Atrial Fibrillation Treatment 2011

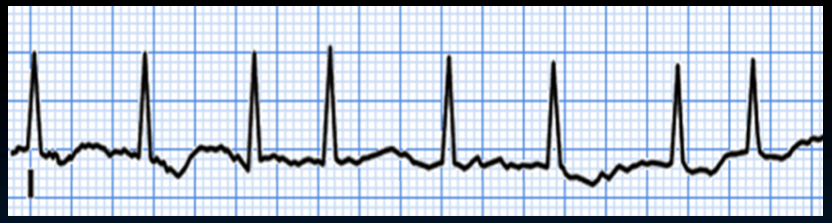
John Mandrola

Disclosures

None

Approach to AF treatment

(after making the diagnosis and exclusion of obvious causes)



Treat Symptoms

Rhythm Control

Prevent Heart Failure

Rate Control

Prevent Stroke

Anticoagulants

Devices

Ablation

Rhythm Control Strategies

Not controlling rhythm → This is Okay

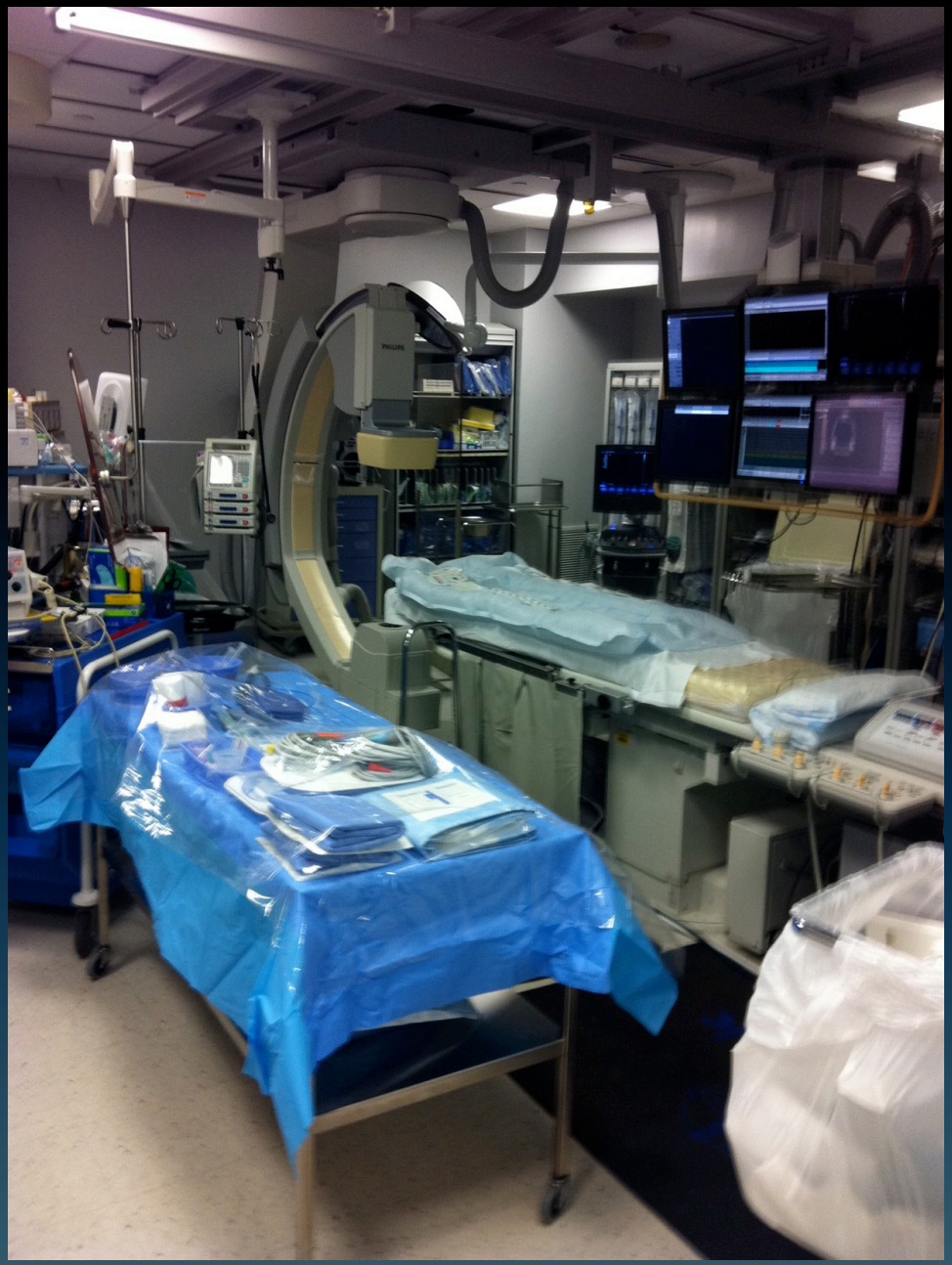
Anti-arrhythmic drugs

AF Ablation

Just get adequate 'Rate Control'

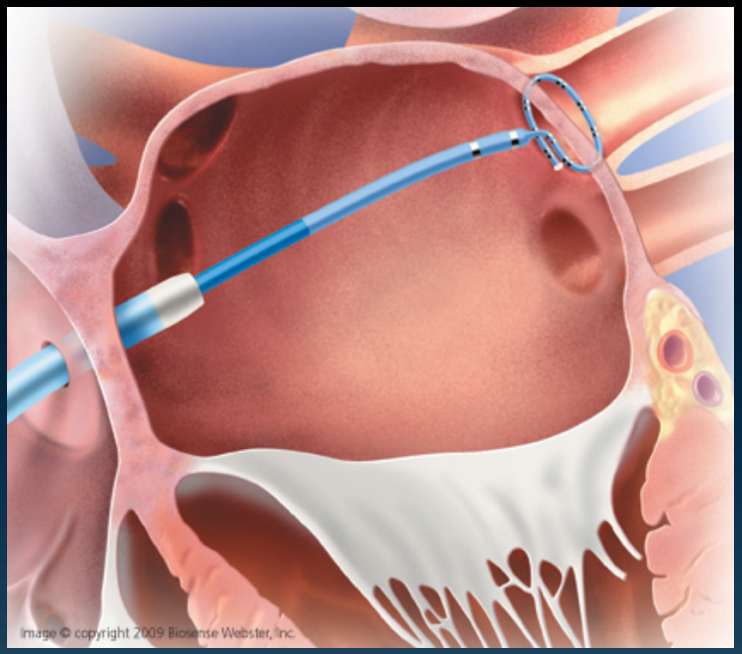
AF Ablation:

