MODERATOR: Hello, I'm Sandeep Jain with the Heart and Vascular Institute at UPMC. I'm presenting an update today. The topic I'm presenting today is contemporary management of atrial fibrillation, rate versus rhythm control. And this is the first in a series of a few different talks dealing with atrial fibrillation. These are my disclosures. I think we all know that atrial fibrillation is the most common abnormal rhythm in the heart. It's characterized by abnormal electrical pathways in the atria, as depicted here. As opposed to the normal sinus node conducting to the AV node in the [INAUDIBLE] system, there is this irregular activity in the top chambers of the atria characterized by P waves normally in sinus rhythm versus an irregular rhythm without clear P waves in the EKG tracing.

This is a supraventricular arrhythmia characterized by chaotic atrial activity resulting in no effective atrial contraction. That then results in irregular and often rapid ventricular response rates. Stasis that results from this predisposes to thrombus in the left atria and then is a cause for potential stroke. If we look at the prevalence of atrial fibrillation, it is a disorder of aging. And as we age, there's a high incidence of atrial fibrillation. It's the most common sustained arrhythmia and some would say even approaching an epidemic in the sense that 1% of those over the age of 60 and 5% of those over the age of 69 have atrial fibrillation. It currently affects up to 5 million Americans. And the prevalence in the general population is 0.5% to 1%.

There's an overall 25% lifetime risk of atrial fibrillation. So it doesn't take much, if we look within our friends and family circle, that it's pretty likely that you know someone who has atrial fibrillation. Why does it matter? Quality of life has clearly been shown to be lower in patients with atrial fibrillation. With an overall lower total functional capacity and lower global life satisfaction. And although we don't think of it this way, the quality of life has been shown to be the same or even worse than those patients who have had an MI or angioplasty. And I would submit that in some cases this is actually more impactful on a day to day basis because this is something patients are living with as opposed to an acute coronary syndrome, where they have an acute event that they recall and may have less impact downstream. The stroke risk is 3 to 5 fold out of the general population. And 15% of strokes that occur in people with atrial fibrillation.

And there is an association with increased all-cause mortality, although this is somewhat controversial even dating back to population studies such as Framingham. The odds ratio is 1.5 to 2 of an increased mortality risk with atrial fibrillation. If we look at the wrist factors for atrial fibrillation, they're listed here. Age, gender, diabetes, hypertension, really any structural heart disease with congestive heart failure or MI or valvular heart disease. If we look at other secondary risk factors or triggers for atrial fibrillation. Hypothyroidism, obesity, sleep apnea, alcohol abuse, severe infections, pulmonary disease, and even anger and hostility have been described to be triggers for atrial fibrillation. I would just highlight that these three that are underlying obesity, sleep apnea, and alcohol abuse, while we used to say these need to be addressed just because it was a healthy thing to do, now there is specific data of treatment of these conditions impacting the outcomes in atrial fibrillation and decreasing atrial fibrillation recurrence rates.

So they are very important in terms of lifestyle modification in our patients with atrial fibrillation and really need to be addressed up front. If we look at the characterization of atrial fibrillation, there are three different types of atrial fibrillation. Paroxysmal atrial fibrillation is AF that converts to sinus rhythm in less than seven days spontaneously. Persistent atrial fibrillation is described in those patients that require us to do something. So that's either an electrical cardioversion or a chemical agent to convert to normal rhythm. If that persistent atrial fibrillation is between 7 days and 12 months, we call it short lasting persistent atrial fibrillation. Versus greater than 12 months, in which it's long lasting or long standing persistent atrial fibrillation.

Permanent atrial fibrillation is really a form of persistent atrial fibrillation in which the patient remains in atrial fibrillation. And we have given up on further attempts to restore sinus rhythm. And this is really nomenclature more than anything else. But patient outcomes have been associated with these different categories and why it's important to know up front what we're dealing with. The three main concerns that occur in atrial fibrillation are thromboembolism and stroke, as described. And there will be a whole series of lectures on this upcoming. Symptoms that we're trying to mitigate, palpitations, chest discomfort, shortness of breath, fatigue, lightheadedness, syncope even, and a wide range of symptoms that patients can present with in atrial fibrillation. And some in the elderly population may have no symptoms at all.

