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Atrial Fibrillation Expert Column

## New ACC/AHA/ESC Guidelines for the Management of Atrial Fibrillation: Highlighting Stroke Prevention and Catheter Ablation

**Hugh Calkins, MD**

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### Editor's Note

*Atrial fibrillation (AF) is the most common clinical arrhythmia, with an estimated 2.2 million people in the United States and 4.5 million in the European Union afflicted with the disorder.<sup>[1]</sup> Moreover, its prevalence is on the rise due to the aging population, the increasing incidence of chronic heart disease, and more frequent AF diagnoses. Over the past 20 years, hospital admissions for AF have increased by 66%, and AF now accounts for about one third of US hospitalizations for cardiac rhythm disturbances. The annual cost of treating the disease is about \$3600 per patient, making AF one of the costliest public health problems. Although not directly life-threatening, AF significantly increases the risk of all-cause mortality, primarily from cardiovascular-related causes such as heart failure and, of primary concern, stroke.*

*Earlier this month, the American College of Cardiology, American Heart Association, and European Society of Cardiology (ACC/AHA/ESC) jointly released revised clinical guidelines for the management of patients with AF.<sup>[1]</sup> This was the first revision in AF management recommendations since 2001. The 2006 guidelines change some of the criteria for antithrombotic therapy and, for the first time, highlight catheter-based AF ablation as a viable treatment option for selected patients.*

*To gain a perspective on the new clinical guidelines, Medscape recently spoke with Hugh Calkins, MD, FACC, Professor of Medicine and Director of the Electrophysiology Lab at Johns Hopkins University School of Medicine (Baltimore, Maryland). In the following interview, Dr. Calkins discusses some of the most important differences between these and previous AF guidelines and provides additional insight into the promising role of catheter-based ablation therapy for the treatment of AF.*

### The New Guidelines in Perspective

**Medscape:** What are the most important differences between the 2001 guidelines<sup>[2]</sup> and the new recommendations on AF management that physicians should focus on?

**Dr. Calkins:** I think there are essentially 2 important changes in clinical recommendations in the new guidelines. The first is the inclusion of catheter ablation of AF as one of the therapeutic

options for patients with more persistent AF, and the second is a fairly striking change in the anticoagulation guidelines. In terms of the latter, the threshold for anticoagulation has actually been raised and the guidelines now are quite specific about risk factors for stroke in various risk groups.

A third change, which is also important, reflects the greater number of studies on rate vs rhythm control that have come out in the past few years. As a result, the guidelines include an expanded section on rate control drugs in both the acute and chronic settings. There are also some minor changes with respect to which antiarrhythmic drugs should (and should not) be used.

## Criteria for Antithrombotic Therapies

### Practice Point

The mortality rate in AF patients is approximately twice that in persons who are in normal sinus rhythm, and increases with age. AF patients also have a higher long-term risk of both heart failure and embolic stroke. In fact, AF is an independent risk factor for stroke. According to the ACC/AHA/ESC guidelines, the rate of ischemic stroke in patients with nonvalvular AF is about 2 to 7 times that of people without AF, and the risk increases dramatically as patients age. In the Framingham Heart Study by Wolf and colleagues,<sup>[3]</sup> the annual risk of stroke attributable to AF was 1.5% in participants aged 50-59 years and 23.5% in those aged 80-89 years.

Anticoagulation therapy is essential in patients with AF to reduce the risk of embolic stroke; however, there is some question about when warfarin (Coumadin) should be used in moderate- to low-risk AF patients.

Recommendations for anticoagulant therapy differ between the 2001 and 2006 guidelines. In 2001, the guidelines recommended using several patient characteristics (including age, gender, heart disease risk, and concurrent conditions) to determine proper antithrombotic therapies. The new guidelines, however, place more emphasis on stroke risk as the primary means to determine the need for anticoagulants, regardless of whether the patient is in sinus rhythm.

### Medscape: Is placing more emphasis on stroke risk as the primary means to determine the need for anticoagulant therapy a positive change?

**Dr. Calkins:** Yes, I think it is a positive change. The problem with the old guidelines was that different organizations published their own anticoagulation guidelines, and each one had slightly different cutoffs for when a patient should be receiving warfarin. Interpreted even in a very conservative fashion, those previous guidelines would lead to the conclusion that any patient over 65 years of age who has at least 1 risk factor for stroke should be getting warfarin. This means that huge numbers of otherwise healthy patients, when they reached the age of 65 years, required a discussion about warfarin and the need for anticoagulation monitoring, which is an enormous lifestyle change and commitment.

