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## COVID-19 & Cardiovascular Considerations

Announcer:

Welcome to CME on ReachMD. This special activity focusing on COVID-19 is part of a special series titled *COVID-19: Clinical Considerations* provided by Medtelligence.

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Dr. Bhatt:

In light of the current ongoing COVID-19 pandemic, we are providing information on the cardiovascular impact of COVID-19, consequences of COVID-19 infection in patients with established cardiovascular disease, and considerations for cardiovascular disease patients with and without COVID-19, healthcare workers, and health systems. Understanding the impact of the COVID-19 pandemic on cardiovascular health and on the cardiovascular community, in general, will be important for optimizing outcomes during this critical period. This is a Medtelligence CME program on ReachMD. I'm Dr. Deepak Bhatt and joining me today to explore the implications of managing cardiovascular disease in the setting of the COVID-19 pandemic is Dr. Mike Gibson, Professor of Medicine at Harvard Medical School. Welcome Mike.

Dr. Gibson:

Hey, Deepak, how are you?

Dr. Bhatt:

I'm pretty well. Well, maybe the real question is how are you? I understand, Mike, that you have COVID-19 yourself, so you're not just a physician dealing with COVID-19, you're a patient?

Dr. Gibson:

Well to be clear, I guess you would say I have a presumptive diagnosis. Back at the CRT conference, people were really stunned when I was up trying to give my talk and I couldn't speak. I couldn't even get through my talk, and I couldn't breathe, I couldn't catch my breath. I then began coughing more and more. Kind of self-quarantined in my room, went home, and I've been self-quarantined, here at home, since that time. Now, I contacted my coworkers and said should I go in and get tested, and at that point, they said the hospital says it will take three weeks for the test to come out and that was when this first erupted. So, I was told to quarantine at home. I've been home. It was horrible Deepak. I had had ARDS when I was 33 as a result of varicella pneumonia and I had a platelet count of 10, the liver inflamed, and this really hit me pretty hard. I was on the couch for weeks. I couldn't really breathe that well. I would get winded just walking across the room, still coughing a lot. I am doing better now in terms of being winded. Thank God I could still Tweet Deepak, but, otherwise, I was really knocked down. Now my daughter-in-law, she hadn't had contact with me. She works in the ICU at The General, and she tested positive for COVID-19. Her symptoms were somewhat atypical. She just had exhaustion. Exhaustion and a headache, and two days later she got short of breath. When she got short of breath, she got tested. She tested positive. My son had all the same symptoms as her, and here's the interesting thing. He tested negative. So we're not sure if he made it through, the infection and then had cleared it when he got tested, but, you know, both of them, if not already, seem to be back on the frontlines battling the virus.

Dr. Bhatt:

Well I hope that all three of you feel better soon. I got to say, that story just points out the real issues here. That is a pretty high rate of infection among healthcare workers and even people that are relatively young, like your son and daughter-in-law getting sick. One case COVID-19 positive, the other one not. And there is so much we seem to not know about this disease, and I know, of course, we're at the steep part of the learning curve and learning a lot every day I would say. But, I think, you know, for three healthy people like yourselves to get sick like this, you got to really worry about our patients that have cardiovascular disease to begin with because it's quite clear from the global data emerging from COVID-19 that people that have underlying cardiovascular diseases are at much higher risk of complications in mortality. Smoking has emerged as a very potent risk factor for pulmonary complications and death as well. So, what are you telling patients in terms of what they ought to do, in particular, our patients as cardiologists. Our folks, in general, have cardiovascular disease. What should they be doing? What should they be on the lookout for? When should they get tested?

Dr. Gibson:

