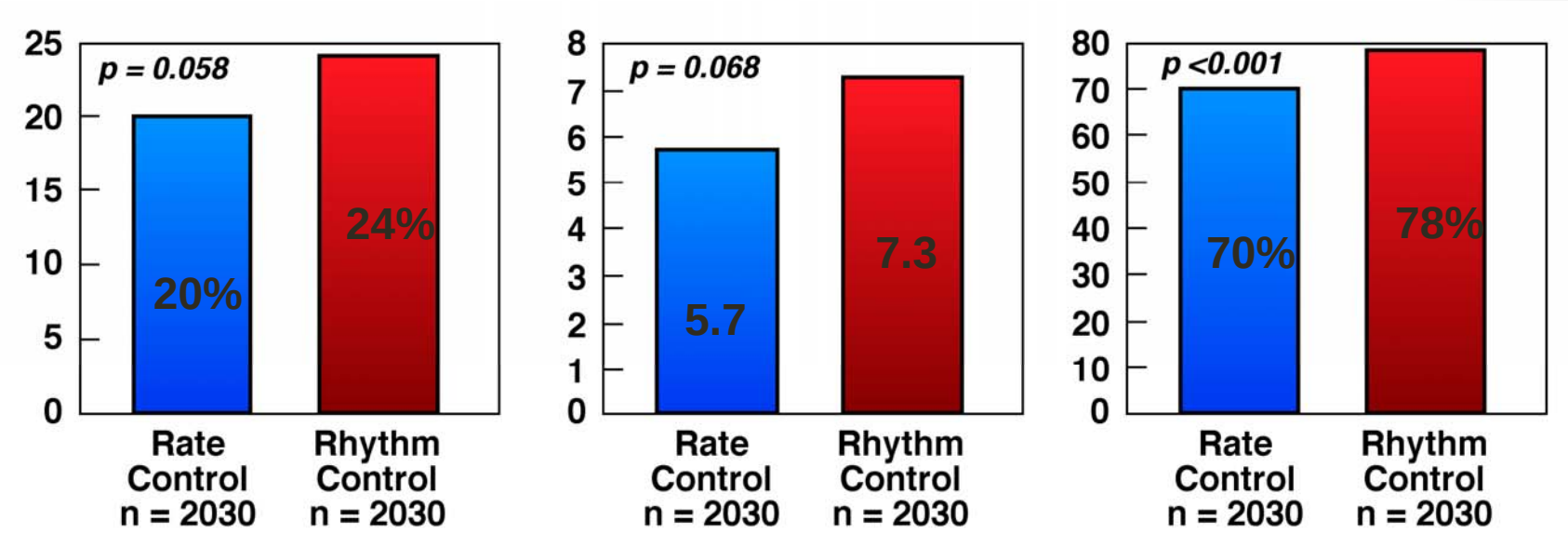
- Other, inhibits Na-K ATPase
- 0.125-0.5 mg daily
- Adverse effects: AV block, bradycardia, dizziness, headache, nausea/vomiting
- Monitor: Cr, electrolytes, drug level

AFFIRM Trial Results

Mortality : No difference

Strokes : No difference

Hospitalizations*



4060 patients; enrolled 1995-99; age > 65 yrs or <65 yrs with HTN, CHF; AF duration > 6 hours