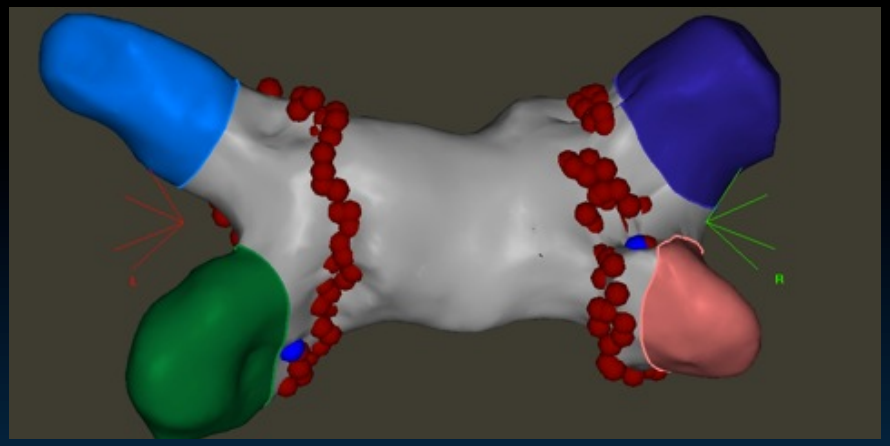
The Journey

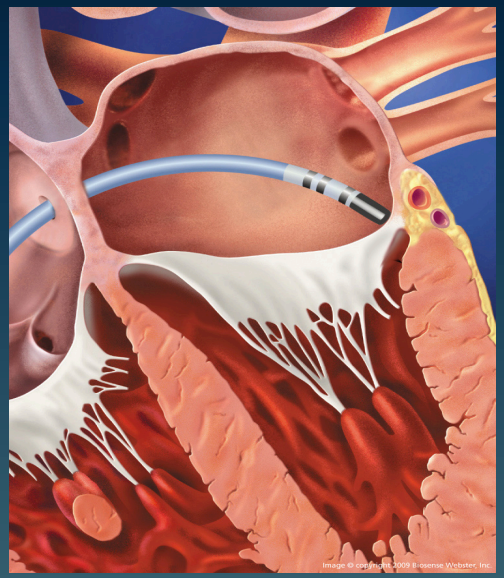


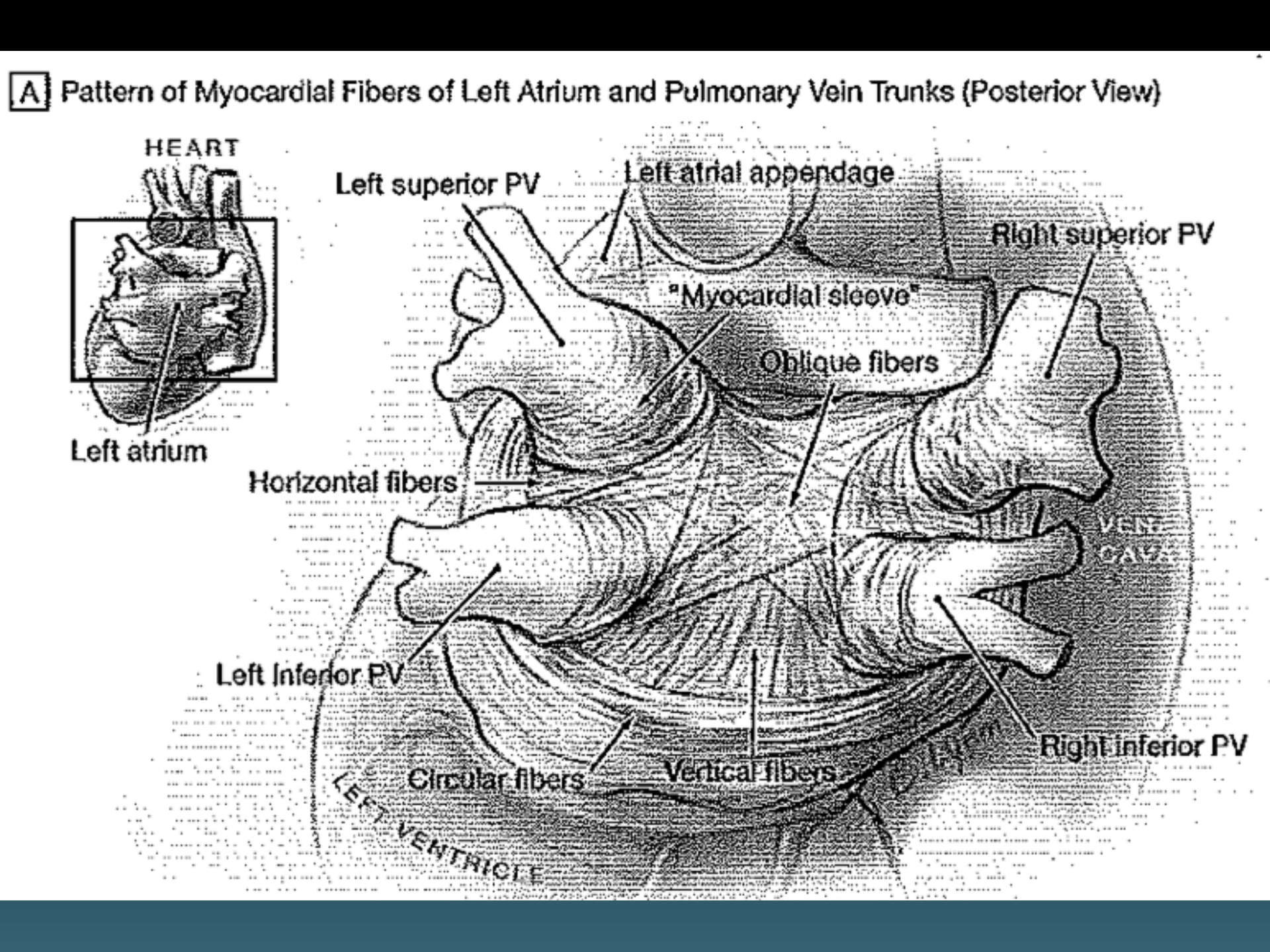
What is AF ablation?

AF ablation = Pulmonary Vein Isolation



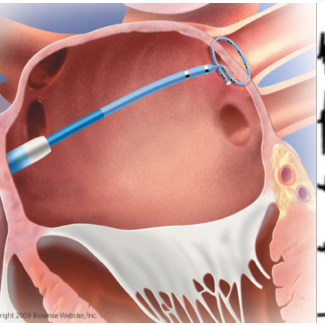





A Pattern of Myocardial Fibers of Left Atrium and Pulmonary Vein Trunks (Posterior View)
HEART
Left atrium
Left superior PV
Left atrial appendage
Right superior PV
"Myocardial sleeve"
Oblique fibers
Horizontal fibers
Left Inferior PV
Right inferior PV
Circular fibers
Vertical fibers
LEFT VENTRICLE

