LESLIE COOPER: As you all know there have been more than 3 million cases of COVID-19 and more than 200,000 deaths. Many of these have involved cardiac complications. We know that a substantial minority, up to 20% or 25% of hospitalized patients, will either have an abnormal finding on echocardiogram or an abnormally elevated troponin. These are important because there are powerful prognostic markers of death and other adverse outcomes.

What we would like to do today is to review the diagnosis and the management of those patients who have developed cardiac involvement in the setting of acute COVID-19 injury. I'm now going to share my screen. I'm going to present first, followed by Dr. Michael Ackerman, and finally, Dr. Sandhu. We will then take questions from the audience.

There are many reasons why people develop acute cardiac injury following infection with the virus SARS-CoV-2. This slide illustrates the spectrum of injury. The first and perhaps the most worrisome is an acute coronary syndrome. The inflammation associated with SARS-CoV-2 is highly thrombogenic and can lead to clots forming in the epicardial coronary arteries. In that setting, as you would in a typical MI, you will find an ST segment elevation or sometimes ST segment depression presentation. These would be treated, as Dr. Sandhu will describe, in standard fashion in the catheterization laboratory.

However, many patients, as we've learned from the New York experience, actually have open epicardial coronary arteries. These patients could have microvascular thrombosis, or they could have a primary heart muscle problem. Disorders that will affect the heart muscle include myocarditis and direct involvement of the virus, cytokine dysregulation with high levels of IL-6 or IL-1 in a setting of a cytokine storm, and even a Takotsubo-like stress cardiomyopathy. Some patients will present with arrhythmias, and there are reasons why high levels of IL-6 or TNF alpha could lead to atrial and ventricular arrhythmias that may occur in the setting of the normal cardiac function or in the setting of cardiogenic shock.

Some of the patients who have acute lung injury will go on to septic shock, and a fraction of those people and a fraction of the people who do not have septic shock will also develop cardiogenic shock. It's important to be mindful and think of the cause of hypotension in that setting. Finally there have been case reports in small a series of pericardial effusions with or without tamponade and thrombotic complications in the large veins and pulmonary emboli.

The next slide illustrates the causes of injury here. There are eight major causes of cardiac injury after infection with SARS-CoV-2. The first, and I would be important to recognize, is hypoxemia. Many of the patients you will see in the hospital or in the intensive care unit in the hospital will have severe lung injury. The hypoxemia would only make worse any other cause of cardiac dysfunction.

In addition, many of the older patients will have pre-existing coronary disease or hypertensive cardiomyopathy that would lead to a decreased ability to respond to the stress of sepsis. As we mentioned, thrombosis, both of the large arteries and veins and the microvasculature, can lead to cardiac dysfunction, as well as the cytokine storm and adrenergic stress, which leads to either a cardiomyopathy or a Takotsubo-like syndrome. Finally, the virus can infect heart muscle cells and macrophages in the heart. This can lead to some cardiac damage in a minority of these patients.

When we think about an algorithm to approach the treatment and diagnosis, first thing in all patients hospitalized is, are there cardiac signs and symptoms. Once you think that there's a cardiac syndrome going on, in addition to standard testing like an EKG, consider a troponin. In this setting, the normal troponin, and sometimes a normal bedside point of care echo, it's OK to continue monitoring these patients carefully in case of future clinical deterioration.

If you detect a decrease in cardiac function either with tachycardia, low blood pressure, or new arrhythmias, then it's important to consider both guideline-directed management, which is that which we would find in our standard US and European guidelines, as well as enrollment in clinical trials. Clinical trials currently are focused on anticytokine therapies and viral therapies and convalescent plasma, a trial that is led by the Mayo Clinic in Rochester.

At that point, patients will divide into a couple of groups-- those who have normal or near normal heart function, who can be managed expectantly with guideline-directed therapy, and those who may require additional intervention because of uncertainty regarding the cause of shock. In those patients, they may benefit from a invasive approach with a PA catheter or perhaps a mechanical circulatory support. Finally, in the recovery phase, after patients are getting better, if there was an uncertainty regarding the mechanism of injury, a cardiac MRI at that time point after they've begun to recover may be of value.

My final slide covers clinical trials that are available at Mayo Clinic in Rochester and likely may be available regionally, if you're doing us from another area. In patients who are relatively well, either in the outpatient setting or in the inpatient setting without a need for ICU care, there is a hydroxychloroquine trial. In the sicker patients, they're divided into mild, moderate, and severe ICU-level care. There are specific trials illustrated of anti-IL-6, anti-IL-1, as well as antiviral therapy.