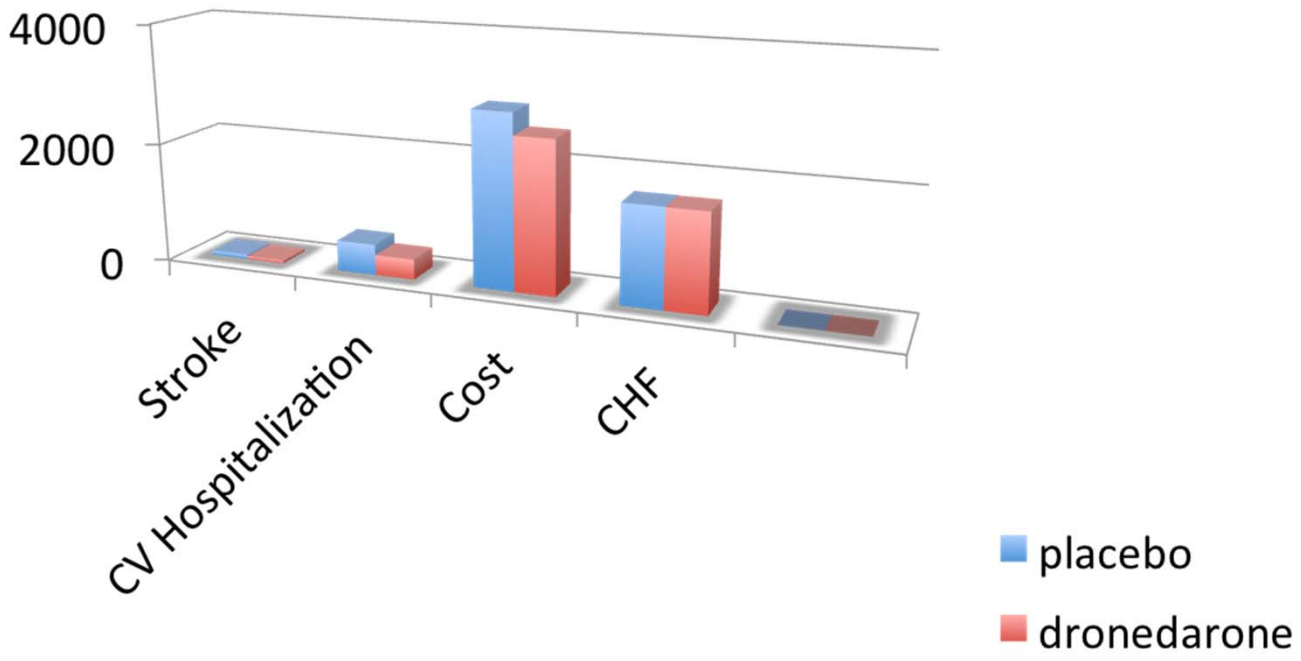
PRIMARY ENDPOINT: Mortality; Secondary endpoints: stroke, QOL

RATE CONTROL: **Digoxin 51%, beta blockers 49%, Calcium channel blocker 41%, ablate and pace 5%**

RHYTHM CONTROL : **Amiodarone 39%, Sotalol 33%, Propafenone 10%, Procainamide 5%, Quinidine 5%.**

AFFIRM Investigators NEJM 2002; 347:1825-33

ATHENA



4628 patients with history of PAF/persistent AF; enrolled 2005-2006, follow-up for one year

