KHRS 2021 The 13th Annual Scientific Session of the Korean Heart Rhythm Society

심방세동 환자의 맥박수 조절 방법

천광진

강원대학교병원 심장내과

Korean Heart Rhythm Society
COI Disclosure

Kwang Jin Chun:

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CC To ABC

ESC European Society of Cardiology
European Heart Journal (2020) 00, 1–125
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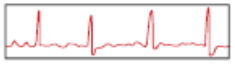
ESC GUIDELINES

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)

The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC)

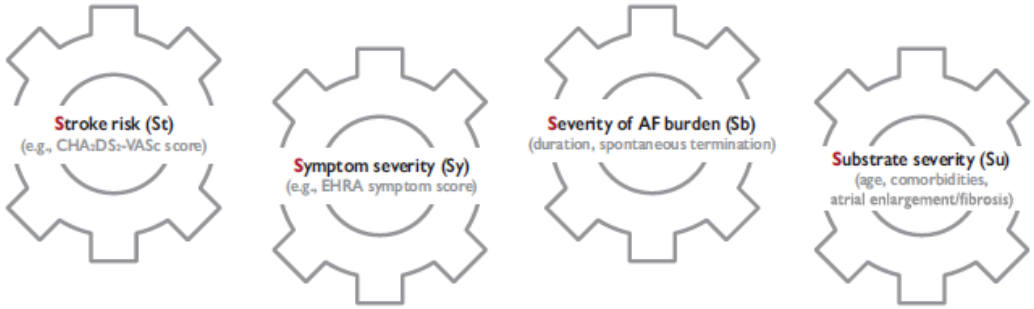
Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

Confirm AF

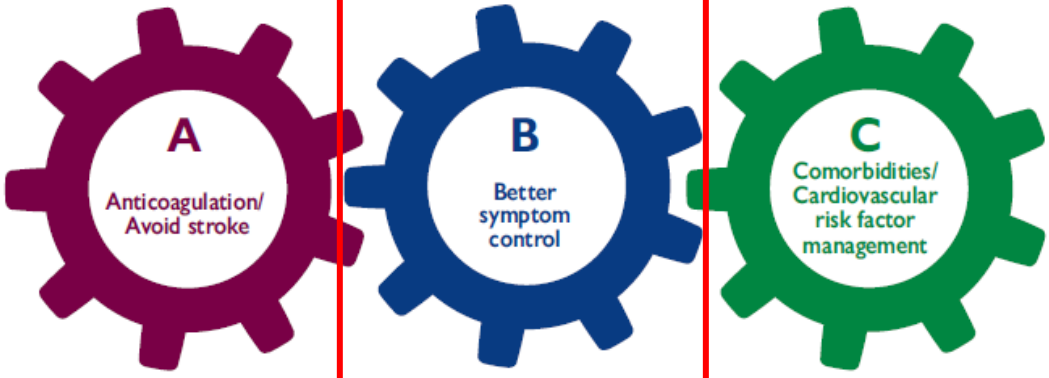


A 12-lead ECG or a rhythm strip showing AF pattern for ≥30 s

Characterise AF (the 4S-AF scheme)



Treat AF: The ABC pathway



1. Identify low-risk patients CHA_2DS_2-VASc 0(m), 1(f)
2. Offer stroke prevention if $CHA_2DS_2VASc \geq 1$(m), 2(f)

Assess bleeding risk, address modifiable bleeding risk factors

3. Choose OAC (NOAC or VKA with well-managed TTR)

Assess symptoms, QoL and patient's preferences

Optimize rate control

Consider a rhythm control strategy (CV, AADs, ablation)

Comorbidities and cardiovascular risk factors

Lifestyle changes (obesity reduction, regular exercise, reduction of alcohol use, etc.)

