# AHA COVID-19 Clinical Guidance Series Diabetes

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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.

## Dr. Jonathan Newman:

I'm Dr. Jonathan Newman, the Eugene Braunwald assistant professor of medicine and cardiology at the Leon H. Charney Division of Cardiology and the Center for the Prevention of Cardiovascular Disease at New York University, Grossman School of Medicine. I'm joined by my colleague, Dr. Lee-Shing Chang from Brigham and Women's Hospital an associate professor and endocrinologist. Through this podcast, we will be discussing and you will get information on the following power bites in this podcast.

# Dr. Jonathan Newman:

COVID-19 is a high-risk, rapidly evolving medical crisis. For you to know, COVID-19 symptoms include fever in a high percentage, 80 to 90% of individuals, a cough in 50 to 80% of people, fatigue, loss of appetite and shortness of breath are also very common. More severe symptoms of COVID-19, that should lead you to seek medical care, include gasping for air, having blue colored lips or face, severe or constant chest pain or pressure, or constant dizziness, or lightheadedness.

## Dr. Jonathan Newman:

As we will review in this podcast patients with diabetes, with or without known heart disease are at increased risk of severe COVID-19 or complications from COVID-19. And many patients with diabetes take medications to control their blood pressure and cholesterol. These medications, by and large, should be continued during COVID-19. However, if you have COVID-19 or symptoms of COVID-19, you may need to stop or reduce the dose of some of your diabetes medications. And it's very important that you discuss this with your doctor or your healthcare provider.

#### Dr. Jonathan Newman:

Hi, welcome to this podcast on diabetes, cardiovascular risks, and COVID-19. I'm joined here today by my colleague, Dr. Lee-Shing Chang from Brigham and Women's Hospital, Lee-Shing.

## Dr. Lee-Shing Chang:

Hi, my name's Lee-Shing Chang. I'm an associate physician at Brigham and Women's Hospital in the division of endocrinology and diabetes. And I'm an instructor of medicine at Harvard Medical School as well.

## Dr. Jonathan Newman:

Terrific. It's a pleasure to be here with you today and Dr. Chang and I are going to discuss some of the relevant issues about COVID-19 and cardiovascular risks for patients with diabetes. And there's a lot for us to cover, so why don't we jump right in?

# Dr. Lee-Shing Chang:

Dr. Neiman, maybe I'll start by asking you, are patients with diabetes more likely to be hospitalized with COVID-19?

#### Dr. Jonathan Newman:

So, that's a great question. I think the data we have from this rapidly evolving situation suggest that there are almost overlapping pandemics or burdens of disease, in that patients or individuals with high blood pressure, who are overweight or obese, are over 65 years of age with diabetes or heart disease, are common risk factors that are present among people hospitalized with COVID-19. So, this early data in the US and in other countries suggest that diabetes is one of the common risk factors for a severe health response to COVID-19. Broadly defined as, needing to be in the hospital or to be in the intensive care unit, or worse, needing more intensive care or even dying from COVID-19.

## Dr. Lee-Shing Chang:

And Dr. Newman, what other conditions or risk factors are associated with COVID-19?

## Dr. Jonathan Newman:

So, touched on this a little bit, but a lot of the other, what we think of as traditional risk factors for heart disease, such as high blood pressure, obesity, prior heart disease, have really in multiple populations and older age, being over age 65 to 70, seem to be the populations that are most at risk for significant COVID-19 illness, needing to be hospitalized or receive more intensive care with COVID-19.

# Dr. Lee-Shing Chang:

And focusing specifically on patients with diabetes, do we know why patients with diabetes are more likely to be sick or at risk of more severe illness with COVID-19?

#### Dr. Jonathan Newman:

Yeah. That's a really interesting question, and we don't yet know exactly why. We certainly know that there is overlapping pathology between the sort of twin pandemics of diabetes and COVID-19, that patients with diabetes who have poorly controlled blood glucose may be more susceptible to infections,

or if they have infections, they may tend to have more complications, more severe infections if they do get an infection to begin with.

#### Dr. Jonathan Newman:

And we know that patients with diabetes, depending on severity and duration of their diabetes, can be relatively immuno-suppressed in a way, and have greater markers of inflammation or systemic inflammatory responses, along with increased levels of coagulation or blood clotting. That may be more of a background or a predisposition to severe illness if they are infected, if they do progress with COVID-19, if they do have COVID-19 illness. So, that's a really interesting question and area that I don't think we fully understand yet.

