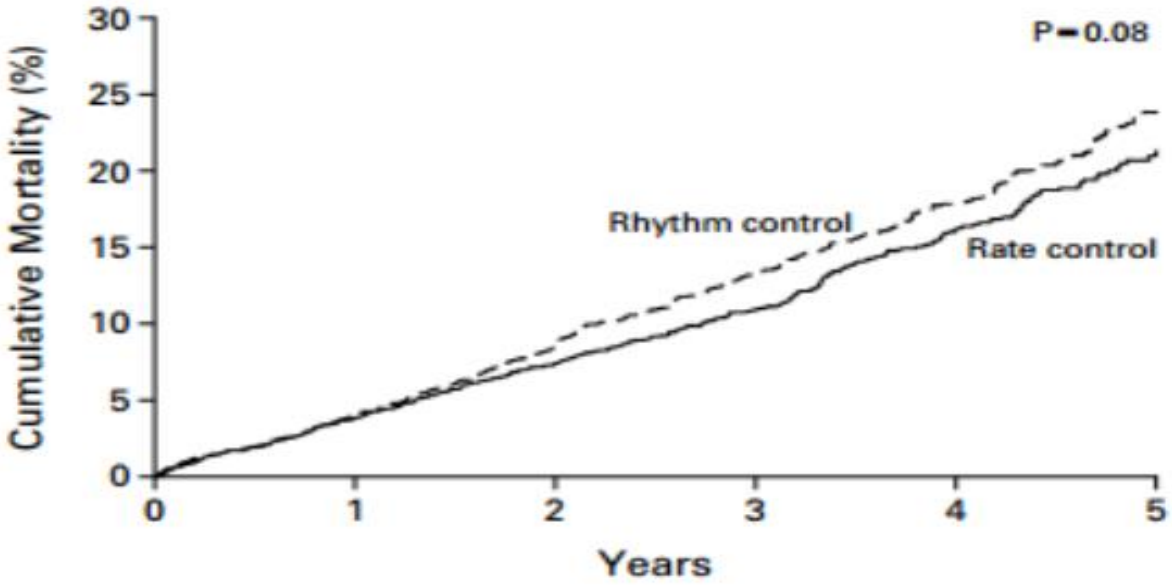
ĐIỀU TRỊ CHUYỂN NHỊP HAY KHỐNG CHẾ TẦN SỐ CHO BỆNH NHÂN RUNG NHĨ: KHI NÀO VÀ NHƯ THẾ NÀO?

TS.BS. Phạm Như Hùng FACC, FHRS, FSCAI, FAsCC.
Tổng thư ký Hội Tim mạch can thiệp Việt nam
Bệnh viện Tim Hà nội

Thử nghiệm AFFIRM



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

Figure 1. Cumulative Mortality from Any Cause in the Rhythm-Control Group and the Rate-Control Group.
Time zero is the day of randomization. Data have been truncated at five years.

NEJ M 2002; 347:1825

Rhythm Control Versus Rate Control and Clinical Outcomes in Patients With Atrial Fibrillation

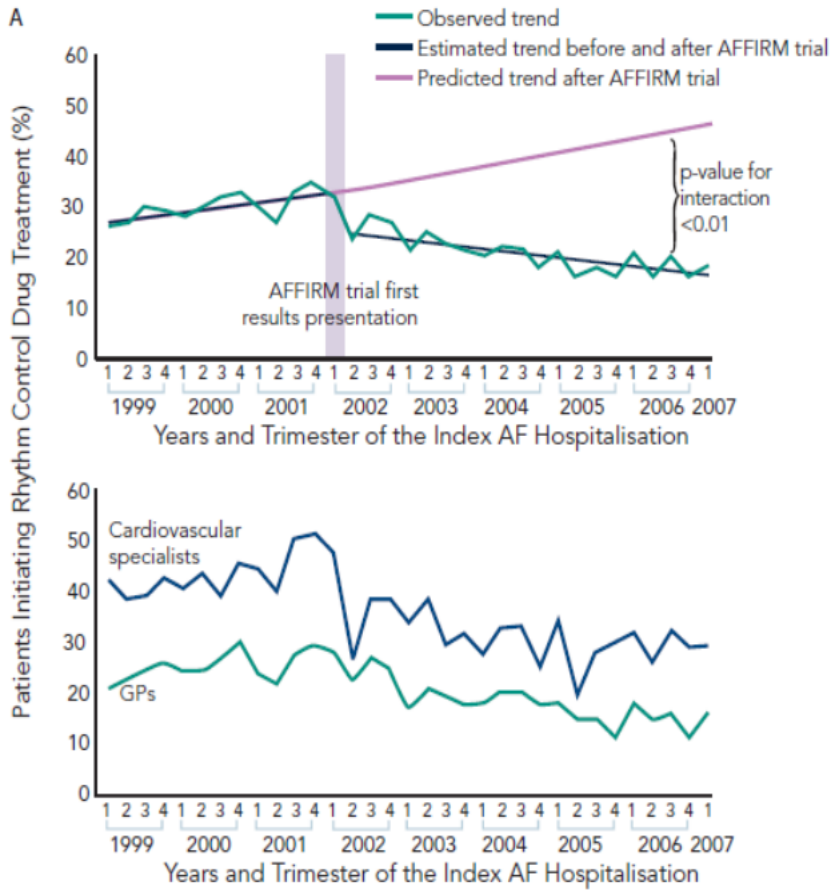
Results From the ORBIT-AF Registry

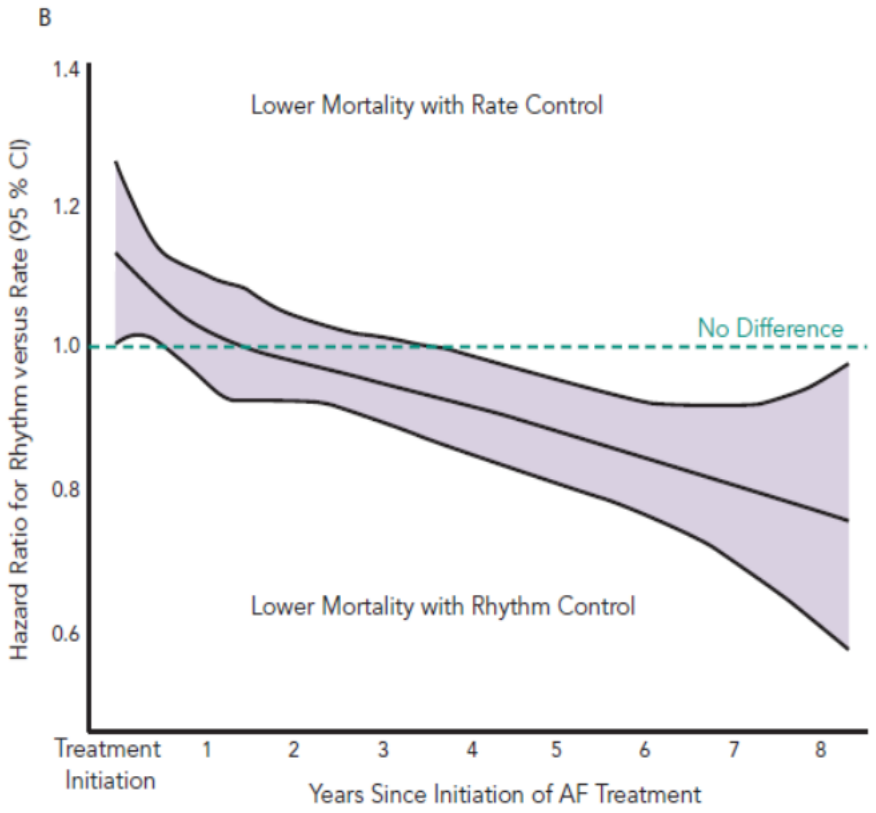
TABLE 2 Incidence of Outcomes by AF Management Strategy and Associations Between AF Management Strategy and Outcomes (N = 6,988)

Outcome	Rhythm Control		Rate Control		Unadjusted Results		Adjusted Results*	
	Events	Rate†	Events	Rate†	HR‡ (95% CI)	p Value	HR‡ (95% CI)	p Value
All-cause death	247	3.81	515	5.79	0.65 (0.55-0.77)	**<0.0001**	0.87 (0.72-1.04)	0.1161
CV death	101	1.56	197	2.23	0.69 (0.52-0.93)	**0.0149**	0.96 (0.69-1.32)	0.7947
First CV hospitalization	992	19.41	1,175	15.92	1.22 (1.09-1.37)	**0.0006**	1.24 (1.10-1.39)	**0.0003**
CV hospitalization or death	1,121	21.93	1,477	20.01	1.10 (0.99-1.21)	0.0664	1.16 (1.05-1.29)	**0.0032**
First stroke, non-CNS embolism, or TIA	73	1.14	135	1.54	0.73 (0.56-0.97)	**0.0282**	0.87 (0.66-1.16)	0.3452
Composite of death, stroke, non-CNS embolism, and TIA	308	4.80	602	6.86	0.69 (0.60-0.80)	**<0.0001**	0.90 (0.77-1.06)	0.2032
New-onset congestive heart failure§	54	1.13	84	1.38	0.83 (0.59-1.17)	0.2796	0.92 (0.63-1.34)	0.6742
First major bleeding event	185	2.94	323	3.77	0.78 (0.66-0.92)	**0.0039**	0.91 (0.76-1.08)	0.2699

J Am Coll Cardiol EP 2016;2:221–9

Thử nghiệm AFFIRM: thời gian nghiên cứu kéo dài hơn





JAMA. 2012;172(13):997-1004

Khống chế tần số hay chuyển nhịp xoang?

