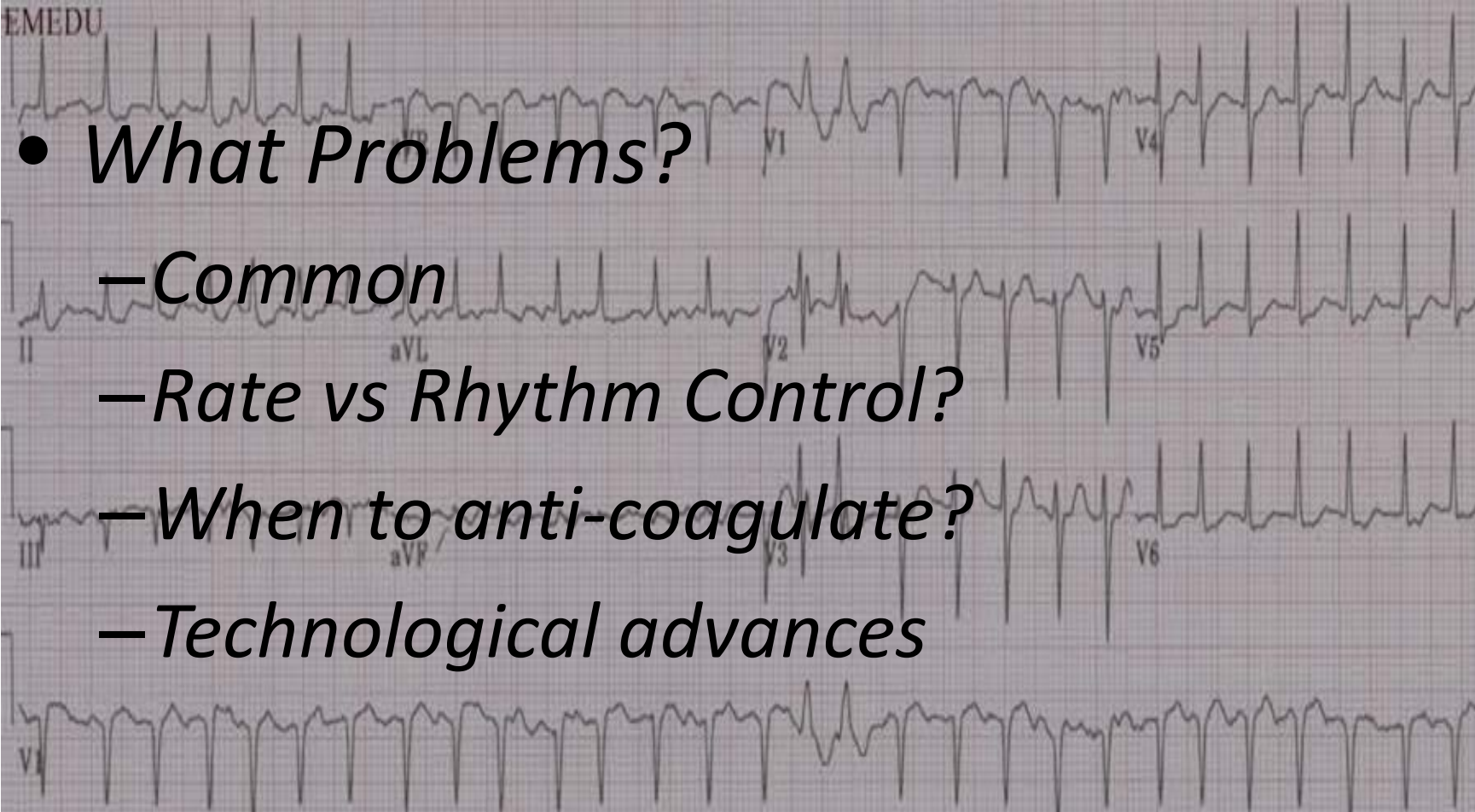


From Evidence to Practice: Atrial Fibrillation

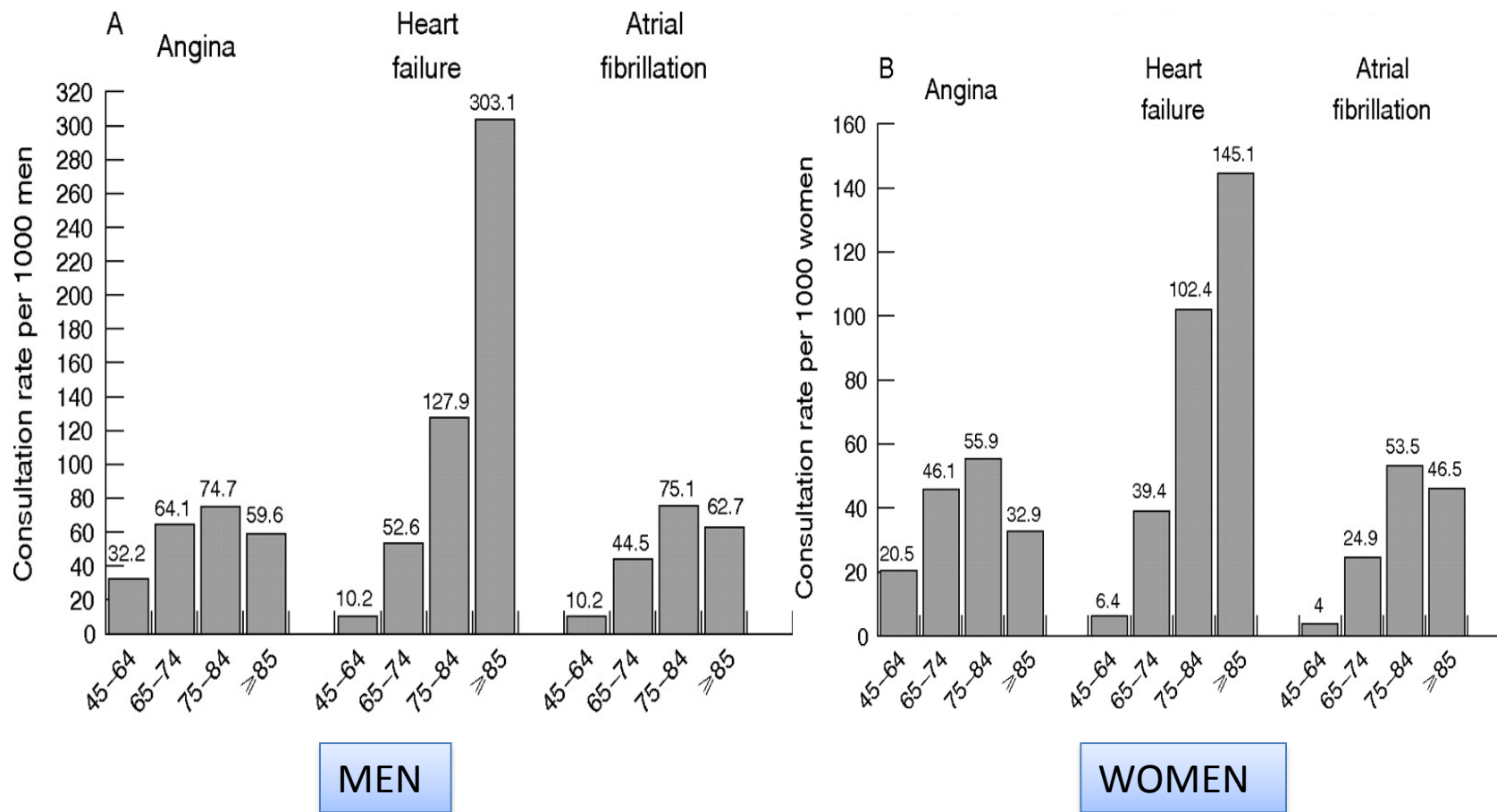
Dr Chris Davidson

Brighton & Sussex Medical School

Problems managing Atrial Fibrillation

- 
- The background of the slide is a 12-lead ECG tracing. The leads are labeled: I, II, III, aVL, aVF, V1, V2, V3, V4, V5, and V6. The rhythm is irregularly irregular, consistent with atrial fibrillation. The text is overlaid on the ECG.
- *What Problems?*
 - *Common*
 - *Rate vs Rhythm Control?*
 - *When to anti-coagulate?*
 - *Technological advances*

Age-stratified general practitioner consultation rates per 1000 population for heart failure, angina and atrial fibrillation in men (A) and women (B).



Murphy N F et al. Heart 2007;93:606-612

Case Studies in AF

- Case 1:
 - 50 yr old University Lecturer
 - Hypertension Rx Nifedipine
 - Palpitations lasting 8-12 hours about once/month