ECG

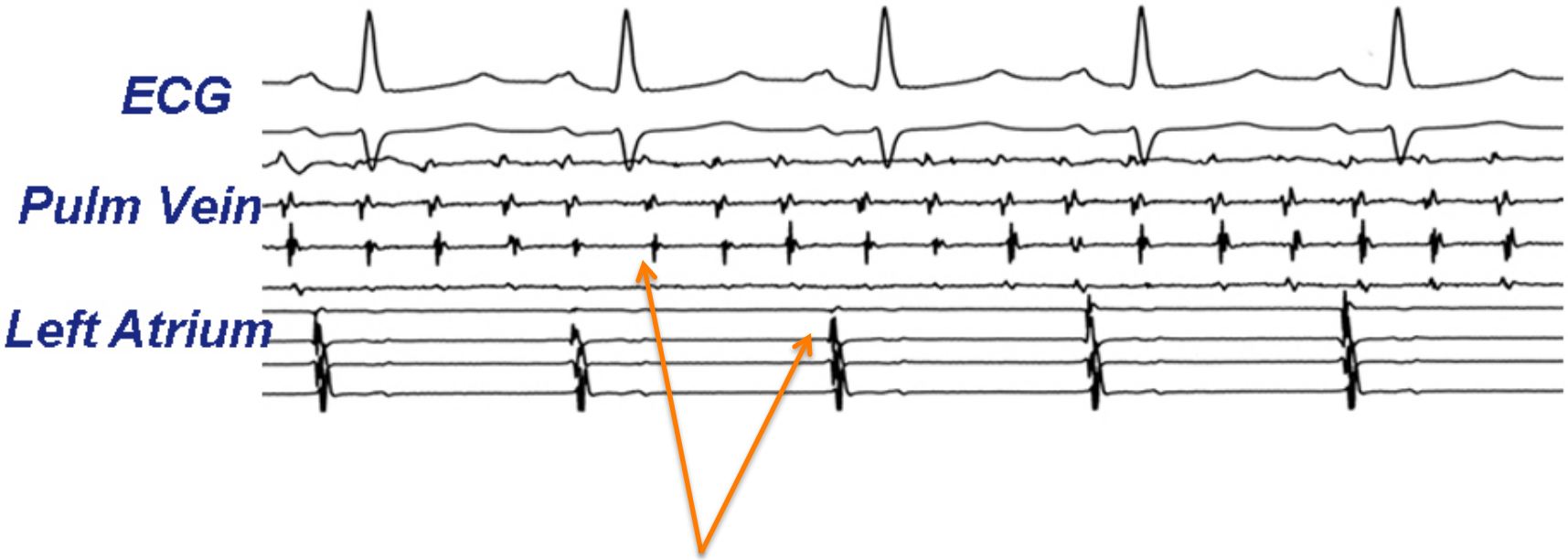
PV



LA

PV isolation results

in AF termination



AF from within a disconnected pulmonary vein

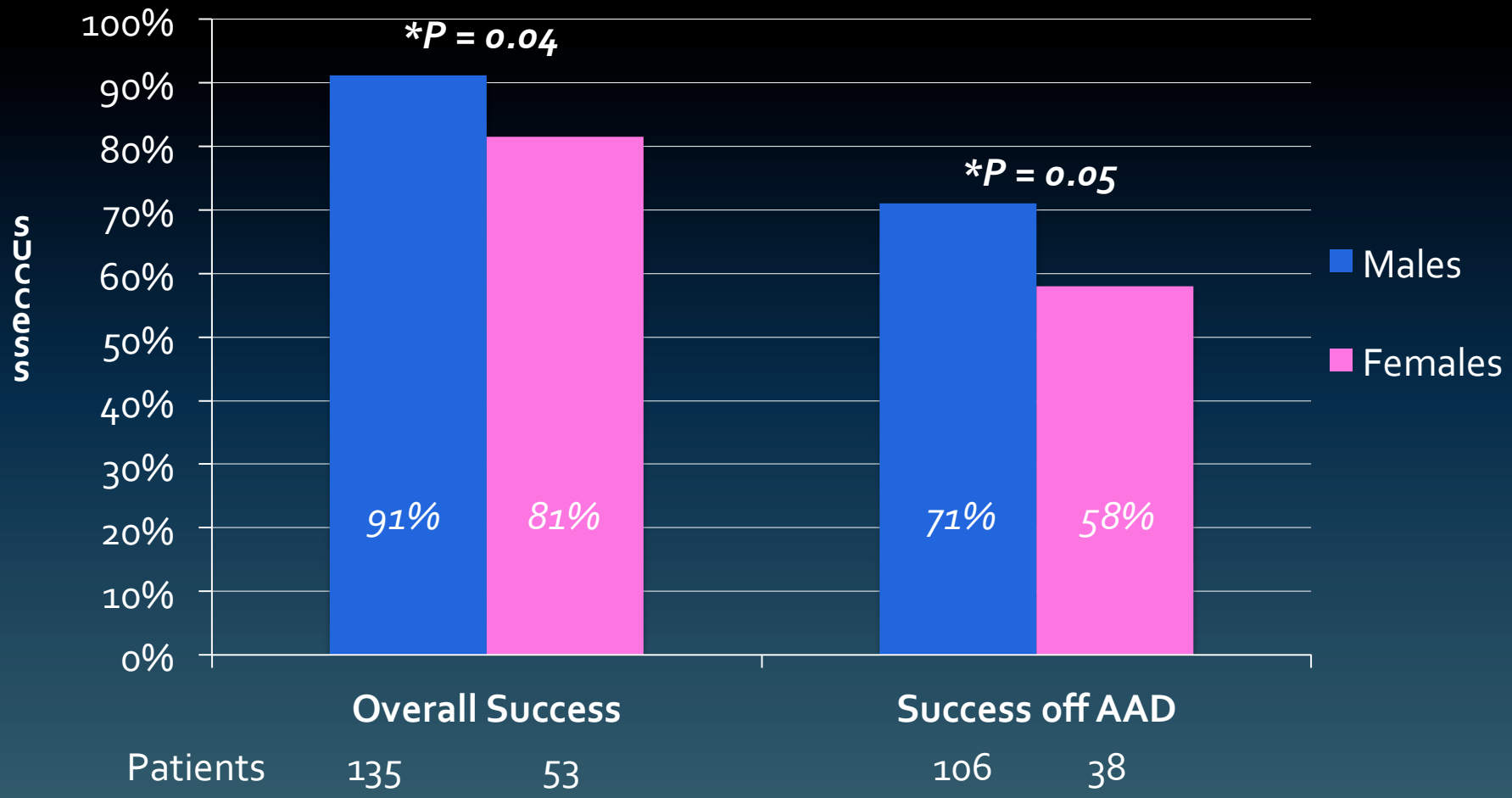
AF ablation Success

Table 18 Randomized clinical trials of catheter ablation vs. antiarrhythmic drugs or no treatment in AF

Study	Reference	Patients (n)	Age, years	Type of AF	Previous use of AAD	Ablation technique	Repeat ablation in the ablation group	Crossed to ablation in the AAD group	AF free at 1 year	
									Ablation	AAD
Krittayaphong *et al.* 2003	Online	30	55 ± 10 (ablation) 47 ± 15 (AAD)	Paroxysmal, persistent	≥1[a]	PVI + LA lines + CTI ablation + RA lines	Not stated	Not stated	79%	40%
Wazni *et al.* 2005 (RAAFT)	134	70	53 ± 8 (ablation) 54 ± 8 (AAD)	Mainly paroxysmal	No	PVI	12%[b]	49%[c]	87%	37%
Stabile *et al.* 2005 (CACAF)[d]	Online	245	62 ± 9 (ablation) 62 ± 10 (AAD)	Paroxysmal, persistent	≥2	PVI + LA lines ± CTI ablation	No exact data	57%	56%	9%
Oral *et al.* 2006[e]	Online	245	57 ± 9	Persistent	≥1 (mean 2.1 ± 1.2)	CPVA	26% for AF; 6% for LA flutter	77%	74%	4%
Pappone *et al.* 2006 (APAF)	135	198	55 ± 10 (ablation) 57 ± 10 (AAD)	Paroxysmal	≥2 (mean 2 ± 1)	CPVA + CTI ablation	6% for AF; 3% for atrial tachycardia	42%	86%	22%
Jais *et al.* 2008 (A4 study)	133	112	51 ± 11	Paroxysmal	≥1	PVI ± LA lines ± CTI ablation	Mean 1.8 ± 0.8, median 2 per patient	63%	89%	23%
Forleo *et al.* 2008[f]	Online	70	63 ± 9 (ablation) 65 ± 6 (AAD)	Paroxysmal, persistent	≥1	PVI ± LA lines ± CTI ablation	Not stated	Not stated	80%	43%
Wilber *et al.* 2010 (Thermocool)[g]	96	167	55.5 (ablation) 56.1 (AAD)	Paroxysmal	≥1 (mean 1.3)[h]	PVI ± LA lines ± CFAEs ± CTI ablation ± RA lines	12.6% within 80 days after 1st procedure[i]	59%[c]	66%	16%
Packer *et al.* 2010 (STOP-AF)[j]	Online	245	56.7 (ablation) 56.4 (AAD)	Paroxysmal	≥1[b]	Cryo-PVI ± LA lines	19% within 90 days after 1st procedure	79%	69.9%	7.3%