Rate Control

- Integral part of AF management
- Often sufficient to improve AF-related symptoms

- Very little robust evidence exists to inform the best type and intensity or rate control treatment

- The optimal heart-rate target is unclear

ACC/AHA/ESC Practice Guidelines

ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation—Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation)

Developed in Collaboration With the European Heart Rhythm Association and the Heart Rhythm Society

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Criteria for rate control vary with patient age but usually involve achieving ventricular rates between 60 and 80 bpm at rest and between 90 and 115 bpm during moderate exercise

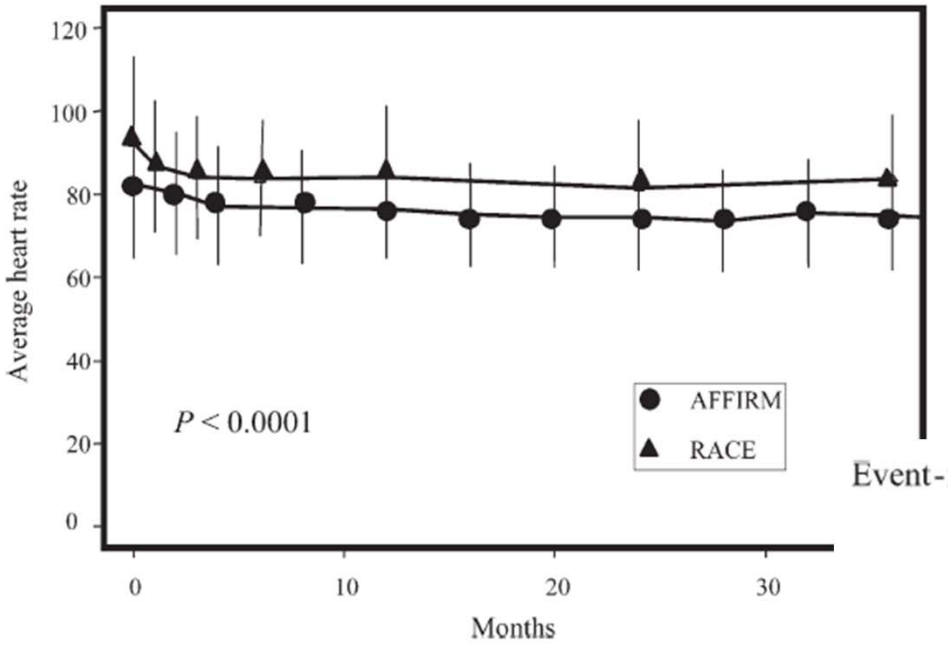
No Clinical Evidence

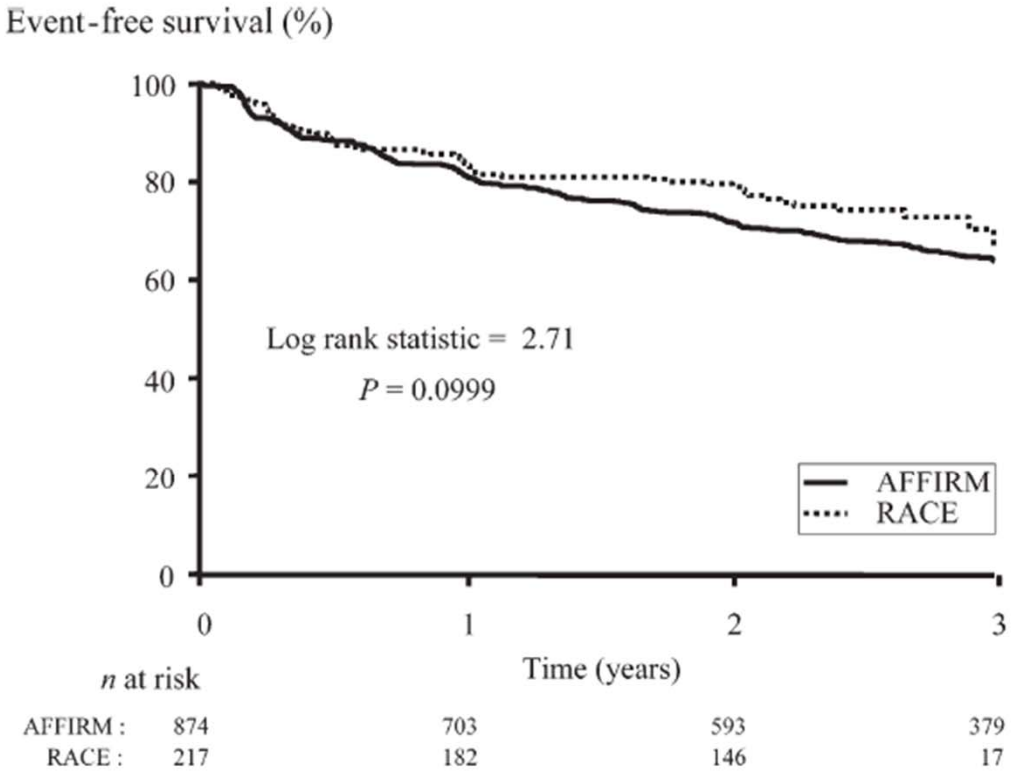
Does intensity of rate-control influence outcome in atrial fibrillation? An analysis of pooled data from the RACE and AFFIRM studies