Throughout the country. We are enrolling in the recombinant-- in the recovered plasma trial led by Mike Joyner. I would encourage all of you to consider that for your patients who are sicker in this case.

I'd now like to introduce Dr. Michael Ackerman, who is the director of the Windland Smith Rice Clinic for Genetic Rhythm Disorders and the Laboratory for the Study of Sudden Death.

MICHAEL ACKERMAN: Thanks a lot, Leslie. Well, it's great to get to be with everyone. And I'm going to pick up where Dr. Cooper left off about heart disease and why did we hear about a month ago that patients with heart disease, quote unquote, "heart disease" are at more risk of serious COVID-19 outcomes.

I'm conflicted. These are some of my conflicts of interest to disclose, and the most relevant one will be a conversation we'll have towards the end of my monologue with my relationship, Mayo Clinic's relationship, and that of a few of our other colleagues, including our chair of cardiovascular medicine here in Rochester, Dr. Paul Friedman with AliveCor.

I'm going to touch on two things-- ACE2 in heart disease in general, and in hypertrophic cardiomyopathy in particular. And then and Dr. Cooper's final slide about what are the various clinical trials, we'll make some comments on the COVID-19 pharmacotherapies that have a QT issue.

We're really excited about this work and this discovery that was just published in *Mayo Clinic Proceedings* just three days ago. It's a 20-year story that began with the first frozen myectomy specimen from our cardiovascular surgeons, Dr. Schaaf and Dr. Dearani in 1999. And over the course of the next 10 years, we obtained over 100. flash frozen myocardial specimens at the time that the patients came for relief of their obstructive hypertrophic cardiomyopathy. And we had upregulated genes, we had downregulated genes.

And with this work from one of our former Fellows, Dr. Virginia Hebl, we didn't quite know what kind of a story to make with it, and we kind of left the data set. And that, as we say, was, oh, so BC-- Before Corona-- because after corona and after we were hearing how the SARS-CoV-2 virus hijacks a particular receptor to gain entry into the various tissues, Frank Brozovich and I about at the same time recalled, and we asked each other, didn't we have ACE2 as one of the up regulated genes in our patients with hypertrophic cardiomyopathy?

And as you can see, yes, we did. Not only was it an upregulated gene, but ACE2, out of our patients entire transcriptome of over 50,000 transcripts, was the single most upregulated gene. And with that we had a story to tell because now ACE2 had new meaning.

And our coequal first author, Martine Bos, dusted off our data set, looked at it, we did new data. And you can see here the aha moment because patients with hypertrophic cardiomyopathy, at the time of their surgery to relieve they're an output tract obstruction, had five times higher levels of not just transcript, but the protein, the ACE2 protein, which we view back then as simply a patho-responsive compensatory reaction where the heart is trying to counter the ill effects of excess angiotensin II. And by generating increased levels of ACE2, we could generate more of the healthy, favorable heptapeptide that has favorable vasodilatory effects, favorable antihypertrophic effects, and favorable anti-inflammatory effects. And you can see in the tissue of a hypertrophic cardiomyopathy individual marked increase in expression of ACE2.

And we think, as shown here, that ACE2 accentuating diseases like hypertrophic cardiomyopathy-- and earlier this week we learned of a handful of heart failure patients, eight of them, where their tissues showed increased levels of ACE2-- that what we're basically doing, or what SARS-CoV-2 is getting to do, is have much, much easier access to steal entry into those tissues that have ACE2 overexpression. And I'm particularly interested about the study that's going on headed out of University of Minnesota with the trial of angiotensin receptor blockers, losartan, because it would make sense that losartan will be a very good idea for patients with ACE2 accentuating diseases.

And so I think this underscores a reason why we should all keep our patients on their ACE inhibitors or their angiotensin receptor blockers until there is evidence to suggest otherwise. There may in fact be protection by being on an angiotensin receptor blocker. So it's going to be very interesting to see what are the other ACE2 accentuating heart diseases. Does hypertension do this, meaning cause this patho response to occur?