The new guidelines are much clearer about who are the highest-risk patients. According to the new guidelines, patients with prior stroke, or transient ischemic attack (TIA), or with rheumatic heart disease are at the highest risk for stroke ( [Table 1](#) ), and they clearly need warfarin. But for patients at lower risk, no longer is 1 moderate risk factor enough to justify warfarin; these patients require  $\geq 2$  of these less severe risk factors before warfarin therapy should be considered.

The new guidelines also provide the full CHAD (Cardiac Failure, Hypertension, Age, Diabetes, and Stroke) scoring system, and they clearly specify when risk factors indicate that aspirin is sufficient and when risk factors suggest a patient is a candidate for warfarin. As shown in [Table 2](#) , aspirin is sufficient in an AF patient with no other risk factors for stroke. If there is 1 moderate risk factor, either aspirin or warfarin can be used, according to patient preference. Warfarin is clearly indicated if a patient has 1 high risk factor or  $\geq 1$  moderate risk factor.

I commend the guideline committee on a superb job of narrowing risk and anticoagulant strategy, because otherwise a large number of patients would be put on warfarin. As much as we don't want patients to have strokes, we also don't want to put massive numbers of patients on warfarin when the stroke risk is only marginal or borderline. A lot of patients at the age of 65 years, and even in their early 70s, are still very active, and committing a patient like that to warfarin just because they reach age 65 years is a fairly big step to take.

## Anticoagulation Therapy in Moderate-Risk Patients

**Medscape: For moderate-risk patients, the guidelines give some leeway as far as whether to use aspirin or warfarin. How do you decide which therapy is appropriate for the moderate-risk patient?**

**Dr. Calkins:** It really depends on patient preference. I have the 'anticoagulation discussion' with all of my AF patients who are eligible for warfarin. We talk about the benefits and risks of warfarin, and patients generally react in 1 of 2 ways. Some patients are incredibly frightened by the notion of a stroke, either because a family member has had a stroke or they have a friend who experienced a stroke, and they tend not to have a problem with warfarin clinics and long-term follow-up. These patients will choose to take warfarin even though their stroke risk is not high.

But most patients opt for the opposite: They strongly dislike taking medications and do not like the idea of going in monthly or weekly to get their INR level checked. With these patients, if you tell them their stroke risk is fairly low and there isn't an enormous difference between the 2 treatment options in terms of outcomes, they are likely to choose aspirin therapy and avoid warfarin clinic visits. I always will document that discussion with the patient, noting that we have talked about the risks and benefits of warfarin therapy and they have elected to proceed with a certain approach; I also include the patient's reasoning behind that decision.

## Rate vs Rhythm Control

### Practice Point

Two landmark studies published in 2002, the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)<sup>[4]</sup> and the Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation (RACE)<sup>[5]</sup> trials, found that treating AF with a rhythm-control strategy involving cardioversion and antiarrhythmic drug (AAD) therapy offers no survival or clinical advantages over simpler rate-control therapy using medications such as calcium channel blockers, beta-blockers, and digoxin. In fact, the potential benefits of a rhythm-control strategy were largely offset by the adverse side effects associated with AAD therapy. These results led many in the medical community to endorse rate control as the better choice for first-line AF therapy. However, there were important limitations to these studies since they primarily enrolled older patients (over age 65 years) with persistent AF who were mildly symptomatic. Moreover, in the AFFIRM study, less than two thirds of those in the rhythm control arm were actually able to maintain normal sinus rhythm. Thus, because the scope of these trials was limited, the results cannot be extrapolated to significant subgroups of patients, including: younger patients; those with new, first-onset AF who may benefit from early conversion to sinus rhythm; patients with persistent AF who are highly symptomatic; and patients with poor left ventricular (LV) function or with significant heart failure.

**Medscape: Have the new guidelines achieved a good balance between rate-control and rhythm-control strategies?**

**Dr. Calkins:** I think the rate- vs rhythm-control issues are well spelled out in the new guidelines. In fact, the guidelines as a whole are incredibly well written, well laid out, and well thought out, and certainly reflect the approach I use in clinical practice. I am also impressed that these guidelines did not just tweak or change slightly the recommendations in only a few sections;

rather, the panel has done a very comprehensive overview of the entire document.