Isabelle C. Van Gelder[1*], D. George Wyse[2], Mary L. Chandler[3], Howard A. Cooper[4], Brian Olshansky[5], Vincent E. Hagens[1], Harry J.G.M. Crijns[6], and the RACE[†] and AFFIRM Investigators[‡]

- AFFIRM trial (n=874) and RACE trial (n=217)
- AFFIRM
  - Resting heart rate ≤80 bpm and daily activity ≤110 bpm
- RACE
  - Resting heart rate <100 bpm
- Primary end point
  - Composite of mortality, cardiovascular hospitalization, and MI

Europace 2006;8:935-942


Average heart rate
120
100
80
60
40
20
0
0
10
20
30
Months
P < 0.0001
AFFIRM
RACE


Event-free survival (%)
100
80
60
40
20
0
0
1
2
3
Time (years)
Log rank statistic = 2.71
P = 0.0999
AFFIRM
RACE
n at risk
AFFIRM : 874 703 593 379
RACE : 217 182 146 17

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 15, 2010 VOL. 362 NO. 15

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*

- RACE II trial
- 614 patients with permanent atrial fibrillation
- Lenient vs. Strict rate control

N Engl J Med 2010;362:1363-1373

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BACKGROUND

Rate control is often the therapy of choice for atrial fibrillation. Guidelines recommend strict rate control, but this is not based on clinical evidence. We hypothesized that lenient rate control is not inferior to strict rate control for preventing cardiovascular morbidity and mortality in patients with permanent atrial fibrillation.

RACE II Trial

- Lenient rate-control strategy
  - Resting heart rate <110 bpm
- Strict rate control strategy
  - Resting heart rate <80 bpm and heart rate during moderate exercise <110 bpm
- Primary end point
  - Composite of cardiovascular death, hospitalization for heart failure, and stroke, systemic embolism, bleeding, and life-threatening arrhythmic events
- Follow-up duration (2~3 years)

- No difference in a composite of clinical events, NYHA class, or hospitalization

