

A 70-Year-Old Man With a Cardiac Rhythm Disturbance

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A 70-year-old man is being evaluated for a several-months history of cardiac palpitation. Approximately 3 months ago, he had experienced several episodes of palpitation that initially had been related to physical effort of doing yardwork, but by week's end, the palpitations had continued into the evening, with associated dyspnea interfering with and awakening him from sleep.

He was subsequently hospitalized, where atrial fibrillation (AF) had been diagnosed with a heart rate of 150 to 160 beats/min. A course of β -blockers had lowered the rate to 100 to 120 beats/min, and results of a thorough cardiac evaluation were negative for acute or subacute myocardial infarction (MI), negative for the presence of coronary artery disease, and negative for valvular heart disease and hyperthyroidism.

Cardiac echocardiography (including transesophageal echocardiography) revealed normal-sized atria and no cardiac thrombi. Contractility was normal, and his ejection fraction was 55%. He spontaneously converted to sinus rhythm on day 3 of hospitalization and was discharged on a β -blocker and rivaroxaban anticoagulation.

Ten days later, he had a recurrence of symptoms and was readmitted. Amiodarone was started, and dose titration was accomplished over a 7-day period, again with eventual conversion to sinus rhythm. However, 3 weeks after the second hospital discharge, his symptoms returned as AF once again recurred. He is now being evaluated regarding how to proceed.

His history is that of a healthy man. He is retired but is quite active with care of his home and property. He participates in athletics even more than usual for a man of his age. He has military- and employment-related tinnitus with some hearing loss but with no need for a hearing aid. He has a remote history of smoking during his active-duty years in Vietnam but has not smoked since then. He has mild hypertension that is well controlled with losartan, 50 mg/day. He is not diabetic and does not use alcohol or drugs.

Physical examination reveals a strongly built man who appears younger than his age. His body mass index is 23 kg/m². His blood pressure is 125/80 mm Hg, and his pulse rate is irregular at 100 beats/min but with periods of sinus rhythm at 80 to 90 beats/min on his cardiac monitor. His chest is clear to auscultation and percussion. He has no pedal edema. His electrocardiogram (ECG) shows atrial fibrillation without ECG criteria for left ventricular hypertrophy or acute, subacute, or remote MI or ischemia.

Which one of the following is the most accurate statement referring to management of this patient's condition?

- Ablation therapy will provide a modestly superior quality of life (QOL) benefit advantage over medical therapy.
- Ablation therapy will provide a superior mortality benefit over medical therapy but with increased toxicity and adverse effects.
- The major difference between ablation therapy and medical therapy is the all-cause and cardiovascular mortality at 4 years.
- Despite the excellent treatment choices now available for AF, the morbidity and mortality associated with AF has remained essentially unchanged in recent decades.

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CITATION:

Rubin RN. A 70-year-old man with a cardiac rhythm disturbance. *Consultant*. 2020;60(12):13-14. doi:10.25270/con.2020.12.00001

DISCLOSURES:

The author reports no relevant financial relationships.

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TAKE-HOME MESSAGE

AF remains the most commonly encountered cardiac rhythm disturbance. A variety of strategies have evolved regarding rate control or rhythm control, optimal rate targets for symptom and morbidity prevention, and, most recently, the use of radiofrequency ablation techniques for long-term rhythm control compared with medical therapy. Good trials seem to indicate that to date, ablation and medical therapy are equivalently effective with regard to all-cause mortality and serious AF morbidities of cardiac arrest, serious bleeding, and disabling stroke. Ablation does seem to have some clinical benefit in QOL measurements. Overall, recent trials do show improved prognosis for the AF population in general compared with previous decades.

Answer: A, ablation therapy will provide a modestly superior QOL benefit advantage over medical therapy

The case presentation here provides the opportunity to once again review aspects of the management of AF, which is still by far the most common rhythm disturbance encountered in clinical medicine and which occurs in approximately 10% of people aged 75 years or older.¹ And, appropriately, AF has been the topic of "What's the 'Take Home?'" discussions 3 times previously at approximately 5-year intervals, with the most recent being in 2016.² There is more than adequate-quality literature to justify this. We have gone from rate vs rhythm issues, to what is the optimal rate regardless of rhythm, and now will address that latest addition to the AF armamentarium: the use of radiofrequency ablation techniques.

Ablation has gained traction and more frequent, early, and widespread use in the past decade.^{1,3,4} Initially, ablation was shown to be a good therapeutic intervention for low-risk patients with recurrent and poorly controlled episodic paroxysmal AF, with the goal end point of fewer episodes being accomplished when compared with antiarrhythmic medical therapy.³ So, over the past 5 years, the questions asked and studied were as follows: 1) What about more general and high-risk patient populations such as older adults and patients with more widespread coexisting cardiac conditions such as coronary artery disease and congestive heart failure? 2) Are there bona fide all-cause and cardiac mortality benefits, the absolute gold standard for essentially any therapy comparison trial? And 3) are there lesser but still important secondary end points (the "silver standard," to extend the metaphor) such as QOL?