And then let's turn our attention-- we're going to leave ACE2, and some of the other treatments where for over a month now center stage has been the use of chloroquine and hydroxychloroquine, where a month ago it received FDA emergency use authorization. Four days before the FDA released that, Mayo Clinic-- again, thanks to *Mayo Clinic Proceedings*-- we released an urgent warning and guidance because we saw the perfect storm assembling to where in these kind of sick patients we were going to have disease-related and potentially treatment-related sudden cardiac deaths.

And so we provided a way to do this. How could we safely navigate, and by identifying who is at risk for an unwanted, tragically unwanted, sudden cardiac death reaction from the so-called "corona cocktail" of hydroxychloroquine and azithromycin. And I want to thank one of our other Fellows, John Giudicessi, for spearheading this work.

And what you'll see is we also offer in that a PPE-sparing approach to how you could obtain this vital sign, this vital sign being in our patients QTC value, for which AliveCor and their smartphone-enabled device received FDA emergency approval as a way to monitor the QTC during COVID-19 therapy. I want to thank a third Fellow, Alan Sugrue, for then being chief architect with me to create a free online resource on calculating the QTC. And you can go to the website www.covid.qtc to get to the QT calculator.

I'm going to show it to you here. And you can see, when you go to the calculator, you can get information about the QT interval. You can be linked to Mayo Clinic Connect page of our Genetic Heart Rhythm Clinic and updated about COVID-19, and COVID-19 as it relates to the QTC. But whether it's from the telemetry or a smartphone-enabled device, you can look through, enter into the QTC, enter your patient's age, gender. And off the telemetry or the smartphone, you see that the QTC measure, the QT interval measured 420 when the heart rate was 85, and you now see that your patient is just entered the red light.

Stop. Be very careful. This patient is telling us that they are QT twitchy, that they are torsadogenic, and that the impending drug-induced cardiac arrest is potentially around the corner. www.covid.qtc.com.

This 500 line must be respected. We see 500 milliseconds in about 1% of all patients who come to Mayo Clinic, inpatient or outpatient, for whatever reason. But it's not 1% if you have COVID-19 and you're being treated with the corona cocktail.

As published earlier this week, 11% have crossed the 500 line. Not only have they crossed the 500 line, but in Brazil with the Brazilian and corona cocktail-- and this is a whopper. This is a stiff dose of chloroquine. We have almost 20% go into the red zone, and you can see 39% who are on high dose corona cocktail, 39% died compared to 15% who were on low dose.

So ACE2 in HCM is potentially the explanation for why some patients with certain heart diseases are at greater risk of bad COVID-19 and COVID-19 pharmacotherapies that affect the QT interval where the QT must be respected, so much so that the FDA, less than a month later after their emergency use authorization, earlier this week released a warning, a safety alert, about the use of these medications, and said, these drugs, hydroxychloroquine and chloroquine, should only be used in the hospitalized patient under careful monitoring or in patients enrolled in clinical trials.

So I look forward to seeing what kind of a conversation we'll have in a few minutes. But now it's my pleasure to turn this over to Dr. Gurpreet Sandhu for our third installment. Gur is the Director and Chair of our Division of Interventional Cardiology at Mayo Clinic here in Rochester, Minnesota. And Dr. Sandhu, it's all yours.

GURPREET SANDHU: Thank you, Mike, and thank you, Les. So I'd like to start by thanking everyone for joining us today, and I'd also like to thank all of her colleagues worldwide who have shared their experience in their cath labs, their cardiology practices, and helped us and others learn from their experience.

So what we know from our own experience so far is here in the state of Minnesota, we have been quite successful in flattening the curve. So we are nowhere close to experiencing the peak that other places have, but at the same time, we expect that once we start seeing higher volumes, this peak will extend for potentially a couple of months.

So in terms of experience, what have we learned? Around the world, what we've seen has been COVID cases start to spike, cath labs are amongst the first to shut down, and there have been numerous reasons for this. One is pretty apparent. If you look on the internet, Twitter, even publications, you see patients coming in with classic-looking ST elevation MI ECGs. But you take them to the cath lab, and you find the coronaries are normal. And at this time, you now have infections in the cath lab personnel, people go into quarantine, and the labs shut down.

And a consequence of this also has been that many labs have decided not to offer primary PCI, and they go straight to offering thrombolytics. There are pros and cons of this. While thrombolytics can definitely help the right patient, we also know that many ACS patients do much better with primary PCI than with lytics. And also if you have a COVID-positive patient, you could potentially put them at risk, both by doing procedures and surgeries, and also giving them lytics when there's no indication.