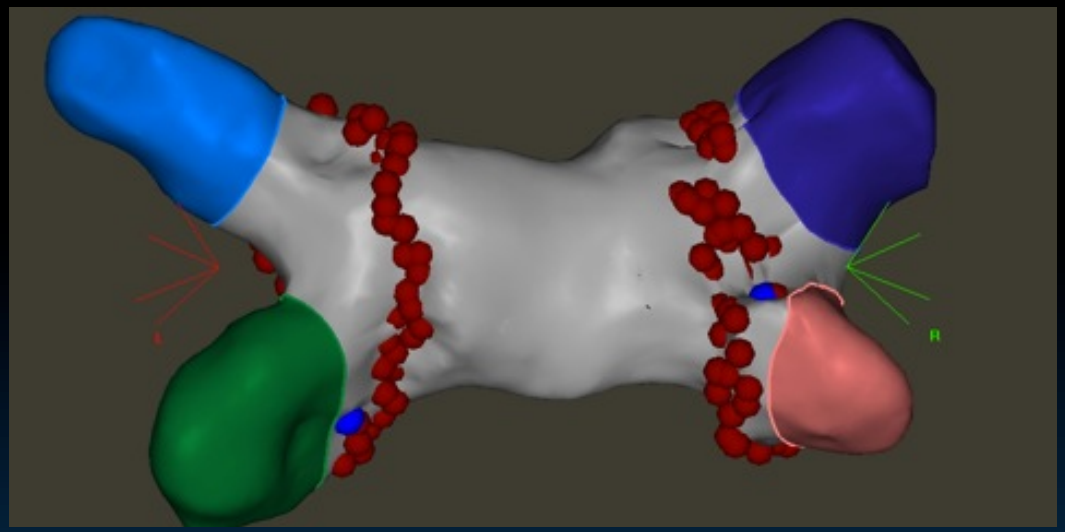
Long-term success by gender

Follow-up duration:
Males: 16.4 months ± 15.5
Females: 16.1 months ± 15.8
p=ns



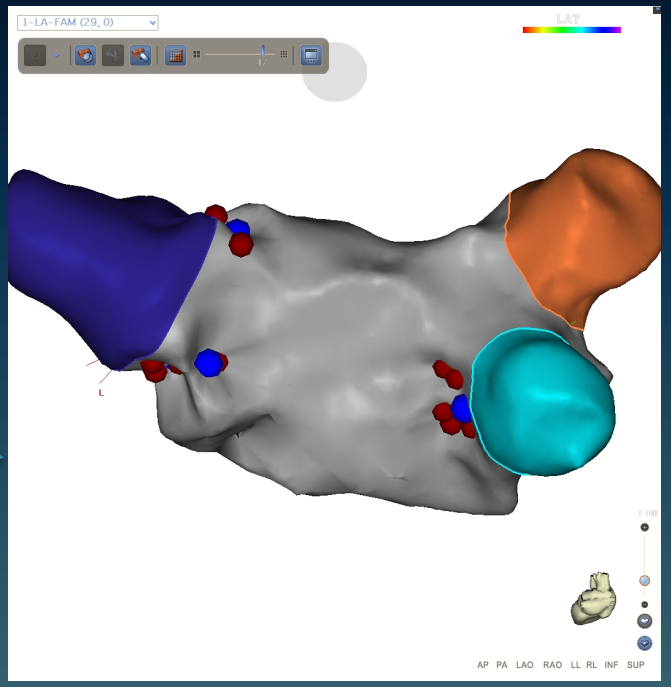
Mandrola et al, AHA 2011

First AF Ablation

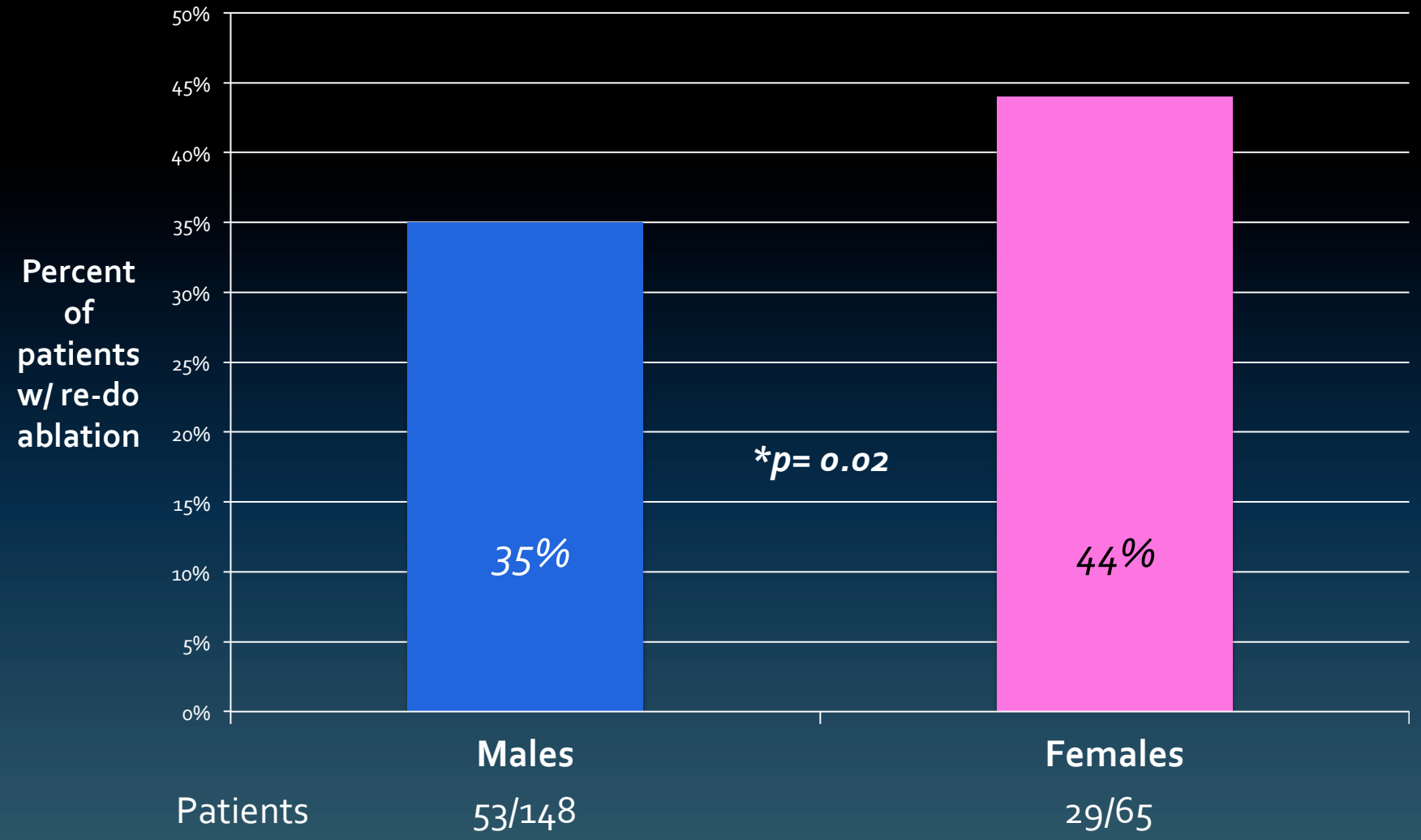


Durability of Lines

Re-do Ablation



Repeat AF ablations by gender



[9 patients (5 Females) had two repeat procedures]

Mandrola et al, AHA 2011

AF ablation

Advantages

- Proven superior to AAD in maintenance of SR
  - Ultimate success rates: 90%
  - Often closes the chapter on AF
- Proven superior to AAD in QOL
- Safer
  - Two-three hours
  - X-Ray times less than 20 min
  - Complications rate 1-2%
  - One day hospital stay
- Preliminary data on stroke and mortality look promising

Cons:

- Success often requires two procedures
- Complications can be serious
- Requires general anesthesia
- Though smaller now, the procedure is not "Mickey Mouse."
- LA contractility and asymptomatic MRI lesions still a concern
- What about outcomes?

CABANA Trial

- *CABANA: Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation*
- *RCT looking at Outcomes:*
  - *Stroke*
  - *Mortality*
  - *Efficacy*
  - *QOL*
- *124 Centers*
  - *Enrolled 492; Target 3000*
  - *Enrollment is problem b/c referred patients want cure—not meds*

COMPARISON OF LONG TERM STROKE OR TIA RISK BETWEEN PATIENTS WITH ATRIAL FIBRILLATION WHO UNDERGO RADIOFREQUENCY CATHETER ABLATION VS. MATCHED PATIENTS WHO HAVE NOT HAD AN ABLATION PROCEDURE

ACC Poster Contributions
Ernest N. Morial Convention Center, Hall F
Sunday, April 03, 2011, 3:30 p.m.-4:45 p.m.