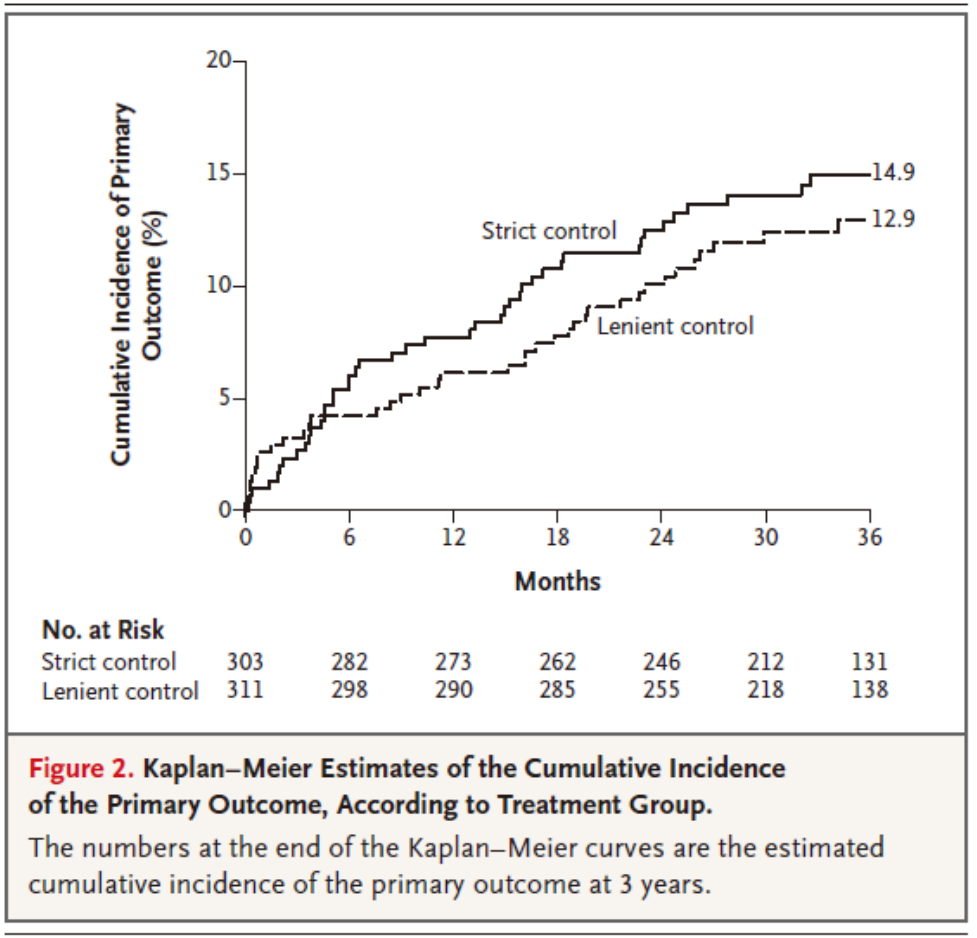


Figure 2. Kaplan–Meier Estimates of the Cumulative Incidence of the Primary Outcome, According to Treatment Group.

The numbers at the end of the Kaplan–Meier curves are the estimated cumulative incidence of the primary outcome at 3 years.

Cumulative incidence of the Composite Primary Outcome

Outcome	Lenient Rate Control (N=311)	Strict Rate Control (N=303)	Hazard Ratio (90% CI)
	no. of patients (%)		
Composite primary outcome	38 (12.9)	43 (14.9)	0.84 (0.58–1.21)
Individual components			
Death from cardiovascular cause	9 (2.9)	11 (3.9)	0.79 (0.38–1.65)
From cardiac arrhythmia	3 (1.0)	4 (1.4)	
From cardiac cause other than arrhythmia	1 (0.3)	2 (0.8)	
From noncardiac vascular cause	5 (1.7)	5 (1.9)	
Heart failure	11 (3.8)	11 (4.1)	0.97 (0.48–1.96)
Stroke	4 (1.6)	11 (3.9)	0.35 (0.13–0.92)
Ischemic	3 (1.3)	8 (2.9)	
Hemorrhagic	1 (0.3)	4 (1.5)	
Systemic embolism	1 (0.3)	0	
Bleeding	15 (5.3)	13 (4.5)	1.12 (0.60–2.08)
Intracranial	0	3 (1.0)	
Extracranial	15 (5.3)	10 (3.5)	
Syncope	3 (1.0)	3 (1.0)	
Life-threatening adverse effect of rate-control drugs	3 (1.1)	2 (0.7)	
Sustained ventricular tachycardia or ventricular fibrillation	0	1 (0.3)	
Cardioverter–defibrillator implantation	0	1 (0.3)	
Pacemaker implantation	2 (0.8)	4 (1.4)	

