심방세동과 최신 항응고요법

울산대 내과
남 기병

AF

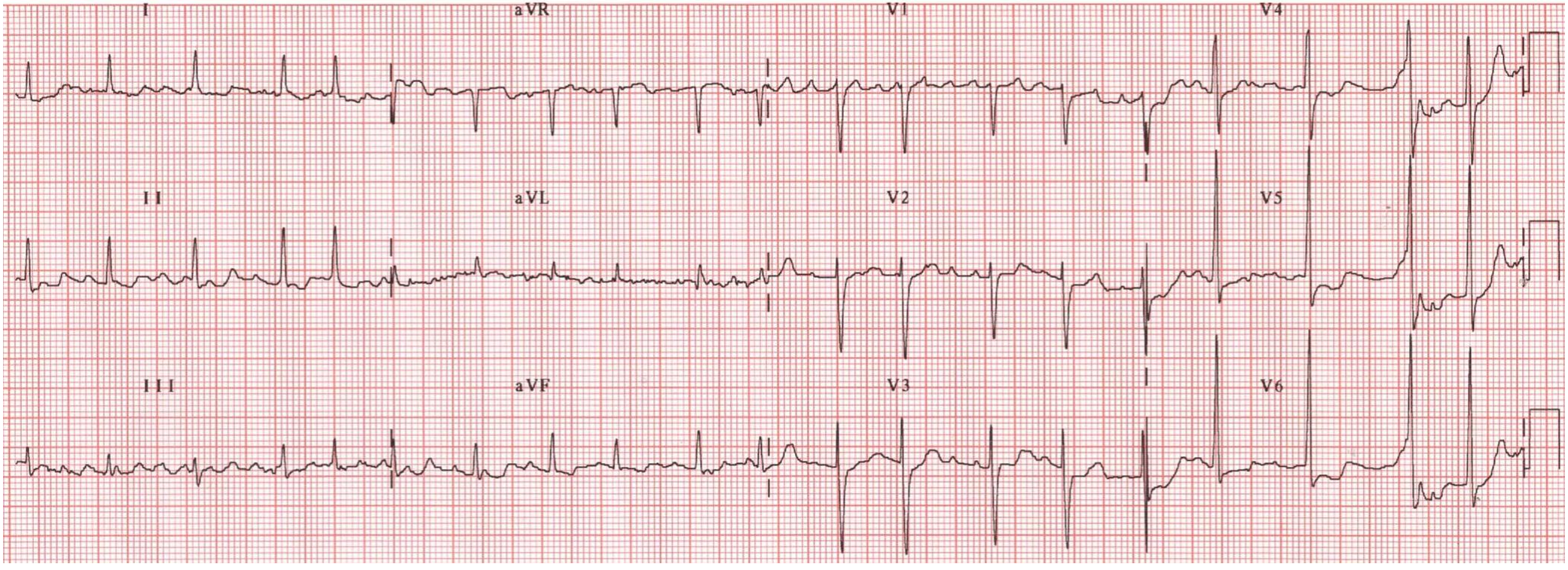
Sinus conversion

Rapid HR ---------- CHF

Rate control

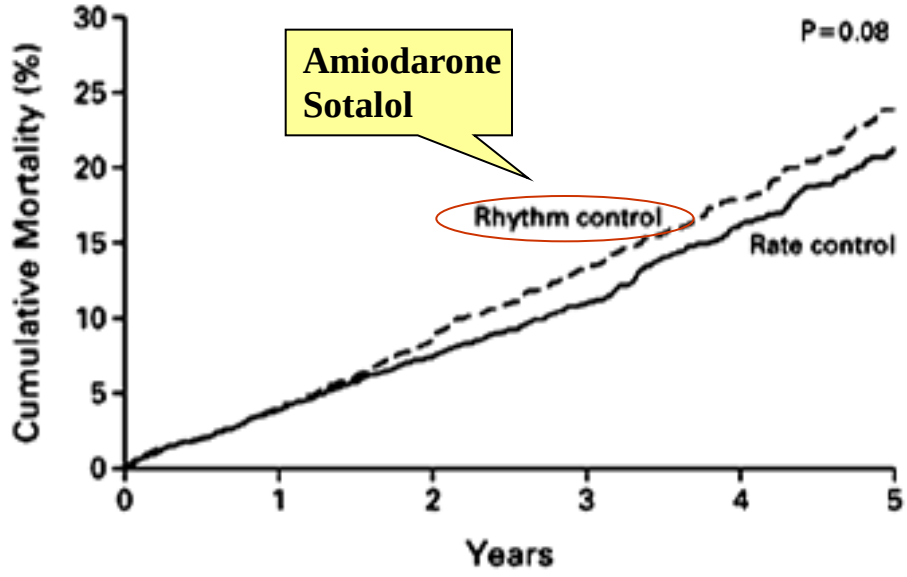
Stasis
Hypercoagulability – **Clots - Stroke**
Injury

Anticoagulation



AFFIRM

4060 enrolled patients from 213 sites in the US, Canada
Age: >65 y.o. (69.7±9.0 years)
Risk factors for stroke
AF lasting > 6 hours, episode lasted at least 2 days (70%)
Mean follow up time: 3.5 years (maximum, 6 yrs)



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)

~~사망율~~
~~심부전~~
~~뇌경색~~
~~병원입원~~
~~삶의 질~~
~~증상개선~~

운동능력

AF-CHF

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 19, 2008 VOL. 358 NO. 25

Rhythm Control versus Rate Control for Atrial Fibrillation and Heart Failure

Denis Roy, M.D., Mario Talajic, M.D., Stanley Nattel, M.D., D. George Wyse, M.D., Ph.D., Paul Dorian, M.D., Kerry L. Lee, Ph.D., Martial G. Bourassa, M.D., J. Malcolm O. Arnold, M.D., Alfred E. Buxton, M.D., A. John Camm, M.D., Stuart J. Connolly, M.D., Marc Dubuc, M.D., Anique Ducharme, M.D., M.Sc., Peter G. Guerra, M.D., Stefan H. Hohnloser, M.D., Jean Lambert, Ph.D., Jean-Yves Le Heuzey, M.D., Gilles O'Hara, M.D., Ole Dyg Pedersen, M.D., Jean-Lucien Rouleau, M.D., Bramah N. Singh, M.D., D.Sc., Lynne Warner Stevenson, M.D., William G. Stevenson, M.D., Bernard Thibault, M.D., and Albert L. Waldo, M.D., for the Atrial Fibrillation and Congestive Heart Failure Investigators*

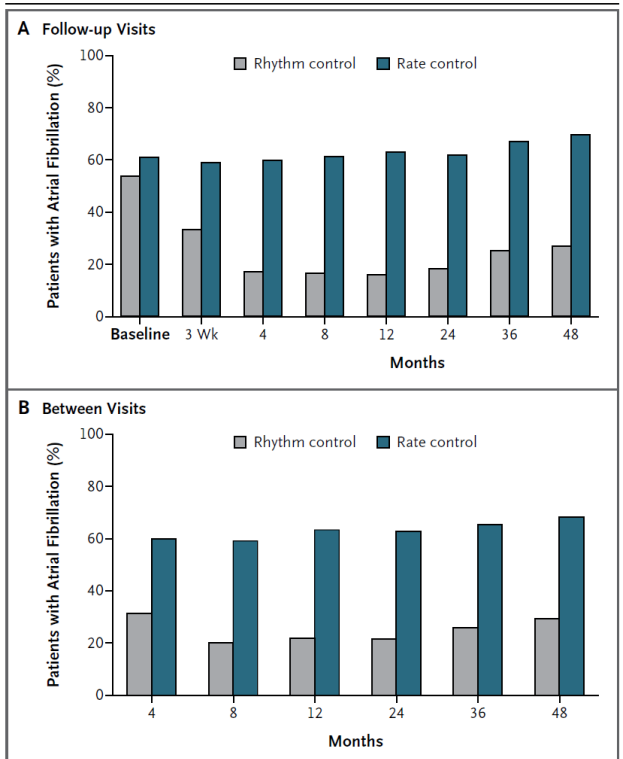


Figure 1. Prevalence of Atrial Fibrillation at Each Follow-up Visit and between Visits.

The presence or absence of atrial fibrillation was confirmed on 12-lead electrocardiography at each follow-up visit (Panel A) and on electrocardiography, as documented through chart review, between visits (Panel B).

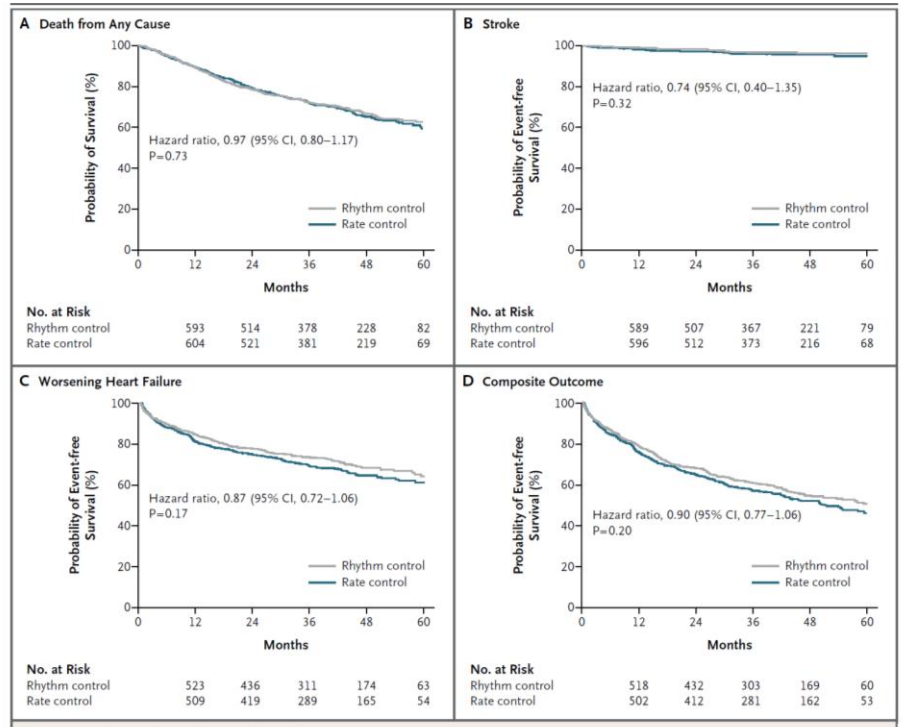


Figure 3. Kaplan–Meier Estimates of Secondary Outcomes.

None of the secondary outcomes differed significantly between the treatment groups. Panel A shows the probability of death from any cause (32% in the rhythm-control group and 33% in the rate-control group), Panel B the probability of ischemic or hemorrhagic stroke (3% and 4%, respectively), Panel C the probability of worsening heart failure, which was defined as heart failure requiring hospitalization, the administration of an intravenous diuretic, or a change in treatment strategy (28% and 31%), and Panel D the probability of the composite outcome of death from cardiovascular causes, stroke, or worsening heart failure (43% and 46%). There were also no significant differences favoring either strategy in any of the predefined subgroups. Hazard ratios are for the rhythm-control group, as compared with the rate-control group.