Case 1: Evaluation



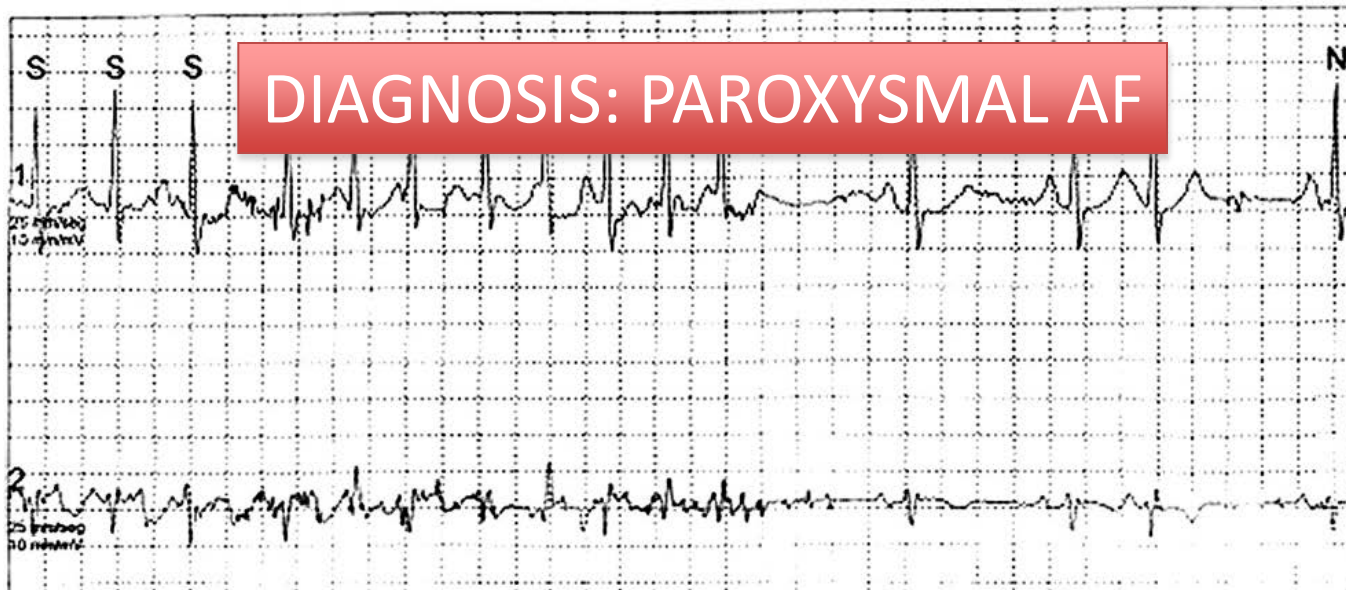
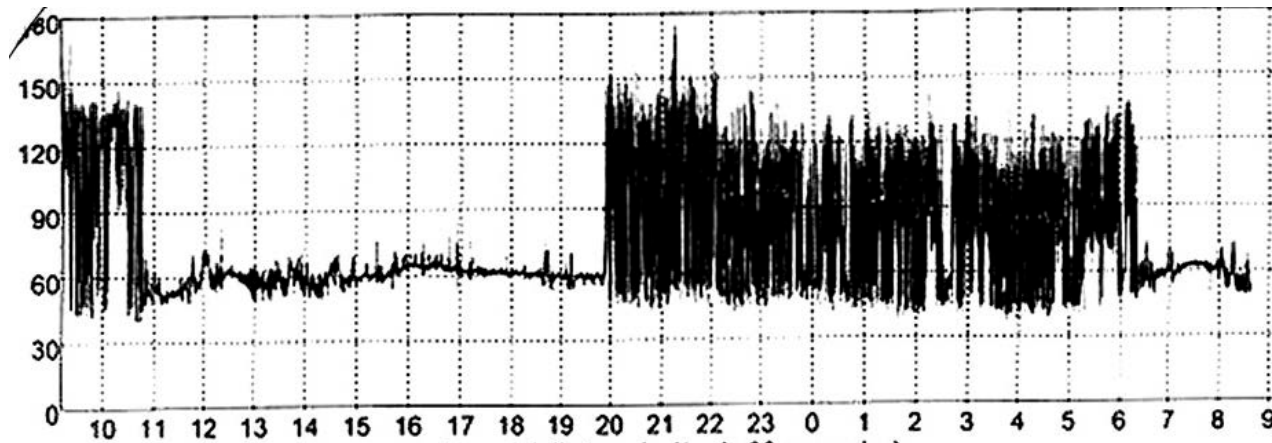
- Clinical Examination:
 - Healthy, but stressed
 - BP 172/96, Cardiac normal, no evidence vascular disease
- Investigations:
 - Normal (routine blood tests, ECG, CXR)
- Current drugs:
 - Nifedipine

Case Studies in AF

What other information would you seek from the patient at this stage?



HOLTER Monitor



Case 1: Paroxysmal AF

Choice of Treatment



Beta-Blocker or ACE Inhibitor?

Either or Both!

Case 1: Choice of Treatment

ACE Inhibitors are Beneficial in PAF



“Overall, ACEIs and ARBs revealed statistically significant preventive effects on AF (odds ratio (OR), 0.65; 95% confidence interval (CI), 0.55-0.76). The preventive effect was similar in the two classes of drugs (ACEI: OR, 0.68; ARB: OR, 0.69).”

The Role of renin-angiotensin system blockade therapy in the prevention of Atrial Fibrillation: a Meta-Analysis. Zhang, P et al Clin. Pharm. Ther. (2010), 521-31

Case 1: Choice of Treatment

Paroxysmal AF



Should he receive Warfarin?

CHADS-2 Score in AF

RISK FACTOR	SCORE
Cardiac Failure	1
Hypertension	1
Age >75 years	1
Diabetes	1
Stroke / TIA	2

JAMA 2001;285:2864 – 2870.

CHADS₂ Score in AF

Table 7 CHADS₂ score and stroke rate

CHADS ₂ score	Patients (n=1733)	Adjusted stroke rate (%/year) ^a (95% confidence interval)
0	120	1.9 (1.2–3.0)
1	463	2.8 (2.0–3.8)
2	523	4.0 (3.1–5.1)
3	337	5.9 (4.6–7.3)
4	220	8.5 (6.3–11.1)
5	65	12.5 (8.2–17.5)
6	5	18.2 (10.5–27.4)

Adapted from Gage BF et al. JAMA 2001; 285:2864–2870.