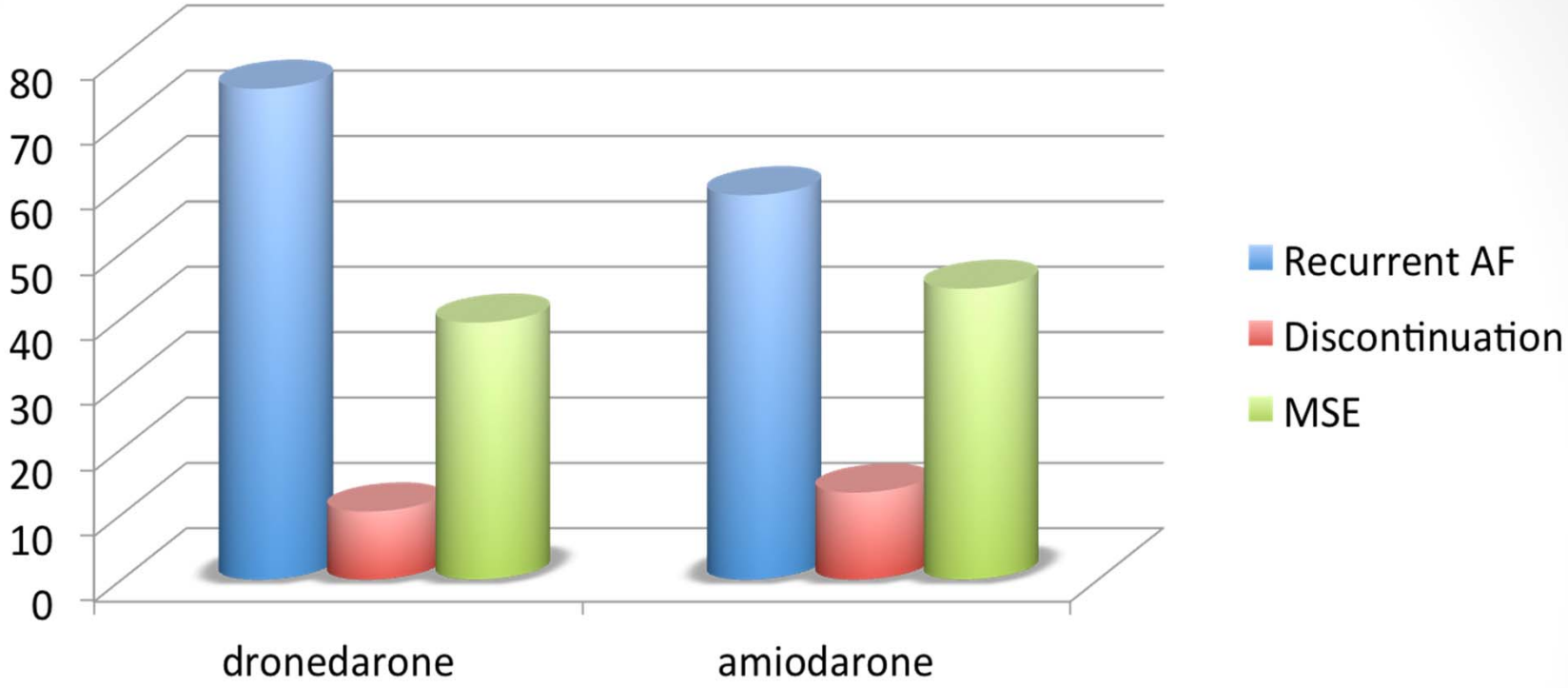
> 70 yr old, HTN, DM, LAE and/or EF <40

PRIMARY ENDPOINT: first cardiovascular hospitalization or any cause death

Greatest benefit of Multaq demonstrated in stroke reduction and CV hospitalization

(Connolly 2009, Reynolds 2013, Hohnloser 2010, Torp-Pedersen 2011)

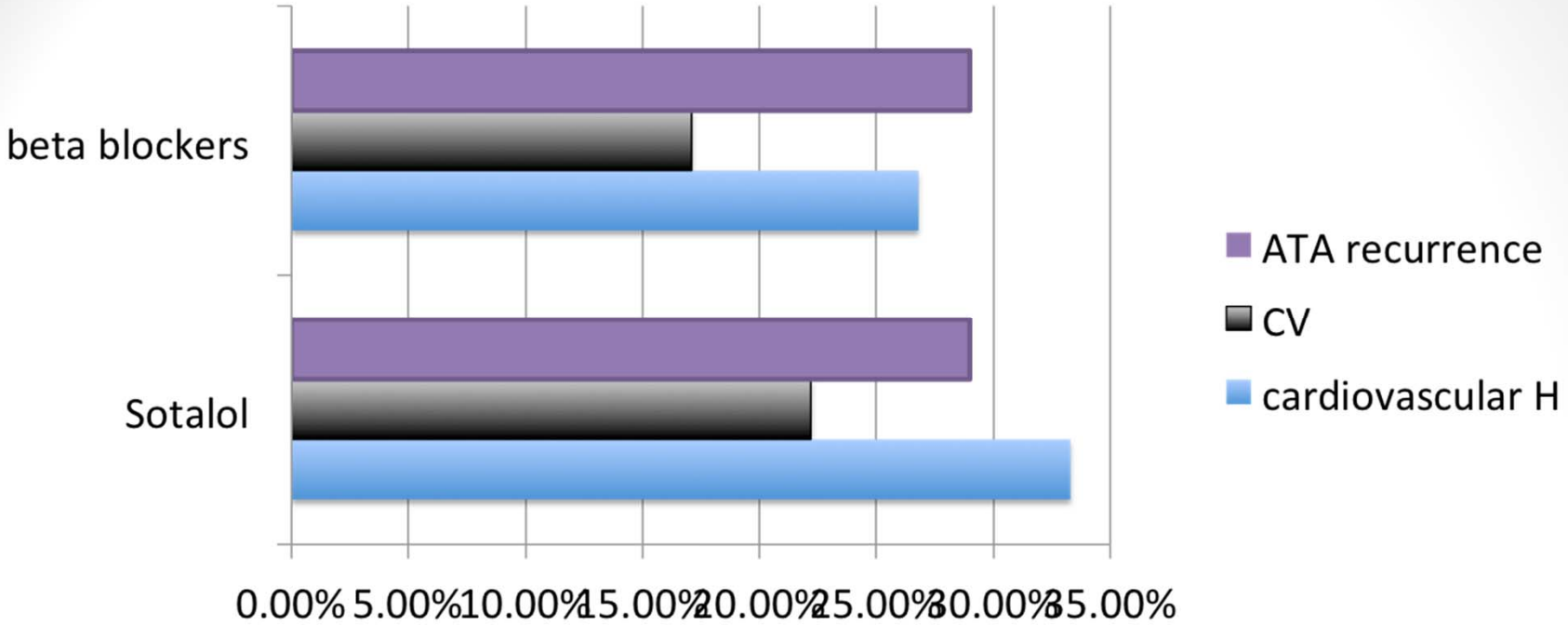
DIONYSUS



404 patients with persistent AF 2007-2008, aged >21, follow-up six mos
PRIMARY ENDPOINT: recurrent AF or premature study discontinuation
MAIN SAFETY ENDPOINT: occurrence of thyroid-, hepatic, pulmonary-, neurologic-, skin-, eye- or GI-specific events