All of the studies that have been performed, including AFFIRM and RACE, have shown that there is no difference between rate and rhythm control in terms of stroke risk and survival. So the real question is: Which patients should use which approach? If a patient has symptomatic AF, particularly if the patient is young, I lean toward rhythm control to maintain sinus rhythm and alleviate the patient's symptoms; whereas as a patient gets older and their symptoms lessen, rate control becomes the dominant therapy.

If you look at the AFFIRM study, the patients who were included in the study were candidates for either rate or rhythm control. The highly symptomatic patients with paroxysmal AF that I see in my practice would not have been in that study because they weren't candidates for rate control alone due to their very symptomatic AF; thus, we shouldn't over-interpret the results of these studies.

The other important issue that the new guidelines make fairly clear is that catheter ablation has come a long way from its infancy to now being a recognized treatment option for patients with AF, and it's actually another reason why it makes sense to try to maintain a patient's sinus rhythm with pharmacologic drugs. By doing this, we can prevent atrial remodeling, which ultimately may make the patient a poor candidate for catheter ablation.

**Medscape: Do you think these guidelines are the final word on rate vs rhythm control, or will the discussion continue?**

**Dr. Calkins:** I think the discussion will clearly continue; most physicians I know feel fairly strongly one way or the other. I think most electrophysiologists generally believe that rhythm control is important and maintenance of sinus rhythm is important. Electrophysiologists are a subset of cardiologists that are more aggressive about trying to preserve and maintain sinus rhythm. But there are other cardiologists who are looking for reasons to proceed with a rate-control strategy alone. And certainly there are data that support either approach, as long as the patient's symptoms can be controlled.

Clearly, we don't have all the answers yet; there are still areas for interpretation and debate, and that's where clinical judgment fits in. I think that, in general, age plays an important role. If we are talking about patients who are  $\geq 75$  years old, I believe every cardiologist and electrophysiologist would agree that in the subset of very elderly individuals, a rate control strategy oftentimes is optimal and sufficient. Whereas if patients are younger (eg, 40 to 70 years old), that is a group, generally speaking, for whom it makes more sense to be more aggressive about treating symptoms by restoration and maintenance of sinus rhythm.

## Drug Choices for Rhythm Control

**Medscape: What are your first-line drug choices for rhythm control?**

**Dr. Calkins:** It depends on the patient; but I think the new guidelines are fairly clear in breaking down which drugs to use in various patient groups. In general, if someone has severe heart failure, we are fairly limited to either amiodarone or dofetilide. On the other hand, if someone has lone AF and is otherwise healthy, I commonly use 1C drugs like flecainide or propafenone initially, although sotalol also is a reasonable option. There are patient groups with differing proarrhythmic risk profiles. In patients with ischemic heart disease, for example, we tend to avoid the 1C agents and use sotalol or dofetilide earlier. By contrast, if someone has significant hypertension, we may want to use a 1C agent before sotalol or dofetilide.

**Medscape: The guidelines also briefly mention the benefits of statin drugs, noting that**

**recent studies have shown that statins can help maintain sinus rhythm after successful cardioversion in patients with persistent AF. Do you think that most rhythm-control patients should be receiving a statin drug to help maintain sinus rhythm?**

**Dr. Calkins:** There are 2 different types of non-AADs that seem to have some benefit for AF patients. I think there is more compelling data with angiotensin converting enzyme (ACE) inhibitors than with statin drugs. The data on ACE inhibitors come from multiple studies suggesting that an ACE inhibitor may help prevent the recurrence of AF. Given these data, I am very aggressive about using ACE inhibitors in anyone with AF, particularly if there is any hint of hypertension, cardiac dysfunction, or heart failure.

In my opinion, the data on statins and rhythm control are much less compelling than the data we have with ACE inhibitors. Certainly, if you interpret the lipid guidelines in the most conservative fashion, you could justify putting most AF patients on a statin drug. But in my practice, I have not routinely put patients with a low level of low-density lipoprotein cholesterol on a statin drug just because they have AF. If there is any hint of hyperlipidemia, however, I definitely prescribe a statin as opposed to relying on weight control, diet, or some other lipid-lowering agent.