ESC recommendation 2010:
Treat if Score 2 or more

Case 1: Choice of Treatment

Intermittent AF



*Is he at lower Risk with
intermittent AF?*

“Patients with paroxysmal AF should be regarded as having a stroke risk similar to those with persistent or permanent AF, in the presence of risk factors.” *ESC Guideline 2010*

Case 1: Progress



- Remains Symptomatic on combination:
 - Nifedipine, atenolol, ramipril
 - In spite of good BP control
- What would you do next?
- Referred to cardiologist:
 - Fails to tolerate flecainide
 - Photosensitivity with Amiodarone

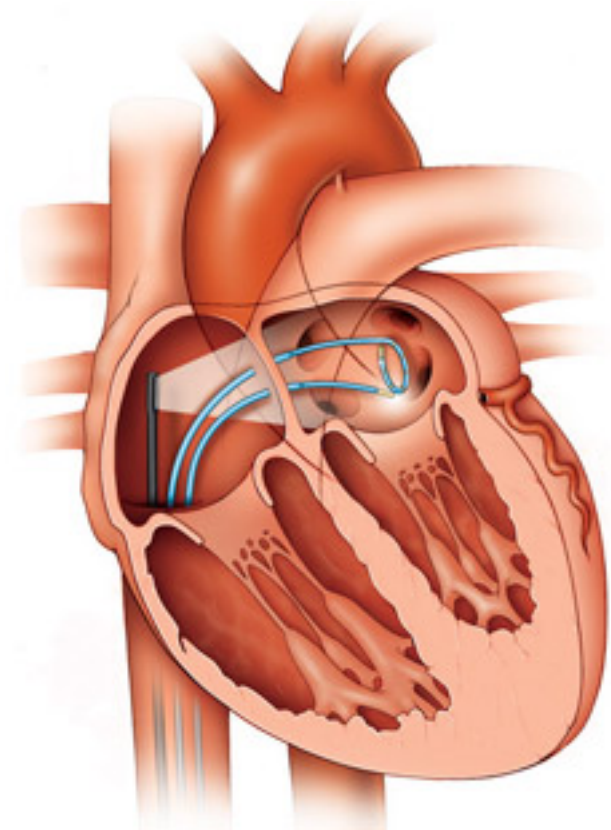
What's New?



DRUGS

- **Dronedarone**
 - Amiodarone related
 - Twice daily
 - Contains no Iodine
 - Licensed for AF
 - Contra-indicated in Heart Failure
- **BUT**
 - FDA warning on liver injury (Jan 2011)
 - FDA warning: increased mortality in chronic AF in PALLAS study (Dec 2011)

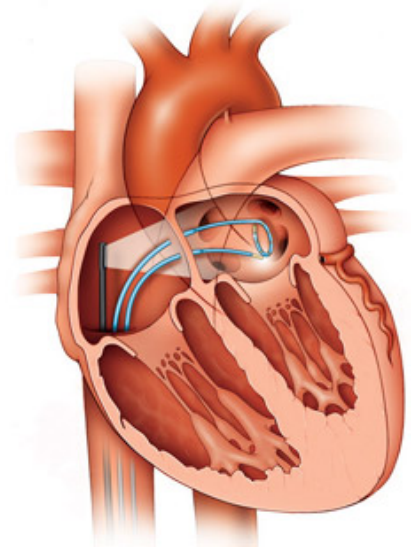
TECHNOLOGY



Radiofrequency Ablation in AF

Catheter Ablation for Atrial Fibrillation: Are Results Maintained at 5 Years of Follow-Up?

Hopital Cardiologique du Haut-Leveque, Bordeaux-Pessac, France
JACC 2011; 57; 160-6



- 100 Patients: 86% male, 64% paroxysmal, mean age 55.7 yrs
- 175 procedures (median 2/patient)
- Complications: Tamponade 3%
- AF free: 87%, 81%, and 63% at 1, 2, and 5 years
- Adverse factors:
 - Persistent AF
 - Valve disease or dilated cardiomyopathy

Case 1: Take-Home Messages:



- *ACE inhibitors (and Angiotensin receptor blockers) can prevent the development of recurrent AF*
- *Emboic risk in paroxysmal AF is equivalent to permanent AF and depends on the CHADS-2 score*
- *Radio-frequency ablation is now available for those unresponsive to drug treatment but long term benefit uncertain*