2010 ESC Guidelines for the management of atrial fibrillation

It is reasonable to initiate treatment with a lenient rate control protocol aimed at a resting heart rate <110 bpm.	IIa	B	98
It is reasonable to adopt a stricter rate control strategy when symptoms persist or tachycardiomyopathy occurs, despite lenient rate control: resting heart rate <80 bpm and heart rate during moderate exercise <110 bpm. After achieving the strict heart rate target, a 24 h Holter monitor is recommended to assess safety.	IIa	B	98

2020 ESC Guidelines for the management of atrial fibrillation

Recommendations for ventricular rate control in patients with AF[a]

Recommendations	Class[b]	Level[c]
Beta-blockers, diltiazem, or verapamil are recommended as first-choice drugs to control heart rate in AF patients with LVEF≥40%.[492,507,511,529]	I	B
Beta-blockers and/or digoxin are recommended to control heart rate in AF patients with LVEF<40%.[486,491,502,512,530–532]	I	B
Combination therapy comprising different rate controlling drugs[d] should be considered if a single drug does not achieve the target heart rate.[533,534]	IIa	B
A resting heart rate of <110 bpm (i.e. lenient rate control) should be considered as the initial heart rate target for rate control therapy.[488]	IIa	B

Drugs

- Beta-blocker
- Diltiazem and verapamil
- Digoxin
- Combination therapy
- Antiarrhythmic drug

- Choice of rate control drugs depends on symptoms, comorbidities and potential side-effects

Beta-blocker (BB)

- First-line rate-controlling agents
- Prognostic benefits of beta-blockers seen in HFrEF patients with sinus rhythm had been questioned in patients with AF

	Intravenous administration	Usual oral maintenance dose	Contraindicated
Beta-blockers[b]			
Metoprolol tartrate	2.5 - 5 mg i.v. bolus; up to 4 doses	25 - 100 mg *b.i.d.*	In case of asthma use beta-1-blockers Contraindicated in acute HF and history of severe bronchospasm
Metoprolol XL (succinate)	N/A	50 - 400 mg *o.d.*	
Bisoprolol	N/A	1.25 - 20 mg *o.d.*	
Atenolol[c]	N/A	25 - 100 mg *o.d.*	
Esmolol	500 µg/kg i.v. bolus over 1 min; followed by 50 - 300 µg/kg/min	N/A	
Landiolol	100 µg/kg i.v. bolus over 1 min; followed by 10 - 40 µg/kg/min[505]	N/A	
Nebivolol	N/A	2.5 - 10 mg *o.d.*	
Carvedilol	N/A	3.125 - 50 mg *b.i.d.*	

Non-dihydropyridine CCB (NDCCB)

- Verapamil and diltiazem
- Provide reasonable rate control and can improve AF-related symptoms

	Intravenous administration	Usual oral maintenance dose	Contraindicated
Non-dihydropyridine calcium channel antagonists			
Verapamil	2.5 - 10 mg i.v. bolusover 5 min	40 mg b.i.d. to 480 mg (extended release) o.d.	Contraindicated in HFrEF Adapt doses in hepatic and renal impairment
Diltiazem	0.25 mg/kg i.v. bolus over 5 min, then 5 - 15 mg/h	60 mg t.i.d. to 360 mg (extended release) o.d.	

Digoxin

- Not effective in patients with increased sympathetic drive
- Observation studies have associated digoxin use with excess mortality in AF patients
  - Due to selection and prescription biases
- Ongoing RCT – digitoxin use in HFrEF patients (DIGIT-HF trial)

	Intravenous administration	Usual oral maintenance dose	Contraindicated
Digoxin	0.5 mg i.v. bolus (0.75 - 1.5 mg over 24 hours in divided doses)	0.0625 - 0.25 mg o.d.	High plasma levels associated with increased mortality Check renal function before starting and adapt dose in CKD patients
Digitoxin	0.4 - 0.6 mg	0.05 - 0.1 mg o.d.	High plasma levels associated with increased mortality