So for our practice, we decided pretty early on, after seeing what's happening around the world, that we will try our best to retain our full functional capacity, and we will try and protect the patients as well as our personnel the best we can. We had time, not more than a couple of weeks, though, because things were changing pretty quickly. But we utilized that to do all the commonsense things.

First, we did the social distancing within the personnel, and we had the same limitations that everyone else had. And we did not have enough N95s. Our personal protective equipment was very, very limited, and was only being deployed when it was critically essential. And also we had no prior roadmap as to what to do in a worldwide pandemic.

So along with the distancing, universal masking, we also decided to convert the face-to-face clinic visits into non-face-to-face, and that helped provide patients the continuity of care, but reduce the risk of patients getting infected during travel to Mayo Clinic. It also gave us time to prepare. Meanwhile, following the national and local government guidelines, we discontinued all elective procedures and only offered the urgent and emergent procedures upfront.

We used this first couple of weeks timeline to also then fine tune our systems, and I'd like to share some of this. You've already heard about the pathophysiology and the management from Dr. Cooper and Dr. Ackerman, so I'll just share some of the practical things that we have done, then I'll go into some more details.

So as part of this preparation, wherever possible in the cath lab and the electrophysiology labs, we decided to divide ourselves into three teams, where one team would be in-house doing procedures, with the second team available as backup. And the third team were simply stay at home and help with other non-clinical or clinical roles online without exposing themselves. This also gave us time then to make sure we had adequate supplies of N95s. And we practiced appropriate donning and doffing and all the safety mechanisms, and make sure all three teams are fully comfortable with this. So once we reached this point, we also then started recycling, resterilizing, and reusing N95s and other PPE, using processes that were fine tuned by our own supply chain people to try and conserve and make sure we didn't burn through our supplies.

So at this point, I'll go over to sharing some slides. So this is an algorithm that was developed in conjunction with our coronary artery disease experts and our coronary intensive care unit colleagues and the emergency department colleagues. This is a pretty high level overview.

So at this time, in the general population, almost anyone coming in with an ACS is a suspected COVID patient. We also obviously have non-COVID patients who are in house in the hospital. So people coming in with an ST elevation on their ECG, once they reach them the emergency department, after the usual screening questions to rule out COVID quickly-- well, you can't rule it out, but at least you can do the usual screening questions because none of the tests would be good enough to or quick enough to give us the results right away.

So if the clinical suspicion is high that this is truly an ACS and a patient would benefit from revascularization, then we simply follow our standard STEMI activation pathways. We go straight to the cath lab, treat the patient, and then move them on to our floor services or the ICU as appropriate.

Down the middle is our pathway where there is uncertainty, where we aren't really sure. Is this truly an ACS? Does the story fit? Could this still be a patient presenting with COVID-19 infection or some other comorbidities where they may or may not benefit from revascularization?

Here our process is to give them full benefit for the revascularization. So as soon as the patient hits the emergency department, the cardiology intensive care unit team, which is in-house 24/7, goes right down and they make a quick assessment. In some cases, this may require doing a bedside echo to look for regionals. If you see regionals, then it's pretty straightforward. Go to the cath lab.

If the story is still unclear, then a coronary CT angiogram is also available, and we get the results back in about 20, 25 minutes. If the coronaries are clean, then we follow all our other diagnostic pathways. But if we see a coronary occlusion or a critical appearing lesion, then they come straight to the cath lab with minimal delay.

Then on the right side, we have our algorithm with what to do with patients who come in with hemodynamic instability, shock, COVID-like symptoms, or a history of contact with a COVID-positive patient, foreign travel, all the risk factors. There, instead of rushing them off and doing procedures, the first step is to safely and sensibly stabilize them medically. Once the patient is stable, once you have your diagnostic testing done, at that point you make a decision. Is this someone who would need to be managed in a COVID unit with medical intensive care unit services versus cardiac intensive care unit versus bringing to the lab for the procedure or some other diagnostic test.

So that is our overview of the inpatient acute ACS algorithm. In the interim period, what we have also done is to ensure that our patients are provided our services safely. So this is something which is being seen repeatedly around the country, around the world. The minute COVID patients start increasing in a population, the number of patients presenting with STEMIs, with acute coronary events, with acute heart rhythm disorders, even heart failure, they seem to dwindle and almost disappear.

