AHA COVID-19 Clinical Guidance Series
Arrhythmias

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Speaker 1:

Welcome and thank you for joining us for this podcast brought to you by the American Heart Association. This podcast is part of a series focused on sharing information with healthcare providers who are caring for patients during the COVID-19 pandemic.

Jeanne E. Poole:

Hello, welcome to our podcast today. This is Jeanne Poole, Section Head of Electrophysiology at the University of Washington. This is your power byte of what you will learn today. We have covered three topics that are very important, the first of which is, what is the real risk of cardiovascular disease in COVID-19, with a special look at arrhythmia risk. It appears to be overall low, but it's not zero and we yet need to better understand why these arrhythmias occur? Whether or not they're directly related to the effects of the virus, combination with the fact that many of these patients have cardiovascular disease? And then, how can we safely use medications once they are proven and shown in randomized trials to be beneficial to patients? How can we provide those medications safely to patients who may be at a risk for QT prolongation or other cardiovascular toxicity?

Jeanne E. Poole:

Welcome to this podcast today discussing the risk of arrhythmias in COVID-19, and I'm joined today by Mina Chung from the Cleveland Clinic who is Professor of Medicine in the Division of Cardiology and the Section of Pacing and Electrophysiology and Dr. DJ Lakkireddy, who is Medical Director for the Kansas

City Heart Rhythm Institute. So we wanted to talk a little bit amongst ourselves and think a bit about the problem of arrhythmias in the COVID-19 disease process.

Jeanne E. Poole:

Certainly, we were perhaps surprised that this has risen to such a visible concern. Early in the reports coming out of China, however, the Chinese were already stating that a significant proportion of patients up to 16 plus percent of patients were manifesting arrhythmias. And so, to understand better why this was, further reviews of those patients revealed that commonly troponin was increased, or in rare cases patients were having myocarditis. But it raised the concern that we might be actually dealing with significant cardiovascular events.

Jeanne E. Poole:

So when you think about why that might be, specifically in terms of arrhythmias, I think about the fact that it could be due to the virus itself. We don't know that much yet, but we're learning more and more. There may be a direct effect of COVID-19 on being cardiotoxic or perhaps from its endothelial and cytokine storm effects.

Jeanne E. Poole:

It also could well be due to the fact that a lot of these patients have high risk for cardiovascular disease and the presence of COVID-19 puts an extra cardiometabolic demand on these patients, that then could worsen their underlying cardiac disease and therefore, result in arrhythmias, both ventricular as well as atrial arrhythmias. And then I think the third issue really has to do with the potential for iatrogenic arrhythmogenesis from the use of drugs that might be cardiotoxic or pro-arrhythmic. So I wanted to turn to my colleagues now and see what they might have to shed light on in terms of thinking about the potential arrhythmic risks of COVID-19. Mina, you've been looking at this a lot, lately reviewing some of the literature, what are your thoughts about why we might be seeing arrhythmias and what's been your experience?

Mina Chung:

Well, I think, Jeanne you've really summarized it well because there's an incidence of myocarditis, but also cytokine storm and there's a lot of research done on the impact of various cytokines and reduction of cardiac function and heart failure. So those kinds of events with just developing heart failure from the cytokine storm or direct viral invasion or myocarditis can certainly lead to arrhythmias of all sorts, atrial arrhythmias, as you said, and ventricular arrhythmias. And actually that initial report from China said that of people requiring an ICU, 44% had some sort of an arrhythmia. So I think it's multifactorial.

Mina Chung:

And the other thing that had been concerning, especially early on, were these reports of people who had been semi-stable and then would suddenly decompensate. So there's also the issue with that as of whether or not there's some neurotropism to this virus. There are ACE2 receptors in the brain. ACE2 happens to be the receptor by which the spike protein on COVID-19 enters host's cells. So people have speculated that perhaps some of the late manifestations might have something to do with invasion of the brain and decrease respiratory drive and apnea and respiratory arrest and secondary arrhythmias. I don't know DJ or Jeanne, if you've seen any of that. I know Jeanne you're in a higher incidence area than we are in Ohio. So that might be.-

DJ Lakkireddy:

So, Mina, thank you. I think all of the mechanisms that you have outlined probably make sense. Some of our experience, we are putting out a large series of ventricular arrhythmia experience during the COVID time period with multiple institutions from the United States and Italy participating. We found that there was a general increase in incidence of arrhythmia. So we pooled all the patients who had COVID or suspected COVID PY status that came to the hospital with either ICD shocks and monomorphic nonsustained VTs and PVCs. If you really tease out the data, what is very interesting is the patients who have COVID positive status, presenting with cardiac arrhythmias, are the ones that do have a significantly higher level of troponins being positive. So just enough involvement of the myocardium to a much greater degree, whether it is direct myocardial injury and the cell necrosis or if it is microscopic capillary thrombosis induced by the COVID infection.