(Le Huezey, 2010)

DAPHNE



135 patients w/dual chamber pacemaker; follow-up 12 months
PRIMARY ENDPOINT: occurrence of atrial CV or cardiovascular hospitalization
ADDTL OBSERVATION: recurrence of ATA

(Capucci, 2008)

Treatment Drugs

- Quinidine
- Flecainide
- Propafenone
- Dronedarone
- Sotalol
- Dofetilide

Quinidine

- Class IA
- 200-600 mg, individualize dose
- Side effects: arrhythmias, AV block, hematologic, hypotension, GI, headache…
- Monitor: Cr, LFTs, ECG

Flecainide

- Class IC
- 50-300 mg daily, divided dose
- Side effects: arrhythmias, CHF, heart block, hematologic, dyspnea, headache, nausea, fatigue
- Monitor: : Cr, electrolytes, ECG

Propafenone

- Class IC
- 150-300 mg daily, divided doses
- Side effects: arrhythmias, AV block, CHF, dizziness, constipation, headache…
- Monitor: electrolytes

Sotalol

- Class III, prolongs action potential
- 80-160 mg daily Q12 hrs
- Adverse effects: CHF, bradycardia, QT prolongation, dizziness, fatigue, diaphoresis
- Monitor: Cr, EKG for QT at initiation and with dose titration

Dofetilide

- Class III
- 500 mcg Q12
- Must be managed by cardiology and initiated in-hospital
- DC if QT longer than 500 ms or > 15% baseline

Dronedarone

- Properties of all four classes
- 400 mg BID
- Side effects: GI, CHF, bradycardia
- Monitor: BUN/Cr, ECG, LFT

Control

- Beta blockers (Class II)
- Calcium channel blockers (Class IV)
- Amiodarone (Class III)

How do I choose?

- Goal
- Comorbidities
- Side effect profile
- Cost

Anticoagulation

- Indication
  - -arrhythmia
  - -CHA2DS2VASc score
- Contraindications
  - -adherence
  - -fall risk
  - -HASBLED score

Indication

- AVNRT, AVRT, AT do not need anticoagulation
- AFL with clear onset and no evidence of AF does not necessarily
- AF of brief duration or no CHA2DS2VASc does not
- AF with unknown onset, long duration and/or CHA2DS2VASc >2 does

(Sparks, 2001)

CHA2DS2VASc

CHA2DS2-VASc Risk	Score
CHF or LVEF <40%	1
Hypertension	1
Age >75	2
Diabetes	1
Stroke/TIA/Thromboembolism	2
Vascular disease	1
Age 65-74	1
Female	1

ESC AF Guidelines:http://escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-afib-FT.pdf

CHA2DS2VASc

CHA2DS2VASc Score	Adjusted stroke rate (%/year)
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	6.7
9	15.2

ESC AF Guidelines:http://escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-afib-FT.pdf

Contraindications

- Medical nonadherance puts patient at greater risk than benefit
- Renal disease/valvular heart disease limits drug choice to warfarin
- Bleeding diathesis or liver failure
- Fall risk
- HASBLED score

HAS-BLED

Risk Factor	Score
Hypertension (systolic BP > 160 mmHg)	1
Abnormal renal/liver function	1 point each
Previous stroke	1
Bleeding history or predisposition	1
Labile INR (unstable/high or <60% time therapeutic)	1
Age >65	1
Drugs (anti-platelet) and/or ETOH	1 point each

(Pisters 2010)

Chronic anticoagulants

- Warfarin
- Apixaban (Eliquis)
- Dabigatran (Pradaxa)
- Rivaroxaban (Xarelto)

warfarin

- Vitamin k antagonist
- Indications: DVT, PE, thromboembolic risk w/AF/valve, MI/CVA
- Long onset, long half life (72-96 hrs, 20-60 hrs)
- Requires lab monitoring
- Cost effective

warfarin

- Many drug interactions
- Food interactions
- Variable once daily dosing
- Must hold 5 days prior to surgery

apixaban

- Factor Xa inhibitor
- Indication: reduce the risk of stroke and systemic embolism in non-valvular AF
- Rapid onset, short half-life (3-4 hrs, 6-12 hrs)
- No lab monitoring
- Costly
- Fewer drug interactions, few food interactions
- Twice daily dosing