## **Recommendations for Atrioventricular (AV) Node Ablation and Permanent Pacing**

**Medscape: The guidelines specifically state that AV node ablation followed by permanent pacing should be used only as a fall-back treatment rather than a primary strategy because of the risk of long-term right ventricular (RV) pacing. Do you agree with that recommendation?**

**Dr. Calkins:** I agree with that completely. There are multiple studies showing that AV node ablation improves quality of life in patients with AF, but I think the pendulum has clearly swayed away from that procedure for a number of reasons. The most important reason is the issue of dyssynchrony and the adverse effects of pacing at the RV apex. The downside of AV node ablation is that you obviously still have AF, you still have the anticoagulation issues, and you now have substituted a permanent pacemaker and instituted a life-long condition or problem that is going to require periodic office visits. Here at Johns Hopkins, the number of AV node ablations we perform has dropped dramatically. Generally, I only perform that procedure in elderly patients — those aged  $\geq 70$  years, in whom pharmacologic rate control has been unsuccessful or poorly tolerated.

The new guidelines also clarify the language concerning when AV node ablation is appropriate. The previous guidelines stated that if pharmacologic rate control fails, then AV node ablation may be indicated. This new document clarifies this by adding that if the patient's rate cannot be controlled adequately with pharmacologic agents, or the patient cannot tolerate rate-control medications, an AV node ablation is reasonable. So the new guidelines make it clear that it is reasonable to do an AV node ablation either if drugs don't work or if patients develop side effects from those drugs.

## **The Role of Catheter Ablation**

Since 2001, significant developments in the field have emerged suggesting the importance (and viability/success) of catheter ablation for AF. In the 2001 guidelines,<sup>[2]</sup> the data on catheter ablation were limited; however, since then, the technique has been much more commonly employed worldwide, although long-term data are still limited. A worldwide survey on catheter-based AF ablation, coauthored by Dr. Calkins and published earlier this year, summarized the experience from 100 centers with AF catheter

ablation programs.<sup>[6]</sup> The survey found that 52% of the ablations performed were curative, with an additional 24% of patients achieving sufficient improvement to make them amenable to antiarrhythmic drugs. However, 24.3% of patients required a second ablation procedure to treat recurring AF and 3.1% required a third procedure. The overall complication rate was 6%.

## Ablation as Mainstream Therapy?

**Medscape:** These new guidelines are the first to classify catheter ablation as a viable treatment option for selected AF patients. Given the steadily improving outcomes that have been achieved over the past several years with catheter-based ablation and the growing use of this treatment approach, how would you characterize the current role of AF catheter ablation, and should it now be considered a mainstream therapy?

**Dr. Calkins:** Catheter ablation of AF is the most common ablation procedure performed today, and I think it certainly should be considered a part of the standard treatment options for AF. The real debate is when should it be used and in whom. The new guidelines carefully outline step by step what drugs to use and when, and the various subgroups for whom the drugs should be used. However, one of the striking changes in these new guidelines is that for the first time, catheter ablation appears as an option for treatment of paroxysmal or persistent AF in patients who have failed  $\geq 1$  course of an AAD regimen.

Catheter ablation is considered as an alternative to amiodarone, if you will. And in my clinical practice, that is the way I treat catheter ablation. I don't generally perform catheter ablation as a first-line therapy for AF. But if a patient has failed prior AADs, I will certainly offer that patient the opportunity to receive catheter ablation and make sure he or she understands the risks and benefits of the procedure.

**Medscape:** Can we define the ideal candidate for catheter ablation at this point?

**Dr. Calkins:** Yes, I think so. I would say an ideal candidate for catheter ablation is a person aged  $< 70$  years with paroxysmal AF who has never been cardioverted, has failed at least 1 AAD, and is highly symptomatic. The patient's left atrial size should be  $< 5$  cm with an ejection fraction  $> 40\%$ , without other significant common cardiac disease.

**Medscape:** Studies have suggested that if patients with paroxysmal, symptomatic AF fail their first AAD, catheter ablation should be the next step, rather than trying a progression of other drugs. Do you agree with this approach?