Well you know you're right Deepak. The cardiovascular patients tend to have a higher risk and it's not clear if it's the cardiovascular disease itself or if cardiovascular disease is kind of like a crater. It's the grand integrator of health. You know, if you have hypertension, diabetes, a host of other conditions, you're older, you tend to have more cardiovascular disease. So is it a marker of frailty in morbidity? It is the cardiovascular disease itself? Not entirely clear. What we are seeing, and I'm sure you've seen this also, Deepak, is all these reports, on social media of here's the case of ST-elevation and you think the person has an ST-elevation MI. They come to the cath lab, but many doctors are reporting that they had clean coronaries. Now, that's by report from some people on Twitter. I asked and you may recall this on an international call the other day if other people were seeing that. Other people said they were not, but nonetheless, it does point out that some people have broad and better ST-elevation MI. Perhaps the pockets you are seeing, triggered by the inflammation from the infection causing plaque rupture, probably during the cytokine storm phase. Some people may have Takotsubo-like pattern. And then thirdly, the pathology studies from China showed that some people have microvascular thrombosis. And I guess that brings us to another issue, Deepak, is what are we doing to manage these people? A lot of these patients do have elevated D-dimers, and there is a lot of talk out there, in social media, about making sure we adequately anticoagulate these patients given their thrombotic risk. So I think everyone is now in tune to that. The other big issue is the issue of ACE inhibitors and losartan. You know, what's fascinating, for instance, is losartan blocks the angiotensin II receptor, that's where the virus binds, but your body in response may upregulate the number of receptors. So, it's somewhat controversial, at least in my mind, about whether the losartan and other drugs like the ACE inhibitors are good or bad. At this point, the AHA has told us to continue those drugs. You don't have to stop them. Based upon the individual patient need. I want to end, Deepak, by talking a little bit about what was disconcerting in China, which says people would begin to recover from the pulmonary part. The Chinese physicians tell us we could ventilate the patient, we could oxygenate them and then they were getting better and then a day or two later, they would have a cardiac arrest, but it wasn't a VT/VF arrest. It was pulseless electrical activity into asystole. So, it's not clear what's going on there. There are some cases now being reported of myocarditis or myopericarditis. That can also cause the ST-elevation. And, there are some reports also of aggressive anti-inflammatory therapy, plasmapheresis treating those patients. So, you know, very complex. I think we're learning a lot every day. What have you been hearing, Deepak?

Dr. Bhatt:

So, I think you hit upon several important points. And I just want to emphasize something. You said there was a lot of buzz about ACE inhibitors and angiotensin receptor blockers should they be stopped, but the current guidance from the American Heart Association and others is continue those. It's true, the ACE II or the angiotensin-converting enzyme II is a receptor, for this particular coronavirus, but there's no good evidence to date that those drugs are bad. In fact, I'd say the opposite in our patients of cardiovascular risk, make sure they're taking their blood pressure meds and their statins and lipid control and glycemic control and everything else. I think that might, if anything, keep them from getting sick. So that's the best guidance for now. It's challenging in these patients that come in with cardiovascular manifestations because you hit the nail on the head. They come in with ST-elevation many times and it could be anything. Like, it could be that they are in fact having plaque rupture in a STEMI. There are now several reports largely on social media are from just a spike in delayed presentation of STEMI. Probably patients toughing it out at home because they don't want to come in because they're worried that the hospital is full of people that are COVID-19 positive. So they're just not coming in as quickly as they normally would. Realizing that, in general, people aren't always coming in that quickly. There's often some degree of delay, but even more delay than usual. So people coming in in really bad shape, delayed presentation of STEMI, so that option is still there. Could this be classic STEMI, just a bit delayed, maybe a bigger infarct. But on top of that, there's myocarditis, myopericarditis. There is possibly some vasospasm, the Takotsubo, and the autopsy confirmation from China, the microvascular thrombosis. So, all these different etiologies are presenting to cath labs around the world and it makes life really challenging because some people have said maybe given that there's an epidemic, the healthcare system is under strain, let's just go ahead and lyse these folks, but I'm not sure that's actually such a good option because a bunch of them don't actually have epicardial thrombosis and exposing the others to thrombolytic therapy could backfire. And furthermore, I am not even sure that that's a sensible strategy because a large percentage of patients, even if it is a

classic STEMI or epicardial obstruction, they're not going to re-perfuse or they're going to end up in the cath lab anyway or perhaps in even worse shape, having failed lysis. So, how are you handling that particular aspect? It is an important branch point. Have you moved towards just lysing these folks or are you sticking with primarily PCI?

Dr. Gibson:

Well, you know, I had worked very actively in the lytic field back in the 90s and I'm a big pro-lysis person, but I got to say, this makes me a little scared, Deepak, because a lot of cases of myocarditis and pericarditis and we wouldn't want to cause bleeding in those patients; either intraparenchymal hemorrhage or pericardial bleed. You're right, a lot of these arteries may be open due to microvascular obstruction. On the other hand, the PCI is not going to open up the microvasculature, this might, the lytic. On that point, there is some data suggesting that lytics, if there is microvascular obstruction, I've done some work on this. Sadly, at the end of the day, it looks like you may precipitate some intramyocardial hemorrhage. So, maybe not a good idea. I think the smart money is still on going to the cath lab, get your PPE on. You know, it's not going to really hurt outcomes by delaying five minutes to make sure you're fully gowned and gloved and everything you need for full PPE, but I agree with you, on all those points, Deepak.