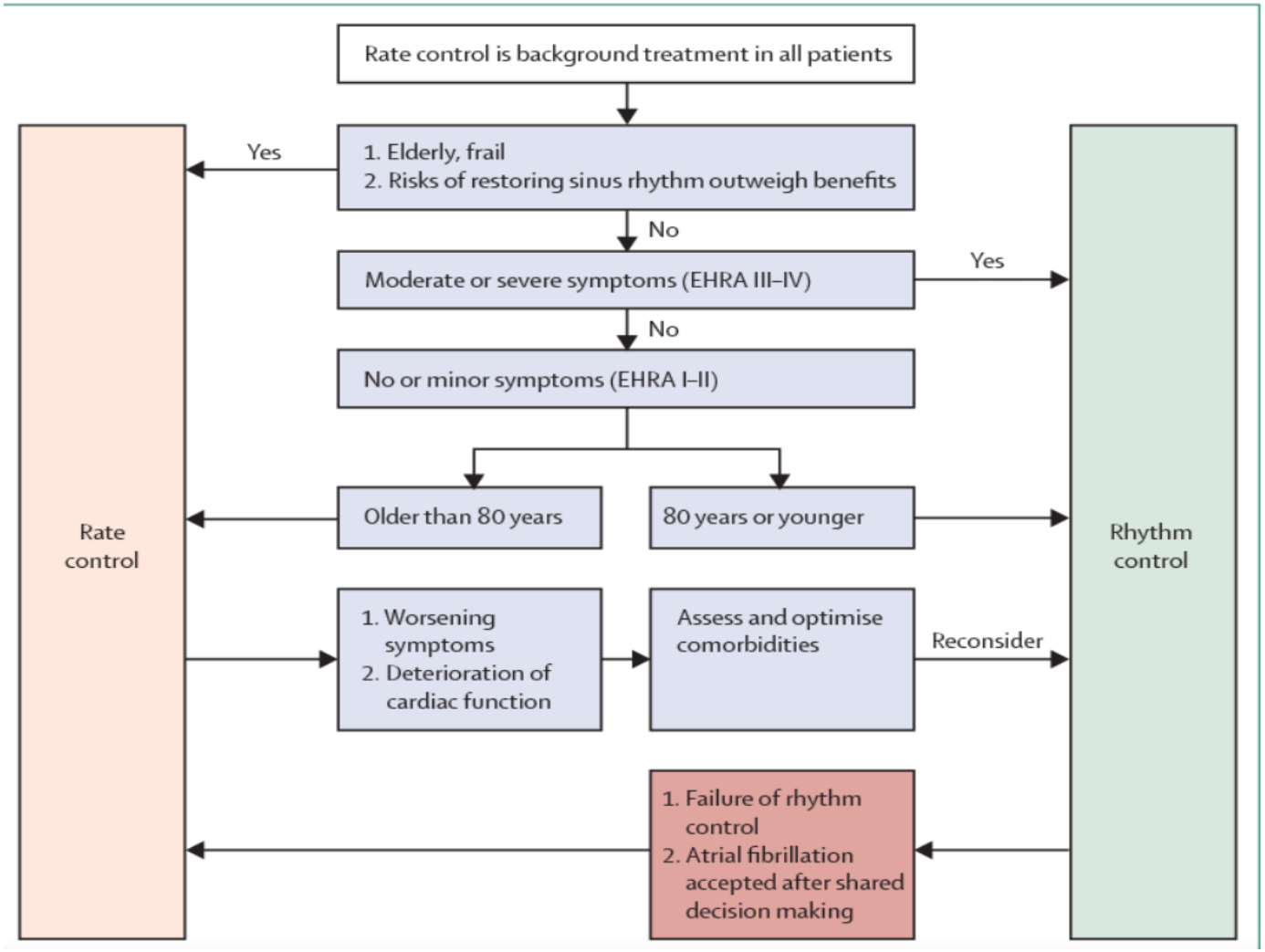
Table 1: Comparison of Rate Control versus Rhythm Control as Management Strategies for Atrial Fibrillation

Therapeutic Strategy	Advantages	Disadvantages
Rate control	• Therapeutically convenient • Less exposure to drug toxicity • Preferred in older, minimally symptomatic AF • Optimal rate control adequate to decrease hospitalisation • Cost-effective	• No effect on disease progression • May not be beneficial in highly symptomatic patients
Rhythm control	• Prevents disease progression • Avoids unfavourable electrical and structural remodelling • Potentially preferable in younger patients • Better quality of life	• Exposure to adverse effects of antiarrhythmic drugs (or risks of ablation procedures) • Generally less cost-effective

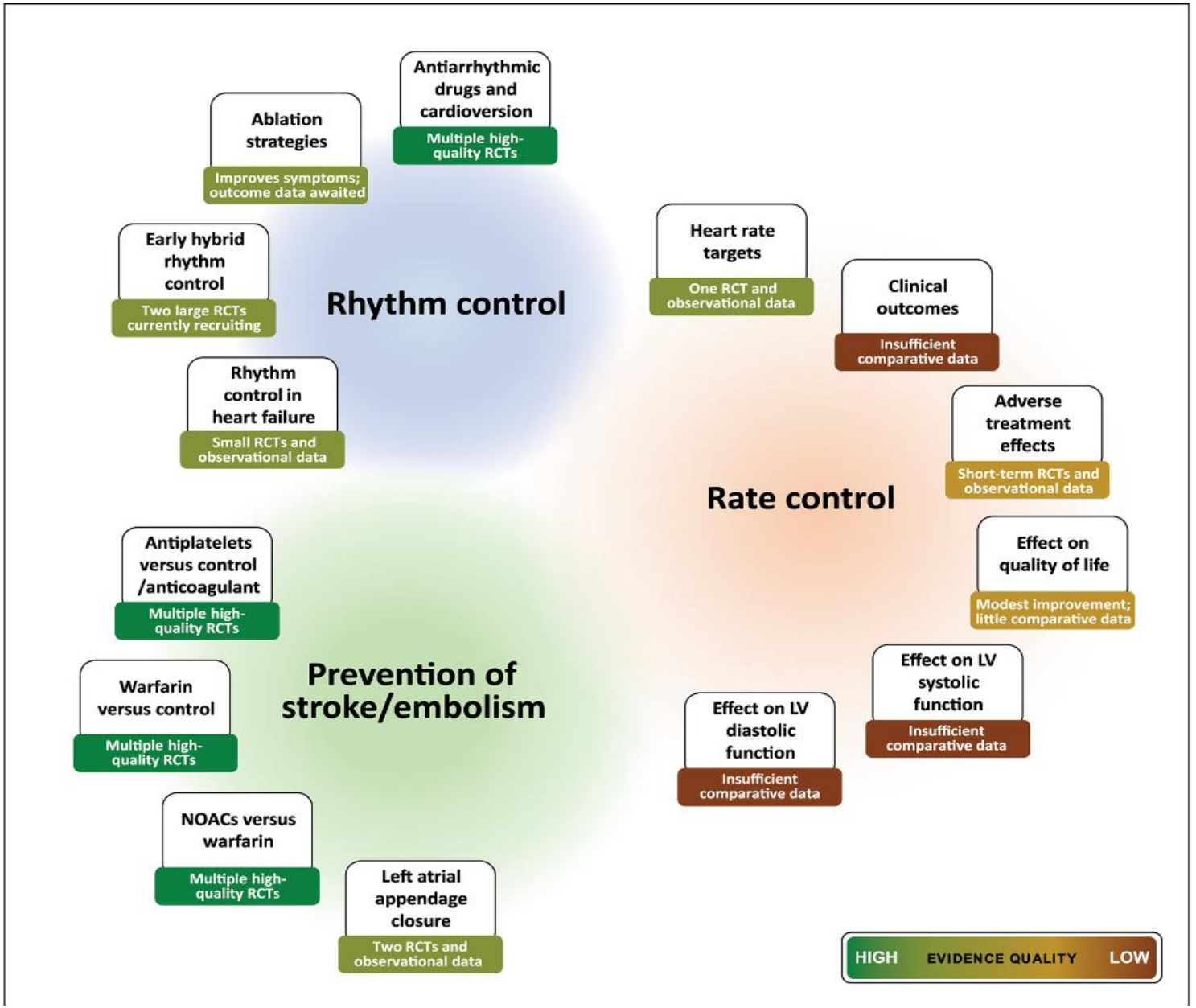
AF = atrial fibrillation.

Arrhythmia & Electrophysiology Review 2013;2(1):30-5

Khống chế tần số hay chuyển nhịp xoang?

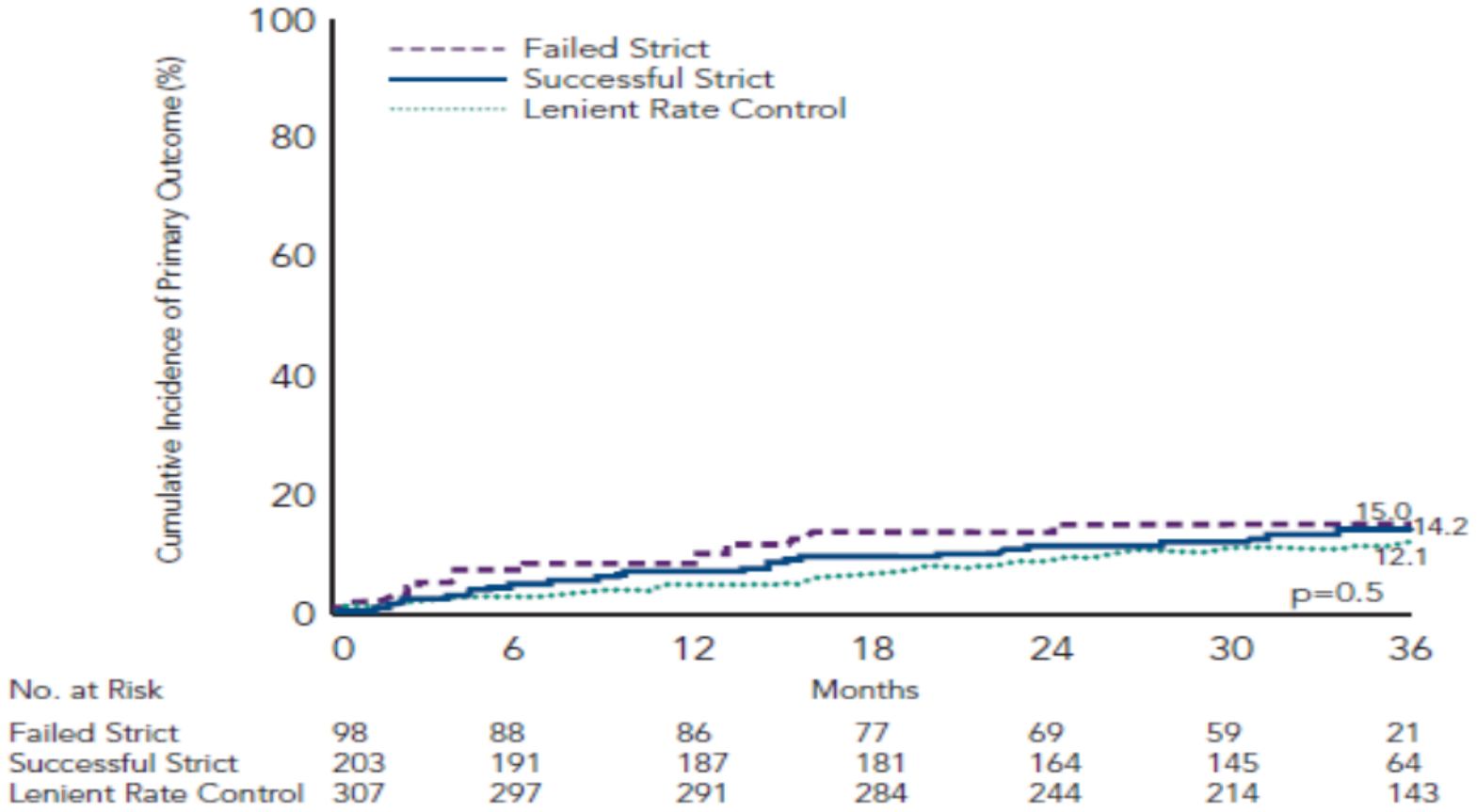


Lancet 2016; 388:, 20–26



BMJ Open 2017;7:e015099.