Session Title: Clinical Electrophysiology --Atrial Fibrillation and Stroke
Abstract Category: 26. Clinical Electrophysiology—Supraventricular Arrhythmias
Session-Poster Board Number: 1056-395

Authors: *Matthew R. Reynolds, Candace Gunnarsson, Tina Hunter, Joseph Ladapo, Jamie March, Sarah A. White, Mingdong Zhang, Steven C. Hao, Beth Israel Deaconess Medical Center, Boston, MA, California Pacific Medical Center, San Francisco, CA*

Background: Evidence informing the role of radiofrequency catheter ablation (RFCA) in the care of patients with AF is growing rapidly, but little is known about long-term outcomes, particularly in regards to the incidence of stroke or TIA. The objective of this study was to compare long term safety for a propensity matched sample of ablation and non-ablation patients with AF.

Methods: We performed a retrospective cohort analysis of the incidence of stroke/TIA in AF patients who underwent RFCA compared to those that were treated with at least two different rhythm-control medications but no ablation. We used a coding algorithm to identify 3,194 RFCA patients and 6,028 non-ablation patients from the Thomson Reuters MarketScan® Research Database. This database contains individual-level claims information from employers, health plans, hospitals, Medicare, and Medicaid. The analytic start date for the RFCA patients was the date of their first ablation and for non RFCA patients it was the date of their second rhythm control medication fill. From this sample, 801 pairs were propensity matched based on 15 characteristics, which included patient demographics, comorbid conditions, medication usage and prior stroke/TIA. The primary outcome measure was a record of stroke or TIA at any time up to 3 years.

Results: Kaplan Meier analysis in the propensity matched pairs demonstrated a significant reduction in stroke/TIA rates for RFCA patients compared to non-ablation patients during the follow-up period. Preliminary findings include a multivariable Cox proportional hazards model, which adjusted for covariates still statistically different after matching (time in the database, baseline diabetes mellitus, rate medication pre time zero), showing a reduction in stroke/TIA rates with RFCA hazard ratio of 0.664 [p=0.04, 95% CI (.45,.98)]. A second multivariable Cox proportional hazards model, which included an additional adjustment of prior stroke/TIA, revealed consistent findings; hazard ratio .695 [p=.07, 95% CI (.47,1.00)].

Conclusion: In this analysis, 801 propensity-matched pairs demonstrated a significant reduction in the risk of stroke/TIA in AF patients treated with RFCA.

Typical Email

- "I have a pending appt. with a cardiologist. I have AFIB and am currently taking Sotolol 80 mg 3 times daily. It allows me to control my Fib if I don't eat to excess. *I am an avid biker and now I am currently tired all the time and short of breath. I used to race (last year) but have retired…damn*. What questions do you think will be useful to ask at my interview. We will be discussing the possibility of ablation which he would be performing.

My typical response

- *You have a quandary. Drug treatment is at least partially effective. But…and this is a big but, the suppressing drug is causing side effects--fatigue and shortness of breath.*

- *AF ablation offers the chance of eliminating AF. To get the treasure of an AF-free or AF-drug-free life, you will have to accept the risk of the procedure, and the likelihood of more than one ablation.*

- *You will have to accept the journey.*

- *This decision lies more with you than the doc. How bad is your life now? How good would it be with no AF or sotalol? How much risk can you accept?*

Are there gender-related differences in AF ablation?

Our AHA presentation

Gender-specific Results of Atrial Fibrillation Ablation in a Private Practice Setting

John M. Mandrola, MD, Vicky A. Swift, APRN, Sean Kettring, Kathryn Grace Thorne, MS, David E Mann, MD • Louisville, Kentucky

BAPTIST HOSPITAL EAST

Introduction/Background

- There are two general strategies used to treat AF:
  - **Rate-control** or **Rhythm-control**
- AF ablation is now an accepted rhythm-control strategy
- In 2011, AF ablation is commonly done outside of academic medical centers
- The evidence base supporting AF ablation comes from trials conducted at academic medical centers
  - These trials enrolled mostly men
- Though scant data exist on gender-related results of AF ablation, a few centers have reported that females fare less well with AF ablation

Hypothesis

We asked two questions:

In a real-world, private practice setting of two electrophysiologists practicing at a community hospital…

1. Are females under-represented in AF ablation but over-represented in palliative AV node ablation?
2. Is AF in females more difficult to ablate?

Methods

- We reviewed hospital records of consecutive patients that had AF ablation or AV node ablation in our 500-bed community hospital from 1/2007 to 8/2011.
- All procedures were done by two electrophysiologists (JM or DM)
- Patients considered for AF ablation had either paroxysmal or persistent AF
  - Permanent AF was not ablated.
- AF was ablated with wide area pulmonary vein isolation (PVI), guided by 3D non-fluoroscopic imaging (Biosense) and a lasso-catheter confirmed PV isolation
- Non-PV triggers, complex-fractionated electrograms and organized atrial flutters were ablated at the discretion of the operators (PVI+)
  - *Left atrial ablation beyond standard PVI* was done either when felt necessary to eliminate persistent AF or when non-AF arrhythmias (left atrial flutter/tachycardia) persisted after PV isolation
- AF ablation success was determined by clinical follow-up:
  - Assessment of symptoms, ECG and ambulatory-ECG monitoring (when indicated)
- Long-term success rates included repeat procedures
- Statistical analysis was performed with chi-square and two-tailed t-tests

AF Ablation – PVI Procedure

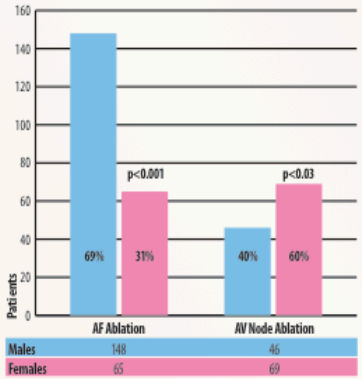
- Point by point RF lesions were made with a saline-irrigated tip catheter
- Maximum RF energy used on the posterior wall was 20-25 watts and 40 watts anteriorly
- All patients after June 2009 had general anesthesia
- Nearly all patients underwent AF-ablation with therapeutic INRs (≥2), or were bridged with low-molecular weight heparin

Results

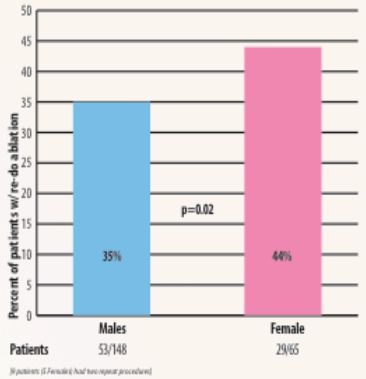
	Males	Females	Total
Patients	148	65	213
AF Procedures	190	92	282
AV-Node Ablation Procedures	46	69	115
Mean Age (AF Ablation)	59 ± 9	61 ± 10	P = ns
Mean Age (AV node ablation)	74 ± 8	79 ± 7	P = 0.03

- PVI was acutely successful in 212 of 213 patients
- 4 patients had severe complications:
  - 1 Right Phrenic Nerve paralysis (resolved at one year)
  - 1 Stroke (non-lethal)
  - 2 Acute tamponade requiring chest tube drainage
- No patient died as a result of the procedure
- No patient had symptoms or findings of PV Stenosis

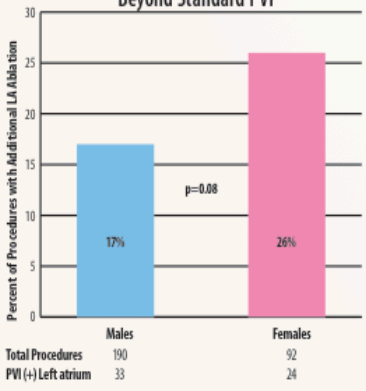
AF Ablation and AV Node Ablation in Males v. Females



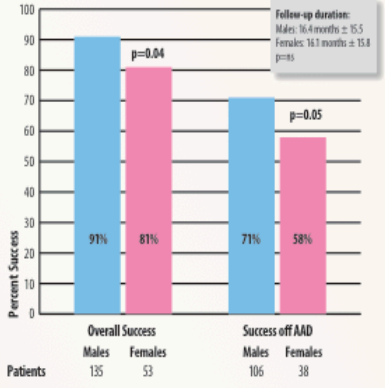
Repeat AF Ablations by Gender



AF Ablation with Left Atrial Ablation Beyond Standard PVI



Long-term Success by Gender



Conclusions

1. Females with AF were significantly under-represented in the AF-ablation group, but over-represented in an older cohort that had AV node ablation.
2. Females were more likely to require repeat AF ablations.
3. Females had lower long term success with AF ablation, either on or off rhythm-control drugs.
4. There was a trend for females to have additional ablation in the left atrium beyond standard PVI.