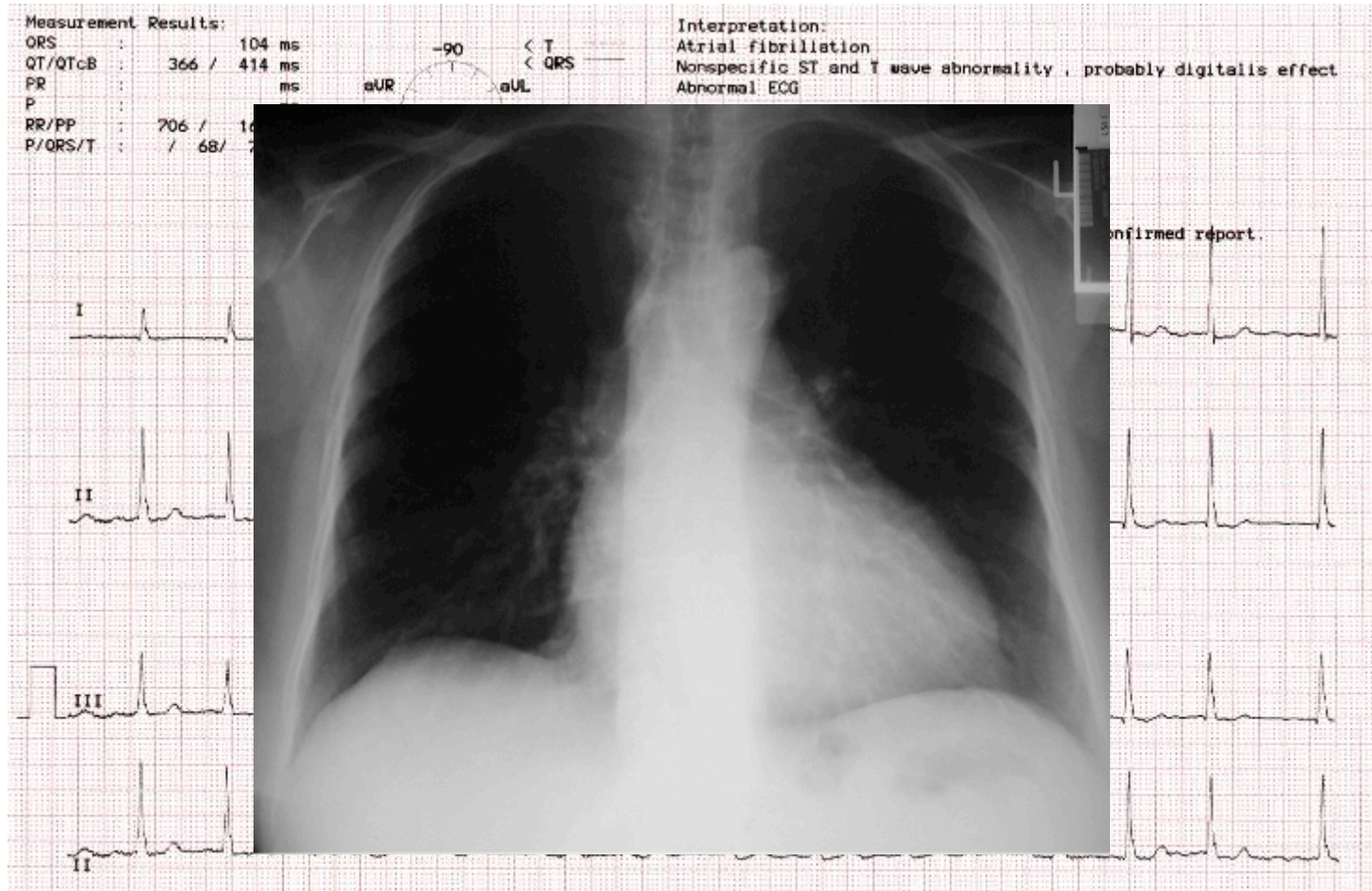
Atrial Fibrillation: Case 2

- Male smoker, 69 years with HT
- Rx Atenolol + thiazide
- AF found on routine examination
- Mild dyspnoea only
- Examination:
 - No heart failure
 - No murmurs



What proportion of patients with AF are asymptomatic?

Atrial Fibrillation: Case 2



Atrial Fibrillation: Case 2

Hypertensive Heart Disease



- Should sinus rhythm be restored?
 - By Electrical cardioversion?
 - OR drugs eg Amiodarone?
 - OR a combination of these?

Rhythm-control vs. Rate-control controversy

“The AFFIRM, RACE, the Pharmacologic Intervention in Atrial Fibrillation (PIAF) trial, and the Strategies of Treatment of Atrial Fibrillation (STAF) trial found no differences in quality of life with rhythm control compared with rate control.” *ESC AF Guideline 2010*

Atrial Fibrillation: Case 2

Hypertensive Heart Disease



Should he be started on long-term anti-coagulants?

CHADS-2 Score in AF

RISK FACTOR	SCORE
Cardiac Failure	1
Hypertension	1
Age >75 years	1
Diabetes	1
Stroke / TIA	2

JAMA 2001;285:2864 – 2870.

Atrial Fibrillation: Case 2

Hypertensive Heart Disease



- *Should he be started on long-term anti-coagulants?*
 - *CHADS-2 score = 1*
 - *2.4 % per annum stroke risk (2.0-3.8)*

What are the problems with the CHADS-2 Score?

CHA₂DS₂-VASc Score

Major Risk Factors

- Prior Stroke / TIA
- Prior Systemic Embolus
- Age > 75 years
- Valvular disease (rheumatic, prosthetic)

Minor Risk Factors

- Heart Failure or LV dysfunction
- Hypertension
- Diabetes
- Age > 65 years
- Vascular Disease
- Female sex

Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fibrillation. *Chest* 2010;137:263 – 272.