Khống chế tần số: Thử nghiệm RACE II



Van Gelder; NEJM 2010; 362:1363

Tần số tim tối ưu

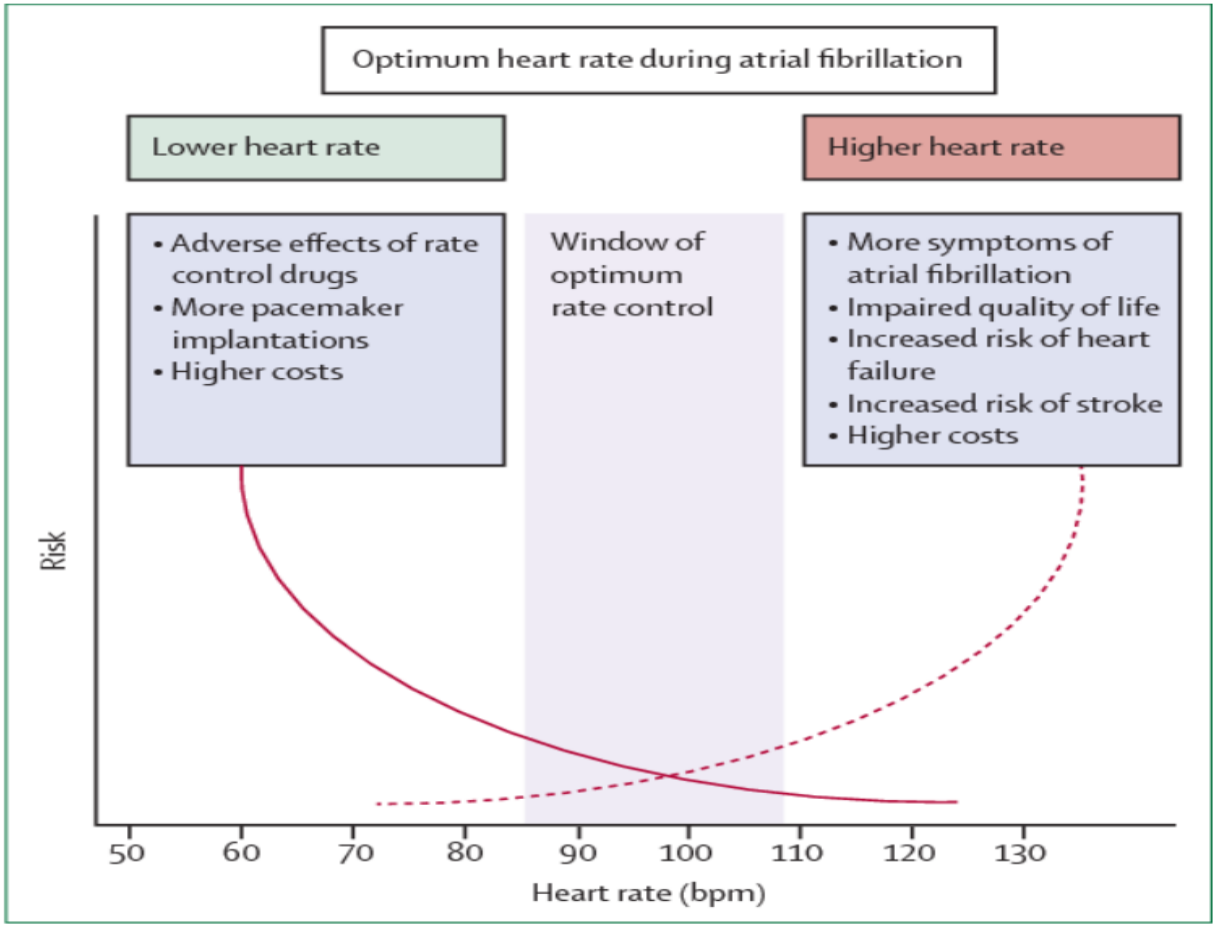
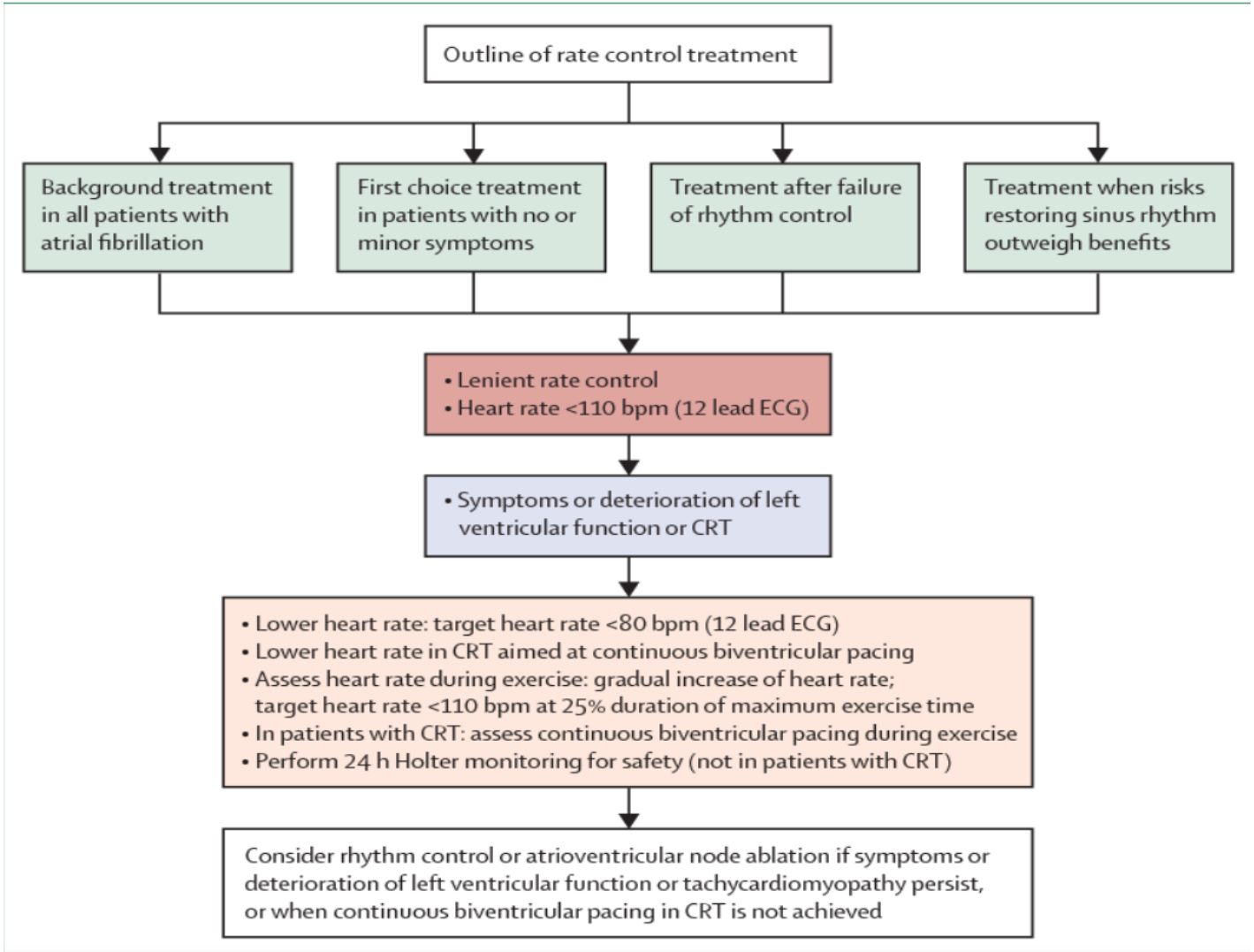