Amiodarone

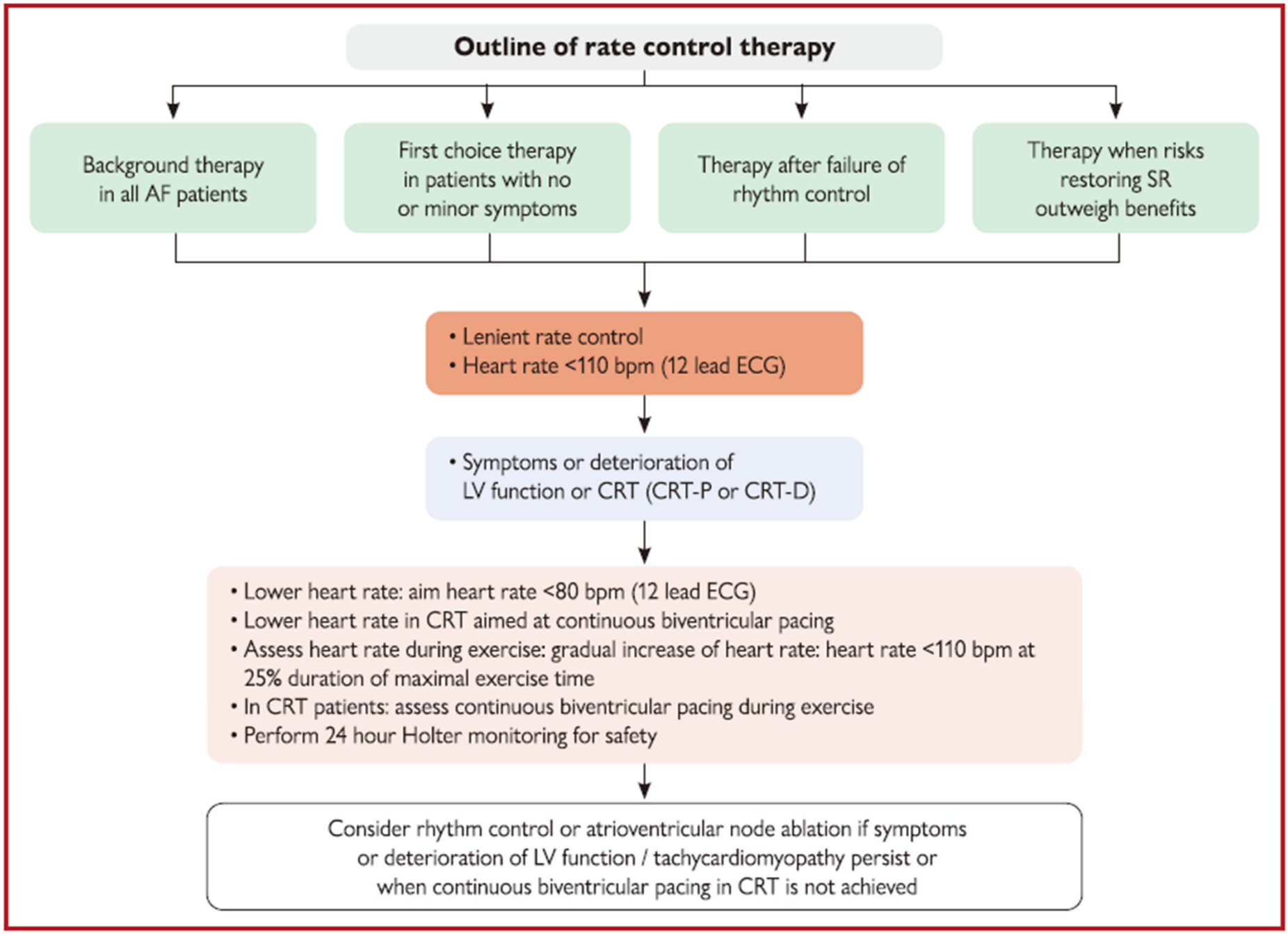
- Useful as a last resort when heart rate cannot be controlled with combination therapy