Table I Characteristics of rhythm control and rate control trials in patients with atrial fibrillation (adapted from Camm *et al.* with permission)[1]

Trial	Patients (*n*)	Mean age (years)	Mean length of follow-up (years)	Inclusion criteria	Primary endpoint	Patients reaching primary endpoint (*n*)		
						Rate control	Rhythm control	*P*
PIAF[8]	252	61.0	1.0	Persistent AF (7–360 days)	Symptomatic improvement	76/125 (60.8%)	70/127 (55.1%)	0.32
AFFIRM[6]	4060	69.7	3.5	Paroxysmal AF or persistent AF, age 65 years or older, or risk of stroke or death	All-cause mortality	310/2027 (25.9%)	356/2033 (26.7%)	0.08
RACE[7]	522	68.0	2.3	Persistent AF or flutter for <1 year and 1 to 2 cardioversions >2 years and oral anticoagulation	Composite: cardiovascular death, CHF, severe bleeding, PM implantation, thromboembolic events, severe adverse effects of antiarrhythmic drugs	44/256 (17.2%)	60/266 (22.6%)	0.11
STAF[9]	200	66.0	1.6	Persistent AF (>4 weeks and <2years), left atrial size >45 mm, CHF NYHA II–IV, LVEF <45%	Composite: overall mortality, cerebrovascular complications, CPR, embolic events	10/100 (10.0%)	9/100 (9.0%)	0.99
HOT CAFÉ[10]	205	60.8	1.7	First clinically overt persistent AF (≥7 and <2 years), 50–75-year old	Composite: death, thromboembolic events; intracranial/ major haemorrhage	1/101 (1.0%)	4/104 (3.9%)	>0.71
AF-CHF[11]	1376	66	3.1	LVEF≤35%, symptoms of CHF, history of AF (≥6 h or ECV <last 6 months)	Cardiovascular death	175/1376 (25%)	182/1376 (27%)	0.59

AF, atrial fibrillation; AFFIRM, atrial fibrillation follow-up investigation of rhythm management; CHF, congestive heart failure; CPR, cardiopulmonary resuscitation; ECV, electrical cardioversion; HOT CAFE, how to treat chronic atrial fibrillation; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PIAF, pharmacological intervention in atrial fibrillation; PM, pacemaker; RACE, rate control versus electrical cardioversion for persistent atrial fibrillation; STAF, strategies of treatment of atrial fibrillation.

Isabelle C. Van Gelder, Europace 2011

Clinical outcomes in AF patients were driven mainly by hospitalizations for arrhythmia/proarrhythmia and other cardiovascular causes, but not by the choice of rate or rhythm strategy. Rhythm-control patients progressed less rapidly to permanent AF.

Real-Life Observations of Clinical Outcomes With Rhythm- and Rate-Control Therapies for Atrial Fibrillation: RECORDAF (Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation) J Am Coll Cardiol 2011;58:493–501

AF → **Rapid HR ---------- CHF**

Sinus conversion — **Rate control**

↘

Stasis
Hypercoagulability
Injury

– Clots - Stroke

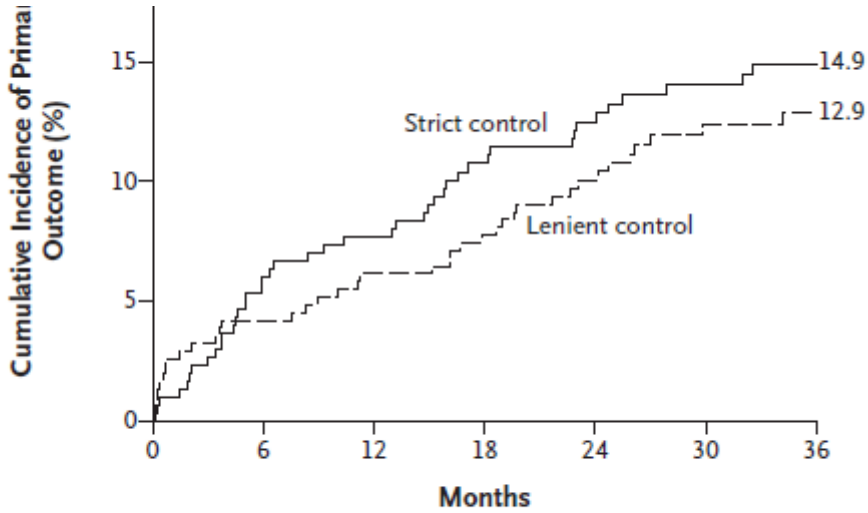
Anticoagulation

RACE II

ORIGINAL ARTICLE

Lenient versus Strict Rate Control in Patients with Atrial Fibrillation

Isabelle C. Van Gelder, M.D., Hessel F. Groenveld, M.D., Harry J.G.M. Crijns, M.D., Ype S. Tuininga, M.D., Jan G.P. Tijssen, Ph.D., A. Marco Alings, M.D., Hans L. Hillege, M.D., Johanna A. Bergsma-Kadijk, M.Sc., Jan H. Cornel, M.D., Otto Kamp, M.D., Raymond Tukkie, M.D., Hans A. Bosker, M.D., Dirk J. Van Veldhuisen, M.D., and Maarten P. Van den Berg, M.D., for the RACE II Investigators*



No. at Risk							
Strict control	303	282	273	262	246	212	131
Lenient control	311	298	290	285	255	218	138

~~사망율~~
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~~증상개선~~

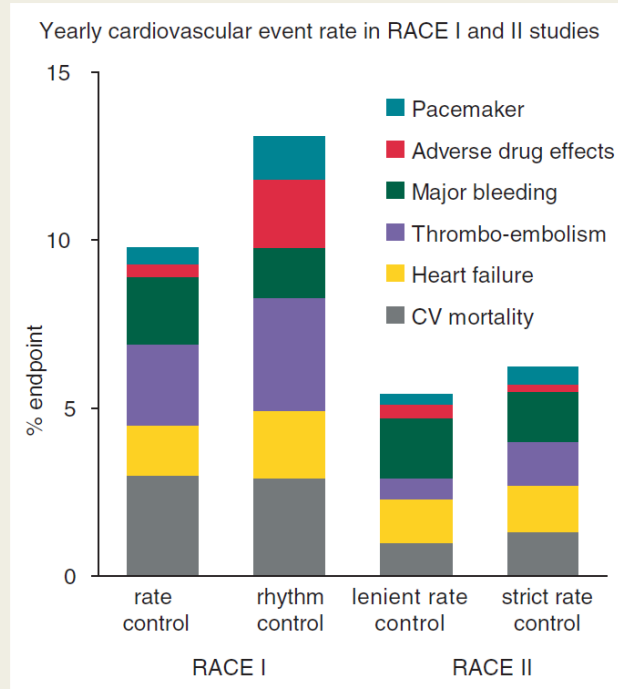


Figure 1 Yearly cardiovascular morbidity and mortality rate in the Rate Control Versus Electrical Cardioversion (RACE) I study (published in 2002) and the RAte Control Efficacy in permanent atrial fibrillation (RACE) II study (published in 2010).[7,20]

AF → **Rapid HR ---------- CHF**

Sinus conversion — **Rate control**

↘

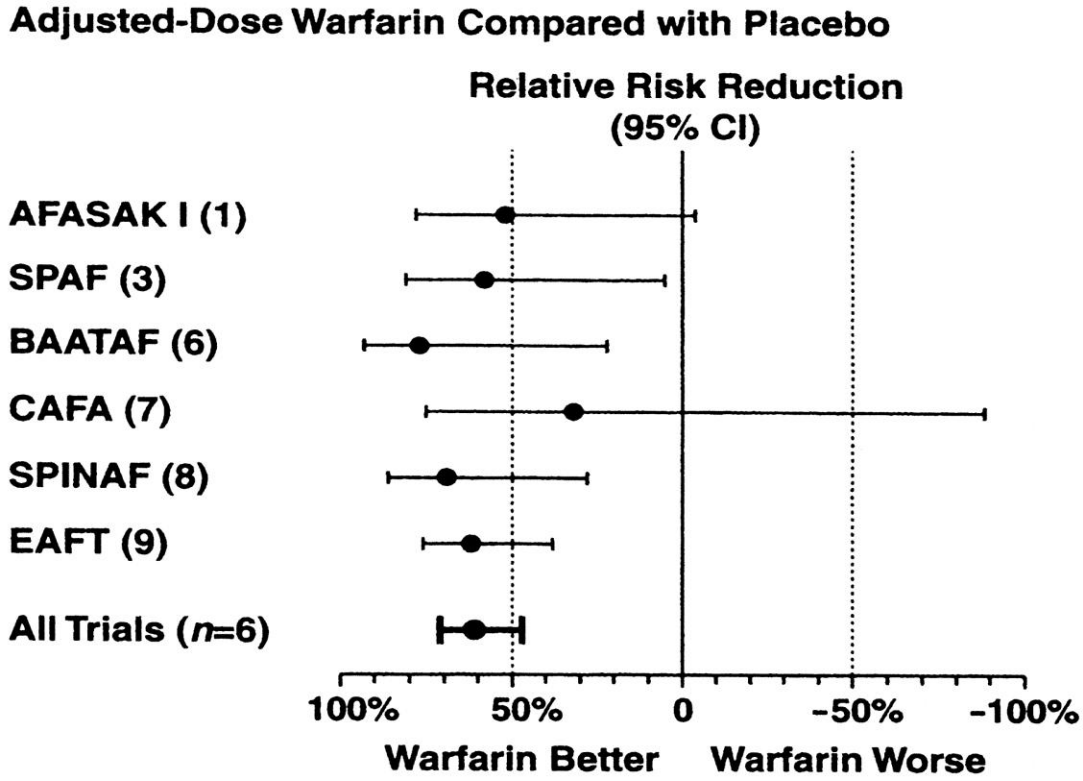
Stasis
Hypercoagulability
Injury

– Clots - Stroke

Anticoagulation

항응고치료의 효과

Warfarin : relative risk reduction, 68%
Annual rate of stroke: from 4.5% to 1.4%/yr
Major hemorrhagic complication: 1.0 to 1.3%/yr
cf. Asprin: relative risk reduction, 33%



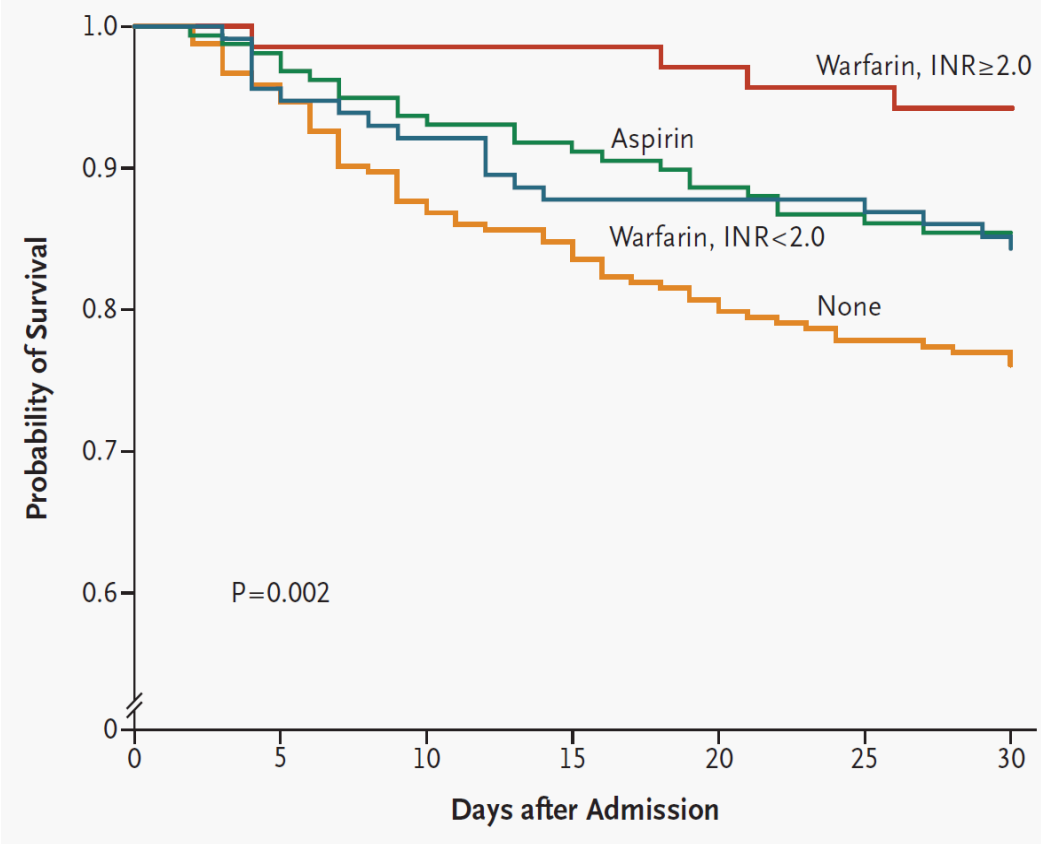
Ann Intern Med 1999;131:492-501

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 11, 2003 VOL. 349 NO. 11

Effect of Intensity of Oral Anticoagulation on Stroke Severity and Mortality in Atrial Fibrillation

Elaine M. Hylek, M.D., M.P.H., Alan S. Go, M.D., Yuchiao Chang, Ph.D., Nancy G. Jensvold, M.P.H., Lori E. Henault, M.P.H., Joe V. Selby, M.D., M.P.H., and Daniel E. Singer, M.D.