***Figure 3*: Advantages and disadvantages of slow and fast heart rate management during atrial fibrillation**

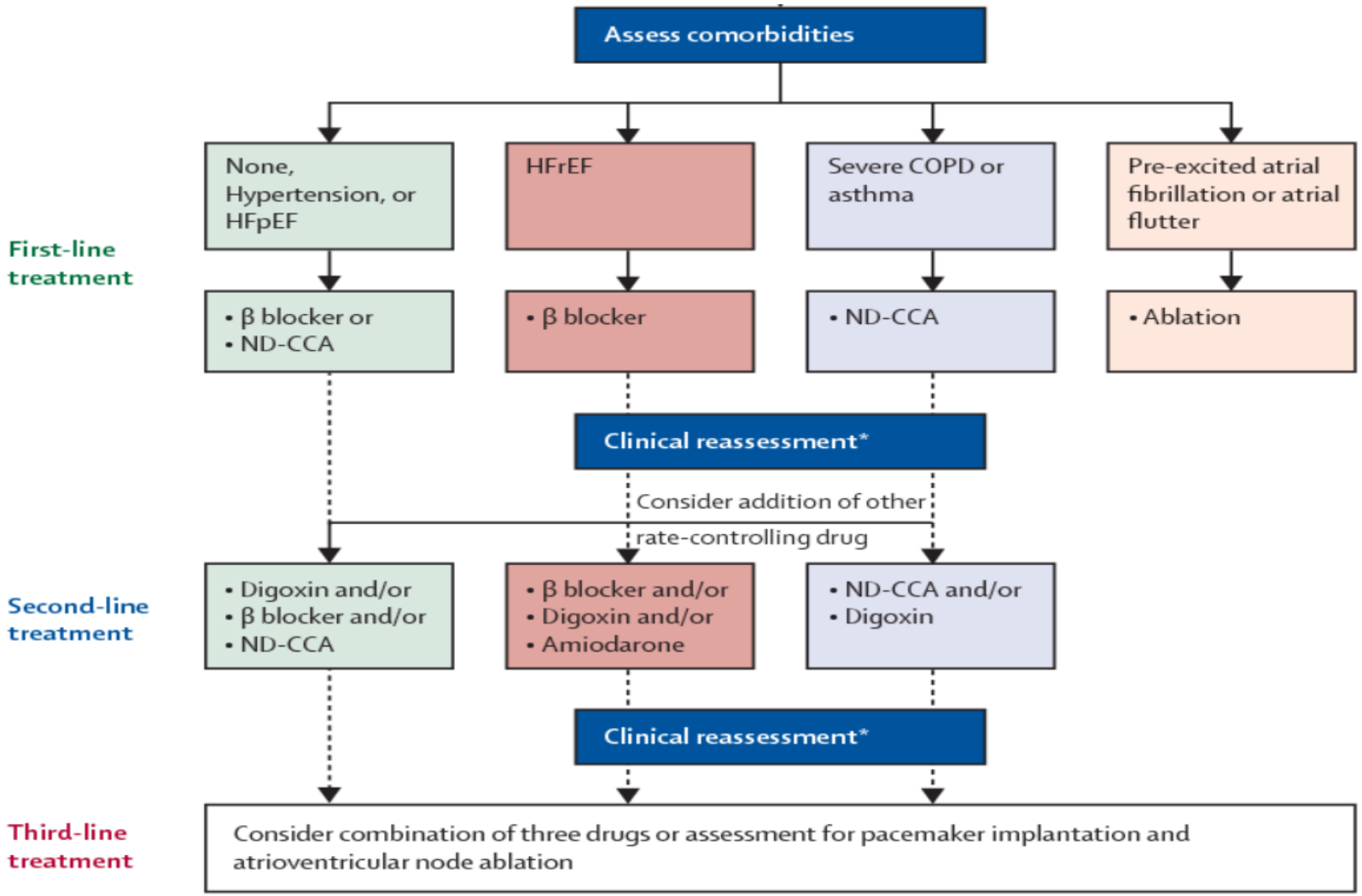
Lancet 2016; 388:, 20–26

Khống chế tần số



Lancet 2016; 388:, 20–26

Lựa chọn thuốc



Lancet 2016; 388:, 20–26

Lựa chọn thuốc khống chế tần số

Comparison of Four Single-Drug Regimens on Ventricular Rate and Arrhythmia-Related Symptoms in Patients With Permanent Atrial Fibrillation

Sara R. Ulimoen, MD[a,*], Steve Enger, RN[a], Jonas Carlson, MSc, PhD[b], Pyotr G. Platonov, MD, PhD[b], Are H. Pripp, PhD[c], Michael Abdelnoor, PhD[c], Harald Arnesen, MD, PhD[d,f], Knut Gjesdal, MD, PhD[e,f], and Arnljot Tveit, MD, PhD[a]

Pharmacokinetics of study drugs

Study Drug	Dose (mg)	Group	Formulation	Half-life (h)	Residence Time (h)	Manufacturer
Metoprolol	100	β_1-receptor blocker	Slow-release tablets	3.5	24	AstraZeneca
Diltiazem	360	Selective calcium channel blocker	Sustained-release capsules	3–6	24	Pfizer
Verapamil	240	Phenylalkylamine calcium antagonist	Modified-release tablets	5–8	13	Abbot
Carvedilol	25	α_1 and nonselective β blocker	Immediate release tablets	6–10	NA	(Roche) Hexal

NA = not available.

Am J Cardiol 2013;111:225

Lựa chọn thuốc

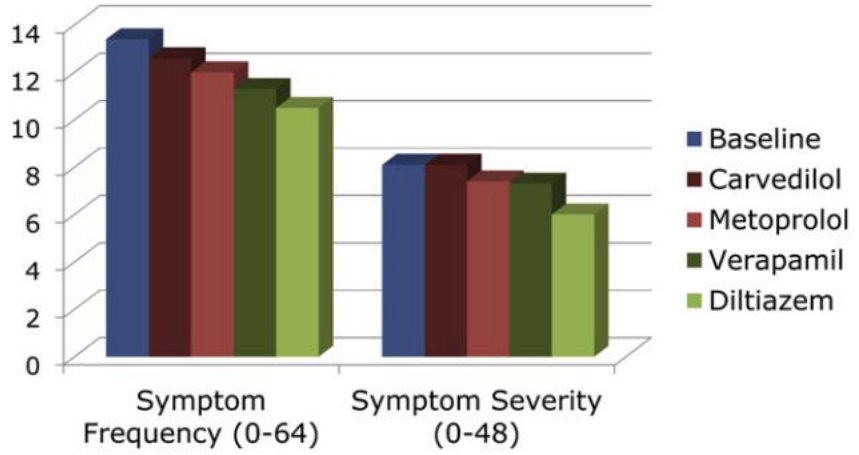


Figure 3. Symptom frequency and symptom severity scores at baseline and during treatment.

Heart rate measures

Treatment	HR at Rest (beats/min)	24-h HR (beats/min)	Daytime HR (beats/min)	Nighttime HR (beats/min)
Baseline	95 ± 15	96 ± 12	106 ± 14	79 ± 12
Diltiazem	77 ± 13	75 ± 10	80 ± 12	66 ± 9
Verapamil	82 ± 16	81 ± 11	82 ± 13	76 ± 12
Metoprolol	81 ± 15	82 ± 11	88 ± 13	72 ± 10
Carvedilol	78 ± 11	84 ± 11	89 ± 12	76 ± 10

Data are expressed as mean ± SD.

HR = heart rate; Daytime = 9:00 A.M. to 9:00 P.M.; Nighttime = 2:00 A.M. to 6:00 A.M.

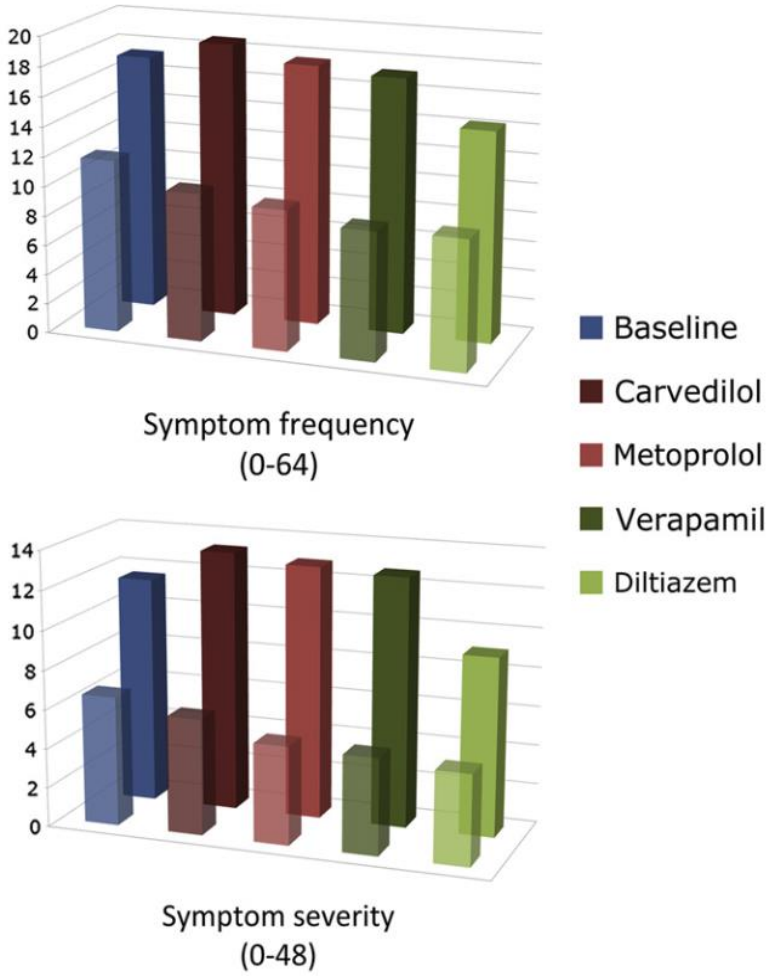
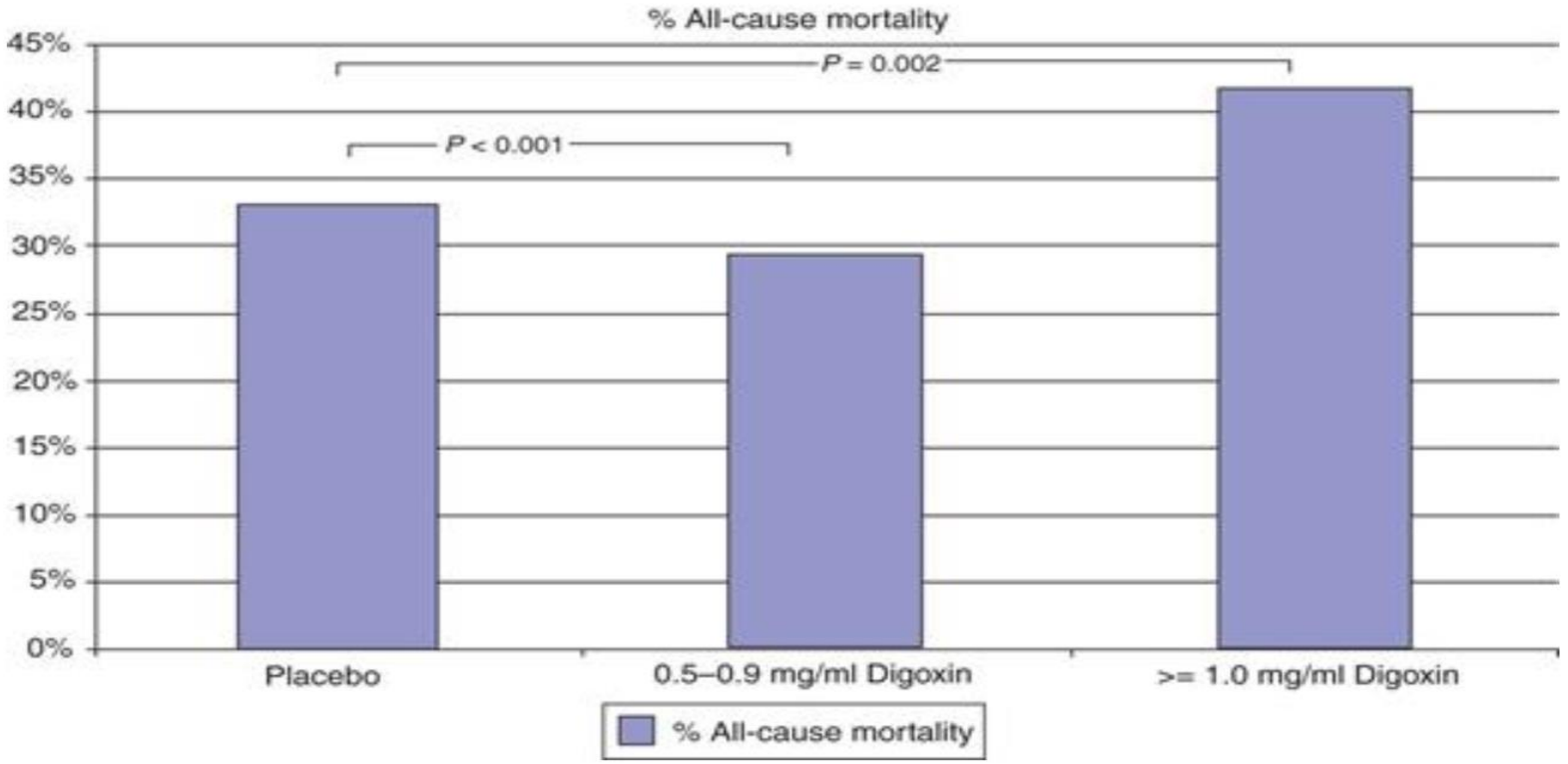


Figure 4. Symptom frequency and symptom severity scores by gender at baseline and during treatment. Back row: women. Front row: men.