	Intravenous administration	Usual oral maintenance dose	Contraindicated
Amiodarone	300 mg i.v. diluted in 250 mL 5% dextrose over 30 - 60 min (preferably via central venous cannula), followed by 900 - 1200 mg i.v. over 24 hours diluted in 500 - 1000 mL via a central venous cannula	200 mg o.d. after loading 3 × 200 mg daily over 4 weeks, then 200 mg daily[536 d](reduce other rate controlling drugs according to heart rate)	In case of thyroid disease, only if no other options

Acute rate control

- In acute settings, physicians should always evaluate underlying causes, such as infection or anemia
- BB and NDCCB are preferred over digoxin
  - Rapid onset and effectiveness at high sympathetic tone
- Target heart rate will depend on the patient characteristics, symptoms, LVEF, and hemodynamics

  ➔ Lenient initial heart-rate approach seems acceptable
- In unstable patients, urgent cardioversion should be considered

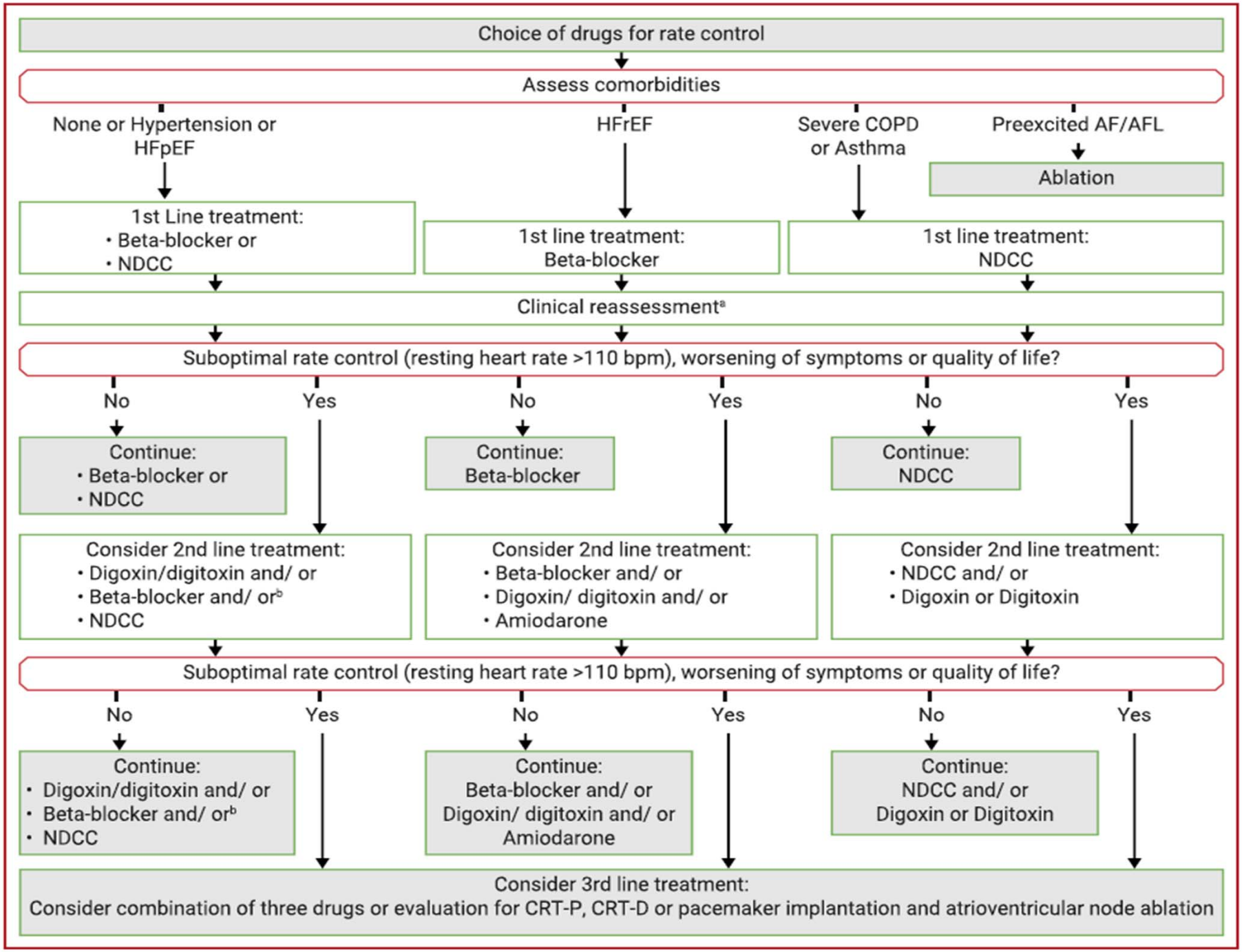


2020 ESC AF Guidelines

Atrioventricular node ablation and pacing

- AV node ablation and pacemaker implantation can control ventricular rate when medication fails
- The procedure is relatively simple and has a low complication rate and low long-term mortality risk
- All other pharmacological and non-pharmacological treatment options have been carefully considered

- His-bundle pacing after AV node ablation may evolve as an attractive alternative pacing mode


Choice of drugs for rate control
Assess comorbidities
None or Hypertension or HFpEF
HFrEF
Severe COPD or Asthma
Preexcited AF/AFL
Ablation
1st Line treatment:
• Beta-blocker or
• NDCC
1st line treatment:
Beta-blocker
1st line treatment:
NDCC
Clinical reassessment[a]
Suboptimal rate control (resting heart rate >110 bpm), worsening of symptoms or quality of life?
No
Yes
No
Yes
No
Yes
Continue:
• Beta-blocker or
• NDCC
Continue:
Beta-blocker