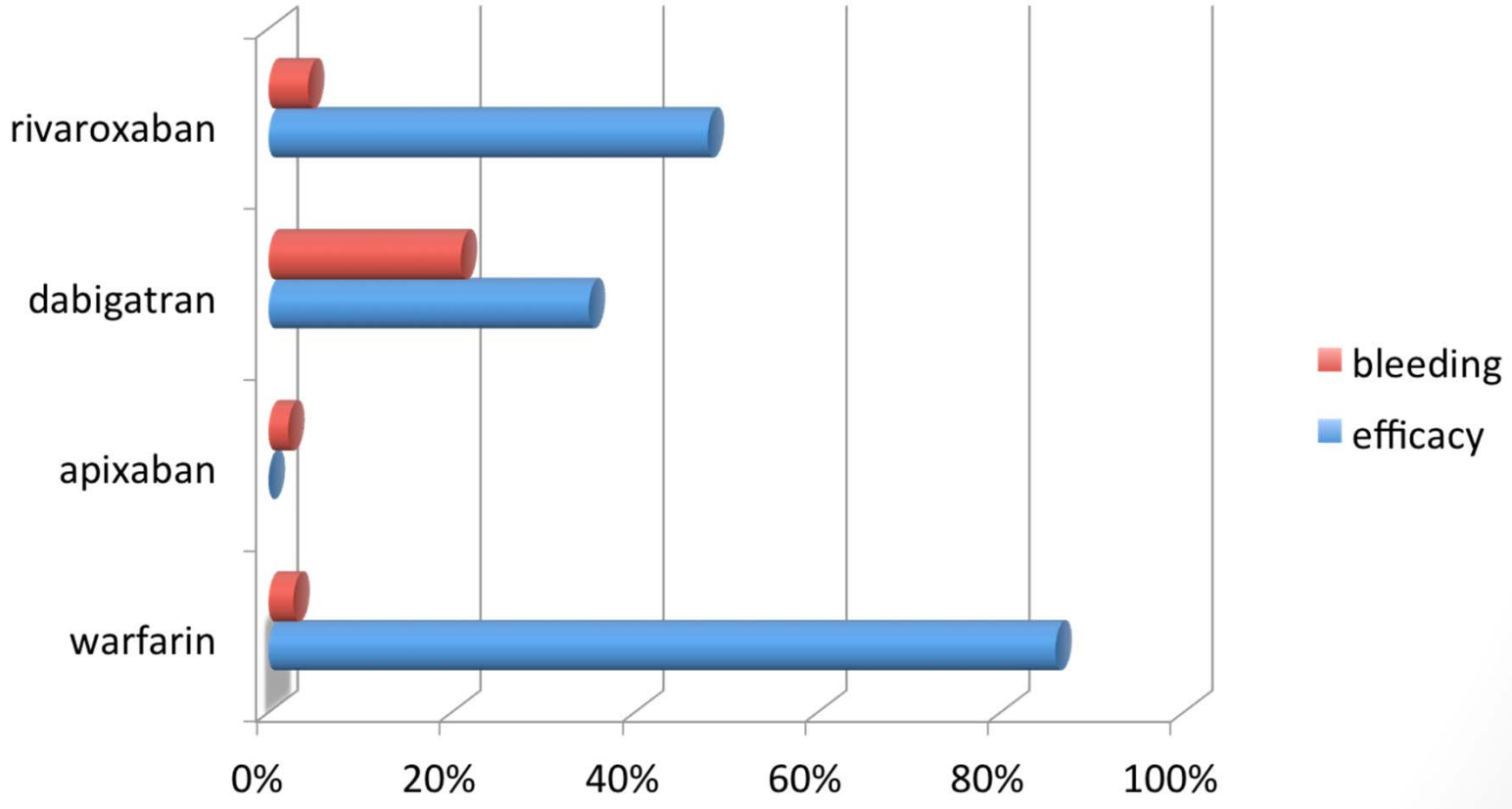
dabigatran

- Direct thrombin inhibitor
- Indication: thromboembolic w/AF
- Rapid onset, short half life (1-2 hrs, 12-17 hrs)
- No lab monitoring
- Reasonable cost
- Fewer drug interactions, no food interactions
- Twice daily dosing

rivaroxaban

- Factor Xa inhibitor
- Indications: thromboembolic w/AF, DVT/PE
- Rapid onset, short half life (2-4 hrs, 5-9 hrs)
- No lab monitoring
- Costly
- Fewer drug interactions, no food interactions
- Once daily dosing

Efficacy vs bleeding



In summary…

- Treat symptomatic SVT, consider referral to cardiology
- Control or treat AF and prevent risk of stroke
- Anticoagulate only those with true risk for thromboembolic event

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