Am J Cardiol 2013;111:225

Digoxin



Eur Heart J, 2006;27: 178 -186

Digoxin

- Digoxin làm chậm tần số tim qua chẹn dẫn truyền NT. Giảm tần số tim khi nghỉ nhưng ít làm giảm tần số khi gắng sức.

-Chẹn bêta thường vượt hơn Digoxin khi làm chậm RN kể cả có hay không có suy tim.

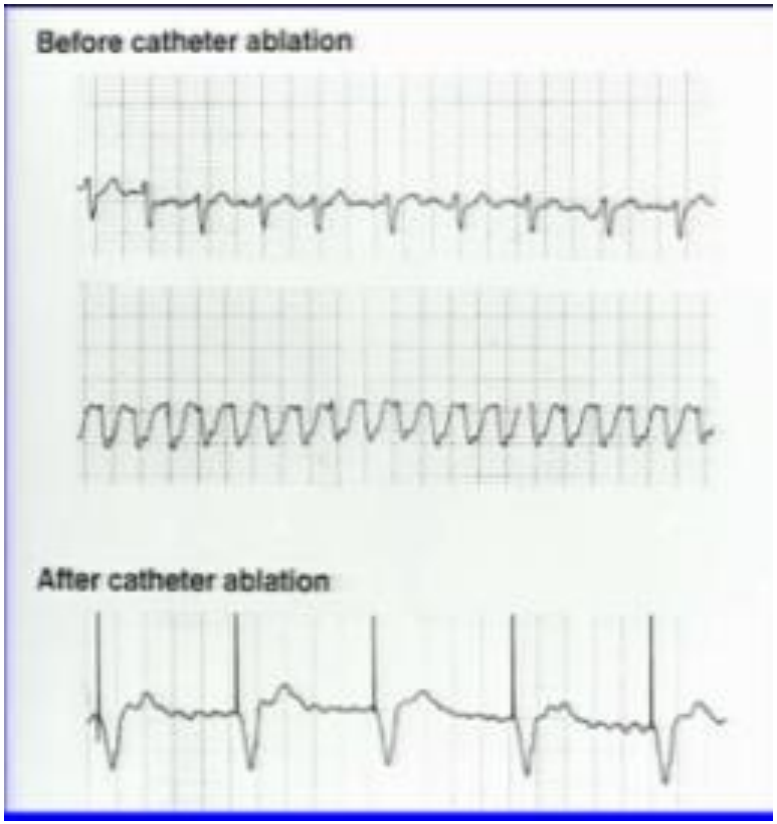
- Digoxin làm tăng tỷ lệ tử vong toàn bộ [HR 1,41; CI95% 1,19-1,67; p < 0,001] ở cả bệnh nhân có hay không có suy tim (nghiên cứu AFFIRM).

- Thường chỉ phối hợp thêm với chẹn bêta hoặc chẹn canxi. Giảm liều.

Eur Heart J, 2013;34: 1468–1470

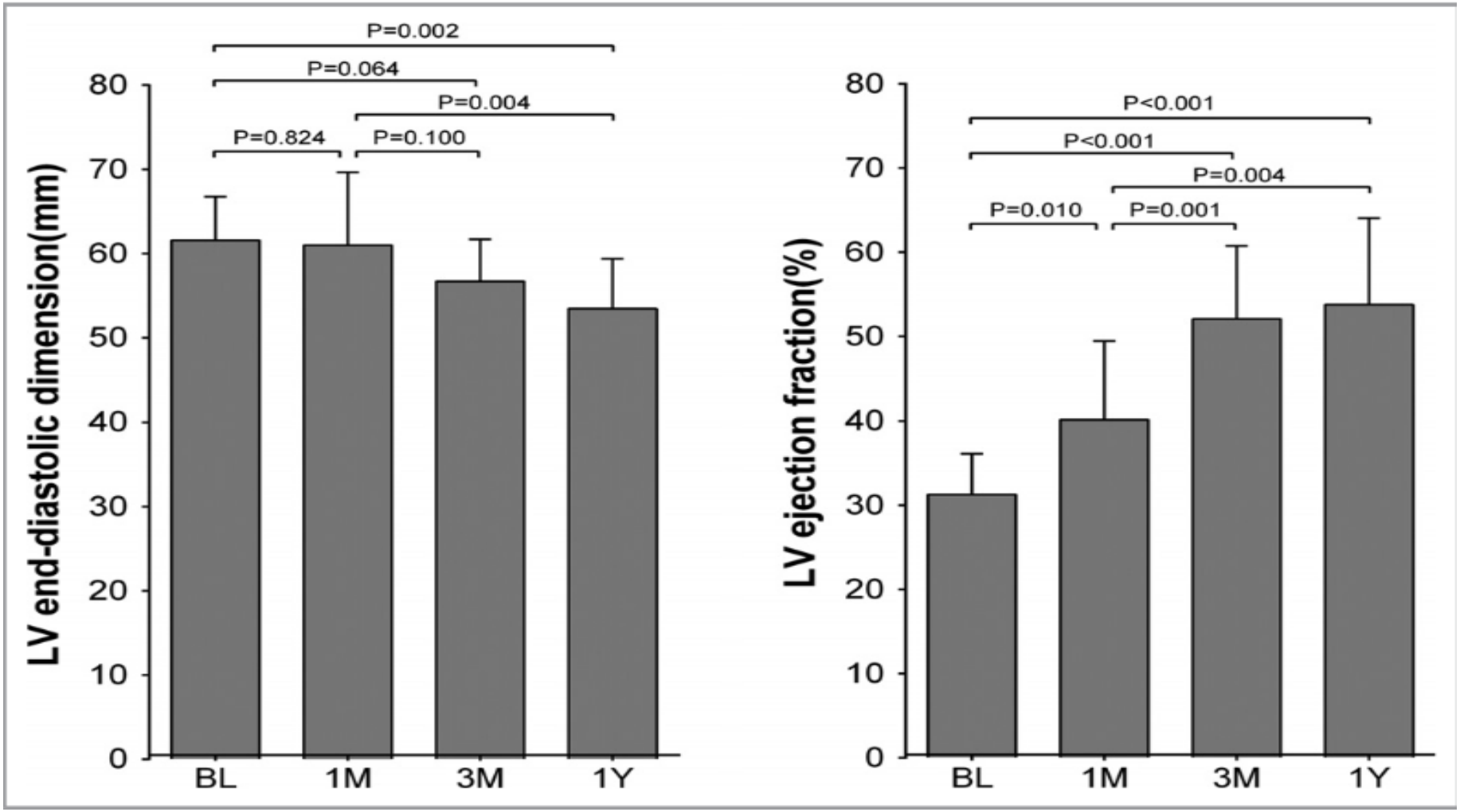
Khống chế tần số: Cắt nút nhĩ thấtt

- Vẫn tồn tại Rung nhĩ.
- Kiểm soát tần số một cách hiệu quả
- Cải thiện:
  - ✓Chất lượng cuộc sống.
  - ✓ Khả năng gắng sức
  - ✓Chức năng thất trái.
- Không khác biệt trên tiên lượng sống còn