CHA₂DS₂-VASc Score

(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA₂DS₂-VASc
(Note: maximum score is 9 since age may contribute 0, 1, or 2 points)

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease ^a	1
Age 65–74	1
Sex category (i.e. female sex)	1
Maximum score	9



CHA₂DS₂-VASc Score

(c) Adjusted stroke rate according to CHA₂DS₂-VASc score

CHA ₂ DS ₂ -VASc score	Patients (n=7329)	Adjusted stroke rate (%/year) ^b
0	1	0%
1	422	1.3%
2	1230	2.2%
3	1730	3.2%
4	1718	4.0%
5	1159	6.7%
6	679	9.8%
7	294	9.6%
8	82	6.7%
9	14	15.2%

ESC recommendation 2010:
Treat if Score 2 or more

Atrial Fibrillation: Case 2

Hypertensive Heart Disease



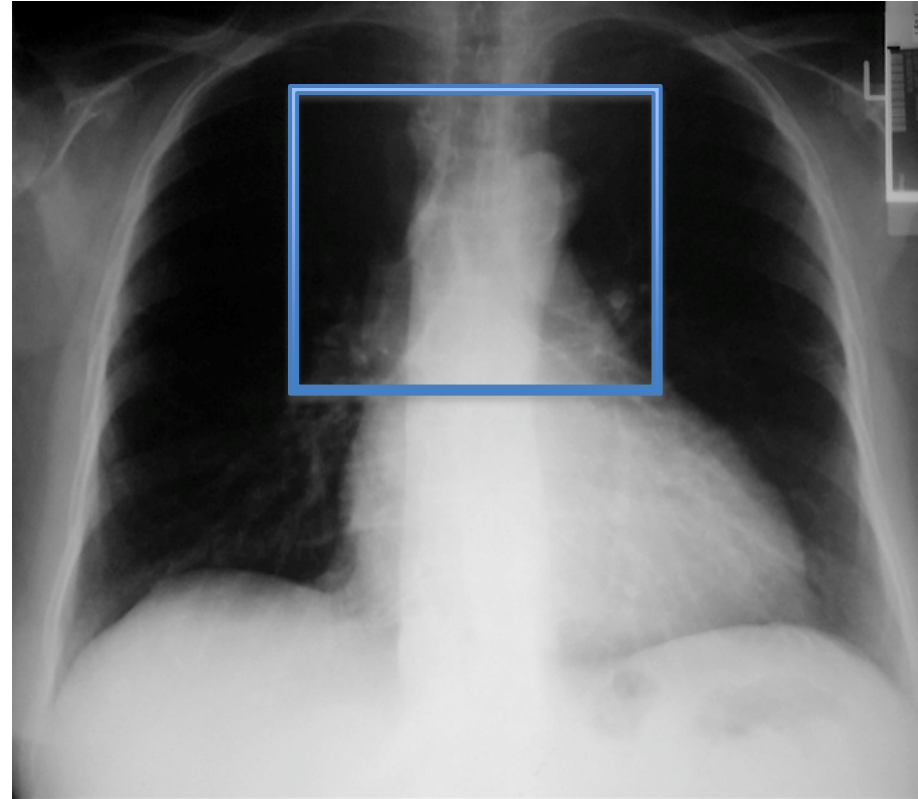
- *Should he be started on long-term anti-coagulants?*
 - *CHA₂DS₂-VASc score = 2*
 - *2.2 % per annum stroke risk*

BUT you note that he has been a heavy smoker – does that change his risk?

Atrial Fibrillation: Case 2

- Male smoker, 69 years with HT
- Re-Examination
 - ? Abdominal bruit
 - Peripheral pulses: dorsalis pedis absent bilaterally

What further test would help?



Peripheral Vascular disease: A growing problem for the internist

EFIM Vascular Medicine Working Group
Eur. J Int Med 2009; 20; 130-8

- PVD present in 16% over age 55 yrs
- Readily identified by **A**nkle-**B**rachial **I**ndex
- Significant additional Risk factor for vascular events

Patient: ABI = 0.76



Atrial Fibrillation: Case 2

Hypertensive Heart Disease



- *Should he be started on long-term anti-coagulants?*
 - *CHA₂DS₂-VASc score = 3*
 - *3.2 % per annum stroke risk*
 - *Risk of Significant haemorrhage on warfarin = 1-2% per annum*

5 years ago had gastric haemorrhage requiring hospitalisation

Atrial Fibrillation: Case 2

Hypertensive Heart Disease



What further information would you like to know to decide whether to prescribe him warfarin or aspirin or neither?

Bleeding Risk in AF Population (Euro-HF survey)

Chest November 1, 2010 138:1032-1033

Bleeding Risk – HAS-BLED Score

Letter	Clinical characteristic ^a	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

www.escardio.org



Overall bleeding rate low (1.5% per year) and Score <3 represents ‘low-risk’

Bleeding risk scores provide mixed results, especially in intermediate-risk patients

Burgess S, Crown N, Louzada ML, et al. Clinical performance of bleeding risk scores for predicting major and clinically relevant non-major bleeding events in patients receiving oral anticoagulant therapy. American Society of Hematology 2011 Annual Meeting; December 13, 2011; San Diego, CA. Abstract **2311**.