Clinical Implications

- Our real-world data, combined with prior studies, suggest that gender-related differences exist in the referral pattern and response to AF ablation.
- These findings have important implications in decision-making when AF ablation is considered in females.
- Further studies are needed to determine if these findings are due to gender bias in the management of females or actual differences in the AF substrate between sexes.

No Author has any disclosures

Most promising in near future…

Dreamy stuff

As presented at ACC 2010:

Specialized Atrial Fibrillation Clinic reduces cardiovascular morbidity and mortality in patients with atrial fibrillation

Jeroen ML Hendriks, MSc
Robert G Tieleman, PhD, MD

Department of Cardiology
Cardiovascular Research Institute
Maastricht University Medical Centre, The Netherlands
Martini Hospital Groningen, The Netherlands

The AF-Clinic

An integrated chronic care program for patients with atrial fibrillation

- Substitution of care by specialized nurses
- Management of AF according to guidelines
- Dedicated knowledge software
- Supervision by cardiologists

Hypothesis

Nurse-led, guideline based, software-supported AF-Clinic, supervised by cardiologists improves clinical outcome in patients with atrial fibrillation in comparison to usual care

visit 1
nurse

visit 2
cardiologist + nurse

follow-up visits
nurse

(under supervision of
cardiologist)

questionnaire

medical history and
medication

physical examination

additional tests

supervision

22 individual patient profiles based on:

- symptoms
- thromboembolic risk
- type of AF
  - paroxysmal
  - persistent
  - permanent
- (contra)indications for medication

patient profile

- ☑ advise treatment underlying disease
- ☑ anti coagulation
- ☐ cardioversion
- ☑ anti-arrhythmic drugs
- ☑ rate control

treatment advise

treatment according to guidelines

(inter)national guidelines on atrial fibrillation and cardiovascular risk management