A cohort of 13,559 non-valvular AF

596 ischemic strokes

32% during warfarin

27% during aspirin

42% none

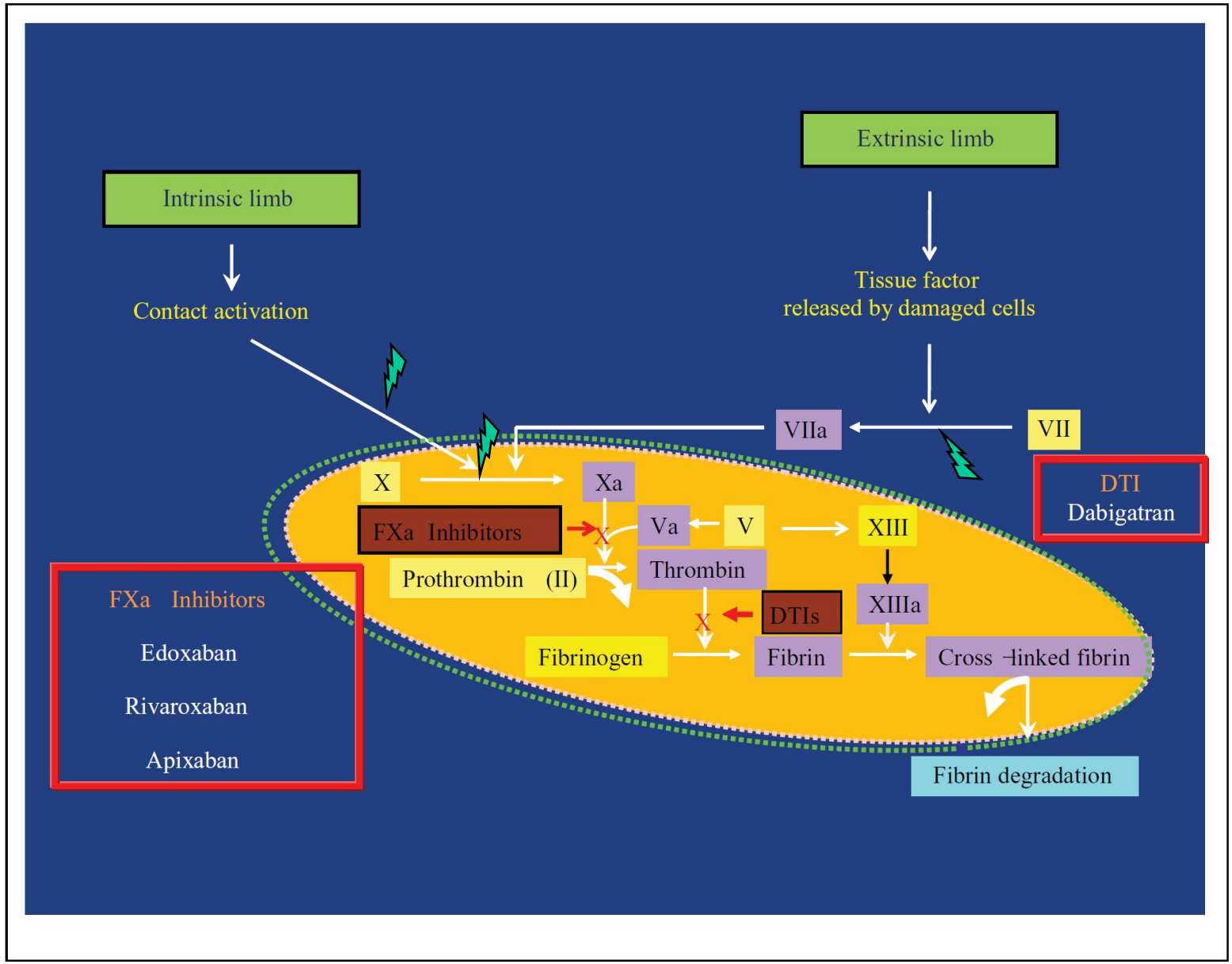
N Engl J Med 2003;349:1019-26.

현재의 항응고 치료방침

1. 심방세동의 type, 지속시간에 무관.
2. 임상적 위험요소에 기반. (CHADS2, CHADS2-VASc)
3. 위험군에서는 아스피린보다는 와파린이 효과적.
4. 아스피린에 클로피도그렐을 추가하는 것이 도움은 되지만 와파린보다는 약함.
5. 기타: 판막 질환(승모판협착증) 환자에서의 심방세동 심율동전환—전3주 후4주 시행

와파린의 단점

1. **INR검사 요망 – 순응도 (교통, 보호자, 경제력…)**
2. **음식물, 약물과 상호작용 심하다 – INR수치 변동**
3. **반감기가 길다**
4. **narrow therapeutic window**
5. **출혈 (뇌출혈, 소화기 출혈)**


Extrinsic limb
Intrinsic limb
Tissue factor
released by damaged cells
Contact activation
VIIa
VII
DTI
Dabigatran
X
Xa
FXa Inhibitors
Va
V
XIII
Prothrombin (II)
Thrombin
DTIs
XIIIa
Fibrinogen
Fibrin
Cross -linked fibrin
FXa Inhibitors
Edoxaban
Rivaroxaban
Apixaban
Fibrin degradation

: warfarin

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*

ABSTRACT

BACKGROUND

Warfarin reduces the risk of stroke in patients with atrial fibrillation but increases the risk of hemorrhage and is difficult to use. Dabigatran is a new oral direct thrombin inhibitor.

METHODS

In this noninferiority trial, we randomly assigned 18,113 patients who had atrial fibrillation and a risk of stroke to receive, in a blinded fashion, fixed doses of dabigatran — 110 mg or 150 mg twice daily — or, in an unblinded fashion, adjusted-dose warfarin. The median duration of the follow-up period was 2.0 years. The primary outcome was stroke or systemic embolism.

RESULTS

Rates of the primary outcome were 1.69% per year in the warfarin group, as compared with 1.53% per year in the group that received 110 mg of dabigatran (relative risk with dabigatran, 0.91; 95% confidence interval [CI], 0.74 to 1.11; P<0.001 for noninferiority) and 1.11% per year in the group that received 150 mg of dabigatran (relative risk, 0.66; 95% CI, 0.53 to 0.82; P<0.001 for superiority). The rate of major bleeding was 3.36% per year in the warfarin group, as compared with 2.71% per year in the group receiving 110 mg of dabigatran (P=0.003) and 3.11% per year in the group receiving 150 mg of dabigatran (P=0.31). The rate of hemorrhagic stroke was 0.38% per year in the warfarin group, as compared with 0.12% per year with 110 mg of dabigatran (P<0.001) and 0.10% per year with 150 mg of dabigatran (P<0.001). The mortality rate was 4.13% per year in the warfarin group, as compared with 3.75% per year with 110 mg of dabigatran (P=0.13) and 3.64% per year with 150 mg of dabigatran (P=0.051).

CONCLUSIONS

In patients with atrial fibrillation, dabigatran given at a dose of 110 mg was associated with rates of stroke and systemic embolism that were similar to those associated with warfarin, as well as lower rates of major hemorrhage. Dabigatran administered at a dose of 150 mg, as compared with warfarin, was associated with lower rates of stroke and systemic embolism but similar rates of major hemorrhage. (ClinicalTrials.gov number, NCT00262600.)

From the Population Health Research Institute, McMaster University and Hamilton Health Sciences, Hamilton, ON, Canada (S.J.C., S.Y., J.E., J.P., E.T.); Lankenau Institute for Medical Research and the Heart Center, Wynnewood, PA (M.D.E., A.P.); Uppsala Clinical Research Center, Uppsala, Sweden (J.O., L.W.); Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT (P.A.R., J.V., S.W.); Working Group on Cardiovascular Research the Netherlands, Utrecht, the Netherlands (M.A.); St. John's National Academy of Health Sciences, Bangalore, India (D.X.); FuWai Hospital, Beijing (J.Z.); Estudios Clínicos Latinoamérica, Rosario, Argentina (R.D.); Lady Davis Carmel Medical Center, Haifa, Israel (B.S.L.); Vivantes Klinikum Neukölln, Berlin (H.D.); University Duisburg-Essen, Essen, Germany (H.-C.D.); and Sunnybrook Health Sciences Centre, Toronto (C.D.J.). Address reprint requests to Dr. Connolly at the Population Health Research Institute, 237 Barton St. E., Hamilton, ON L8L 2X2, Canada, or at connostu@phri.ca.

*Members of the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Study Group are listed in the Appendix and the Supplementary Appendix, available with the full text of this article at NEJM.org.

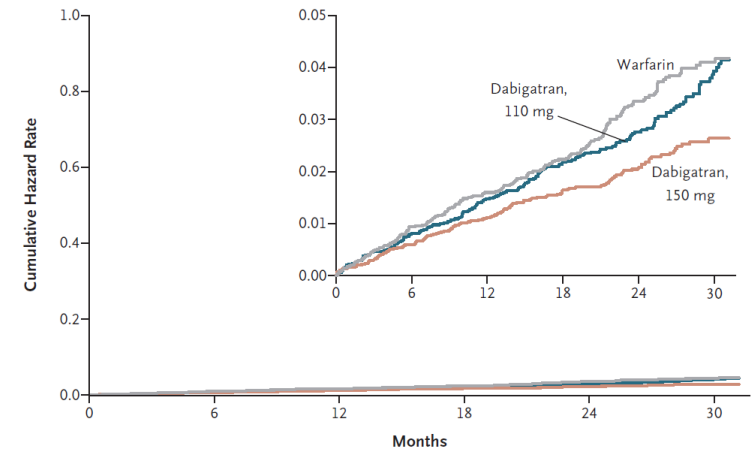
Drs. Connolly, Ezekowitz, Yusuf, and Wallentin contributed equally to this article.

This article (10.1056/NEJMoa0905561) was published on August 30, 2009, and updated on September 16, 2009, at NEJM.org.

N Engl J Med 2009;361:1139-51.

Warfarin
Dabigatran 110mg
Dabigatran 150mg

Primary outcome : stroke or systemic embolism



No. at Risk

Warfarin	6022	5862	5718	4593	2890	1322
Dabigatran, 110 mg	6015	5862	5710	4593	2945	1385
Dabigatran, 150 mg	6076	5939	5779	4682	3044	1429

Figure 1. Cumulative Hazard Rates for the Primary Outcome of Stroke or Systemic Embolism, According to Treatment Group.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 8, 2011 VOL. 365 NO. 10

Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation

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ABSTRACT

BACKGROUND

The use of warfarin reduces the rate of ischemic stroke in patients with atrial fibrillation but requires frequent monitoring and dose adjustment. Rivaroxaban, an oral factor Xa inhibitor, may provide more consistent and predictable anticoagulation than warfarin.

METHODS

In a double-blind trial, we randomly assigned 14,264 patients with nonvalvular atrial fibrillation who were at increased risk for stroke to receive either rivaroxaban (at a daily dose of 20 mg) or dose-adjusted warfarin. The per-protocol, as-treated primary analysis was designed to determine whether rivaroxaban was noninferior to warfarin for the primary end point of stroke or systemic embolism.