# Dr. Lee-Shing Chang:

Shifting gears a bit, Dr. Newman, I'd like to talk a bit about medications and use of medications with diabetes and cardiovascular disease, or increased risk for cardiovascular disease, in the setting of COVID-19. To start with, we know many patients with diabetes take medications to help control blood pressure or to protect their kidneys. Do we know anything about these medications and their use in the setting of COVID-19?

#### Dr. Jonathan Newman:

So, that's another great question. There's been a lot of concern about medication use for patients at risk for, or with COVID-19 illness. And it's been recognized that the virus, the SARS coronavirus 2, interfaces with a part of the system in the physiologic system called the Renin-angiotensin-aldosterone system, that is involved with blood pressure regulation and neural hormonal response and control the blood pressure, that the SARS virus uses a specific protein of this pathway to access cells, and cells of the lungs in particular, for infection. Certain medications, called ACE inhibitors or angiotensin-converting enzyme inhibitors, or angiotensin receptor blocker type twos, ARBs, interact with levels of this receptor.

#### Dr. Jonathan Newman:

And there was concern that these agents may either potentiate infection, or increase risk of infection, or progression of infection, or potentially even be protective. But I can tell you now that the totality of current evidence, including some work that we're doing here at NYU, and I'm sure that's ongoing at other institutions, suggest that this is not the case and that these medications, these class of medications, like ACE inhibitors for blood pressure, or for protecting the kidney for people with diabetes, they have well-established benefits for diabetes. And that statements from the American Heart Association, the American College of Cardiology and others recommend continuing these medications, the RAAS inhibitors like ACE inhibitors and ARBs, in the COVID-19 pandemic. But we recognize that we need to know more about what's going on and potential medication interactions. But as of now, I would say that the consensus is to continue these medications during this ongoing pandemic.

# Dr. Lee-Shing Chang:

Great, thanks Dr. Newman, I think this is a very hot area of research that we're looking into currently, overall, and it's very helpful to know that as far as we know currently, there's no contraindication to using RAAS or renin-angiotensin-aldosterone system inhibitors in the setting of COVID-19, as far as we currently know.

#### Dr. Jonathan Newman:

Yes. I agree, as far as we know right now.

## Dr. Lee-Shing Chang:

What about other medications that we use to lower heart disease risk in diabetes such as statins? Is there anything we should know about using statins in the setting of people with diabetes and COVID-19?

#### Dr. Jonathan Newman:

Yeah. It's another really interesting issue and as you know, the use of statins is really foundational for management of people with diabetes and lowering cholesterol, whether or not you've already had established heart disease or established cardiovascular disease, system-wide. There's very limited data that statins may, in fact, be protective for viral infections or bacterial respiratory infections, regardless of your diabetes status. But the data is very limited, but I think more conclusively is that there's no signal of harm, meaning as a potential person with diabetes, with or without a history of heart disease, statins are very beneficial over the long-term to reduce your risk of vascular complications. And they don't appear to increase your risk at all for any respiratory or viral infections, COVID-19 related or otherwise.

#### Dr. Jonathan Newman:

So, that's another clear one, clear medication that we really should continue and continue to monitor, but certainly to continue during this burden of COVID-19 illness. I would also add that, as you know, there's a potential for anti-inflammatory properties of statins that may give some other benefit for COVID-19 or other infectious etiologies. But again, we don't have clear evidence to suggest that there's an additional benefit, but certainly no risk of continuing these medications currently. Maybe I can start to ask you some questions, Lee-Shing, as I know you're really an expert in a lot of the use of glucose lowering medications for our patients with diabetes.

#### Dr. Jonathan Newman:

As you asked initially, that we know that glucose control may be important in reducing the likelihood of infection severity. What do we know about using medications to control glucose for patients with diabetes in the setting of COVID-19? Is there anything you can tell us about things we should be aware of that providers and patients should think of as they continue to care for their patients?

## Dr. Lee-Shing Chang:

Sure, Jonathan, I think this is an important and very relevant question, as many people with diabetes and COVID-19 are going to require adjustments to their diabetes medications, should they contract and have to deal with COVID-19. As you know, generally, oral glucose lowering medications should be held in most patients who have any sort of prolonged poor oral intake and acute illness. So, in particular, metformin is contraindicated in patients with impaired or compromised renal function, or with hemodynamic instability due to the increased risk of lactic acidosis. Also, sulfonylureas, which many patients with diabetes are on, can cause hypoglycemia in patients with poor oral intake as well. And in many cases in the setting of acute illness, decreased oral intake should be held.