And luckily rare, but extremely important to pick up on is a tachycardia induced cardiomyopathy. So unchecked rapid ventricular response rates essentially whipping the heart and weakening systolic function, resulting in congestive heart failure is a dreaded concern and sequela of atrial fibrillation. Luckily, again, it happens rarely. It's not that uncommon, but important to pick up early because if caught in time, can be fully reversible. The treatment options for these conditions, again, anticoagulation and other options to prevent thromboembolism that you'll hear about in future talks-- medication to control heart rate and restoration of sinus rhythm either through electrical cardioversion, medications, or invasive strategies.

When we look at lifestyle importance in the cascade that results in atrial fibrillation, these other conditions as mentioned, hypertension, age, sleep apnea, really many different conditions that can cause stress inflammation. Alcohol being one of them. All of these result and the end result is atrial fibrosis and enlargement. That then is thought to derail the electrical system of the heart, resulting in atrial fibrillation.

One of the recognized sources of atrial fibrillation is electrical instability in the pulmonary veins. And that's where catheter ablation has been used to treat atrial fibrillation. Again, you'll hear about ablation and other technologies in the next talk. One of the common controversies over many years is, how do you manage patients with atrial fibrillation and how do you decide whether to pursue rate control only versus rhythm control? The purported advantages of each are listed here.

In rate control, avoidance of antiarrhythmic agents with their attendant side effects, as well as reduced need for potentially invasive procedures, cardioversions, admissions to the hospital to enact these therapies are the potential advantages of rate control. In rhythm control, there is the potential advantage of improved cardiac function, improved quality of life, prevention of thromboembolic events-- although not completely proven, there is a signal there-- and it is important, at least today, to realize that the maintenance of sinus rhythm does not necessarily eliminate stroke risk. So that the rhythm you're seeing the patient in the clinic that day does not necessarily tell you that they are without risk if they're in sinus rhythm that day. When they have a history of atrial fibrillation with appropriate CHADS score or other risk stratifying mechanism, they should be treated with anticoagulation.

When we look at the guidelines and how to achieve pharmacologic rate control, class I guidelines are guidelines that are completely indicated and have data that's proven behind it. And rate control with a beta blocker and on dihydrate carotene calcium antagonist is usually the mainstay for initial management of rate control. If there is no pre-excitation, IV beta blocker or a calcium channel blocker can be used in the acute setting. IV digoxin or amiodarone are approved for atrial fibrillation in the setting of congestive heart failure when there is no accessory pathway present. If there are symptoms with activity, then rates should really be monitored and more aggressively treated. Oral digoxin for rate control in patients with atrial fibrillation with CHF or LV dysfunction can also be considered.

When we look at class III recommendations in the guidelines, which are really contraindications or things that should not be done, digoxin should not be used as a sole agent for rate control in paroxysmal atrial fibrillation. It's rarely sufficient enough to provide enough rate control. Catheter ablation of the AV node, which is the ultimate in rate control where a catheter is placed in the AV node and ablation is performed without a prior trial for medical rate control is contraindicated. So clearly medical rate control before jumping to AV node ablation. Decompensated heart failure in atrial fibrillation, in those patients a calcium antagonist is not recommended. Because of its negative [INAUDIBLE]. IV digoxin or a calcium antagonist in patients with atrial fibrillation and pre-excitation is also not recommended because it may accelerate conduction down the accessory pathway and result in dangerous ventricular arrhythmias.