RESULTS

In the primary analysis, the primary end point occurred in 188 patients in the rivaroxaban group (1.7% per year) and in 241 in the warfarin group (2.2% per year) (hazard ratio in the rivaroxaban group, 0.79; 95% confidence interval [CI], 0.66 to 0.96; P<0.001 for noninferiority). In the intention-to-treat analysis, the primary end point occurred in 269 patients in the rivaroxaban group (2.1% per year) and in 306 patients in the warfarin group (2.4% per year) (hazard ratio, 0.88; 95% CI, 0.74 to 1.03; P<0.001 for noninferiority; P=0.12 for superiority). Major and nonmajor clinically relevant bleeding occurred in 1475 patients in the rivaroxaban group (14.9% per year) and in 1449 in the warfarin group (14.5% per year) (hazard ratio, 1.03; 95% CI, 0.96 to 1.11; P=0.44), with significant reductions in intracranial hemorrhage (0.5% vs. 0.7%, P=0.02) and fatal bleeding (0.2% vs. 0.5%, P=0.003) in the rivaroxaban group.

CONCLUSIONS

In patients with atrial fibrillation, rivaroxaban was noninferior to warfarin for the prevention of stroke or systemic embolism. There was no significant between-group difference in the risk of major bleeding, although intracranial and fatal bleeding occurred less frequently in the rivaroxaban group. (Funded by Johnson & Johnson and Bayer; ROCKET AF ClinicalTrials.gov number, NCT00403767.)

From the Duke Clinical Research Institute (M.R.P., K.W.M., J.G., J.P.P., R.C.B.) and Duke Translational Medicine Institute (R.M.C.), Duke University Medical Center, Durham, NC; Johnson & Johnson Pharmaceutical Research and Development, Raritan (G.P., C.C.N.), and Bayer HealthCare Pharmaceuticals, Montville (J.F.P., S.D.B.) — both in New Jersey; Massachusetts General Hospital and Harvard Medical School — both in Boston (D.E.S.); Ruprecht-Karls-University, Heidelberg (W.H.), and Hospital of the University of Münster, Münster (G.B.) — both in Germany; the Cardiovascular Institute, Mount Sinai Medical Center, New York (J.L.H.); Royal Perth Hospital, Perth, WA, Australia (G.J.H.); and the University of Edinburgh and Royal Infirmary of Edinburgh — both in Edinburgh (K.A.A.F.). Address reprint requests to Dr. Patel at Duke Clinical Research Institute, Duke University Medical Center, Rm. 0311 Terrace Level, 2400 Pratt St., Durham, NC 27705, or at manesh.patel@duke.edu.

*A complete listing of the steering committee members and trial investigators in the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF) is provided in the Supplementary Appendix, available at NEJM.org.

This article (10.1056/NEJMoa1009638) was published on August 10, 2011, at NEJM.org.

N Engl J Med 2011;365:883-91.

CHADS2: 3.5

Rivaroxaban was noninferior to warfarin for the prevention of stroke or systemic embolism.

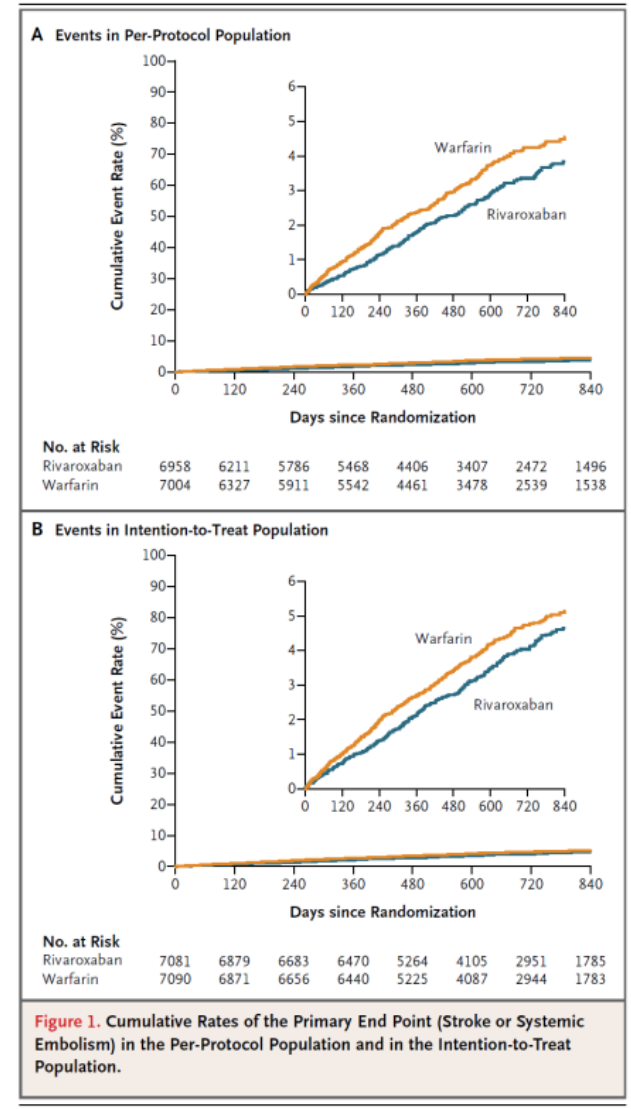


Figure 1. Cumulative Rates of the Primary End Point (Stroke or Systemic Embolism) in the Per-Protocol Population and in the Intention-to-Treat Population.

The NEW ENGLAND JOURNAL of MEDICINE

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., Alvaro Avezum, M.D., Ph.D., M. Cecilia Bahit, M.D., Rafael Diaz, M.D., J. Donald Easton, M.D., Justin A. Ezekowitz, M.B., B.Ch., Greg Flaker, M.D., David Garcia, M.D., Margarida Geraldes, Ph.D., Bernard J. Gersh, M.D., Sergey Golitsyn, M.D., Ph.D., Shinya Goto, M.D., Antonio G. Hermosillo, M.D., Stefan H. Hohnloser, M.D., John Horowitz, M.D., Puneet Mohan, M.D., Ph.D., Petr Jansky, M.D., Basil S. Lewis, M.D., Jose Luis Lopez-Sendon, M.D., Prem Pais, M.D., Alexander Parkhomenko, M.D., Freek W.A. Verheugt, M.D., Ph.D., Jun Zhu, M.D., and Lars Wallentin, M.D., Ph.D., for the ARISTOTLE Committees and Investigators*

ABSTRACT

BACKGROUND

Vitamin K antagonists are highly effective in preventing stroke in patients with atrial fibrillation but have several limitations. Apixaban is a novel oral direct factor Xa inhibitor that has been shown to reduce the risk of stroke in a similar population in comparison with aspirin.

METHODS

In this randomized, double-blind trial, we compared apixaban (at a dose of 5 mg twice daily) with warfarin (target international normalized ratio, 2.0 to 3.0) in 18,201 patients with atrial fibrillation and at least one additional risk factor for stroke. The primary outcome was ischemic or hemorrhagic stroke or systemic embolism. The trial was designed to test for noninferiority, with key secondary objectives of testing for superiority with respect to the primary outcome and to the rates of major bleeding and death from any cause.

RESULTS

The median duration of follow-up was 1.8 years. The rate of the primary outcome was 1.27% per year in the apixaban group, as compared with 1.60% per year in the warfarin group (hazard ratio with apixaban, 0.79; 95% confidence interval [CI], 0.66 to 0.95; P<0.001 for noninferiority; P=0.01 for superiority). The rate of major bleeding was 2.13% per year in the apixaban group, as compared with 3.09% per year in the warfarin group (hazard ratio, 0.69; 95% CI, 0.60 to 0.80; P<0.001), and the rates of death from any cause were 3.52% and 3.94%, respectively (hazard ratio, 0.89; 95% CI, 0.80 to 0.99; P=0.047). The rate of hemorrhagic stroke was 0.24% per year in the apixaban group, as compared with 0.47% per year in the warfarin group (hazard ratio, 0.51; 95% CI, 0.35 to 0.75; P<0.001), and the rate of ischemic or uncertain type of stroke was 0.97% per year in the apixaban group and 1.05% per year in the warfarin group (hazard ratio, 0.92; 95% CI, 0.74 to 1.13; P=0.42).

CONCLUSIONS

In patients with atrial fibrillation, apixaban was superior to warfarin in preventing stroke or systemic embolism, caused less bleeding, and resulted in lower mortality. (Funded by Bristol-Myers Squibb and Pfizer; ARISTOTLE ClinicalTrials.gov number, NCT00412984.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Granger at the Duke Clinical Research Institute, Duke University Medical Center, DUMC Box 3850, Durham, NC 27715, or at christopher.granger@duke.edu.

*The members of the steering committee, as well as other committee members and investigators in the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) study, are listed in the Supplementary Appendix, available at NEJM.org.

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

N Engl J Med 2011.

In patients with atrial fibrillation, apixaban was superior to warfarin in preventing stroke or systemic embolism, caused less bleeding, and resulted in lower mortality.

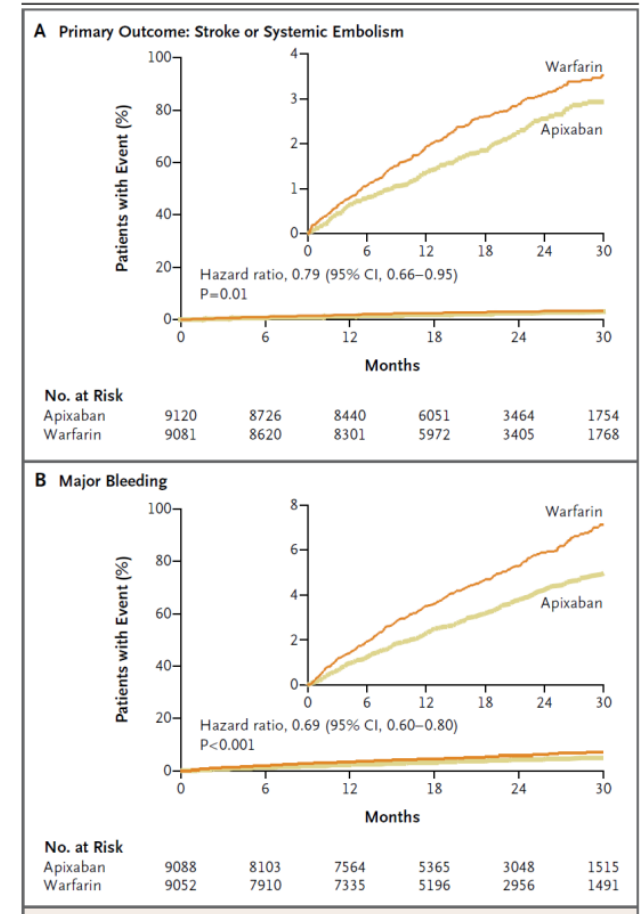
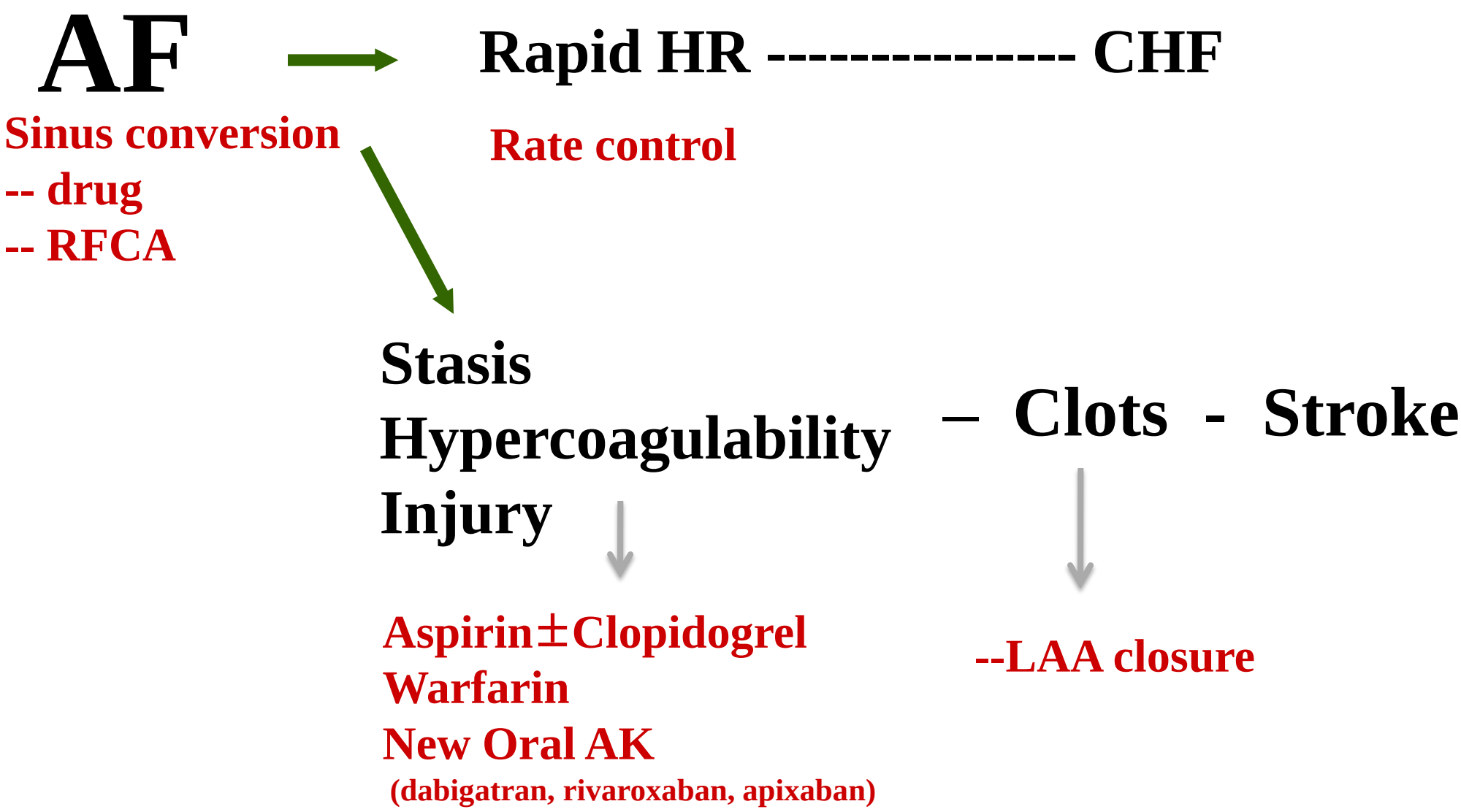