**Dr. Calkins:** Yes, once patients have failed 1 AAD, chances are they are going to fail the second, the third, and the fourth. The exception is amiodarone, which has a significantly different side-effect profile. If you give a patient a first-line therapy, such as flecainide, or propafenone, or sotalol, and that doesn't work, it is very unlikely that switching from sotalol to flecainide or flecainide to sotalol is going to make any difference. The real question is, do you go to amiodarone or do you go with catheter ablation?

When I have this discussion with patients, I go over in great detail the risks of the ablation procedure and the efficacy of the procedure. I make sure they know that this is a relatively young procedure that has been developed over the past 7 years and continues to evolve. And, as with the anticoagulation issue, patients tend to fall into 2 groups: those who want to schedule the procedure immediately and those who want to try all the possible drugs before going ahead with an ablation procedure. It warrants noting that catheter ablation for AF has a 3% to 6% major complication rate and a success rate of certainly no better than 70% for the first procedure.

## Complications and Recurrences Following Catheter Ablation

**Medscape:** As discussed above, you recently coauthored a worldwide survey on AF catheter ablation that showed an overall incidence of major complications of 6%.<sup>[6]</sup> Was it surprising to you that the complication rate was so high, and do you think that this is going to decline with growing operator experience?

**Dr. Calkins:** No, I wasn't surprised by the 6% number because that reflected my own experience. If you look at simple catheter ablation procedures for AV node re-entry, Wolff-Parkinson-White syndrome, or atrial flutter, the early multicenter series published on those procedures demonstrated relatively high rates of complications. For example, one of the series I wrote reported a 3% major complication rate. AF ablation is an order of magnitude more involved and more complex than those procedures, so it is not surprising to me at all that the complication rate would be roughly twice that of a standard, simple ablation.

It is also true that with increased operator experience and development of the procedure worldwide, the complication rate is falling. We have learned a lot and we continue to learn, and this is reducing the rate of complications. But even in the most experienced center in the most experienced hands, I think the complication rate at best would be 3%, and in other circumstances it certainly can be as high as 6% or 8%. Now when we say major complications, we aren't talking about complications that affect long-term quality of life or are lethal; we are talking about a complication that requires intervention. One of the most common complications is a hematoma at the site of access in the thigh, and that is a complication that can extend hospital stay, can cause pain and discomfort, may require a transfusion, and may require surgical repair of a vessel, but doesn't cause long-term disability or problems. So we have to separate major complications from lifelong complications.

**MEDSCAPE:** Another area of concern is the percentage of patients who require a second ablation after their initial procedure. In the survey you co-authored, 24.3% of patients required a second procedure and 3.1% required a third. Are there signs that this is also improving as experience with the procedure grows?

**Dr. Calkins:** One of the main problems, as you point out, is the fact that a second procedure is required in a very significant number of AF ablation patients. If you look at published series, up to half of patients in some series require 2 procedures to achieve whatever success is achieved. That is an enormous problem. It is a problem in terms of costs and it is a problem in terms of risk, because the risks of a procedure are incremental. Each time you undergo a procedure you are accepting the same risks. Clearly, this is something we need to improve and I think we are doing better. Operators now are more aware of the fact that most recurrences occur because of pulmonary vein conduction. The question now is: once you isolate the pulmonary veins, how long do you wait before you pull the catheter out and say the procedure is complete?

I think, certainly in my experience, it makes sense to wait at least 30 minutes to look for early recurrences. This enables you to do a touch-up right then and there, rather than bringing the patient back 3 or 6 months later for a second procedure.

## Future of Catheter Ablation

**Medscape:** How would you characterize the future of ablation therapy? Will the procedure continue to improve and expand to a larger number of patients? And if so, who would you think might be a candidate in the future?

**Dr. Calkins:** There is no question that the procedure is expanding at an extraordinarily rapid rate

worldwide. Certainly this new guideline document, which now officially lists catheter ablation as one of the accepted therapies for AF, will further fuel enthusiasm and the widespread acceptance and performance of this procedure. I think what is clear is that in the optimal patient, which we discussed earlier, this procedure really works. It has quite high efficacy, it has reasonable safety, and I think it is, and will remain, a mainstay of therapy.

One of the debates now is whether catheter ablation should become first-line therapy. There have been several small, randomized studies suggesting that it is reasonable to consider catheter ablation as a first-line therapy, although that certainly remains an area of debate. I think what is much less clear is what to do with patients with more severe forms of AF; the extreme would be patients with chronic or permanent AF. For example, if we have a patient who has been continuously in AF for 5 years, has a left atrial size of 6 cm, and is 75 years old, the question is, what is the real safety and efficacy of catheter ablation in that patient? Is this something that is going to be a mainstay treatment option for patients like that?