Dr. Bhatti:

Yeah, I thought you were the best person to ask because, of course, I remember all the pivotal work you've done in lytics and I'm also a fan of lysis in the right setting, but here I just think primarily PCI or even before that, angiography is probably the way to go. Now, I'm not opposed, however, if it's a really equivocal case, to having them stop at the CT scanner and getting a coronary CT angio. That is, you know, if it looks like a Takotsubo pattern on the echocardiogram in the emergency department realizing the Takotsubo isn't so easy to determine although it's on a transthoracic echo, but, you know, if the ECG patterns sort of diffuse ST-elevation, they are not really fitting the pattern of an epicardial artery, I mean I'm not opposed to stopping in the coronary CT non-invasive angio. What do you think of that strategy?

Dr. Gibson:

You know, I'm not opposed either. I think that is a very, very reasonable strategy in this setting. I think the other thing I've been hearing, Deepak, and I would be interested to see if you're hearing it as well, is that the end NSTEMIs seem to have gone down. And people tend to be toughing it out at home rather than coming in, and what we're seeing is probably the same volume of STEMIs in many countries, but less NSTEMIs.

Another issue that's come up, Deepak, that's really been talked about a lot is chloroquine and hydroxychloroquine. These are antimalarial agents. There are some provocative pictures posted on social media showing that those areas in the world where you have malaria, well they don't seem to have as much coronavirus. I think those images were roundly criticized as being horribly confounded by the fact that there is not a lot of testing in those regions and I think they were largely dismissed, but there is some data coming, from France in very, very limited numbers of people in a nonrandomized look at this issue that these agents may clear the viral load more quickly. Now that being said, we don't have any of the kind of randomized trial data that you and I are familiar with randomizing people to hydroxychloroquine or not. I do see that in his executive order, Governor Cuomo, indicated that you shouldn't be writing prescriptions for these drugs outside of a randomized trial. So, I was happy to see that. So, I think those are being investigated. A word of caution, you and I both know, Deepak, that these drugs can cause some QT prolongation, and we saw some pictures of this on social media including a case of a torsade. There are a couple of other drugs out there like the HIV drug, lopinavir/ritonavir (Kaletra), which also causes QT prolongation, but failed in a trial in *The New England Journal of Medicine* to improve outcomes with coronavirus. Remdesivir from Gilead, really looks to be pretty good from a cardiovascular safety profile. I was pleased that we were able to get a couple of young cardiologists that drug on compassionate use. Compassionate use has now been restrained, and you need to get that drug, as part of a protocol. And then there's some rheumatoid arthritis drugs, tocilizumab (Actemra) and others that are IL-6 blockers that block that cytokine storm, that may be helpful too, but I haven't really seen any cardiovascular side effects from those drugs. Maybe, I'm wrong Deepak. Are you hearing any other side effects from those drugs?

Dr. Bhatti:

Yeah, I think that you've shown that all these different drugs that are out there have potential cardiovascular complications and that's on top of this natural history of the disease itself and that's why I think cardiology is going to be a big part of the treatment of these patients and treatment of the complications of some of the therapies. I think it is also an important point you made in terms of what the governor said and really these things need to be tested and trialed. And, of course, there is a natural tendency for us in medicine to just do anything we can for the patient in front of us. That's completely understandable. I feel that way in an old patient, but to the extent possible if we can test these in randomized trials, we'll get to the truth much more quickly. And you mentioned that the trial of the HIV drug published in *NEJM*. You know, there was something that seemed promising, but then the trial was negative and that's a drug with potentially serious side effects including cardiovascular ones. So, I think the key is, as a medical community, we've got to be really rigorous in our evaluation of these therapies and how to do it in a very quick and efficient way. How can we keep track of our patients

and make sure they're doing okay? And I think telemedicine is going to be really big – it's already getting used quite a lot during this COVID-19 epidemic. In fact, we are doing things that the U.S. healthcare system should have been doing years ago, but because of various regulatory and reimbursement hurdles, problem, it wasn't happening, but I'm actually hopeful that these sorts of changes that are being done in crisis mode, in an epidemic, will carry over and be things we can do back once life, hopefully, returns to normal. Actually, Dr. Wendy Wang, a fellow at the Brigham and I wrote something about this in the *Journal of Invasive Cardiology*, that this is an opportunity, this crisis, to really transform healthcare delivery in the U.S. for the better by adopting things like telemedicine and really embracing a lot of these novel technologies.

Dr. Gibson:

Yep. Great ideas. Well, Deepak, as usual, we're out of time. It's been great talking to you. It's been a great discussion. I'm going to thank you for asking me to join you today. This is such an important topic. I want to thank Medtelligence CME and ReachMD. And I want to thank all of you out there for joining us today. This has been a great discussion.

Announcer:

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