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Atrial fibrillation: More reasons to do less
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A-fib and rate control: Don't go too low

For patients with atrial fibrillation, more relaxed heart rate control is as effective as stricter control—with fewer adverse effects.

PRACTICE CHANGER

Aim for a heart rate of <110 beats per minute (bpm) in patients with permanent atrial fibrillation. Maintaining this rate requires less medication than more stringent rate control, resulting in fewer side effects and no increased risk of cardiovascular events.[1]

STRENGTH OF RECOMMENDATION

B: Based on 1 long-term randomized controlled trial (RCT).

Van Gelder IC, Groenveld HF, Crijns HJ, et al. Lenient versus strict rate control in patients with atrial fibrillation. *N Engl J Med.* 2010;362:1363-1373.

ILLUSTRATIVE CASE

A 67-year-old man comes in for a follow-up visit after being hospitalized for atrial fibrillation with a rapid ventricular rate. Before being discharged, he was put on warfarin and metoprolol, and his heart rate today is 96 bpm. You consider increasing the dose of his beta-blocker. What should his target heart rate be?

Atrial fibrillation, the most common sustained arrhythmia,[2] can lead to life-threatening events such as heart failure and stroke. Studies, including the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) and Rate Control versus Electrical Cardioversion (RACE) trials, have found no difference in morbidity or mortality between rate control and rhythm control strategies.[2,3] Thus, rate control is usually preferred for patients with atrial fibrillation because of adverse effects associated with antiarrhythmic drugs.

Guidelines cite stringent targets

The American College of Cardiology/American Heart Association Task Force/European Society of Cardiology (ACC/AHA/ESC) guidelines make no definite recommendations about heart rate targets. The guidelines do indicate, however, that rate control criteria vary based on age, "but usually involve achieving ventricular rates between 60 and 80 [bpm] at rest and between 90 and 115 [bpm] during moderate exercise."[4]

This guidance is based on data from epidemiologic studies suggesting that faster heart rates in sinus rhythm may increase mortality from cardiovascular causes.[5] However, strict control often requires higher doses of rate-controlling medications, which can lead to adverse events such as symptomatic bradycardia, dizziness, and syncope, as well as pacemaker implantation.

Pooled data suggest a more relaxed rate is better

A retrospective analysis of pooled data from the rate-control arms of the AFFIRM and RACE trials found no difference in all-cause mortality between the more stringent rate-control group in AFFIRM and the more lenient control in RACE.[6] This finding suggested that more lenient heart rate targets may be preferred to avoid the adverse effects often associated with the higher doses of rate-controlling drugs needed to achieve strict con-
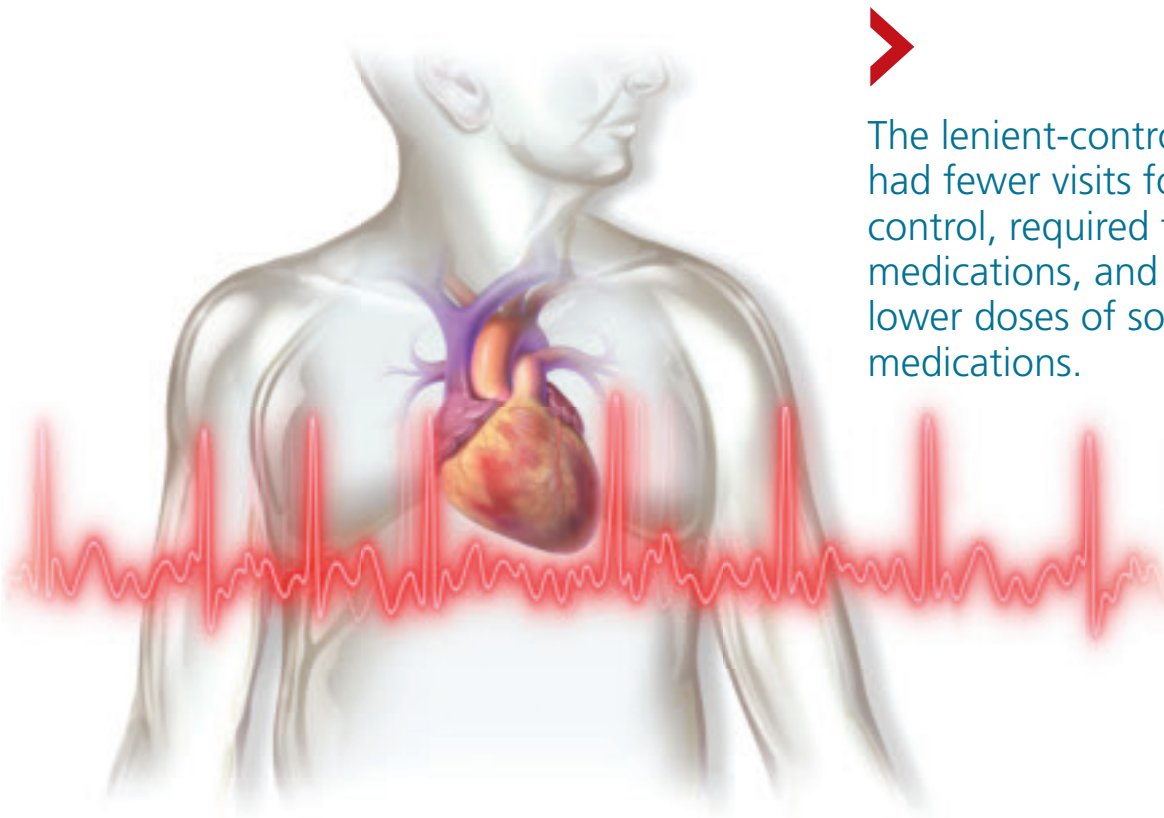
> The lenient-control group had fewer visits for rate control, required fewer medications, and took lower doses of some medications.