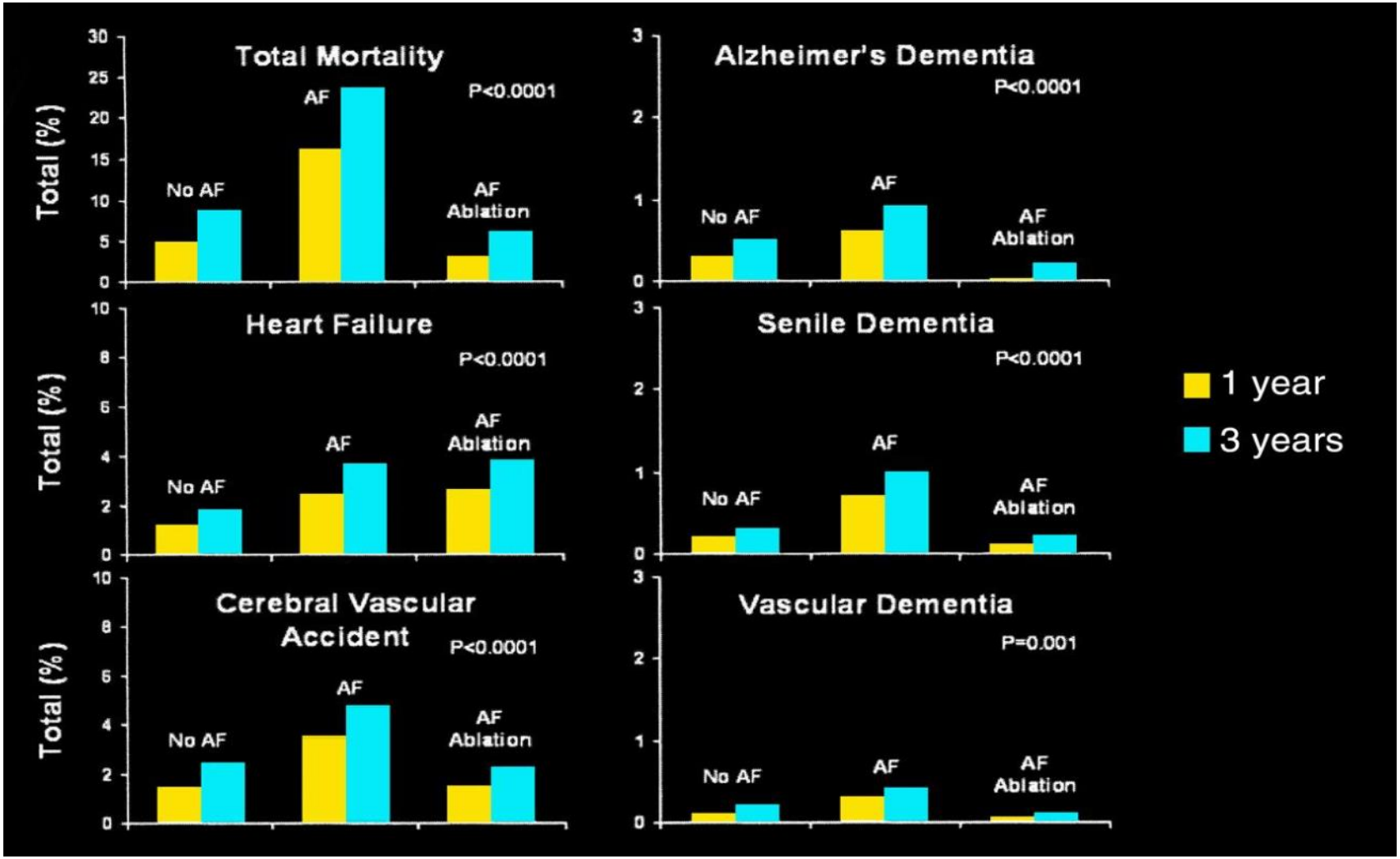


Benefits of Permanent His Bundle Pacing Combined With Atrioventricular Node Ablation in Atrial Fibrillation Patients With Heart Failure With Both Preserved and Reduced Left Ventricular Ejection Fraction

Weijian Huang, MD; Lan Su, MD; Shengjie Wu, MD; Lei Xu, MD; Fangyi Xiao, MD; Xiaohong Zhou, MD; Kenneth A. Ellenbogen, MD

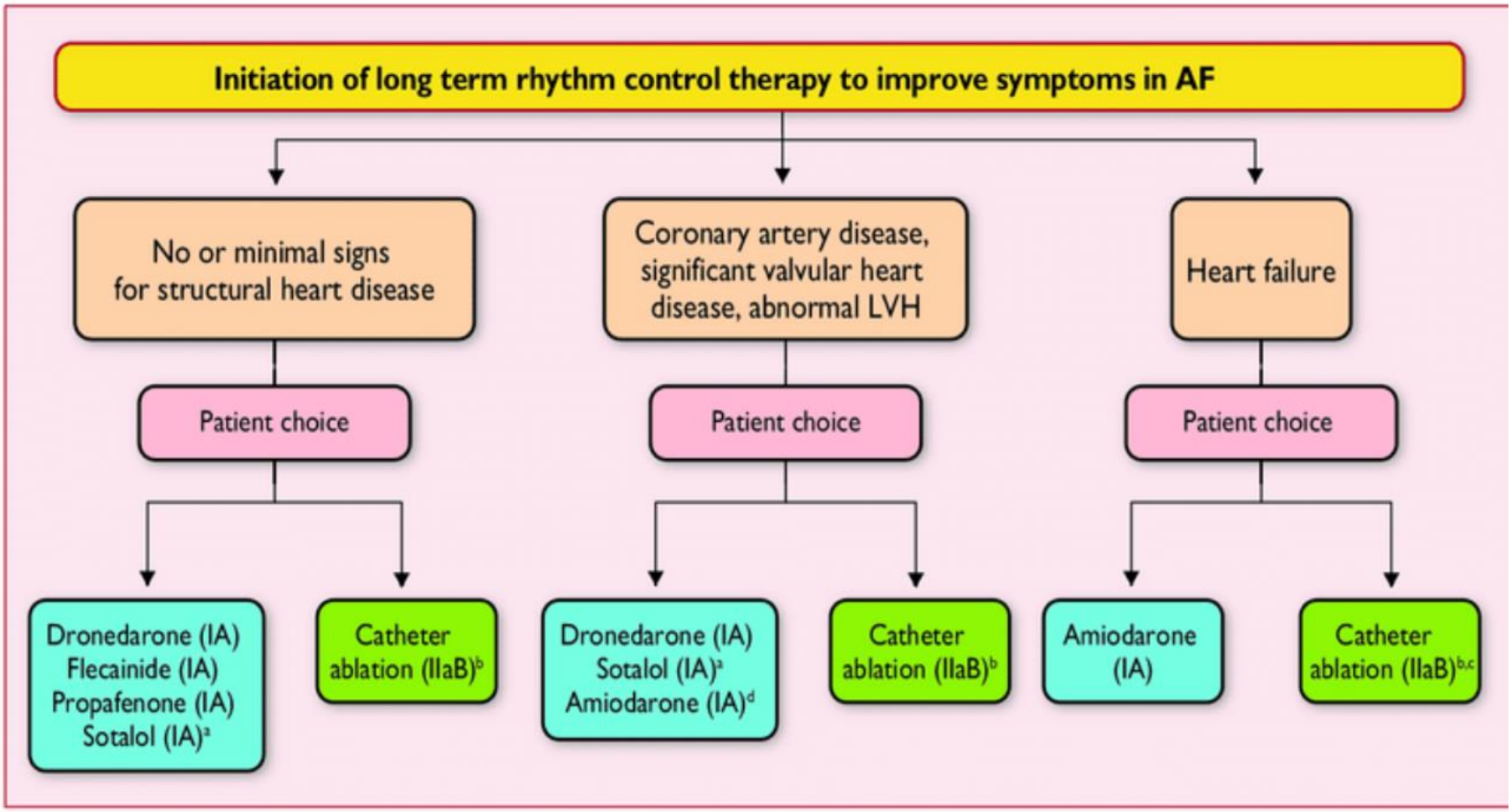


Tiên lượng bệnh nhân có RN và không có RN



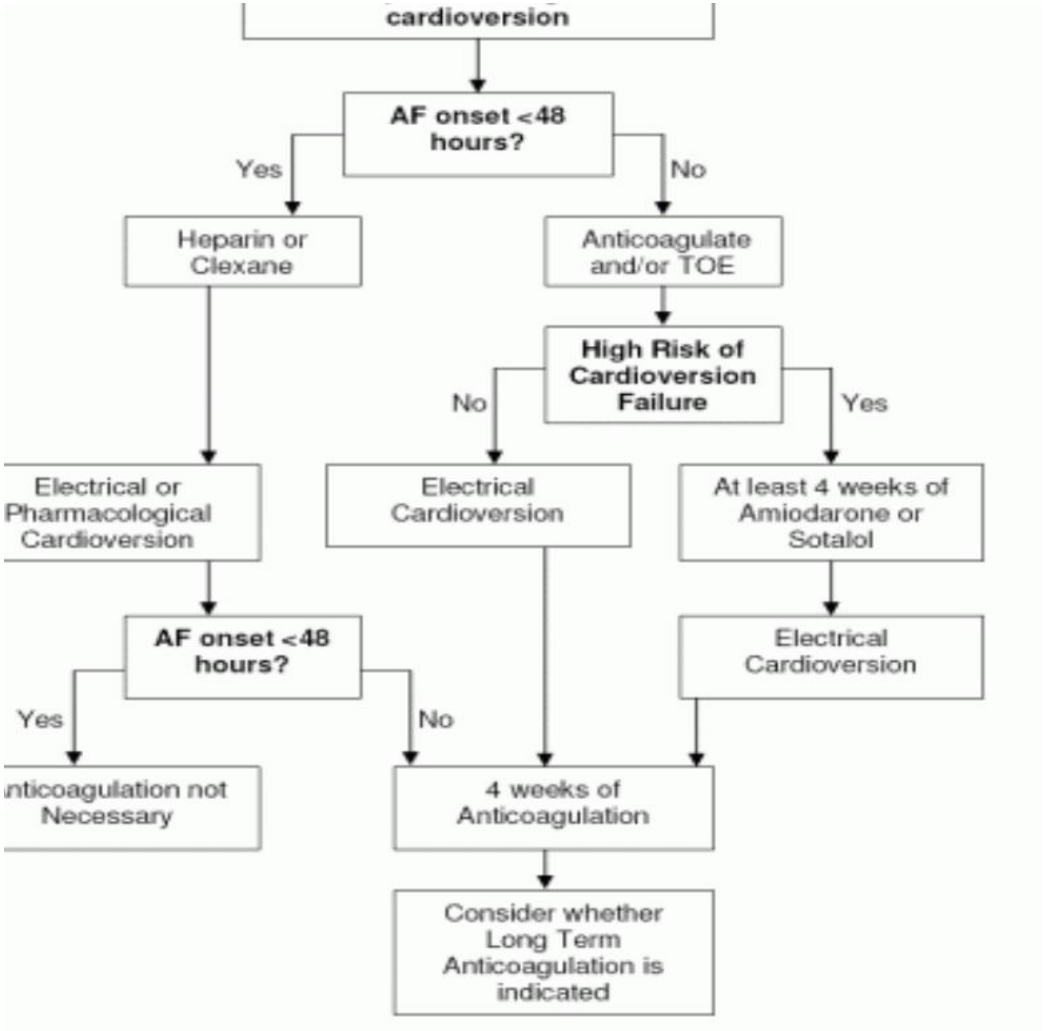
J Cardiovasc Electrophysiol2011; 22: 839

Khống chế nhịp



ESC Guideline 2016

Khống chế nhịp



Lancet 2016; 388:, 20–26

Rhythm Control Does Not Replace Anticoagulation

- ***No*** **evidence that AF reduction via antiarrhythmic therapy reduces the risk of stroke/thromboembolism**
- **Patients *must* continue on appropriate anticoagulation according to their individual embolic risk ($CHADS_2$ VASC score)**

Skanes AC, Healey JS et al., *Can J Cardiol* 2012 Mar;28(2): 125-136

Chuyển nhịp bằng thuốc

Table 4. Recommendations for Antiarrhythmic Drug Use

No Structural Heart Disease	Coronary Artery Disease	Heart Failure	Severe Ventricular Hypertrophy (Hypertrophic Cardiomyopathy)
First line			
Flecainide	Sotalol	Amiodarone	Amiodarone
Propafenone	Amiodarone	Dofetilide	
Dronedarone	Dronedarone		
Sotalol	Dofetilide		
Second line			
Amiodarone			Disopyramide
Dofetilide			
	Avoid flecainide, propafenone	Avoid flecainide, propafenone, dronedarone	Avoid flecainide, propafenone

Circulation. 2012;125:381-389

Chuyển nhịp bằng thuốc

Table 5. Selected Studies of Comparative Efficacy of Antiarrhythmic Drugs

Study	No. of Patients, Average Duration of Follow-Up	Drugs	Percentage of Patients Without Documented AF Recurrence
CTAF[51]	403, 16 mo	Amiodarone	65
		Sotalol	37
		Propafenone	37
SAFE-T[52]	665, 33 mo	Amiodarone	65
		Sotalol	25
		Placebo	10
PAFAC[53]	848, 9 mo	Sotalol	33
		Quinidine plus verapamil	35
		Placebo	17
DIONYSOS[34]	504, 7 mo	Amiodarone	58
		Dronedarone	36

AF indicates atrial fibrillation; CTAF, Canadian Trial of Atrial Fibrillation; SAFE-T, Sotalol Amiodarone Atrial Fibrillation Efficacy Trial; PAFAC, Prevention of Atrial Fibrillation After Cardioversion; and DIONYSOS, Efficacy and Safety of Dronedarone Versus Amiodarone for the Maintenance of Sinus Rhythm in Patients With Atrial Fibrillation.