DJ Lakkireddy:

You do find a significant amount of troponin bump in these patients. And what's incredible about this is that you're not going to see monomorphic VTs in this case. What are you going to see is mostly PVCs, nonsustained VTs, torsades, via RS interval type of a thing. But interestingly, mortality in these patients is primarily due to electromechanical dissociation and primary pump failure rather than ventricular arrhythmias. And then, we saw this other category of patients who all presented to the hospitals with ventricular tachycardia storms, VT storms, and most of these patients actually are known ICD patients who have a preexisting cardiomyopathy. And we were worried that all of these patients had COVID-19. So we treated them as PIs (primary immunodeficiency) , we isolated them. And then the tests come back to be negative, but all these patients have VT storms. I mean, you would be surprised that amongst all these hospitals, we have close to 40 plus VT ablations that were done during the COVID era, clearly suggesting that maybe the environmental stress or the physical stress of the COVID pandemic itself has resulted in VT exacerbations in these patients, which we ended up ablating and taking care of.

DJ Lakkireddy:

So I think there is a clear cut dichotomy in the way these ventricular arrhythmias present. Depending on whether they are truly affected by COVID versus than they are in a COVID environment, but they are really not infected by the COVID virus. So I think there's a difference in how we should differentiate these people.

Jeanne E. Poole:

Mm-hmm (affirmative). Well it's interesting in Seattle, we've seen what you've described. However, the frequency is actually quite low, at least what we think right now. I think time will better show us as we start to collect more data, especially on patients who are being discharged from the hospital, but we've seen all of what you've mentioned. We've had patients with atrial arrhythmias, frequent PVCs, very rarely patients with ventricular tachyarrhythmias. We've seen patients who probably fit into that latter category that you were talking about DJ in the COVID environment. Although in a few cases, patients have subsequently tested positive for COVID, but they clearly had an underlying primary cardiac event. And that makes you wonder about the interplay between COVID-19 and their underlying cardiovascular disease.

Jeanne E. Poole:

When you look at some of the data that has come out of both New York, as well as Italy and their sudden death rates that are remarkably higher in this year, this COVID-19 experience, a timeframe

compared to the year before. It'll be really interesting and very important to understand a lot more about those patients and whether or not the cardiac arrests were due to something like what I just described that interplay between COVID-19 and underlying cardiovascular disease. Is it because patients had delayed presentation to the hospitals because they were afraid to ask for medical help in the standard way? So there's a lot yet to be learned, but I would say that over all the arrhythmia risk in patients hospitalized with COVID-19 has been relatively low in the Seattle experience.

Mina Chung:

I'm curious, have you seen bradyarrhythmias in AV block? I've heard that reported as well.

Jeanne E. Poole:

We have had very little that's been documented. What I would say is that we are mostly looking at those kinds of events in the University of Washington system of hospitals. And so that doesn't reflect necessarily the experience of some of the other Seattle and Seattle metropolitan area hospitals.

DJ Lakkireddy:

Perhaps the global survey of electrophysiologists across the world on the arrhythmia experience has been quite in line with what you said, Jeanne. So I think atrial fibrillation and atrial arrhythmias are relatively common that's to be expected when people have severe lung disease, the RDS (respiratory distress syndrome) type of scenario. And then PVCs followed by nonsustained ventricular tachycardia I think are also relatively common and primary pump failure and EMD interestingly was a lot higher than what you would anticipate in a typical wide syndrome. So I think that's something that's very unique about Corona.

Jeanne E. Poole:

Yeah. I think this issue of patients who recover from their respiratory illness and are discharged home and then have sudden cardiac death is very disturbing. And as you've mentioned, in cases where monitoring, or there's first response rhythms that have been available, it may not be to a ventricular tachyarrhythmia. Well, Mina, what about the potential for iatrogenic arrhythmias and the havoc that we might cause in trying to help patients. This has certainly been a intense area of focus with quite a few reports coming out of literature now about the use of hydroxychloroquine, chloroquine, and azithromycin.