Figure 1. Kaplan–Meier Curves for the Primary Efficacy and Safety Outcomes.
The primary efficacy outcome (Panel A) was stroke or systemic embolism. The primary safety outcome (Panel B) was major bleeding, as defined according to the criteria of the International Society on Thrombosis and Haemostasis. The inset in each panel shows the same data on an enlarged segment of the y axis.

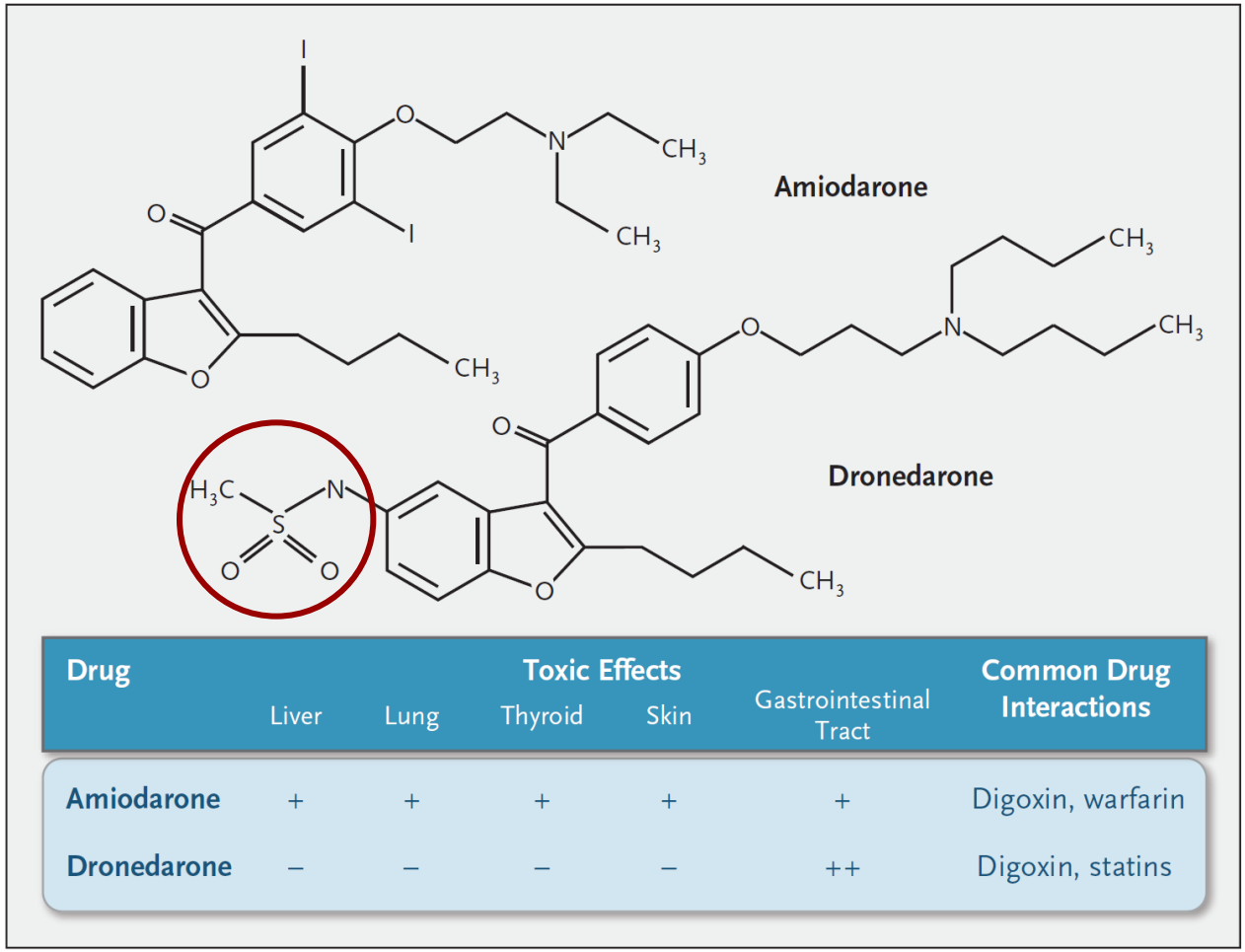
	Dabigatran (Boehringer)	Rivaroxaban (J&J, Bayer)	Apixaban (BMS, Pfizer)
복용	110mg bid 150mg bid (cf. 75mg bid)	20mg qd (15mg qd)	5mg bid (2.5mg bid)
results	Superiority	Non-inferiority	Superiority Mortality data
TTR (time in the therapeutic range)	Mean 64%	Mean 55%	Mean 62.2%
Study design			
CHADS2 score	2.1 (32%, CHADS2=3-6)	3.5 (87%, CHADS2=3-6)	2.1 (30%, CHADS2=3-6)
FDA	yes	yes	pending
Renal excretion	80%	66% (half inactive)	25%
Myocardial infarction	increased	No effect (favorable effect in ATLAS study)	No effect (APPRAISE, negative)

New Oral Anticoagulant
: Are they always good?

1. Forgetting more than one dose can put the patient at a pro-thrombotic risk.
2. There is no antidote to neutralize the action.
3. It is difficult to validate patient compliance.


AF
Rapid HR ---------- CHF
Sinus conversion
-- drug
-- RFCA
Rate control
Stasis
Hypercoagulability
Injury
– Clots - Stroke
Aspirin±Clopidogrel
Warfarin
New Oral AK
(dabigatran, rivaroxaban, apixaban)
--LAA closure

Dronedarone: A new antiarrhythmic drug



Drug	Toxic Effects					Common Drug Interactions
	Liver	Lung	Thyroid	Skin	Gastrointestinal Tract	
Amiodarone	+	+	+	+	+	Digoxin, warfarin
Dronedarone	–	–	–	–	++	Digoxin, statins

N Engl J Med 2009: 360;18

iodine radical
methane sulfonyl radical

반감기

전신독성 (간, 폐, 갑상선)
Torsade de Pointes

심방세동의 심박수 조절
발작성 심방세동 예방

심한 심부전 환자에서는 금기

심혈관계 사망을 감소시킨
유일한 부정맥제

ORIGINAL ARTICLE

Effect of Dronedarone on Cardiovascular Events in Atrial Fibrillation

Stefan H. Hohnloser, M.D., Harry J.G.M. Crijns, M.D., Martin van Eickels, M.D., Christophe Gaudin, M.D., Richard L. Page, M.D., Christian Torp-Pedersen, M.D.,