Circulation. 2012;125:381-389

Cardioversion for Rhythm Control

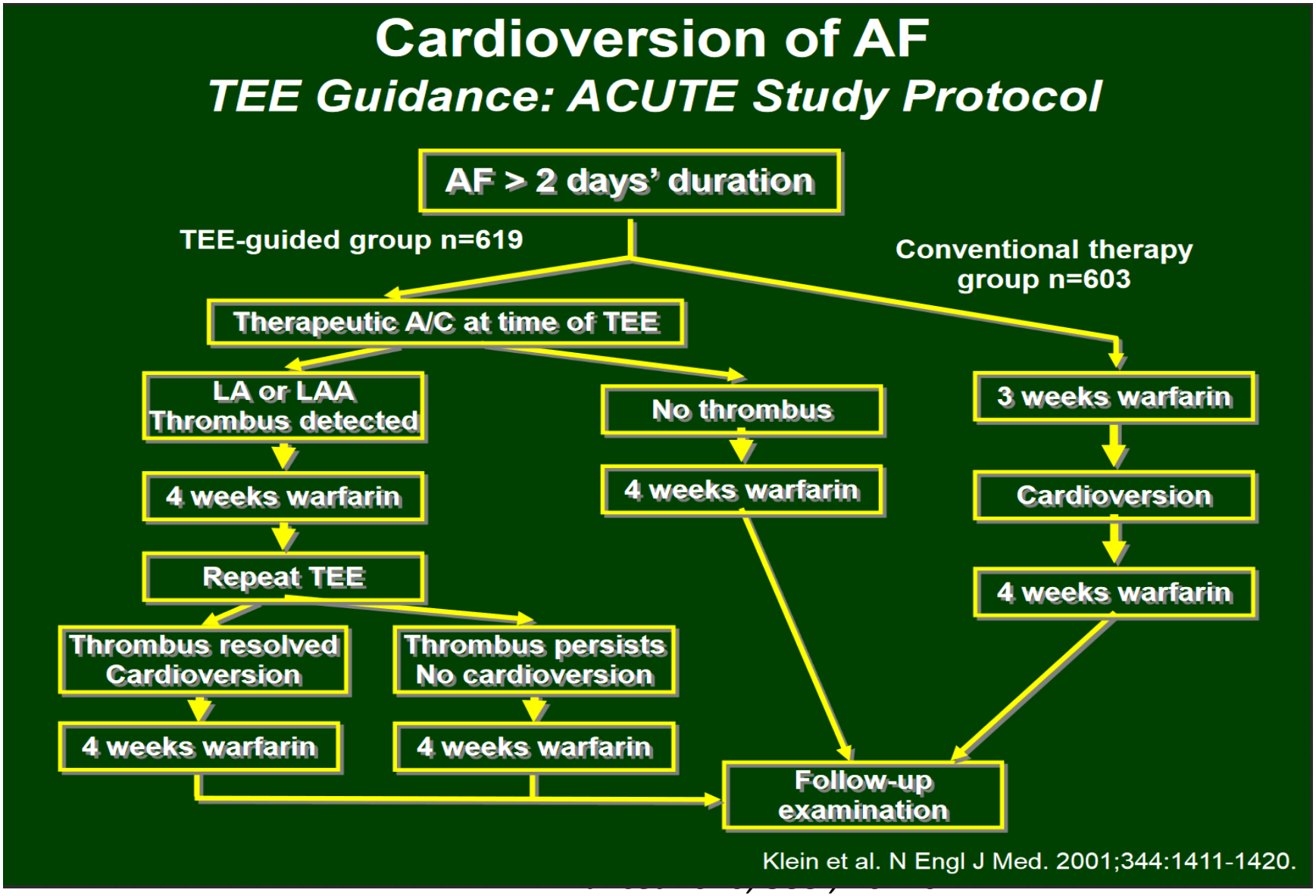
We recommend electrical or pharmacologic cardioversion for restoration of sinus rhythm in patients with AF/AFL selected for rhythm control therapy who are unlikely to convert spontaneously.	**Strong Recommendation Low Quality Evidence**
We recommend pre-treatment with antiarrhythmic drugs prior to electrical cardioversion in patients who have had AF recurrence post-cardioversion without antiarrhythmic drug pre-treatment.	**Strong Recommendation Moderate Quality Evidence**

Values and preferences

These recommendations place a high value on the decision of individual patients to pursue a rhythm control strategy for improvement in quality of life and functional capacity.

Skanes AC, Healey JS et al., *Can J Cardiol* 2012 Mar;28(2): 125-136

Sốc điện


Cardioversion of AF
TEE Guidance: ACUTE Study Protocol
AF > 2 days' duration
TEE-guided group n=619
Conventional therapy group n=603
Therapeutic A/C at time of TEE
LA or LAA Thrombus detected
No thrombus
3 weeks warfarin
4 weeks warfarin
4 weeks warfarin
Cardioversion
Repeat TEE
4 weeks warfarin
Thrombus resolved Cardioversion
Thrombus persists No cardioversion
4 weeks warfarin
4 weeks warfarin
Follow-up examination
Klein et al. N Engl J Med. 2001;344:1411-1420.

Sốc điện: chống đông

Recommendations	COR	LOE
With AF or atrial flutter for ≥48 h, or unknown duration, anticoagulate with warfarin for at least 3 wk prior to and 4 wk after cardioversion	I	B
With AF or atrial flutter for ≥48 h or unknown duration requiring immediate cardioversion, anticoagulate as soon as possible and continue for at least 4 wk.	I	C
With AF or atrial flutter for <48 h and high stroke risk, IV heparin or LMWH or factor Xa or direct thrombin inhibitor, is recommended before or immediately after cardioversion, followed by long-term anticoagulation.	I	C
Following cardioversion of AF, long-term anticoagulation should be based on thromboembolic risk.	I	C

2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation, Circulation, March 28, 2014

Chỉ định cắt đốt RN

2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation

Hugh Calkins, MD (Chair),[1] Gerhard Hindricks, MD (Vice-Chair),[2,*]
Riccardo Cappato, MD (Vice-Chair),[3,¶] Young-Hoon Kim, MD, PhD (Vice-Chair),[4,§]
Eduardo B. Sa

Indications for catheter ablation of atrial fibrillation

A. Indications for catheter ablation of atrial fibrillation

Symptomatic AF refractory or intolerant to at least one Class I or III antiarrhythmic medication	Paroxysmal: Catheter ablation is recommended.	I	A
	Persistent: Catheter ablation is reasonable.	IIa	B-NR
	Long-standing persistent: Catheter ablation may be considered.	IIb	C-LD
Symptomatic AF prior to initiation of antiarrhythmic therapy with a Class I or III antiarrhythmic medication	Paroxysmal: Catheter ablation is reasonable.	IIa	B-R
	Persistent: Catheter ablation is reasonable.	IIa	C-EO
	Long-standing persistent: Catheter ablation may be considered.	IIb	C-EO

Heart Rhythm, 2017: Vol 14, No 10: e275-e443

Chỉ định cắt đốt RN

2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation

Hugh Calkins, MD (Chair),[1] Gerhard Hindricks, MD (Vice-Chair),[2,*]
Riccardo C... [3,¶] ... [4,§]
Eduardo B...

B. Indications for catheter atrial fibrillation ablation in populations of patients not well represented in clinical trials

Congestive heart failure	It is reasonable to use similar indications for AF ablation in selected patients with heart failure as in patients without heart failure.	IIa	B-R	233–237,384,386–395,1042
Older patients (>75 years of age)	It is reasonable to use similar indications for AF ablation in selected older patients with AF as in younger patients.	IIa	B-NR	396–398,401–404
Hypertrophic cardiomyopathy	It is reasonable to use similar indications for AF ablation in selected patients with HCM as in patients without HCM.	IIa	B-NR	385,1043,1044
Young patients (<45 years of age)	It is reasonable to use similar indications for AF ablation in young patients with AF (<45 years of age) as in older patients.	IIa	B-NR	405,1045
Tachy-brady syndrome	It is reasonable to offer AF ablation as an alternative to pacemaker implantation in patients with tachy-brady syndrome.	IIa	B-NR	381–383
Athletes with AF	It is reasonable to offer high-level athletes AF as first-line therapy due to the negative effects of medications on athletic performance.	IIa	C-LD	370–372
Asymptomatic AF**	Paroxysmal: Catheter ablation may be considered in select patients.**	IIb	C-EO	416,418
	Persistent: Catheter ablation may be considered in select patients.	IIb	C-EO	417

Heart Rhythm, 2017: Vol 14, No 10: e275-e443

Lựa chọn bệnh nhân đốt RN

Selection of patients for AF ablation

Better candidates	Worse candidates
Age <70 years	Age ≥70 years
Highly symptomatic	Oligosymptomatic or asymptomatic
LA diameter <45 mm	LA diameter ≥45 mm
Paroxysmal AF (especially <48 h)	Persistent AF
No other arrhythmia	Associated AT or AFL
"Lone" AF	Structural heart disease
Normal cardiac function	Heart failure
Normal BMI	Obesity
Normal pulmonary function	COPD
Normal thyroid function	History of thyrotoxicosis
Amiodarone not used	History of amiodarone failure