Mina Chung:

Yeah, certainly those three drugs can prolong the QT, especially when used in combination, commonly hydroxychloroquine, and azithromycin, there are some other QT prolonging drugs that are used as well. Antivirals, lopinavir/ritonavir, tocilizumab and using fingolimod. But, mostly I think what people have been getting is hydroxychloroquine, plus/minus azithromycin. Now, whether or not those are effective or not, we're still waiting to see, may or may not be. But, we do have some experience where Larry Epstein and Moussa Saleh published their New York City experience in *Circulation AE* (Arrhythmia and Electrophysiology) recently. And they had 200 patients and actually showed that yes, QTC can go up, but they had no cases of torsades. These are people who, if you're in the hospital, you would be watching either with telemetry or some other means of QT.

Mina Chung:

And so there's some opportunity there to hold the medication. And in some cases they even use lidocaine to shorten. But clearly if you had the combination use of hydroxychloroquine, or chloroquine with azithromycin they had more QTC prolongation. But, I think in general, the use of hydroxychloroquine and chloroquine has been pretty widespread for malaria and been used presumably safely. But I think in these sick people and in conjunction with azithromycin, we have to be a little careful. The criteria for what to do when they're on it, such as with, how often do you check EKGs or monitoring. Those are issues in this time, because you want to minimize exposure of personnel and you have issues with contamination of your equipment. Some people have been using telemetry and adapting telemetry leads to be able to read QTCs and change in QTCs and some regions where COVID-19 has been overwhelming and you run out of telemetry space. Some of the MCOT (mobile cardiac outpatient telemetry) devices have been used as well.

Jeanne E. Poole:

Okay. Let me ask you about the specific issue of how do you monitor patients safely? I'm speaking on inpatients now who are being treated with these medications, that became quite a huge issue for us in our hospitals. In terms of what EP (electrophysiologists) could recommend and assist the teams taking care of these patients, who were of course, very concerned about anything that would add exposure between the staff and the patients. So maybe you can let us know what your approach to this has been.

DJ Lakkireddy:

So, I think avoiding doing EKGs on patients. If you don't have to do one, I think it's very reasonable. What we have done within the Health CA system. And also the Kansas City Heart Rhythm Institute, is if patients QT interval need to be monitored and they are COVID positive. And you really wanted to minimize exposure to these people. Then we have used the telemetry leads and when occasionally we have had scenarios where the patients actually had the KardiaMobile app already on their phones. So we actually were able to use the patient's phone to record those in a couple of cases. Even though it was an interesting way to do it. But I think the telemetry data is good enough to give us... It's not the perfect QTC interval that you could measure, but I think you could get by with it, given the situation.

DJ Lakkireddy:

I think to me at this point, there has been a lot of hype about this rather than a true concern. I think that was primarily driven by some very early reports of, "Oh my God, there is going to be 30 plus percent of the people who are going to have bad ventricular arrhythmias," But in the reality seemed to be quite the contrary. So, having grown up in a tropical country like India, we used to give out chloroquine to people left and right, right, so. And I haven't seen anybody drop dead because of torsades or other arrhythmias. So that really makes you wonder if there are geographic and genetic differences in how people respond to chloroquine that I think has to be taken into consideration. Perhaps a lot of these patients that we're trying to put hydroxychloroquine on and chloroquine on are very sick, they have a very high comorbidity profile or renal function, hypoxia, electrolyte abnormalities. I think that picture is completely different than what we see in a routine outpatient prescription of a normal, younger people that we're prescribing hydroxychloroquine to, connective tissue disorder, or malarial prophylaxis or therapy. Right? So I think all of those points need to be taken note of.

Jeanne E. Poole:

Yeah. I think you've made some really important points. I agree. I think that the fact that it's been used safely in otherwise healthy people, maybe it doesn't help us so much with COVID-19. This is a different

situation. These are patients with high cardiovascular risk, but the data nevertheless is interesting that torsades has not actually been seen. QT prolongation, yes. Especially when you combined hydroxychloroquine plus azithromycin. I think that was something that clearly came out of some of these recent articles, including the one from NYU, and that the QT can stay prolonged for a few days, that's not surprising because of the half life. So, Mina what's your take from this in terms of, what do you think is the best way to think about this risk? And what should we be considering if hydroxychloroquine... well it is it is being used a lot in outpatients, we just don't have the same kind of data as we do from the inpatients. But how do you think this should be approached?