If you look at the guidelines right now, they do not list catheter ablation as one of the therapeutic options for permanent AF. That reflects the paucity of data in that patient group and also the fact that the world is struggling with what is the right ablation strategy for those patients. I remain optimistic and am convinced that we will figure this out, and that catheter ablation will play a role in the management of all types of AF. However, with a patient who has permanent AF, catheter ablation may be more like a drug, where it may control the patient's AF for a year or more, but the word 'cure' may be presumptuous in that patient group.

**Medscape: What kind of studies would you like to see conducted at this point to answer some of these remaining questions about catheter ablation for AF?**

**Dr. Calkins:** A significant number of studies still need to be performed for catheter ablation of AF. One of the main limitations now is that most of the data published to date encompasses single-center experiences. There are a few, small multicenter studies involving 2-3 centers, but there are no larger studies, say with data from 10-20 centers. That is a very basic step to take at this point. Part of that is the issue of having ablation systems or tools to use that have been subjected to the rigors of a clinical trial to gain regulatory approval. There are quite a few different ablation catheters, energy sources, and so forth that are being evaluated as part of multicenter clinical trials. Most of those are randomized clinical trials, and I think these will be very helpful in providing us with data about real safety and efficacy, real complication rates, and also to compare antiarrhythmic drug therapy with catheter ablation.

## **Amiodarone as Rate Control and Ablation for Chronic or Permanent AF**

**Medscape: Are there any recommendations in the guidelines that you disagree with or areas where you'd like to see greater emphasis?**

**Dr. Calkins:** One thing mentioned in the guidelines (and it was in the previous guidelines as well) that goes against what I would do in clinical practice involves the use of amiodarone as a rate-controlling drug. The short-term side effects of amiodarone are very few, but if you look at the longer term, 3-5 years down the road, at least half of the patients you put on amiodarone will develop side effects, and some of the side effects are significant. For that reason, I would not put a patient on amiodarone solely to control their ventricular response to AF. I think amiodarone is a highly effective drug for AF and it is a first-line therapy in patients with heart failure; but for other patients, it should be a second- or third-line therapy. However, I don't think it should be used purely for rhythm control. I certainly would never leave a patient in permanent AF on amiodarone purely to control the ventricular response. I was surprised when I read the new guidelines

carefully and found that amiodarone can be used as a rate-controlling drug. I don't know if that reflects the fact that this was cowritten by the ESC and that in Europe the threshold for amiodarone use is much lower than in the United States. But certainly my practice, and my impression of the US standard of care, is *not* to use amiodarone as a rate-controlling drug.

The second thing that strikes me is the issue of whether catheter ablation should play a role in the treatment of patients with chronic or permanent AF. I believe it should, but in these guidelines it is not included in the treatment flow sheet for those patients. I think that reflects the relatively small amount of data that we have right now, but that is changing and the data are increasing fairly rapidly. When these guidelines are rewritten 5 years from now, I would expect to see catheter ablation appear as part of the chronic AF treatment strategy.

**Table 1. ACC/AHA/ESC 2006 Guidelines: Risk Factors for Stroke**

Less Validated/Weaker Risk Factors	Moderate Risk Factors	High Risk Factors
Female gender	Age $\geq$ 75 yrs	Previous stroke, TIA, or embolism
Age 65-74 yrs	Hypertension	Mitral stenosis
Coronary artery disease	Heart failure	Prosthetic heart valve
Thyrotoxicosis	LVEF $\leq$ 35%	
	Diabetes mellitus	

LVEF = left ventricular ejection fraction; TIA = transient ischemic attack

**Table 2. ACC/AHA/ESC 2006 Guidelines: Recommended Therapies According to Stroke Risk**

Risk Category	Recommended Therapy
No risk factors	Aspirin, 81-325 mg daily
One moderate risk factor	Aspirin, 81-325 mg daily, or warfarin (INR 2.0-3.0, target 2.5)
Any high risk factor or > 1 moderate risk factor	Warfarin (INR 2.0-3.0, target 2.5)*

\*If mechanical valve, target INR greater than 2.5

INR = international normalized ratio

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