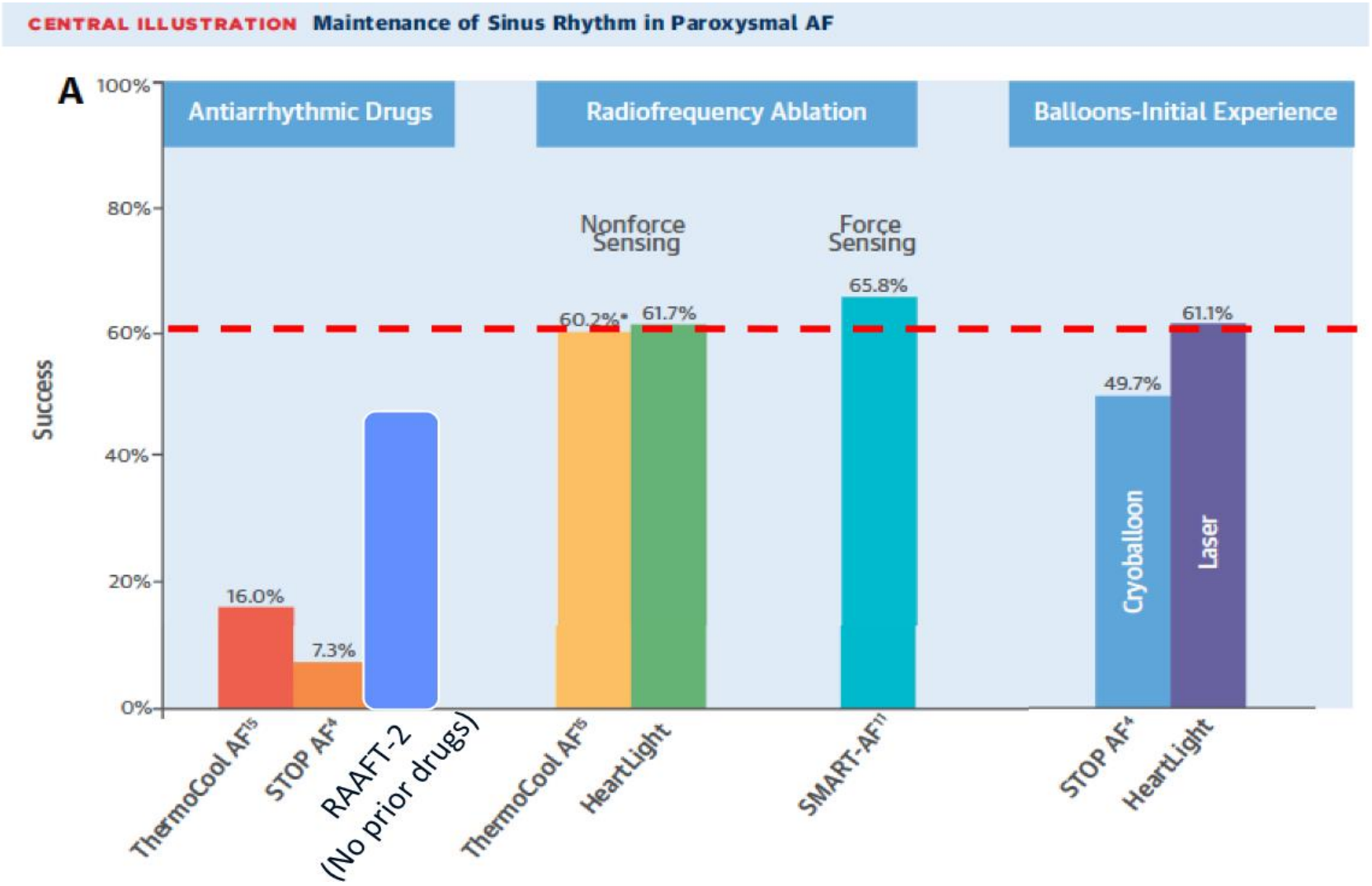
LA left atrium, *AF* atrial fibrillation, *AT* atrial tachycardia, *AFL* atrial flutter, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease

Kết quả điều trị rung nhĩ bằng bằng mapping 3D tại BV tim Hà nội. (n=152)

- Tỷ lệ thành công sau thủ thuật: 92,3%.
- Tỷ lệ bệnh nhân không còn cơn rung nhĩ: 60%.
- Tỷ lệ bệnh nhân giảm cơn rung nhĩ và giảm triệu chứng sau đốt: 11%.
- Biến chứng trong thủ thuật: 5,5%.

Pham Nhu Hung et al. on printing

Triệt đốt cho Rung nhĩ kịch phát

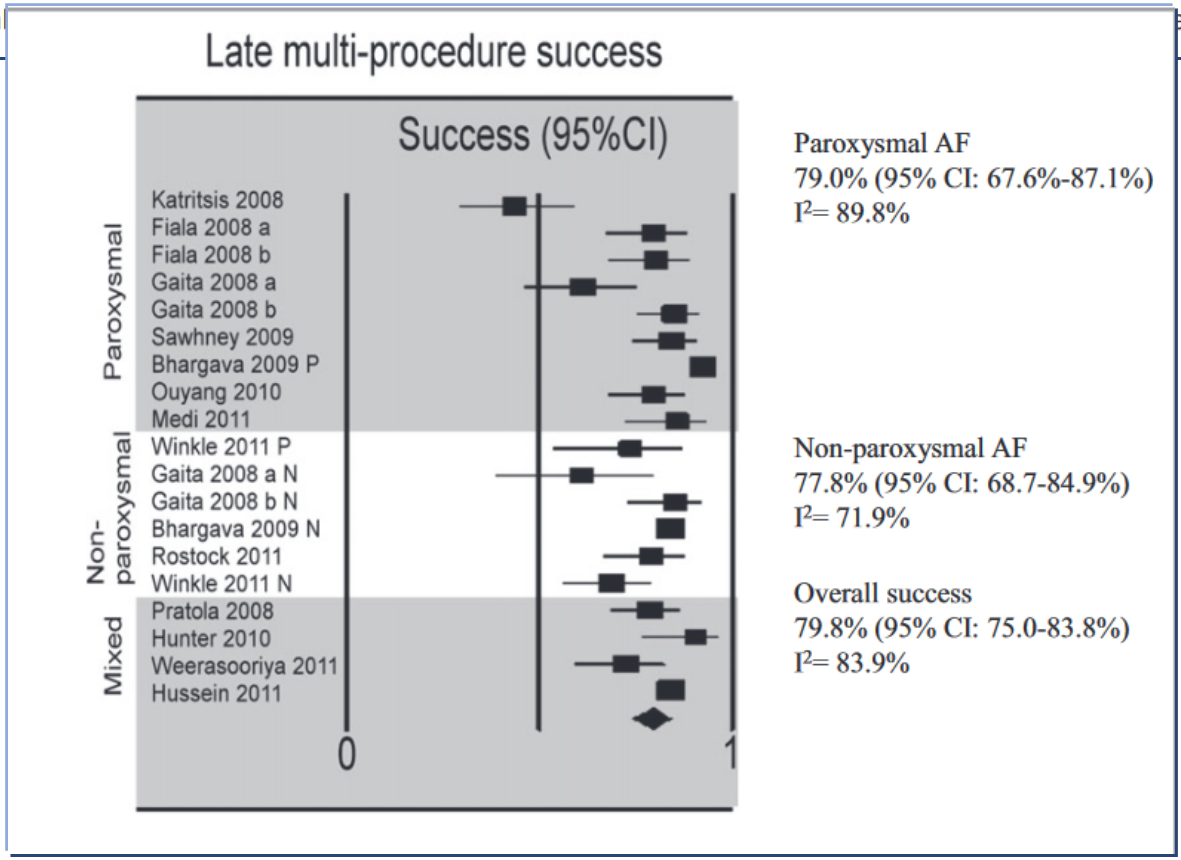


J Am Coll Cardiol. 2015;66:1350-1360

Kết quả điều trị rung nhĩ

Long-term Outcomes of Catheter Ablation of Atrial Fibrillation: A Systematic Review and Meta-analysis

Anand N. Ganesan, MBBS, PhD; Nicholas J. Shipp, PhD; Anthony G. Brooks, PhD; Pawel Kuklik, PhD; Dennis H. Lau, MBBS, PhD; Han S. Lim, MBBS, Ph… …ers, MBBS, PhD



J Am Heart Assoc. 2013;2:e004549

Khống chế tần số hay khống chế nhịp trong suy tim

- Cân nhắc chuyển nhịp sớm bằng amiodarone hoặc sốc điện.
- Các thuốc chuyển nhịp: amiodarone và Dofetilide. Cân nhắc khi dùng Dronedarone, Sotalol. Chống chỉ định: flecainide, propafenone.
- Triệt đốt RN có thể tiến hành trên bn ST với tỷ lệ thành công từ 50-87%.

Atrial fibrillation management strategies and early mortality after myocardial infarction: results from the Valsartan in Acute Myocardial Infarction (VALIANT) Trial

So sánh chiến lược điều trị khống chế tần số và khống chế nhịp sau NMCT cấp:

- Trong giai đoạn sớm, khống chế nhịp làm tăng tỷ lệ tử vong lên *(0–45 days: HR: 1.9, 95% CI 1.2 to 3.0, p=0.004)*

- Trong giai đoạn muộn, 2 chiến lược điều trị không khác biệt trên tỷ lệ tử vong *(45–1096 days: HR 1.1, 95% CI 0.9 to 1.4, p=0.45)*

- Không khác biệt về tỷ lệ TBMN *(0–45 days: HR 1.2, 95% CI 0.4 to 3.7, p=0.73; 45–1096 days: HR 0.*

Heart 2010;96 (11):838–842.

Khống chế tần số hay khống chế nhịp trong BCT phì đại

- Không rõ các bằng chứng lâm sàng.
- Khống chế tần số: chẹn bêta or chẹn canxi
- RN làm tăng gấp 4-6 lần tỷ lệ tử vong trên BCT phì đại. Với RN có triệu chứng hoặc tần số tim quá nhanh, tái lập nhịp xoang là cần thiết:
  - Amiodarone: lựa chọn đầu tiên
  - Disopyramide: lựa chọn thứ 2 đặc biệt sau mổ khoét vách.
  - Cắt đốt: tỷ lệ thành công thấp.

Kết luận

- Khống chế nhịp hay khống chề tần số vẫn còn nhiều các tranh cãi trên lâm sàng.
- Xu hướng khống chế nhịp cho RN mới mắc, suy tim với nhiều ưu thế đặc biệt qua triệt đốt bằng đường ống thông.
- Chống đông là một điều trị nền tảng khi CHAD2VASC ≥ 2.

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