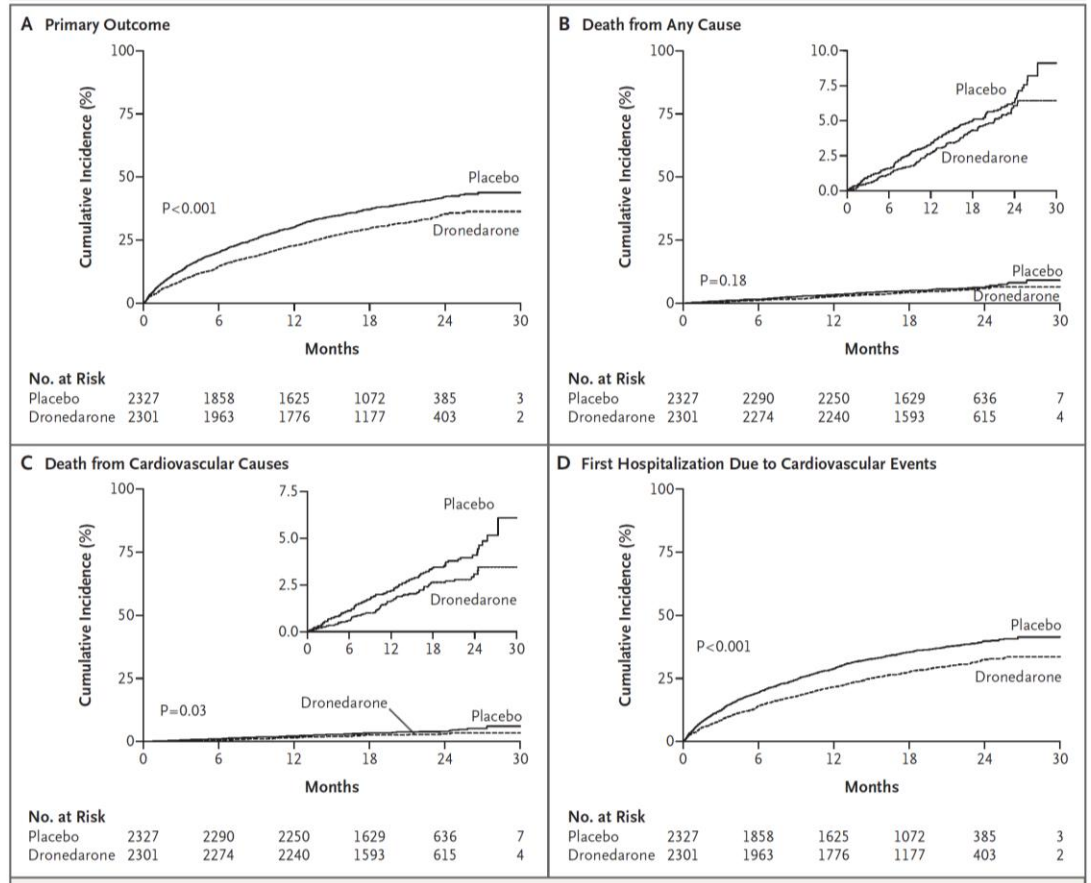


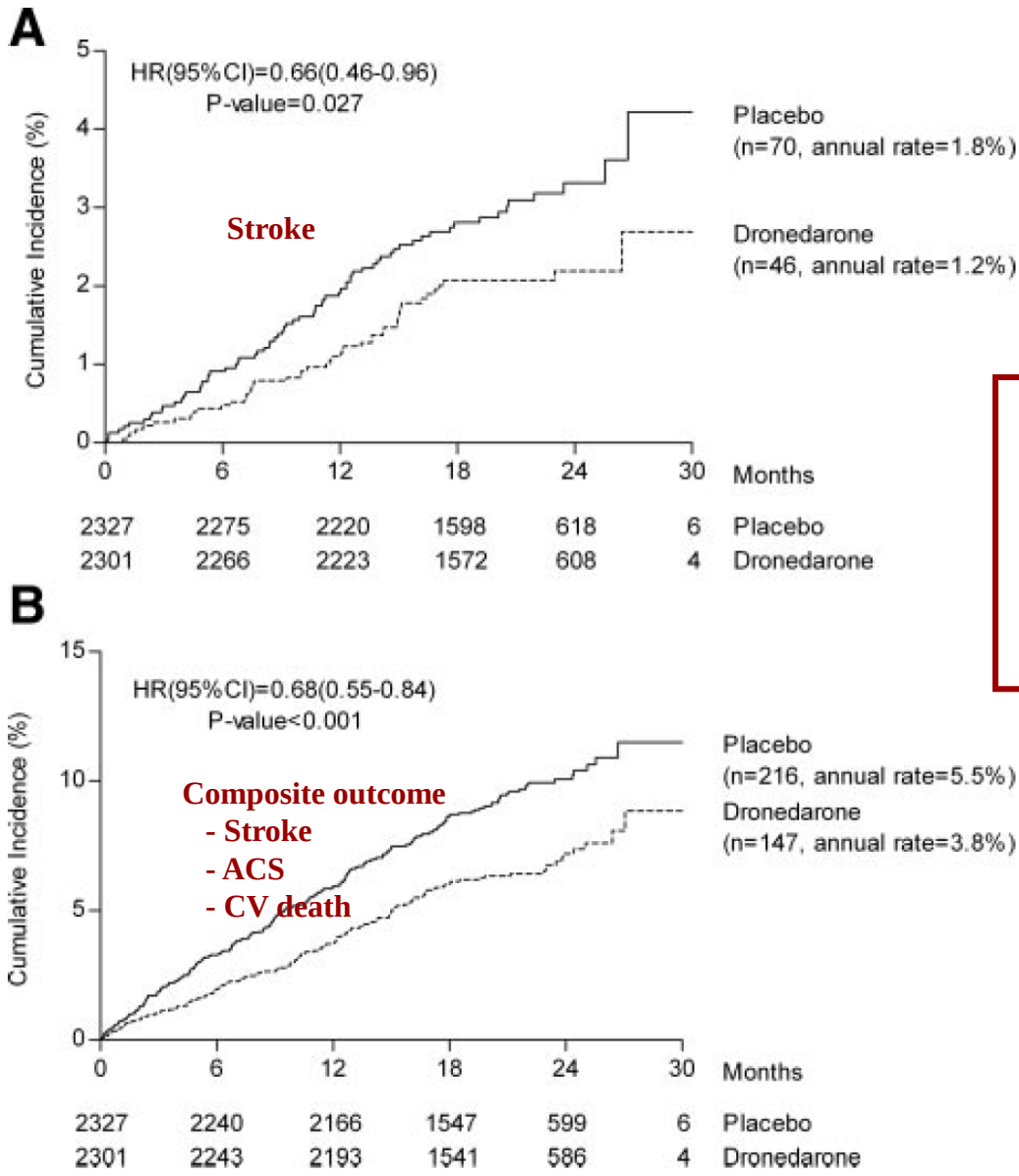
Figure 2. Kaplan–Meier Cumulative Incidences of the Primary and Secondary Outcomes.

Cumulative incidences are shown for the primary study outcome (composite of first hospitalization due to cardiovascular events or death from any cause) (Panel A) and for secondary study outcomes: death from any cause (Panel B), death from cardiovascular causes (Panel C), and first hospitalization due to cardiovascular events (Panel D). The number of patients is the number for whom the variable was assessed. The hazard ratios for the dronedarone group as compared with the placebo group were 0.76 (95% confidence interval [CI], 0.69 to 0.84; P<0.001) for the primary outcome, 0.84 (95% CI, 0.66 to 1.08; P=0.18) for death from any cause, 0.71 (95% CI, 0.51 to 0.98; P=0.03) for death from cardiovascular causes, and 0.74 (95% CI, 0.67 to 0.82; P<0.001) for first hospitalization due to cardiovascular events.

N Engl J Med 2009;360:668-78

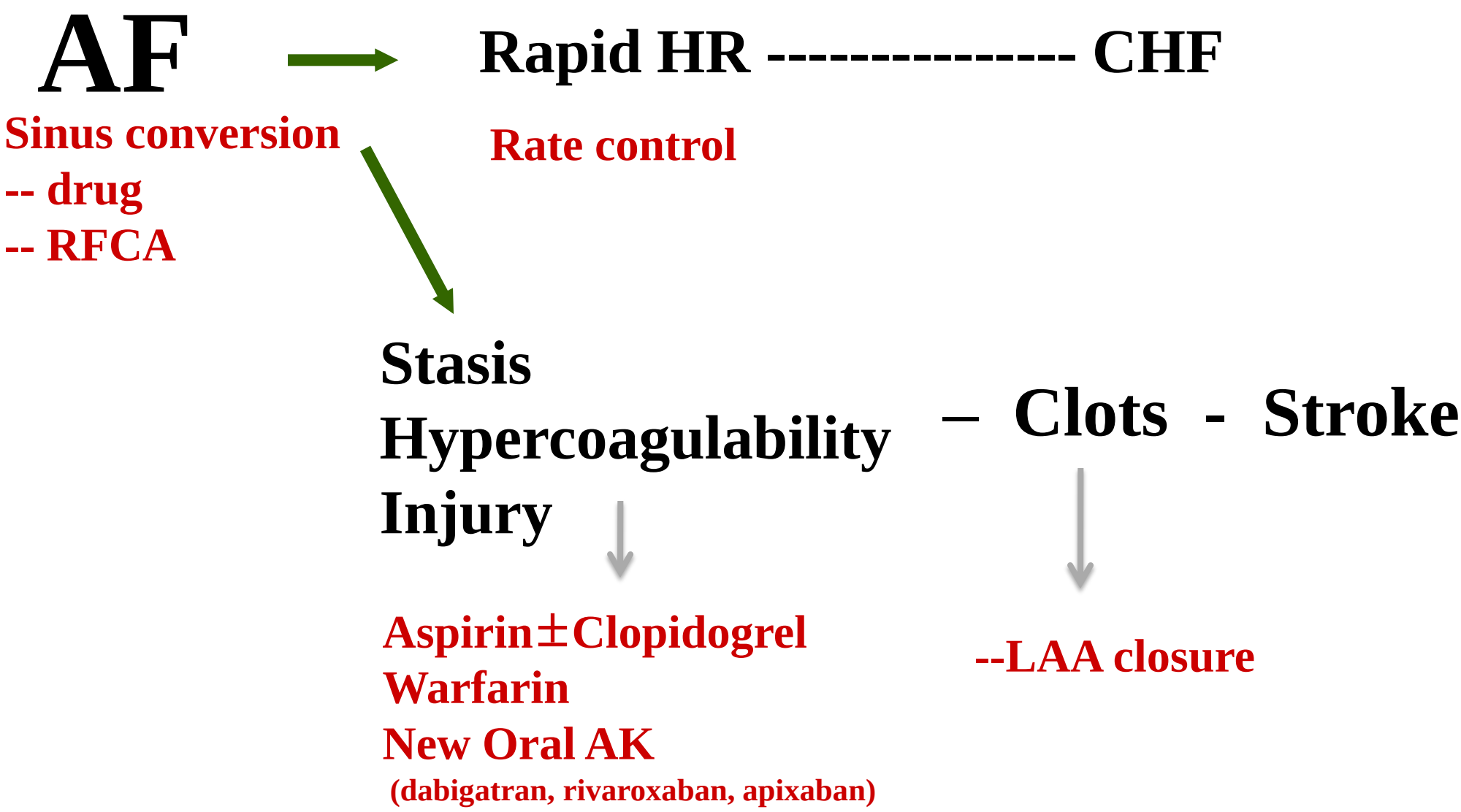
Dronedarone and Thromboembolism

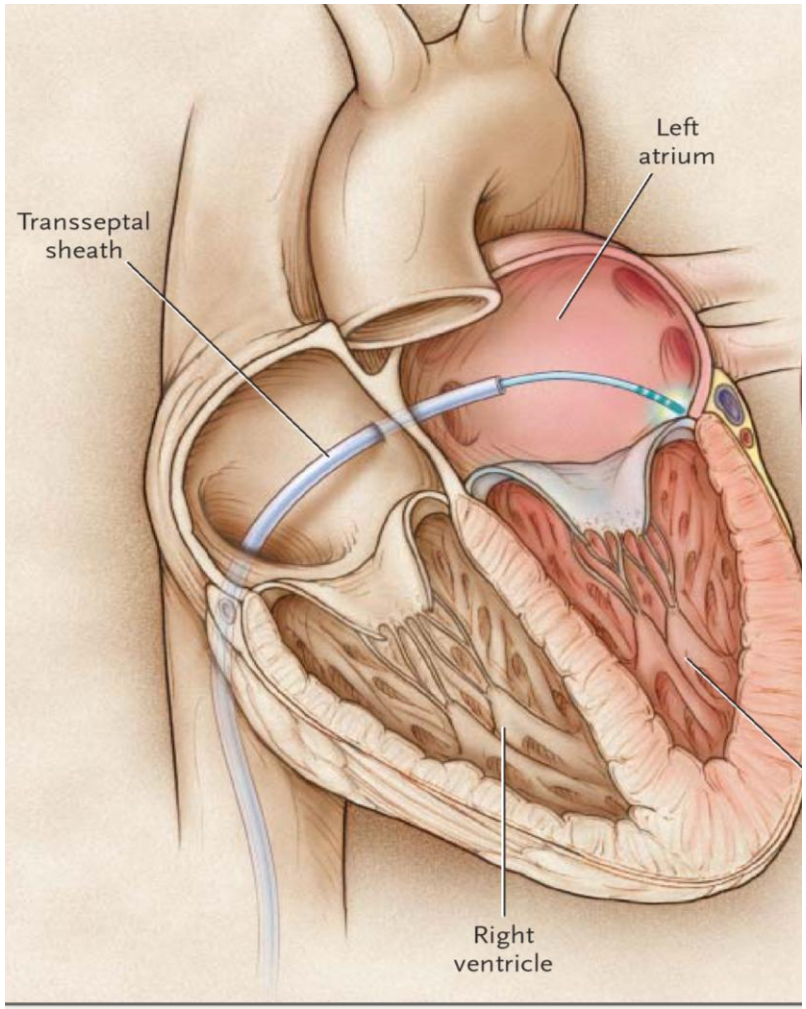
post-hoc analysis



In post hoc analysis of ATHENA, stroke was reduced from 1.8% per year to 1.2% per year with dronedarone, a 34% reduction that was statistically significant.