One of the questions I think that's often asked is, what should I target for rate control when I'm choosing a rate control strategy? And how strict should we be in controlling those rates? So the RACE II study, now published over a decade ago in the New England Journal showed lenient versus strict rate control in patients with atrial fibrillation. And studied this in a randomized fashion. And what was targeted were less than 110 beats per minute arrest for lenient rate control, versus strict rate control of less than 80 beats per minute at rest and with exercise less than 110. There was a combined outcome in this study of death from cardiovascular causes, congestive heart failure, stroke, embolism, bleeding, and life threatening arrhythmias. And when we look at this combined event rate, the kaplan-meier survival curve shown here, the cumulative incidence of this primary outcome was really no different in the strict control versus lenient rate control groups. And with a trend of actually worse outcomes in the strict rate control groups.

So based on this data, it's relatively well-accepted that lenient rate control-- again, assuming no symptoms with lenient rate control-- is a reasonable strategy to pursue when the decision has been made to pursue rate control. When we look at-- again, this is taken from the European Society of Cardiology atrial fibrillation guidelines-- how to think about acute heart rate control in atrial fibrillation, I think that it's very reasonable to first dichotomize between low ejection fraction, and preserved ejection fraction. In those with preserved ejection fraction, more choices. Beta blocker or calcium channel blocker. And targeting a heart rate of less than 110. And if you haven't achieved that, consider adding digoxin.

In patients with an ejection fraction that's depressed or signs of congestive heart failure, using a small dose of beta blocker. And if that's not sufficient, amiodarone would be an option. And add digoxin, again, if you haven't achieved adequate rate control. When choosing rhythm control strategy or maintaining sinus rhythm, here are some of our options. DC Cardioversion, which is a sedation procedure. Takes 5 to 10 minutes to do with an external shock to the heart. Extremely effective at achieving sinus rhythm, but no chance or no ability to discern whether you'll maintain sinus rhythm afterwards, which often requires another agent, such as an antiarrhythmic agent to maintain sinus rhythm longer term.

Other options that you'll hear about in the future talks, AF ablation, surgical MAZE, or the hybrid procedure. Again, once a decision is made to pursue rhythm control antiarrhythmics are our classic way of trying to maintain sinus rhythm that have been around for a long time. What I tell all of my patients based on this list here, is any time that we have multiple options for a therapy as we do with all these antiarrhythmic listed here, the downside of this is that none of them are perfect. It means none of them are perfect and we're usually battling side effects. Otherwise we'd just have one or two antiarrhythmics. In general, class I agents are used in structurally normal hearts. And class III agents in potentially abnormal hearts.

And I think it's very important and not lost on any audience that have dealt with antiarrhythmic agents that they can come with side effects. And this is an example where I think it highlights a situation why we need to be very careful about administering antiarrhythmic in patients with atrial fibrillation. It needs to be done in a controlled setting. So this is a patient with 2 to 1 atrial flutter, shown here. With a ventricular response rate of 150 beats per minute. Administered flecainide. And what flecainide will do is it can slow this flutter rate, now allowing the AV node to actually conduct one to one at 200 plus beats per minute. And we've given the patient a problem that's bigger than what they started with while trying to treat atrial fibrillation. So that, for example, any patient treated with an antiarrhythmic such as flecainide should be given an AV nodal agent concomitant to help prevent one to one conduction. Just highlighting one example of where we can get into issues of pro-arrhythmia with antiarrhythmic agents.

If we look at a schematic of the guidelines-- ACCHA and Heart Rhythm Society guidelines for management with atrial fibrillation-- of how to decide what to do for rhythm control, again, similar to the rate control discussion, looking at no structural heart disease versus structural heart disease. And then looking at coronary patients versus heart failure patients and different antiarrhythmic options. Most of those, the class III antiarrhythmics with ablation and amiodarone as an option. In those with no structural heart disease, more options for antiarrhythmic. But in those that fail those, ablation or amiodarone and potentially ablation as first line with some of the newer data you'll hear about later.