Two papers on a very large and well-done trial (Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation [CABANA]), and an accompanying editorial, have gone a long way in answering these questions. The first and most important CABANA paper⁴ compared 2 well randomized and equivalent groups in large numbers (2204 patients across a wide spectrum of hospitals, not a single institution) and assessed whether ablation is superior to standard medical therapy with regard to

mortality, and the second paper⁵ assessed, in my opinion, the far less important "net" end point of mortality plus admissions for cardiovascular problems, in a 4-year follow up period. I will emphasize the mortality aspect and deemphasize the combined secondary end point, because although I agree with the authors that recurrent hospitalization is clinically "important," its weight is trivial compared with mortality and seems to belong to the second paper's QOL comparison.

As regards cumulative risk for death, disabling stroke, serious bleeding, or cardiac arrest, at 4-year follow-up, the absolute difference between groups was a net 1.7% (8.9% in the medical group vs 7.2% in the ablation group, which was not statistically significant). All-cause mortality alone was even closer to equivalent, 4.7% for ablation vs 5.3% for medical therapy (an absolute difference of 0.6%).⁴ Thus, there are now strong data that appear to show no advantage (or disadvantage) for ablation therapy when mortality or even mortality plus severe morbidities are the issue. This makes **Answer B** and **Answer C** incorrect statements.

An interesting sidelight discussed in the papers was the lower-than-expected mortality and morbidity across the *entire* study—ablation and medical groups combined—compared with historical expectations and assumptions. For example, the control group (medical therapy) had 5.3% mortality at 4 years compared with a projected 12% mortality at 3 years, and the occurrence rate of disabling stroke was a very small 0.7%. The authors therefore wondered whether an even larger study might indeed demonstrate a benefit—a frequent lament when something does not work as well as had been expected beforehand. But I wonder, if it takes thousands of ablations to prevent very few deaths in absolute numbers, is that such a truly major advance? I agree far more with Drs Albert and Bhatt, who in an editorial accompanying the papers suggest that this is very good news for all patients with AF—the prognosis overall seems better than ever.⁶ And, to give a pat on the back to my own

specialty of hematology, what an advance the direct oral anticoagulants have been regarding ease of use, adherence, and safety in patients with AF (and essentially all other patients requiring anticoagulation), and perhaps the tiny stroke incidence observed in CABANA is related to that advance. This discussion thus renders **Answer D** to be an incorrect one.

In the second paper,⁵ the CABANA investigators then looked at a variety of QOL parameters and how these separated the treatment groups. As discussed above, in the initial paper, the end point of hospital admissions in a 4-year period was lumped in with mortality, but intellectually and cerebrally, I will include them here as QOL issues. This is especially true if we add them to the complicated QOL measures—the AF Effects on Quality of Life (AFEQT) questionnaire and the Mayo AF-Specific Symptom Inventory (MAFSI). The AFEQT is chock-full of domains and data, with a net score of 0 to 100! And the larger the spread of numbers, the more amplification of any differences. The MAFSI scheme ranges from 0 to 40 in severity. Also remember that the ablation group experienced a major procedural intervention in a surgical suite, whereas the medical group did not—there was no sham procedure. The patients in the ablation group likely had a stronger emotional input into the therapy being successful. In any event, the results showed that ablation outscored medical therapy, 86.4 to 80.9 points on AFEQT, at 12 months, a mean difference of 5.3 points, which was statistically significant ($P < .001$), while the MAFSI similarly favored ablation with a similar P value.⁵ Thus it is fair to say that ablation resulted in a statistically significant improvement in QOL at 12 months, with a very narrow “covering of the point spread”—5.3 points on a 100-point scale—such that **Answer A** is the correct choice.

Allow me the editorial privilege to add the following opinion comments. I realize how rapidly medicine changes these days, and I will continue to follow the literature closely and change my practice as needed, as I have always done. But I have also learned in my nearly 50 years of being a physician that when things *really* work—“game changers,” in today’s parlance—and really mark a substantial change (for example, historically, penicillin for pneumonia, cardiac bypass and stenting for coronary artery disease, and chimeric antigen receptor T-cell therapy for malignant lymphoma of the CD-19 variety), that Kaplan-Meier curves open early and widely. They sustain these graphs of separation that you can drive a truck through. And the end points are the no-doubt-about-it variety: who has remained alive, and who has died.

There has been no need to create 100-point criteria tables with expansion of end points to create “significance” requiring an ECG caliper and magnifying glass to see separations. So let us carefully apply new evidence like that concerning ablation therapy for AF, but bear in mind that there should be no mandate,⁶ or a too loosely applied use of the adjectives like “best,” at least for now.

PATIENT FOLLOW-UP

A thorough discussion of the options, risks, and benefits of the treatment approaches took place with the patient. There was agreement that a good course of medical therapy had been tried, but that the patient continued to experience clinically significant relapses. And, he had a strong desire to maintain his active and energetic lifestyle. He opted for ablation, which was performed without complications. He was in sinus rhythm at 4 months without relapse and had returned fully to his previous activities. Nevertheless, several weeks later, the AF recurred, and he is being now being evaluated as to what therapeutics and plan of care are next. ■

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