- 321 consecutive patients enrolled at a single academic medical center.
- Risk Scores
 - Outpatient Bleeding Risk Index (OBRI),
 - Contemporary Bleeding Risk Model (CBRM),
 - HAS-BLED,
 - HEMORR2HAGES
- Four major bleeding risk scores used in clinical practice identified patient risk differently, with each of the screening tools having a limited ability to predict risks of major bleeding and clinically relevant non-major bleeding
- Overall, the bleeding risk scores were able to identify patients at high risk for bleeding but had limited ability to identify patients at intermediate risk, report investigators.

What's New in Atrial Fibrillation?

Problems with Warfarin

- Poor control of INR
- Inconvenience for patients
- Medical resources for testing and follow-up
- Drug interactions

New Anti-Thrombins

- DABIGATRAN
 - No testing required
 - Few drug interactions
 - Efficacy equivalent to warfarin

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NEW PILL TO STOP STROKES

Patients can get wonder drug NOW

A PILL, costing less than £2 a day is being hailed as the biggest breakthrough in stroke prevention in 60 years. The drug, which slashes the risk of suffering a stroke by over a third, will help more than 1 million Britons. Production is now available for use in the UK. It is thought to significantly reduce the risk

of a stroke in patients with an irregular heartbeat, known as atrial fibrillation. This is one of the most common of strokes. The drug, taken twice a day at a cost of 23.28 already prevents thousands of strokes each year from blood clots after hip or knee replacements.

TURN TO PAGE 4



ORDER IN THEIR HOUSE BIG BROTHER SALLY AND THE SPEAKER BACK TOGETHER

PICTURE EXCLUSIVE - SEE PAGE NINE

The NEW ENGLAND JOURNAL of MEDICINE

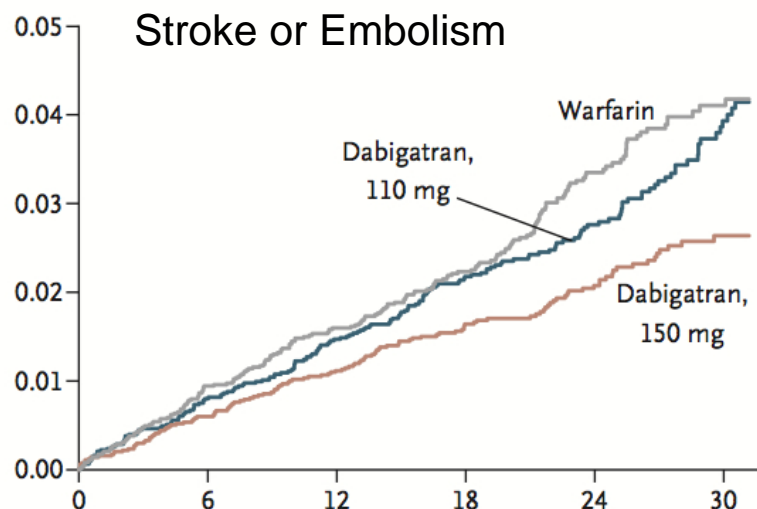
ESTABLISHED IN 1812

SEPTEMBER 17, 2009

VOL. 361 NO. 12

Dabigatran versus Warfarin in Patients with Atrial Fibrillation

Stuart J. Connolly, M.D., Michael D. Ezekowitz, M.B., Ch.B., D.Phil., Salim Yusuf, F.R.C.P.C., D.Phil., John Eikelboom, M.D., Jonas Oldgren, M.D., Ph.D., Amit Parekh, M.D., Janice Pogue, M.Sc., Paul A. Reilly, Ph.D., Ellison Themeles, B.A., Jeanne Varrone, M.D., Susan Wang, Ph.D., Marco Alings, M.D., Ph.D., Denis Xavier, M.D., Jun Zhu, M.D., Rafael Diaz, M.D., Basil S. Lewis, M.D., Harald Darius, M.D., Hans-Christoph Diener, M.D., Ph.D., Campbell D. Joyner, M.D., Lars Wallentin, M.D., Ph.D., and the RE-LY Steering Committee and Investigators*



Non-Inferiority to Warfarin:

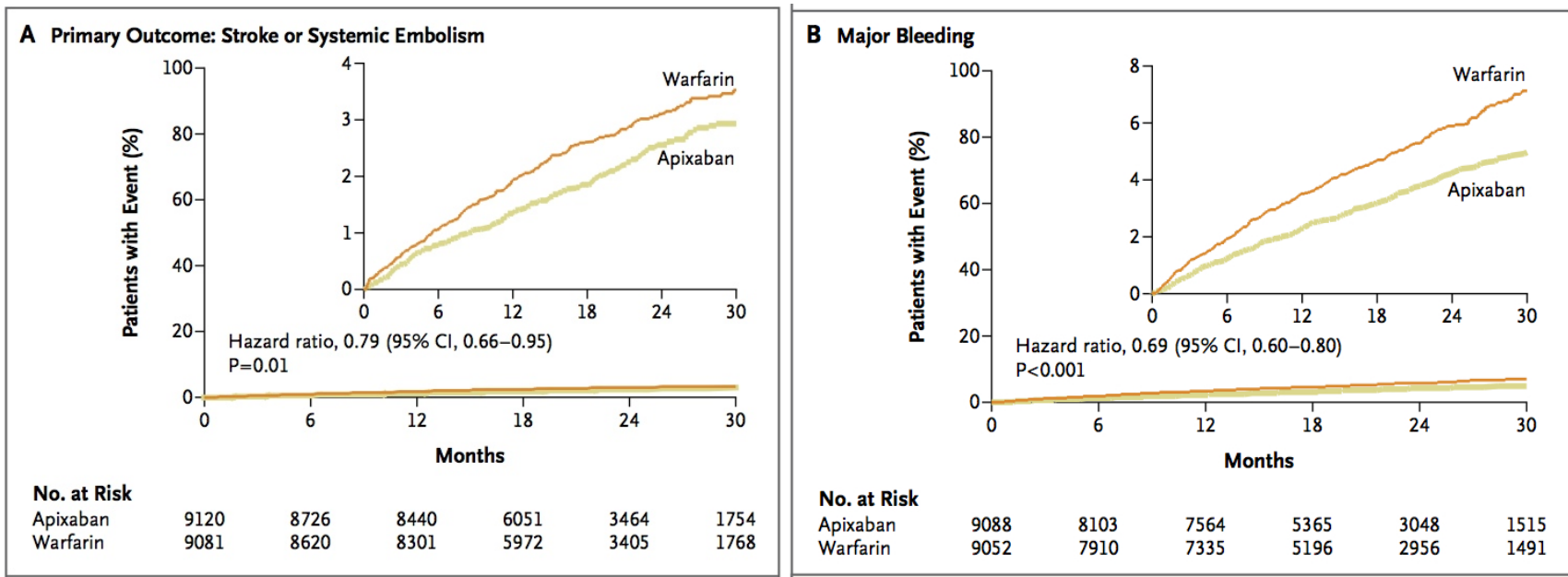
No significant difference in mortality, major bleeding or primary outcome

BUT apparent increase in MI:
RR 1.38 (150mg)

ORIGINAL ARTICLE

Apixaban versus Warfarin in Patients with Atrial Fibrillation

Christopher B. Granger, M.D., John H. Alexander, M.D., M.H.S.,
 John J.V. McMurray, M.D., Renato D. Lopes, M.D., Ph.D., Elaine M. Hylek, M.D., M.P.H.,
 Michael Hanna, M.D., Hussein R. Al-Khalidi, Ph.D., Jack Ansell, M.D., Dan Atar, M.D.,



This article (10.1056/NEJMoa1107039) was published on August 28, 2011, at NEJM .org.

ONLINE FIRST

Dabigatran Association With Higher Risk of Acute Coronary Events**Meta-analysis of Noninferiority Randomized Controlled Trials**

Ken Uchino, MD; Adrian V. Hernandez, MD, PhD

Arch Intern Med. Published online January 9, 2012. doi:10.1001/archinternmed.2011.1666**ABSTRACT**

Background The original RE-LY (Randomized Evaluation of Long-term Anticoagulant Therapy) trial suggested a small increased risk of myocardial infarction (MI) with the use of dabigatran etexilate vs warfarin in patients with atrial fibrillation. We systematically evaluated the risk of MI or acute coronary syndrome (ACS) with the use of dabigatran.

Methods We searched PubMed, Scopus, and the Web of Science for randomized controlled trials of dabigatran that reported on MI or ACS as secondary outcomes. The fixed-effects Mantel-Haenszel (M-H) test was used to evaluate the effect of dabigatran on MI or ACS. We expressed the associations as odds ratios (ORs) and their 95% CIs.

Results Seven trials were selected (N = 30 514), including 2 studies of stroke prophylaxis in atrial fibrillation, 1 in acute venous thromboembolism, 1 in ACS, and 3 of short-term prophylaxis of deep venous thrombosis. Control arms included warfarin, enoxaparin, or placebo administration. Dabigatran was significantly associated with a higher risk of MI or ACS than that seen with agents used in the control group (dabigatran, 237 of 20 000 [1.19%] vs control, 83 of 10 514 [0.79%]; OR_{M-H} , 1.33; 95% CI, 1.03-1.71; $P = .03$). The risk of MI or ACS was similar when using revised RE-LY trial results (OR_{M-H} , 1.27; 95% CI, 1.00-1.61; $P = .05$) or after exclusion of short-term trials (OR_{M-H} , 1.33; 95% CI, 1.03-1.72; $P = .03$). Risks were not heterogeneous for all analyses ($I^2 = 0\%$; $P \geq .30$) and were consistent using different methods and measures of association.

Conclusions Dabigatran is associated with an increased risk of MI or ACS in a broad spectrum of patients when tested against different controls. Clinicians should consider the potential of these serious harmful cardiovascular effects with use of dabigatran.

Atrial Fibrillation:

Take Home Messages

- *Most patients require effective Rate-Control rather than multiple cardioversion*
- *Most patients need long-term warfarin*
- *New Risk scores(CHA₂DS₂-VASc and HAS-BLED) enable more informed decision making*
- *New drugs (anti-thrombin and Factor X inhibitors) has the potential to revolutionise our approach to prophylactic anti-coagulation*