***Circulation*. 2009;120:1174-1180**


AF
Rapid HR ---------- CHF
Sinus conversion
-- drug
-- RFCA
Rate control
Stasis
Hypercoagulability
Injury
– Clots - Stroke
Aspirin±Clopidogrel
Warfarin
New Oral AK
(dabigatran, rivaroxaban, apixaban)
--LAA closure



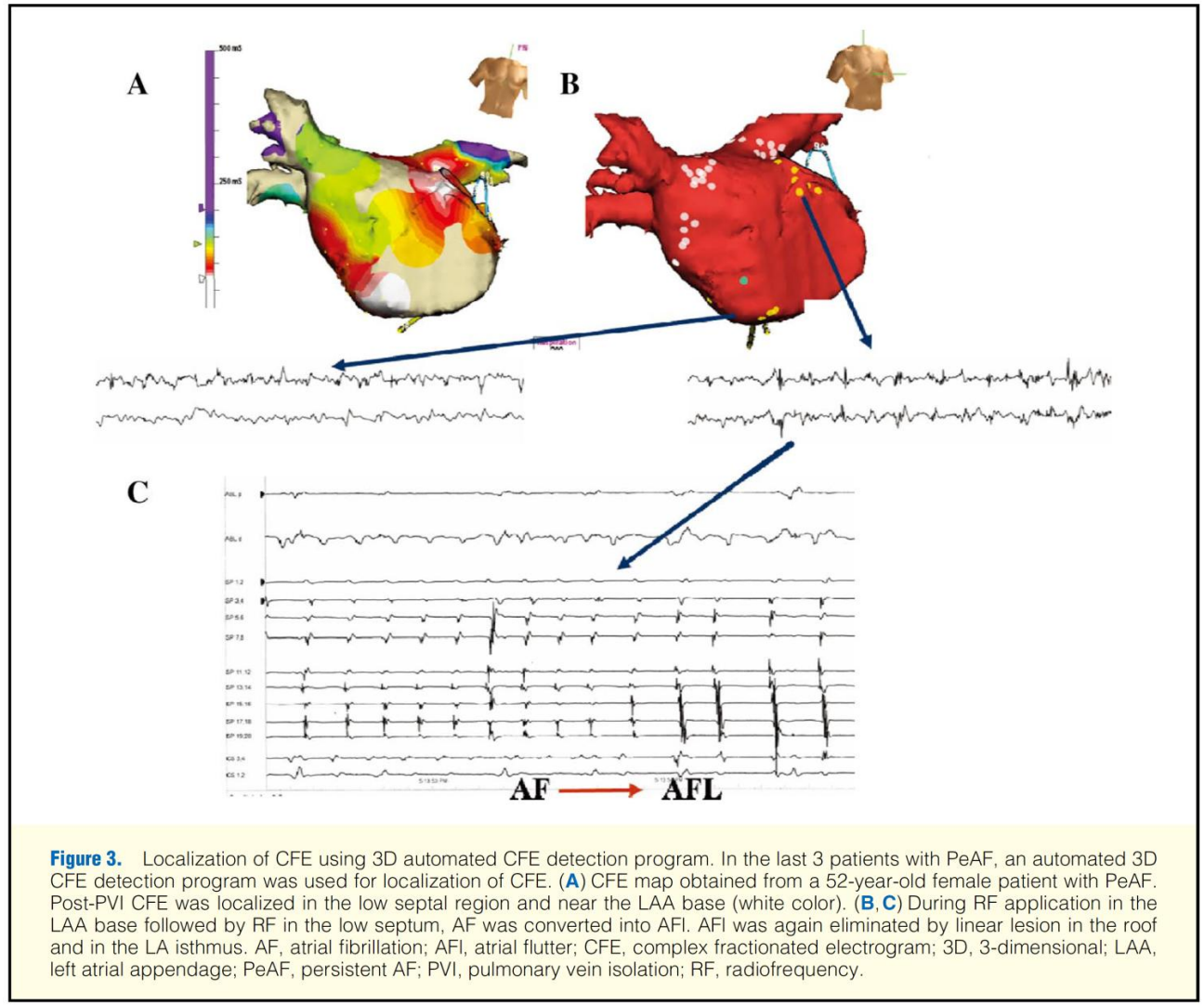


Figure 3. Localization of CFE using 3D automated CFE detection program. In the last 3 patients with PeAF, an automated 3D CFE detection program was used for localization of CFE. (**A**) CFE map obtained from a 52-year-old female patient with PeAF. Post-PVI CFE was localized in the low septal region and near the LAA base (white color). (**B**, **C**) During RF application in the LAA base followed by RF in the low septum, AF was converted into AFl. AFl was again eliminated by linear lesion in the roof and in the LA isthmus. AF, atrial fibrillation; AFl, atrial flutter; CFE, complex fractionated electrogram; 3D, 3-dimensional; LAA, left atrial appendage; PeAF, persistent AF; PVI, pulmonary vein isolation; RF, radiofrequency.

Mortality, Morbidity, and Quality of Life After Circumferential Pulmonary Vein Ablation for Atrial Fibrillation

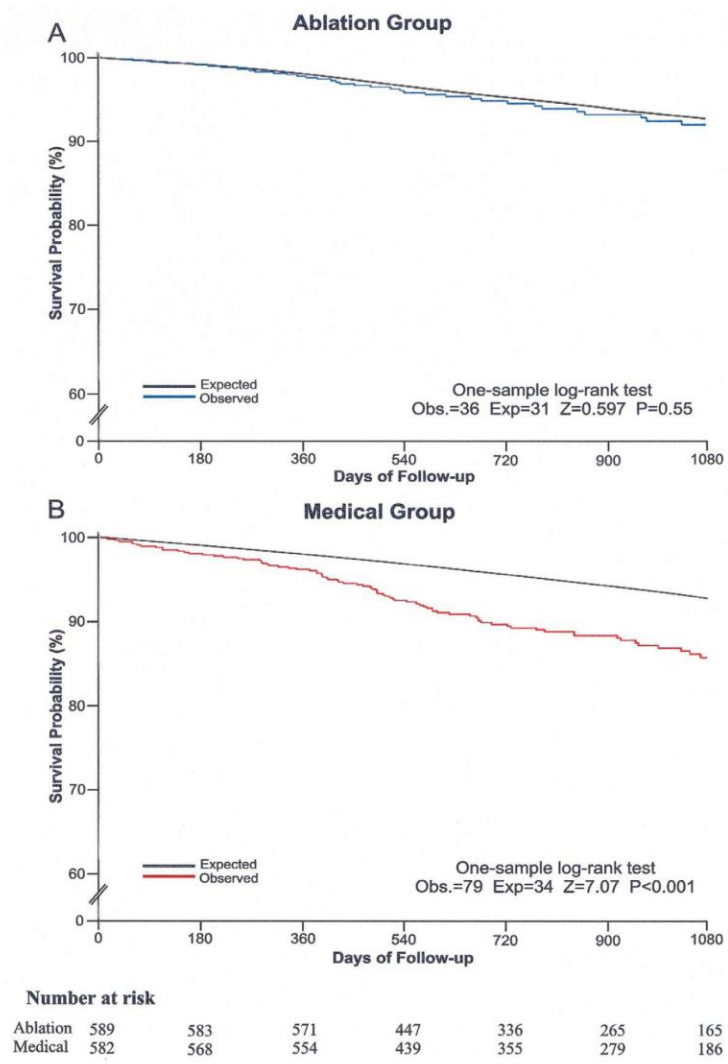


Figure 2. Observed and expected survival in the ablation and medical groups. The observed survival among ablation patients did not differ ($p = 0.55$) from the expected **(A)** and was significantly longer than that observed in the medical group, whose survival proved worse than that expected **(B)**. Observed survival probabilities were 98%, 95%, and 92% at one, two, and three years, respectively, among ablated patients, and 96%, 90%, and 86%, respectively, among those medically treated ($p < 0.001$).

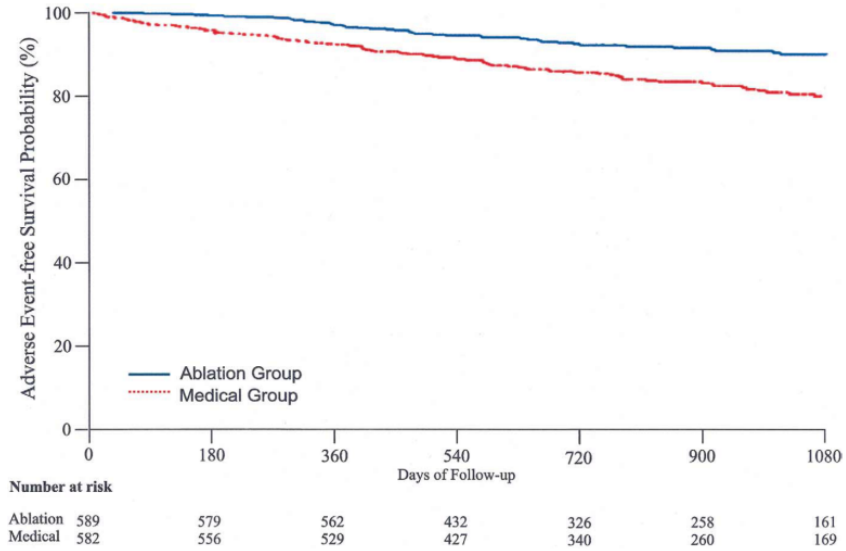
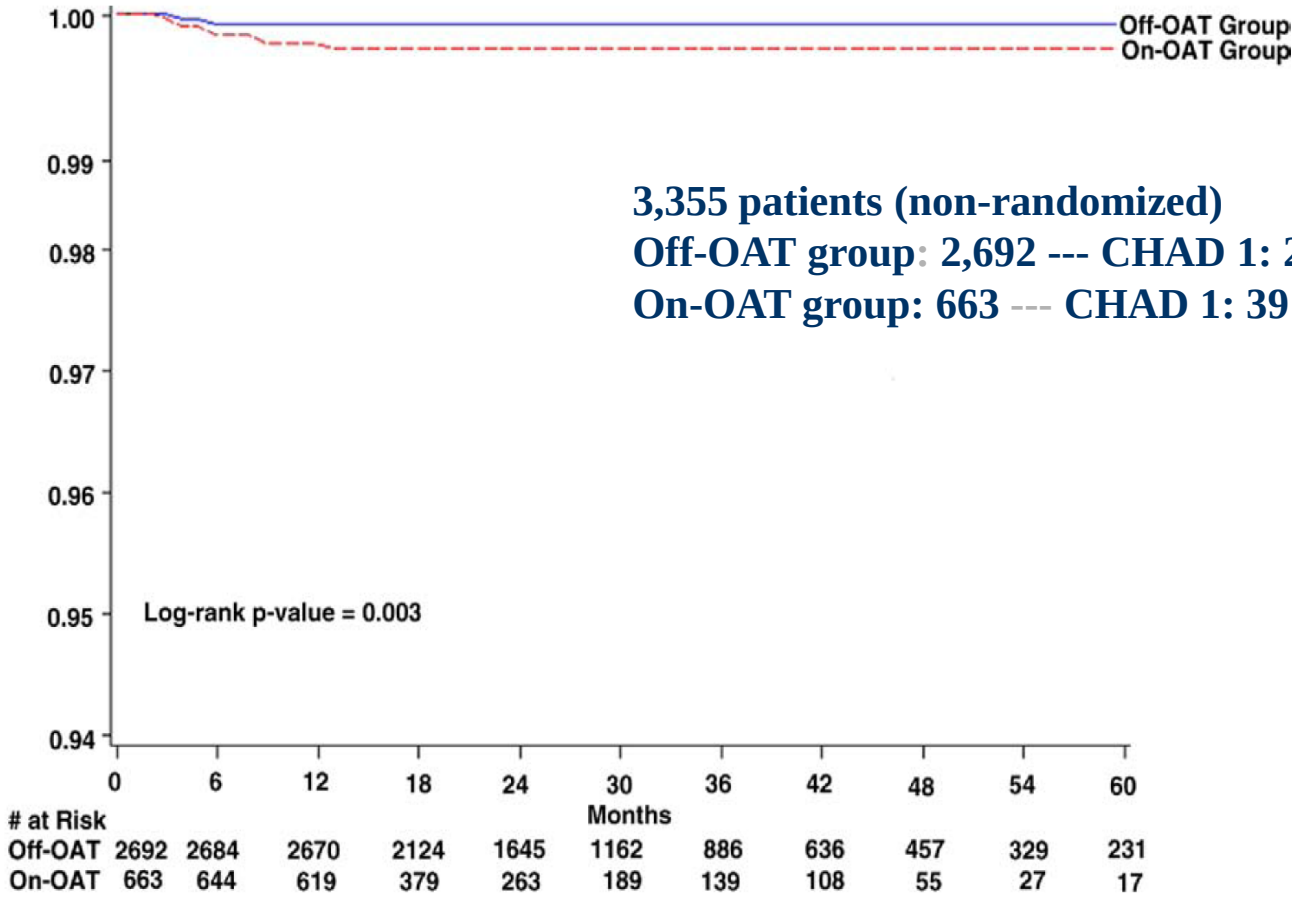


Figure 4. Kaplan-Meier estimates of the percentages of patients remaining free of any adverse events. Percentages of patients event-free were 97%, 94%, and 91% at one, two, and three years, respectively, among ablated patients, and 93%, 87%, and 81%, respectively, among those medically treated ($p < 0.001$).