Continue:
NDCC
Consider 2nd line treatment:
• Digoxin/digitoxin and/ or
• Beta-blocker and/ or[b]
• NDCC
Consider 2nd line treatment:
• Beta-blocker and/ or
• Digoxin/ digitoxin and/ or
• Amiodarone
Consider 2nd line treatment:
• NDCC and/ or
• Digoxin or Digitoxin
Suboptimal rate control (resting heart rate >110 bpm), worsening of symptoms or quality of life?
No
Yes
No
Yes
No
Yes
Continue:
• Digoxin/digitoxin and/ or
• Beta-blocker and/ or[b]
• NDCC
Continue:
Beta-blocker and/ or
Digoxin/ digitoxin and/ or
Amiodarone
Continue:
NDCC and/ or
Digoxin or Digitoxin
Consider 3rd line treatment:
Consider combination of three drugs or evaluation for CRT-P, CRT-D or pacemaker implantation and atrioventricular node ablation

Summary

Recommendations for ventricular rate control in patients with AF

Beta-blockers, diltiazem, or verapamil are recommended as first-choice drugs to control heart rate in AF patients with LVEF≥40%.[492,507,511,529]	I	B
Beta-blockers and/or digoxin are recommended to control heart rate in AF patients with LVEF<40%.[486,491,502,512,530–532]	I	B
Combination therapy comprising different rate controlling drugs[d] should be considered if a single drug does not achieve the target heart rate.[533,534]	IIa	B
A resting heart rate of <110 bpm (i.e. lenient rate control) should be considered as the initial heart rate target for rate control therapy.[488]	IIa	B
Atrioventricular node ablation should be considered to control heart rate in patients unresponsive or intolerant to intensive rate and rhythm control therapy, and not eligible for rhythm control by LA ablation, accepting that these patients will become pacemaker dependent.[516,523,535,536]	IIa	B
In patients with haemodynamic instability or severely depressed LVEF, intravenous amiodarone may be considered for acute control of heart rate.[504,514,515]	IIb	B

경청해 주셔서 감사합니다