# Dr. Lee-Shing Chang:

I think, a particularly relevant area for us to talk about is SGLT2 inhibitors and GLP-1 receptor agonists, because many patients with diabetes and knowing their increased cardiovascular risk are taking these

medication classes, given the recent robust evidence from cardiovascular and renal outcome trials and increasing guidance from the AHA and other professional societies to use these agents, given their known benefits with these population over the past several years.

# Dr. Lee-Shing Chang:

So, regarding SGLT2 inhibitors, in particular, I've been counseling patients in particular to hold them [inaudible 00:13:33] in the setting of acute illness and decreased oral intake, as they can cause ketosis and a risk of dehydration or volume depletion. In particular, SGLT2 inhibitor use in certain settings has been associated, rarely, but there's a known association with diabetic ketoacidosis or DKA in some cases of acute illness or surgery. And, interestingly, this can occur at uncharacteristically mild to moderate levels of hyperglycemia. Sometimes we call it euglycemic DKA because it's not the type of high glucose levels above 500, or so, that we're used to seeing. Sometimes it's more like glucose levels, even in the 200s or 250s, and we're still seeing frank DKA. I know in our hospital, even over the past two weeks, we've seen several cases of DKA and euglycemic DKA in patients with type two diabetes and COVID-19.

# Dr. Lee-Shing Chang:

So, I do think that this is something that's important for us to watch out for. Personally, I've been telling my patients on SGLT2 inhibitors, that if they get sick or if their oral intake drops, and certainly in the setting of COVID-19, to hold their SGLT2 inhibitors until they're back to baseline. Regarding GLP-1 receptor agonists, these can cause nausea, they can cause gastrointestinal symptoms and they can suppress appetite as well. So, generally speaking, they should be held in the setting of acute illness and decreased oral intake as well.

# Dr. Lee-Shing Chang:

I think it's an interesting balance overall, certainly if patients are feeling well, I think these medications have really powerful and promising benefit in the setting of cardiovascular and renal risk reduction, but certainly in the setting of if patients are dealing with either a significant decreased oral intake or acute illness in the setting of COVID-19, they should be aware that they need to be vigilant about either dose reducing or stopping some of these medications.

## Dr. Lee-Shing Chang:

I think as clinicians, this is something that we can effectively counsel patients about. I'll comment too, Jonathan, I think the current evidence suggests that overall in hospitalized patients with COVID-19, that insulin is probably going to be the most prudent option for glycemic management, especially in cases of acute illness or critical illness, as is the case, generally speaking, in acute or critical illness in hospitalized patients with diabetes.

#### Dr. Jonathan Newman:

That's really helpful. I mean, I think whether it's for ... The data, I think, we have now for RAAS inhibition and statin use, seems to be more on the side of continuing, even though the benefit there is more long-term. And I think as you're illustrating with the glucose lowering medications, we need to be more cautious given the changes in oral intake and the effects on acute metabolic effects in the setting of acute illness, and use of these agents with more long-term established cardiovascular benefits, certainly for, as you're illustrating or describing with the SGLT2 inhibitors and the GLP-1s, that's really helpful.

#### Dr. Jonathan Newman:

And we too have seen some cases of, as you described, the euglycemic DKA for patients that are on SGLT2 inhibitors, who have come into the hospital, both prior to the COVID-19 pandemic and ongoing. So, it's really a relevant point that I think people need to keep in mind as they think about their medical care as the days move forward. So, do you have any suggestions that you can tell our audience about recommendations to patients about controlling my diabetes and heart disease risk, but also staying safe from COVID-19? It's a real balance, a real change in recommendations for, let's say, patients going to cardiac rehab or to the gym regularly to exercise, how are you counseling patients about continuing good lifestyle modification to minimize their risks and help control their diabetes in the setting of COVID-19?

## Dr. Lee-Shing Chang:

Jonathan, I think this is a key question for all the patients that we're seeing on a regular basis who have not developed COVID-19, but who have to deal with all the effects of social distancing and this new reality for the upcoming foreseeable future. Obviously, COVID-19 has caused upheaval in nearly every part of our lives from social interactions to diet, to what we put in our mouths, to exercise, to sleep, to stress levels and all of these can impact diabetes and heart disease, as we well know, and often in very negative ways. I wanted to focus at least on the diet and exercise aspects of COVID-19 life nowadays. In terms of diet, what I've noticed is two major changes in eating patterns in patients in this COVID-19 era. The first, is a decreased flexibility and access to food.