Mina Chung:

Well, first of all, there are still a lot of issues about whether or not hydroxychloroquine, and azithromycin are effective. So if you're in a center like our center and the patients qualify for a clinical trial then actually the FDA said that we shouldn't be giving them hydroxychloroquine, that they should be in the clinical trial if they qualify for it. So I think there's still equipoise at this point, and we really need more data on whether or not to even use it. And if you have somebody who has a prolonged QTC over 500 or 550 milliseconds, or whatever your cutoff is with prolonged QRS or pacing or that kind of thing, then you have to really think long and hard about the risk benefit ratio. If they're on a monitor, it really is very regionally dependent in some cases, depending on what your resources are for monitoring. And I think if you are going to use it and you're concerned about what the baseline QTC is then by all means get the EKG at baseline. You can consider getting an EKG after a couple of doses or just using telemetry. And I think, one of the big unknowns is what about the outpatients, right? And should we be monitoring them in some form? And that is-

Jeanne E. Poole:

No, I agree it's critical because you know, it is being used out there. We are at the University of Washington. Well, not me, the infectious disease folks are leading the outpatient hydroxychloroquine and the combination of hydroxy plus azithromycin, it's a placebo control trial. That's sponsored by the Gates Foundation and those patients are all being monitored. So I think that... I agree with you. I think that having the randomized clinical trials is what's most important. And I do think that there's also a take home message in general from having gone through this experience, which is that, patients receiving QT prolonging drugs need to be considered carefully, need to look at the other medications that they're taking.

Jeanne E. Poole:

And, this hopefully we'll highlight that for people who maybe don't always think about the patient's antidepressant medication or antipsychotic medication, or all these other medications that can prolong the QT interval, that really safety has to be the first concern for patients.

Jeanne E. Poole:

Well, I'd like to change topics a little bit, because as electrophysiologists, we've had a little bit of a surreal experience over the last several months in terms of how do we manage our patients? How do we take care of them? How do we get them into the electric physiology laboratory? And I know that both of you are involved in the COVID-19 Task Force. That is a consensus between the major scientific organizations. And so I'd like to hear what your thoughts are on, how do we get back to normal? What are the positions that we should implicate in terms of continuing to think about safety, yet, be able to provide our patients with their necessary services. DJ, do you want to lead off on that?

DJ Lakkireddy:

Yeah absolutely, Jeanne. So I think it's a very important question that I think everybody have started asking. We were quick to respond to this pandemic and shut down anything that is non-essential so that we can protect our patients and protect our healthcare personnel and conserve resources for what we have been going through. But then again, to your point, the world just cannot shut out forever. And we have to figure out a way of how to rise from the ashes if you may want to call it, and how do we do that, right? So I think the way I look at this is we've got to really have a better sense of understanding of the severity of the disease burden in that geographic area... Any geographic area, that one lives in. And you've got to really figure out, is this a higher prevalence and incidence area, or is it a medium prevalence and incidence or a low prevalence and incidence.

DJ Lakkireddy:

And that would give you a ground level of understanding of how the disease process is going to really impact operationally and what you intend to do. Then the second part to this puzzle is does your facility have adequate resources to really deal with not only deal with the ongoing COVID crisis, but have the ability to really create a microcosm of relative COVID, safe environment in terms of the lab space or the PPEs or other resources that this intense process is going to require. And then the third and the most important of all of this is our capabilities for testing, right? That was the biggest bottleneck that we faced in the United States compared to countries like South Korea or Taiwan, or Singapore, for that matter. They're all relatively smaller countries, so they can do a lot of these things a lot faster than us.

DJ Lakkireddy:

And they have been a shining example of how they have effectively leveraged aggressive testing in order to resume life back to near normal. And do we have those capabilities here? I think we have done a reasonably good job in wrapping up our supply chain. But I think a lot of times there's a significant amount of discrepancy in access to the testing in different places. So one has to be able to test the patients. What kind of testing are you able to offer to people? Can you get a PCR test on everybody or what you have is only a serologic testing? And so understanding the limitations of both the PCR testing and the serologic testing, interpreting it, and how do you really apply it to both your healthcare teams and patients as you slowly bring them back into the fold? I think it's an important question that one has to keep on mind.