lifestyle and education

smoking cessation

anti coagulation

cardioversion

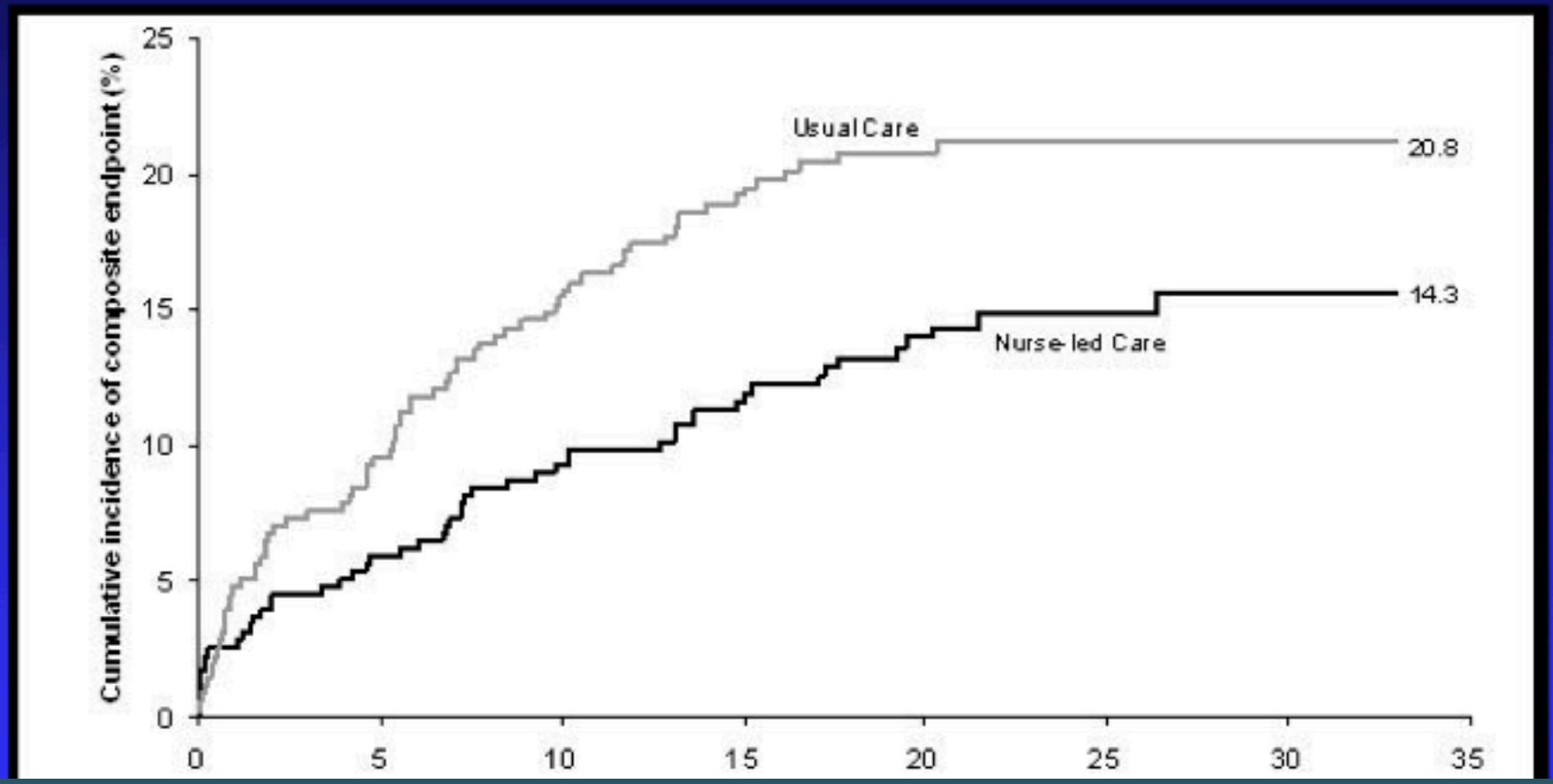
pacemaker therapy

anti-aritmic drugs

rate control medication

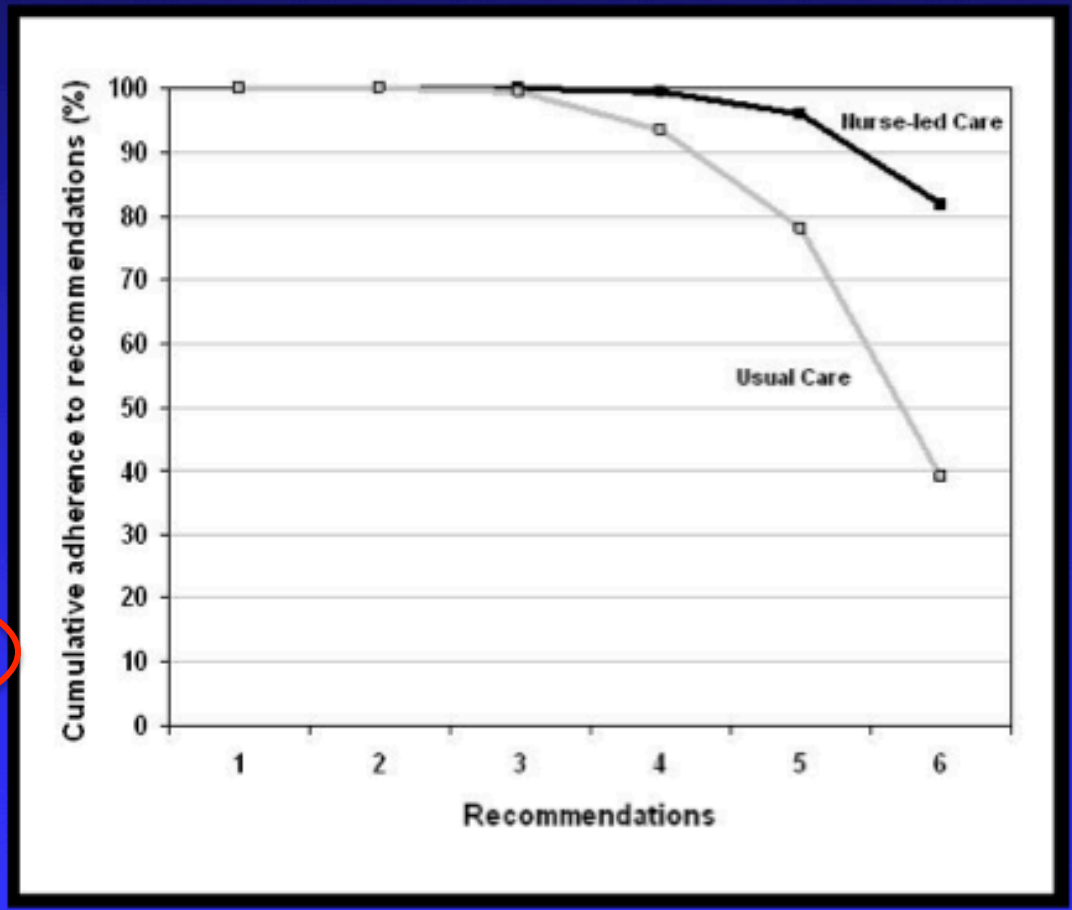
database: data available to be used for correspondence, management and research activities

Incidence of Composite Endpoint:
CV Death or Hospitalization



Results: guideline adherence

- Echocardiogram performed
- Laboratory assessment of Thyroid Stimulating Hormone
- Application of appropriate anti-thrombotic treatment
- Appropriate prescription of Vaughan-Williams class I or III
- Avoiding rhythm control strategy in asymptomatic patients
- Avoiding rhythm control drugs in patients with permanent AF



Conclusion

Management of atrial fibrillation patients in a specialized AF-Clinic improves outcome compared to usual care.

My tired lines to AF patients…

- *"Welcome to the club. I am sorry. I am a member too."*
- *"You have company: 3 million Americans and more than 5 million Europeans also have AF."*
- *"AF isn't terrible, but it may require us to be friends."*
- *"Worrying about AF is like worrying about getting gray hairs, wrinkles or needing reading glasses."*
- *"AF can be rough, but it isn't life-threatening. We must never make AF treatment worse than AF."*

Thanks…

For more real world information on AF and heart rhythm disorders, visit my blog:
www.drjohnm.org

Not used slides
Back up

- Where possible, patients at intermediate risk should be considered for oral anticoagulation rather than aspirin, since undertreatment is more harmful than overtreatment.[28,29] Full discussion with the patient with one combination risk factor would enable agreement to use oral anticoagulation instead of aspirin to allow greater protection against ischemic stroke, especially if these patients value stroke prevention much more than the (theoretical) lower risk of hemorrhage with aspirin and the inconvenience of anticoagulation monitoring.[10] As mentioned, the BAFTA trial found no difference in major bleeding between warfarin (INR 2-3) and aspirin 75 mg in an elderly AF population in primary care,[2] and aspirin cannot be regarded as a much safer alternative to VKA.

Dabigatran and Decreased ICH risk:

Is it Dabigatran, or just that warfarin is bad?

Anticoagulation With the Oral Direct Thrombin Inhibitor Dabigatran Does Not Enlarge Hematoma Volume in Experimental Intracerebral Hemorrhage

Arne Lauer, BSc; Flor A. Cianchetti, BSc; Elizabeth M. Van Cott, MD; Frieder Schlunk, BSc; Elena Schulz, BSc; Waltraud Pfeilschifter, MD; Helmuth Steinmetz, MD; Chris B. Schaffer, PhD; Eng H. Lo, PhD; Christian Foerch, MD

Background—The direct thrombin inhibitor dabigatran etexilate (DE) may constitute a future replacement of vitamin K antagonists for long-term anticoagulation. Whereas warfarin pretreatment is associated with greater hematoma expansion after intracerebral hemorrhage (ICH), it remains unclear what effect direct thrombin inhibitors would have. Using different experimental models of ICH, this study compared hematoma volume among DE-treated mice, warfarin-treated mice, and controls.

Methods and Results—CD-1 mice were fed with DE or warfarin. Sham-treated mice served as controls. At the time point of ICH induction, DE mice revealed an increased activated partial thromboplastin time compared with controls (mean±SD 46.1±5.0 versus 18.0±1.5 seconds; $P=0.022$), whereas warfarin pretreatment resulted in a prothrombin time prolongation (51.4±17.9 versus 10.4±0.3 seconds; $P<0.001$). Twenty-four hours after collagenase-induced ICH formation, hematoma volume was 3.8±2.9 μL in controls, 4.8±2.7 μL in DE mice, and 14.5±11.8 μL in warfarin mice (n=16; Welch ANOVA between-group differences $P=0.007$; posthoc analysis with the Dunnett method: DE versus controls, $P=0.899$; warfarin versus controls, $P<0.001$; DE versus warfarin, $P=0.001$). In addition, a model of laser-induced cerebral microhemorrhage was applied, and the distances that red blood cells and blood plasma were pushed into the brain were quantified. Warfarin mice showed enlarged red blood cell and blood plasma diameters compared to controls, but no difference was found between DE mice and controls.

Conclusions—In contrast with warfarin, pretreatment with DE did not increase hematoma volume in 2 different experimental models of ICH. In terms of safety, this observation may represent a potential advantage of anticoagulation with DE over warfarin. (***Circulation*. 2011;124:00-00.**)