## Dr. Lee-Shing Chang:

Given social distancing I'm seeing a lot of people that obviously aren't able to go to the grocery store as often as they'd like, and hence the quality and the variety in their diets is taking a big hit. The second, is changes in food intake, so for example, grazing and increased snacking with people being at home, being near the fridge, or being near the pantry, we've heard comments about people, "gaining the COVID-19," or gaining 19 pounds, or just gaining weight overall in the setting of all these changes. And I think this is something that's important for us as clinicians to be proactively asking patients about and thinking through with them, what are behavioral changes that they need to be thinking about making?

# Dr. Lee-Shing Chang:

What are practical changes in cooking and food selection that they can make from their more limited availability? And then also, again, those behavioral modifications in terms of what is triggering them to graze, what is triggering them to snack? And thinking about ways to avoid that.

# Dr. Jonathan Newman:

Yeah. Those are really important points, especially, I think, as we're learning, you alluded to sleep disruption and stress. I mean, all of the downstream effects of some of the physical distancing, and those are really interesting perceptions that you've made and described eloquently about changes in diet and food behavior in general. I think that's a very interesting question. Personally, I've, in New York city, which has really been an epicenter of COVID-19, as you know, for my own sanity of trying to maintain my physical activity, I tend to go early in the morning to exercise in the park. And physical distancing usually at that hour of the day is pretty easy to do, but certainly later in the day it can become more challenging. And there's some concern about how best to protect oneself and others with social distancing policies. So, that was really helpful.

#### Dr. Lee-Shing Chang:

Yeah. I totally agree with you, especially about the physical activity. I've been proactively asking patients, "What are you doing to stay physically active in these times?" And been getting a lot of different answers. There's one camp of patients who are actually finding themselves being much more physically active than usual because they have free time to, and the luxury of exercise machines or other things in their homes to use, or they're able to go on more walks outside while still maintaining social distancing, if they do have more public access.

# Dr. Lee-Shing Chang:

And there's another large camp of patients who are much more sedentary than they even usually are. And for those, I think, being proactive in making recommendations or really asking them, "How are you staying active?" Is helpful. I'd say, anecdotally, for me, personally, Jonathan, I actually was thinking about this and I bought a jump rope. I haven't jump-roped in 20 years, but I've been jump-roping several times a week. And just thinking about new ways of exercising that, I think, are really helpful to give ideas to patients and to really speak from our own experience as well, I think that's really resonated.

#### Dr. Jonathan Newman:

That's a great one. I'm a firm believer in jump rope. I actually, a couple of years ago, I started doing that and it is an easy way to get some physical activity in the hectic lives that we all lead, now even more so. As you're recommending and identifying, personalizing some of the preventive recommendations to the current environment is really important and that's really helpful to hear.

## Dr. Lee-Shing Chang:

Agreed.

#### Dr. Jonathan Newman:

Okay. So, maybe I'll make a couple points here as a call to action and then my colleague, Dr. Chang can also chime in and reiterate anything and emphasize. So, COVID-19 is a high risk, rapidly evolving medical crisis, and given the cardiovascular risk for patients with diabetes, with or without established or known heart disease, or vascular disease, along with some of the emerging data we have about the cardiovascular effects of COVID-19, the intersection of the dual epidemics, as we're calling it, of COVID-19 and diabetes, really warrants careful attention, monitoring and personalized treatment decisions. And with integration of the data and the work that we're doing, we can strive to improve outcomes and care for all our patients through the COVID-19 epidemic. Few closing thoughts, Dr. Chang, anything that you'd like to close with?

# Dr. Lee-Shing Chang:

I think, as we know, John, this is still a very rapidly evolving area of research. And so, as far as we best know, just to summarize, we can still continue to use RAAS inhibitors and statins in these settings. But I totally agree with your key recommendation to individualized care, especially with things like glucose-oriented regimens and patients with diabetes, and just really being responsive to patient's needs and unique situations at this time, especially about lifestyle counseling and changes.

## Dr. Jonathan Newman:

That's terrific. I would like to remind our audience to please return online to the AHA Professional Heart Daily for additional podcasts that are planned and ongoing for this series, which include COVID-19 and

stroke, pulmonary hypertension, and other concurrent or risk factors for heart disease, during this really disruptive time in our delivery of healthcare.

# Speaker 1:

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