DJ Lakkireddy:

And then the fourth one is creating a nice process with effective communication at all levels, starting from the healthcare teams to the administrators, to the community in general, and then the patients and creating this care continuum that is effective. I think is going to really play a role in that. So if we take these basic principles and apply them to create your own reboot program at each institution, and applying the general guidelines from CDC, regional, statewide and your institutional policies along with it. I think would be able to help anybody to recreate a safe pathway. So that's kind of what I think people should do.

Jeanne E. Poole:

Mina do you have any thoughts on this?

Mina Chung:

Yeah. I think, first of all, as we all are facing opening up. We have to be agile and be able to model and follow incidence, look at testing. In order to see whether or not this is causing a second wave. And, that could be just as devastating to then have to re-close down again. So I think it's important to have the capacity to do the analytics. To be able to figure out where you are in terms of your PPE, your resources, out. Because it's possible that we could be opening up and then have to shut down again. We have to increase the confidence of our patients to come back. And I have to say that here in our hospital we have hand sanitizer everywhere. Everybody is wearing a mask. We have cloth masks, we've instituted that.

Mina Chung:

And so, DJ's point about a relative COVID safe area, for bringing people in, everybody coming in for procedures, cardioversions, or otherwise, even a stress echo, they're being told they have to get tested ahead of time. We've been lucky to have the capacity to ramp up to be able to do that. So we've started that and we'll probably start routinely in sampling healthcare workers and the population. So there are a lot of pieces to this reboot and hopefully we can avoid second waves. A lot of it, we are going to depend on our regional state leadership as they hopefully ramp up slowly, so we can watch to see what the effect is.

Mina Chung:

But, I think the other thing is perhaps hasn't been talked about as much is contact tracing. One of the things that other countries have done better than us is really institute contact tracing using cell phones and that kind of technology. And it can be done with privacy in mind. And, to at least let you know, if you got near somebody who was COVID positive, that could affect things. So hopefully we'll see more of that come to pass.

Jeanne E. Poole:

Well, the principles very much are the same as what the entire country and world for that matter are talking about in terms of being able to open up the economy and people getting back to work safely. In our cases, it's not only keeping the staff and workers safe, but very importantly, keeping our patients safe. And as you both mentioned, providing them an environment that they feel safe to come to. Because again, we don't want to have patients who are not getting care in a timely fashion and it ends up causing them to have a greater burden of disease or have any declination in their cardiac status. So all of these issues that you all have outlined in the reboot are really very important and it would be very helpful to have that in a nice way that the rest of us can refer to and see how we can apply to our own situations. So, any final thoughts from any of you on any of the topics that we've talked about today?

Mina Chung:

I want to thank DJ for leading the way in terms of these documents coming out. In terms of as we ramped down and he really took the lead for that document and also on rebooting.

Jeanne E. Poole:

Yes, I thank you also, DJ. In that case, I would like to hear if you have any final thoughts or further wisdom for the audience?

DJ Lakkireddy:

No, I think thank you both for being such an amazing part of the heart rhythm team in your respective institutions and what you've contributed to the scientific world and all the support that I've gotten from you both in getting these documents out. I think we've got to keep pushing the envelope. We have to explore the processes in place. We've got to push our administrators to really provide us access to aggressive testing. I think that is something that has to happen. And if there is an agenda item on our list, when we sit down with our administrative counterparts, that is something that we've got to make happen. I think that would really change the equation in a big way. And once we identify more of these patients, we can isolate them better and then we can probably slowly try to shut it out, over the next few months. So, thank you for the opportunity to be here and sharing these discussions with you both.

Mina Chung:

Thank you.

Jeanne E. Poole:

Thank you. And then finally, how do we get back to work? And I think that both Mina and DJ have summed this up very nicely. It's really going to be dependent upon our ability again, to provide a safe environment through testing, protecting ourselves, the staff, and protecting our patients from the risk of COVID-19 infection. Thank you for joining us today. We invite you all to share this podcast with your colleagues and others who you believe would benefit. Please stay safe.

Speaker 1:

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