I think very important, again, although amiodarone is in the guidelines, often not our first line agent because of the potential long term toxicities. Lung, liver, thyroid, and not ideal, again, for long term use. So now that we know how to manage rate control and rhythm control, how do we decide which one to do? There have been multiple studies over the years of rate versus rhythm control. And I would submit that the jury in some cases is still out. And the fact that atrial fibrillation is not the same in all patients and not all AF is the same that the answer is going to be different and individualized, tailored response is what's needed.

If we look at all the historical studies, now many years old, looking at hard outcomes of death, stroke, total mortality, in the largest study done to date, which is AFFIRM of 4,000 patients randomized to rate versus rhythm control, there has been no significant difference shown thus far. This is the results of the AFFIRM trial, now almost 20 years ago published in the New England Journal. That showed no significant benefit, and if anything, a trend towards worse outcomes in rhythm control in these 4,000 patients randomized to rate versus rhythm control.

So let's look a little deeper at some of these studies and specifically AFFIRM that said, well, rate control is good enough. How well did we really achieve rhythm control? This was an intention to treat analysis and, if you look at it carefully, in the rhythm control group we were only able to achieve rhythm control in 60% of the patients. In the rate control group, without even trying those patients converted to sinus rhythm in a 1/3 or more of the time. So when we're comparing these groups, we're not comparing sinus rhythm versus atrial fibrillation. We're comparing a strategy to manage and we didn't have a very good management strategy with the antiarrhythmic available at that time to maintain sinus rhythm.

So what if we took patients in AFFIRM a little differently? So what if we added up all the patients in sinus rhythm at the end of the study and put them in one category. And compared those to all the patients in atrial fibrillation regardless of what treatment strategy they were assigned. So this would be what you consider on treatment analysis. If you look at that, there's actually a 47% reduction in mortality in the sinus rhythm group. So, again, we have to be very careful about reaching too far in terms of conclusions on these type of post hoc analyses.

But when the signal is so large and you have half the mortality in the group that maintains sinus rhythm, I think you have to ask, well, why is that? Why are those patients less likely to die when they're in sinus rhythm? Is it because we had a toxic effect and really poor efficacy of antiarrhythmics? Or is it really just that the ability to maintain sinus rhythm is a marker of less serious disease? So that those that we couldn't maintain sinus rhythm, regardless of their treatment strategy, are they just sicker patients and did poorly? And I think it's likely a combination of both of these effects that we don't have-- for this study, did not have and still don't have-- the perfect way of maintaining sinus rhythm.

And if we did, would the outcomes be different? I think it's important to highlight that these studies are in persistent atrial fibrillation not paroxysmal. So the young 45-year-old or 55-year-old with paroxysmal atrial fibrillation who is a highly symptomatic was not included in AFFIRM or these other studies listed. The population was basically an asymptomatic patient once you achieve rate control. It's not the patient who's highly symptomatic. And it's important to note that. Because those patients usually move on to rhythm control earlier in their disease state.

So with AFFIRM now almost 20 years ago, I think there was a big push to state, appropriately so, that rate control may be good enough in most patients with atrial fibrillation. Especially if they're asymptomatic and have persistent atrial fibrillation. More recently, just last year in 2020, there was the East AFNET 4 study published in the New England Journal, which is a European cohort of early rhythm control strategy in patients with atrial fibrillation. And what they said is, well, what if we take patients who are earlier in their disease process-- less than one year of with diagnosis of atrial fibrillation-- and randomize them to rate versus rhythm control now that, 20 years later, we have other strategies such as catheter ablation that we think is better at maintaining sinus rhythm and potentially less toxic effect of those antiarrhythmics. The outcomes in this study were a combined outcome of cardiovascular death, heart failure, or acute coronary syndrome and hospitalizations. There were 2,789 patients randomized at 135 centers, so broad applicability with long term follow up of a median of five years of follow up.