Adverse event‡			
Congestive heart failure	32	57	89
Myocardial infarction	7	8	15
Peripheral embolism	1	3	4
TIA	8	27	35
Ischemic stroke	4	15	19
Hemorrhagic stroke	2	7	9
Total	54	117	171
No. of patients with events	46	98	144

J Am Coll Cardiol 2003;42:185–97

The Risk of Thromboembolism and Need for Oral Anticoagulation After Successful Atrial Fibrillation Ablation



3,355 patients (non-randomized)
Off-OAT group: 2,692 --- CHAD 1: 27%, CHAD 2이상: 13%
On-OAT group: 663 --- CHAD 1: 39%, CHAD 2 이상: 37%

JACC 2010;55:735

Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation: Results of the CABANA Pilot Study

Funded by St. Jude Medical Foundation,
St. Paul, Minnesota

Research Relationships (DLP) with Biosense, Acuson, Siemens, Cryocath, EPT, St. Jude, Cardiofocus, Symphony, Prorhythm, NIH
Royalties from IP licensed by St. Jude Medical
Unpaid consulting relationships: Medtronic, Boston Scientific, St. Jude, Biosense, Siemens, Cryocath

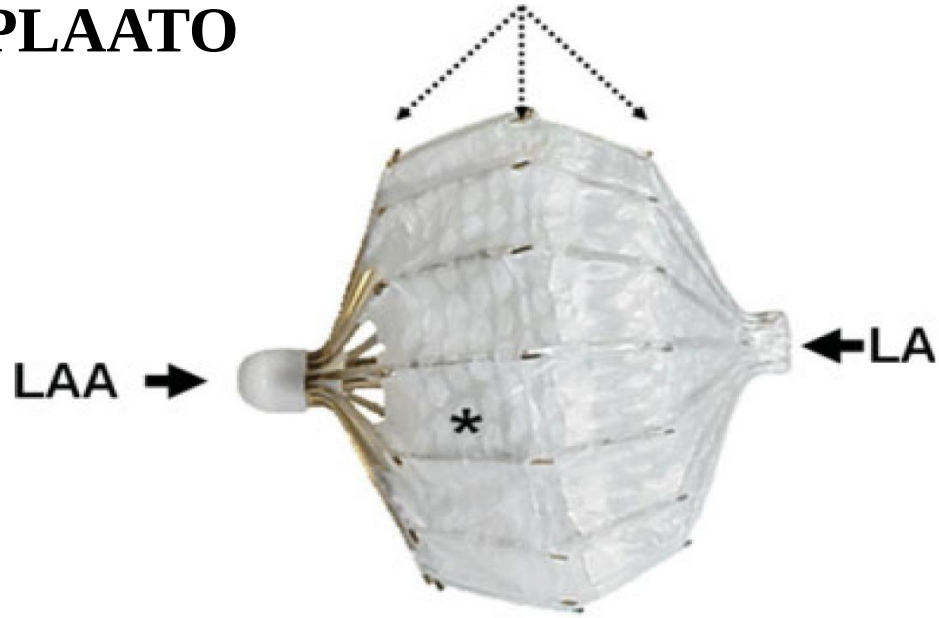
Appendage Obliteration to Reduce Stroke in Cardiac Surgical Patients With Atrial Fibrillation

Thrombi were localized to, or were present in the left atrial appendage and extended into the left atrial cavity in 254 of 446 (57%) of patients with rheumatic atrial fibrillation. In contrast, 201 of 222 (91%) of nonrheumatic atrial fibrillation-related left atrial thrombi were isolated to, or originated in the left atrial appendage ($p < 0.0001$).

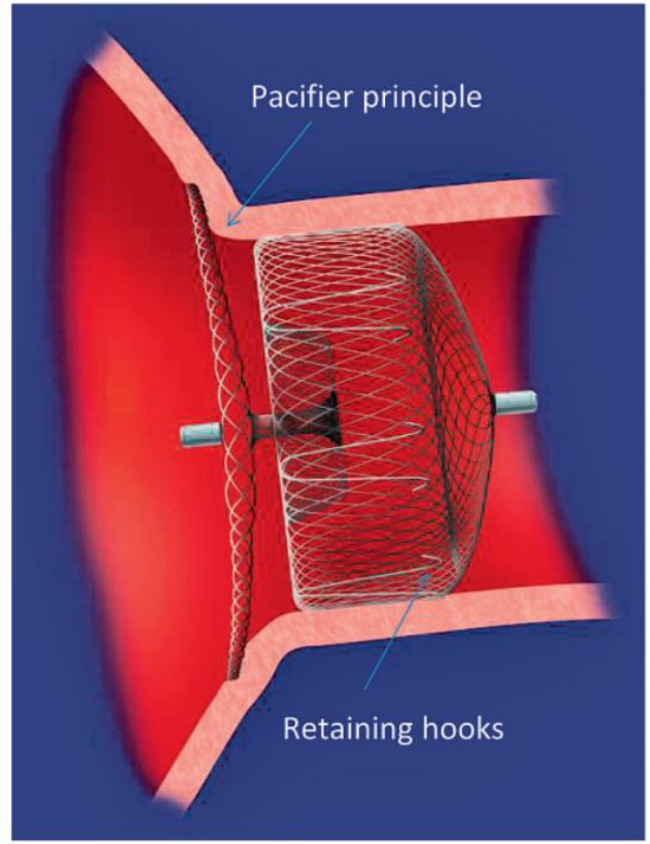
These data suggest that left atrial appendage obliteration is a strategy of potential value for stroke prophylaxis in nonrheumatic AF.

(Ann -Thorac Surg 1996;61:755-9)

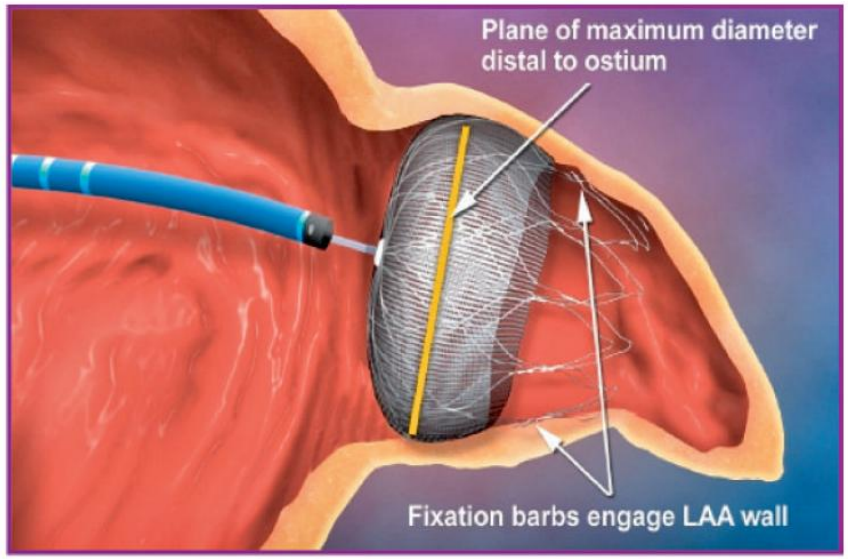
PLAATO



Amplatz

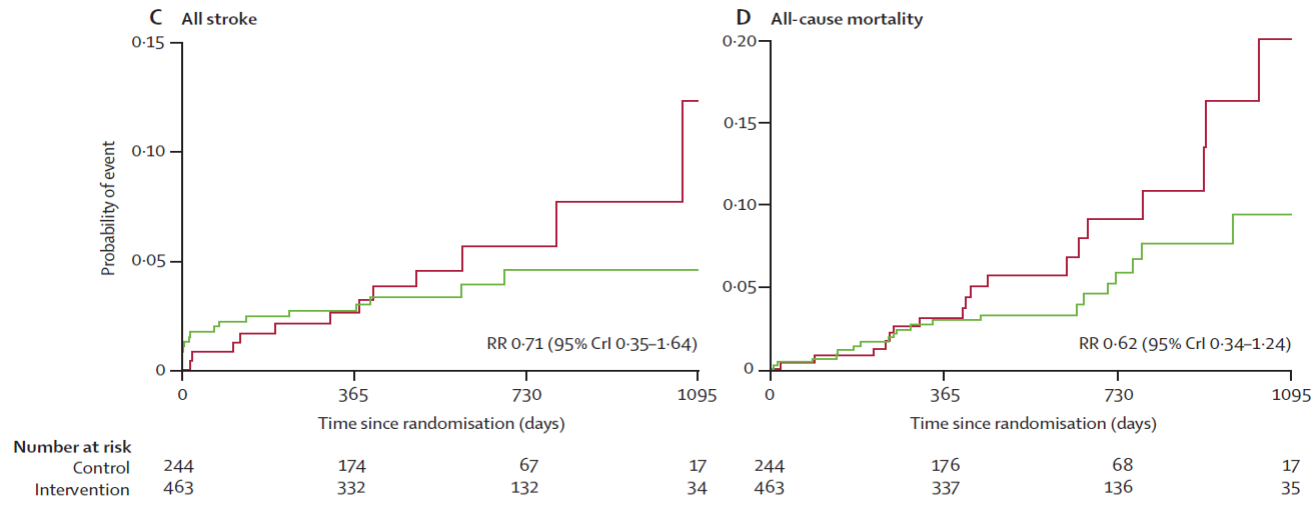


Watchman



Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial

*David R Holmes, Vivek Y Reddy, Zoltan G Turi, Shephal K Doshi, Horst Sievert, Maurice Buchbinder, Christopher M Mullin, Peter Sick, for the PROTECT AF Investigators**



	Intervention (n=463)	Control (n=244)
Serious pericardial effusion*	22 (4·8%)	0
Major bleeding†	16 (3·5%)	10 (4·1%)
Procedure-related ischaemic stroke	5 (1·1%)	0
Device embolisation	3 (0·6%)	0
Haemorrhagic stroke‡	1 (0·2%)	6 (2·5%)
Other§	2 (0·4%)	0

*Defined as the need for percutaneous or surgical drainage. †Major bleeding is defined as a bleeding event that required at least 2 units of packed red blood cells or surgery to correct. ‡Of the seven haemorrhagic strokes, six resulted in death (intervention group, n=1; control group, n=5). §An oesophageal tear and a procedure-related arrhythmia.

Table 3: **Adverse events**

요약

1. 심방세동의 **rhythm control, rate control**은 기대이하의 결과.
2. 와파린을 이용한 뇌졸중 예방만이 효과.

   임상적 위험요소에 기반. **(CHADS2 score, CHADS2-VASc)**

   고위험군에서는 반드시 와파린.

   최근의 새로 개정된 권고안에 의하면 위험요소가 하나라도 있으면 와파린이 추천됨

   아스피린에 클로피도그렐을 추가하는 것이 도움은 되지만 와파린보다는 약함.

3. 단기: 새로운 항응고제 - **Dabigatran (direct thrombin inhibitor),**
   Rivaroxaban (factor Xa inhibitor)
   시술(LAA obliteration)

   장기: 새로운 항부정맥제**(Dronedarone)**, 도자절제술