trol. The Rate Control Efficacy in Permanent Atrial Fibrillation: a Comparison between Lenient versus Strict Rate Control II (RACE II) study we report on here provides strong evidence in favor of lenient rate control.

STUDY SUMMARY
Lenient control is as effective, easier to achieve
RACE II was the first RCT to directly compare lenient rate control (resting heart rate <110 bpm) with strict rate control (resting heart rate <80 bpm, and <110 bpm during moderate exercise). This prospective, multi-center study in Holland randomized patients with permanent atrial fibrillation (N=614) to either a lenient or strict rate-control group. Eligibility criteria were (1) permanent atrial fibrillation for up to 12 months; (2) ≤80 years of age (3) mean resting heart rate >80 bpm; and (4) current use of oral anticoagulation therapy (or aspirin, in the absence of risk factors for thromboembolic complications).

Patients received various doses of beta-blockers, nondihydropyridine calcium-channel blockers, or digoxin, singly or in combination as needed to reach the target heart rate. In both groups, the resting heart rate was determined by 12-lead electrocardiogram after the patient remained in a supine position for 2 to 3 minutes. In the strict-control group, heart rate was also measured during moderate exercise on a stationary bicycle after the resting rate goal had been achieved. In addition, patients in the strict-control group wore a Holter monitor for 24 hours to check for bradycardia.

Participants in both groups were seen every 2 weeks until their heart rate goals were achieved, with follow-up at 1, 2, and 3 years. The primary composite outcome included death from cardiovascular causes; hospitalization for heart failure, stroke, systemic embolism, major bleeding, or life-threatening adverse effects of rate-control drugs; arrhythmic events, including sustained ventricular tachycardia, syncope, or cardiac arrest; and implantation of a pacemaker or cardioverter-defibrillator.

■ **At the end of 3 years,** the estimated cumulative incidence of the primary outcome was 12.9% in the lenient-control group vs 14.9% in the strict-control group. The absolute difference was -2.0 (90% confidence interval [CI], -7.6 to 3.5); a 90% CI was acceptable because

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the study only tested whether lenient control was worse than strict control. The frequency of reported symptoms and adverse events was similar between the 2 groups, but the lenient-control group had fewer visits for rate control (75 vs 684; P<.001), required fewer medications, and took lower doses of some medications.

Heart rate targets were met in 97.7% of patients in the lenient-control group, compared with 67% in the strict-control group (P<.001). Of those not meeting the strict control targets, 25% were due to an adverse medication event. There were no differences between the 2 groups in symptoms or in New York Heart Association functional class status.

However, the major outcomes were determined with relative objectivity and were not different between the 2 groups, so it is unlikely that this knowledge would have a major effect on the results. Nonetheless, this is a single study, and the findings are not yet supported by other large, prospective studies.

The researchers did not enroll patients >80 years, who have a higher incidence of atrial fibrillation and are less likely than younger patients to tolerate higher doses of rate-controlling medications. Also excluded were sedentary patients and those with a history of stroke, which resulted in a lower-risk study population. However, 40% of the subjects had a CHADS score ≥2 (an indication of high risk of stroke in patients with atrial fibrillation), and subgroup analysis found that the results applied to higher-risk groups.

Finally, it is possible that it may take longer than 3 years (the duration of study follow-up) for higher ventricular rates to result in adverse cardiovascular outcomes and that there could be a benefit of strict rate control over a longer period of time.

> **Virtually all (97.7%) of the patients in the lenient-control group reached their target heart rate, compared with 67% of those in the strict-control group.**

WHAT'S NEW

Now we know: It doesn't pay to go too low

A heart rate <80 at rest and <110 during exercise is difficult to maintain. This more stringent target often requires high dosages of drugs and/or multiple medications, which may lead to adverse effects. This RCT—the first to compare outcomes in patients with lenient vs strict heart rate control—found that morbidity and mortality were similar between the 2 groups. This means that, in many cases, patients will need less medication—leading to a reduction in risk of side effects and interactions.

CAVEATS

Unblinded study excluded very old, high risk

This was not a blinded study, so both patients and providers knew the target heart rates.

CHALLENGES TO IMPLEMENTATION

Guidelines do not reflect these findings

These findings are not yet incorporated into the ACC/AHA/ESC guidelines or those issued by other organizations. Clinical inertia may stop some physicians from reducing medications for patients with atrial fibrillation, but in general, both doctors and patients should welcome an easing of the drug burden. **JFP**

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