And again, this composite outcome, as mentioned in the kaplan-meier survival curve of cumulative incidence of the primary outcome, early rhythm control fared better than usual care with rate control. The number of days those patients spend in the hospital were no different in terms of procedures and rhythm control strategies. With antiarrhythmics one might think more hospitalisations. Safety outcomes in terms of arrhythmia from antiarrhythmic is also equal. When we look at the division or subgroups of what comprise that primary outcome that we see here with a 0.79 hazard ratio, death and stroke showed a significant improvement. Whereas hospitalization for heart failure or coronary syndrome, there were trends. So that each of the subgroups in the primary outcome showed at least a trend in the right direction, favoring early rhythm control.

The secondary primary outcome of nights spent in the hospital, as mentioned before, about five days here. Which were no different in each group. So when we take all of this data, how do we start thinking about how to decide rate versus rhythm control? I think that rhythm control is preferable in a first time diagnosis of atrial fibrillation or this early AF. Concomitant congestive heart failure modulated by atrial fibrillation likely deserves a trial for rhythm control. And those that are symptomatic despite adequate rate control should be considered for a rhythm control strategy.

Young patients to avoid long term remodeling, there's more and more data that this is a group that should be considered for rhythm control. And patients that you think have a reversible cause. A one time post-op, atrial fibrillation or thyrotoxicosis or holiday heart with alcohol should likely be considered for an initial rhythm control strategy. Rate control is probably preferred in older patients with comorbid conditions that have no symptoms. So that if their rate control, no symptoms, and their heart function is normal, not unreasonable to pursue rate control. Those that have recurrent atrial fibrillation that you're struggling to maintain sinus rhythm or those who have failed antiarrhythmic circulation and again, those with significant structural heart disease with a large left atrial size, rate control may be the only strategy that we're able to achieve adequate control of the rates. Because we're not able to achieve rhythm control.

And I'll sum up a lot of what we've discussed with what I think is underappreciated or under emphasized in terms of atrial fibrillation. We've discussed management once a patient has atrial fibrillation. But those lifestyle factors that were discussed-- obesity, alcohol use, sleep apnea-- have really been shown now to play a major impact. This is a study the AF- Arrest trial in performed in Australia where patients who were undergoing ablation, so they're already destined and decided to undergo ablation, and after ablation they were told they were randomized. So one group being told lose weight, exercise regularly, and watch your diet. The other aggressively were manage with risk factor modification with trainers, dieticians, and they had almost a doubling of the improvement of maintaining sinus rhythm. And this is after an ablation. So that even the ablation outcome was modulated by lifestyle modifications.

And I think this is very important in terms of what we tell our patients and early on the education that they need to receive about atrial fibrillation management in terms of these risk factors. And this is why at UPMC we have a dedicated center for atrial fibrillation with the goal of diminishing the prevalence of undiagnosed atrial fibrillation and mitigating the downstream sequelae such as stroke and heart failure to try and reach as many affected patients as possible early in their disease course. Because we know that patients managed earlier do better with this type of care. And really provide the expertise to all of the potential options for treatment at our HBI sites.

This involves an initial educational and, if you will, a triage session visit often through a physician extender, coordinated care between electrophysiology and cardiac surgery to provide cutting edge technology such as catheter ablation, appendage ligation, a MAZE procedure that you'll hear about in the future talks. We offer a 24/7 consult service with the Center for Atrial Fibrillation with quick turnaround time appointments. This has been piloted at [INAUDIBLE] and in the Oakland and Pittsburgh area to have triage so that many avoidable admissions when we know that a patient can be followed up in short order. Especially if they can be prescribed, for example, a doac in the ER or in the PCP's office with close patient follow up in our Center for Artial Fibrillation.

And the real focus of this is patient education to promote disease literacy. So that they can take charge of their own care in these modifiable risk factors. They all go home with specific patient educational packets that outline what's atrial fibrillation as well as a risk score for their CHADS score and stroke risk. This is the contact information for atrial fibrillation. And again, thank you for joining this virtual continuing education series for the Heart and Vascular Institute update.