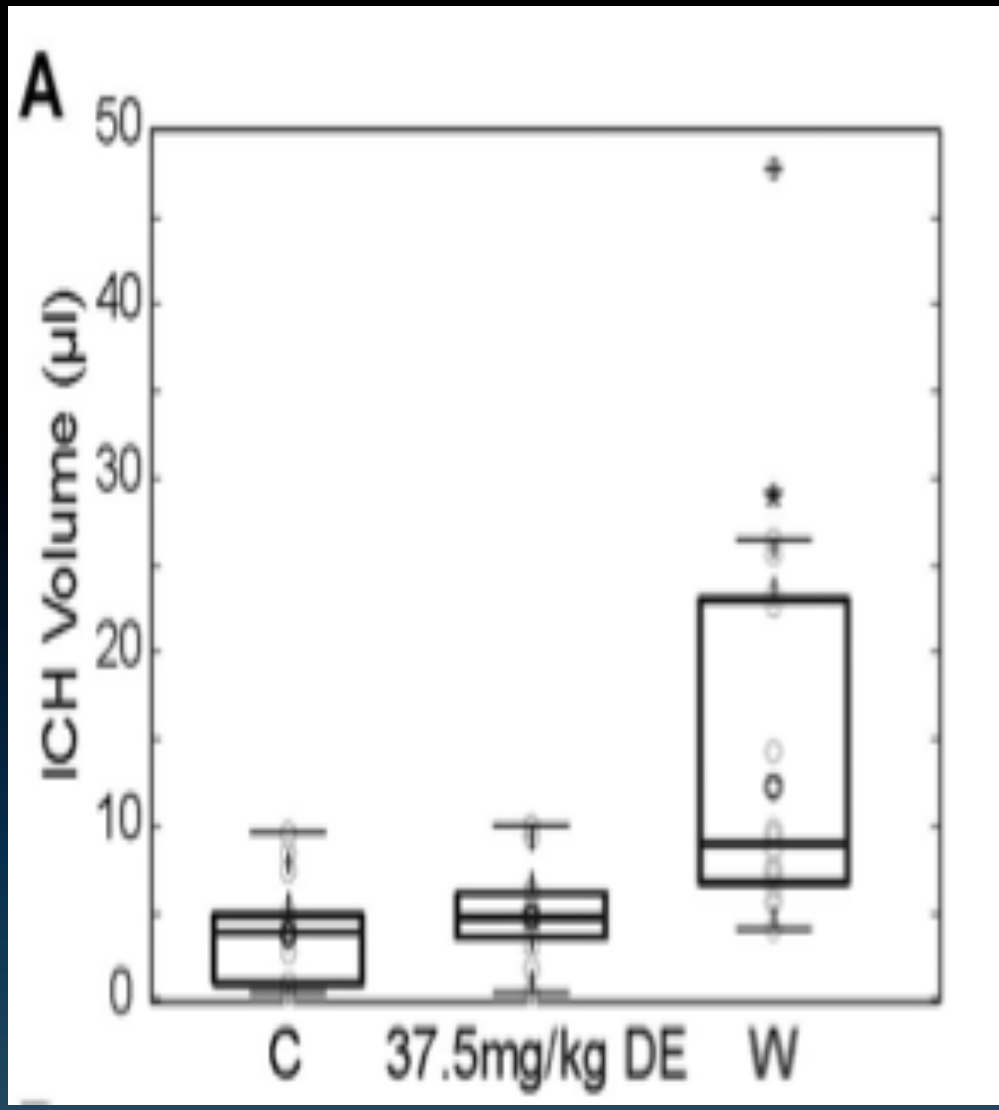
Key Words: anticoagulants ■ cerebral hemorrhage ■ intracerebral hemorrhage ■ warfarin ■ dabigatran ■ stroke

Dabigatran biochemistry

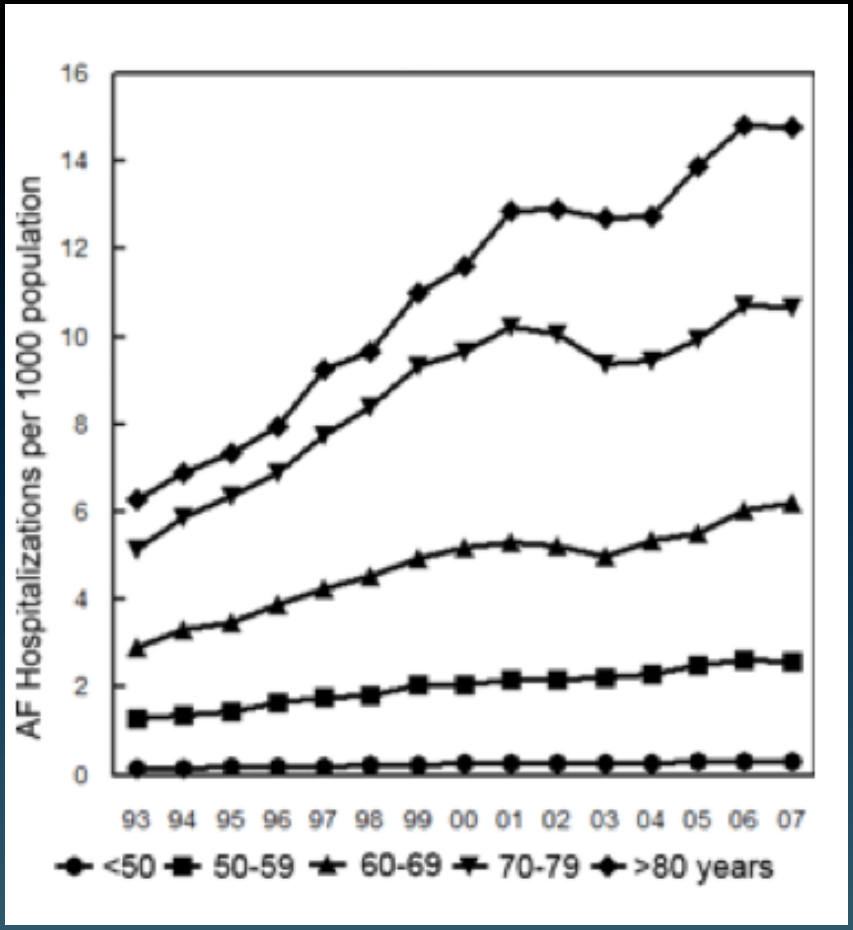
- Compared to warfarin, dabigatran-treated mice fared better with induced ICH

Potential reasons:

- DTI do not inhibit thrombin-activatable fibrinolysis inhibitor generation whereas drugs that target factor Xa (warfarin) do.
  - Dabigatran is a uni-(not bi)valent binder to thrombin. This allows for Dabig-mediated decreases in Factor II activity and sufficient clotting in ICH
- Microhemorrhages induced in warfarin-treated mice more often expand toward having increased RBC and blood plasma diameters whereas microbleeds in DE mice do not differ from controls. Thus, we may speculate that in the RE-LY trial, the absolute number of cerebral micobleeds was similar in the warfarin and the dabigatran groups but that microhemorrhages under warfarin more often expanded to- ward symptomatic ICH.



Is the increasing prevalence of AF related to just age?



RE-LY: Safety Outcomes

Table 3. Safety Outcomes, According to Treatment Group.*

Event	Dabigatran, 110 mg		Dabigatran, 150 mg		Warfarin		Dabigatran, 110 mg, vs. Warfarin		Dabigatran, 150 mg, vs. Warfarin		Dabigatran, 150 mg vs. 110 mg	
							Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value
	no. of patients	*%/yr*	*no. of patients*	*%/yr*	*no. of patients*	*%/yr*						
Major bleeding	322	2.71	375	3.11	397	3.36	0.80 (0.69–0.93)	0.003	0.93 (0.81–1.07)	0.31	1.16 (1.00–1.34)	0.052
Life threatening	145	1.22	175	1.45	212	1.80	0.68 (0.55–0.83)	<0.001	0.81 (0.66–0.99)	0.04	1.19 (0.96–1.49)	0.11
Non–life threatening	198	1.66	226	1.88	208	1.76	0.94 (0.78–1.15)	0.56	1.07 (0.89–1.29)	0.47	1.14 (0.95–1.39)	0.17
Gastrointestinal†	133	1.12	182	1.51	120	1.02	1.10 (0.86–1.41)	0.43	1.50 (1.19–1.89)	<0.001	1.36 (1.09–1.70)	0.007
Minor bleeding	1566	13.16	1787	14.84	1931	16.37	0.79 (0.74–0.84)	<0.001	0.91 (0.85–0.97)	0.005	1.16 (1.08–1.24)	<0.001
Major or minor bleeding	1740	14.62	1977	16.42	2142	18.15	0.78 (0.74–0.83)	<0.001	0.91 (0.86–0.97)	0.002	1.16 (1.09–1.23)	<0.001
Intracranial bleeding	27	0.23	36	0.30	87	0.74	0.31 (0.20–0.47)	<0.001	0.40 (0.27–0.60)	<0.001	1.32 (0.80–2.17)	0.28
Extracranial bleeding	299	2.51	342	2.84	315	2.67	0.94 (0.80–1.10)	0.45	1.07 (0.92–1.25)	0.38	1.14 (0.97–1.33)	0.11
Net clinical benefit outcome‡	844	7.09	832	6.91	901	7.64	0.92 (0.84–1.02)	0.10	0.91 (0.82–1.00)	0.04	0.98 (0.89–1.08)	0.66