There are many theories as to why this happens, but common sense tells us people are afraid to come into the hospital and seek care for other life-threatening illnesses because they don't want to come in and get infected with COVID-19. So here I would like to reassure everyone and hope that all our viewers also reassure their patients that it is actually very safe to come into the hospital, and that they should not jeopardize their own health and well-being because of an infection that is being managed well by teams within hospitals.

So for our outpatient practice, while we are not doing any elective procedures, we have now started a system where all of our patients who call in, who need to come in, their first point of contact is a phone call or a video call using secure systems, and these are usually done by our nurses. They have their usual COVID screening questions. They are counseled on wearing masks, avoiding visitors, social distancing, et cetera.

And then if they need to be brought in for a visit, they come in on day one whee we do COVID testing. Both a PCR is done as well as we'll be having serology available in the next week or so. They get their other routine cardiac workup also-- ECGs, blood draws. If in the prior workup, during the screening questions or the COVID PCR, they turn out to be positive, then they're redirected to seek appropriate care from their local physicians or emergency rooms.

But if at this point everything looks good and they do need to come in for a semi-urgent non-elective procedure, then they have a face-to-face clinic visit. And following that, they can then proceed to the cath lab or the heart rhythm lab, or get their TEE, and then move on to have surgery.

So this is basically our generic overview of what we think is a pathway that will keep our patients safe, protect our personnel. And I think I'll stop at this point, and I'll hand it back to Dr. Cooper for any questions that people may have.

LESLIE COOPER: Gury, thank you very much for that overview of the cath lab procedure and what we're doing to keep our patients safe. Obviously, we know from the Wuhan experience in China, a substantial number of the people who were infected were actually health care personnel. So the safety of everyone is critical during these type of procedures.

We've received a number of questions from the audience, and we're going to start with one for Michael, Michael Ackerman. This question is how do you evaluate the QTC interval if the patient has a baseline left bundle branch, right bundle branch block, or paced rhythm?

MICHAEL ACKERMAN: Thanks, Les, and thanks, Mohamed, for that question. It's a really good one. And it's so good, in fact, that I'd like to show you with the calculator how to do it. And so I'm going to take us to the calculator for a second.

And just in that example that I showed you from the calculator, this was with a normal rhythm and a normal QRS. And this person had entered the red zone at 500 milliseconds, for which we would need to be very, very careful about exposing or adding to that patient additional QT aggravating factors. But like Mohamed asked, what about when the QRS is wide? And it can be wide for a variety of reasons-- wide for bundle branch block, wide because there's ventricular pacing, wide because perhaps the SARS-CoV-2 virus has infected the muscle and has infected and affected the conduction system.

So we've created a way to do that where you click the Wide QRS button, and now you measure and add the QRS. And anything above 120 milliseconds gets adjusted, corrected, as if depolarization was normal. So let's say in that patient, where you measured everything at 420, heart rate was 85. But now the QRS, because of the bundle branch block, was 180 milliseconds, for example.

Now you enter to that, and you see that patient isn't in the red light at all, even though the computer will have measured the QTC at 500 milliseconds and above, but did not make a wide QRS adjustment. So this is a very simple way of making a wide QRS adjustment, keeping the same normal QTC distribution curves of the action lines of respect to the 500 millisecond line, rather than making you and I, Mohamed, have to remember the JTC distributions by starting after the QRS.

So I hope that helps and I hope you find the covid.qtc.com calculator very helpful for you. So thanks for that question.

LESLIE COOPER: Thank you, Michael. The next two questions have to do with the ACE2 protein on the surface of cardiac myocytes. The first is, do we know whether ACE2 is upregulated specifically in the SARS-CoV-2 infection? And the related question is, do we know, if this is upregulated, is this a risk factor for developing the COVID-19 infection? Perhaps that would go to you also, Michael.

MICHAEL ACKERMAN: I'll start with that. And Les, I'd be curious what you think about it. But I would say first, for Heidi, which I love the question, is the virus itself isn't upregulating the ACE2 gene. It's not upregulating the density of the ACE2 receptor. The ACE2 receptor wasn't designed to eventually have some coronavirus come along and hijack it as its path to viral entry into the tissue.

But we do know that there are specific heart diseases where ACE2 protein levels are absolutely increased. We showed it this week very convincingly in the myocardium of patients with obstructive hypertrophic cardiomyopathy. There is another data set showing it in patients with heart failure, that the muscle tissue from the heart has more ace to protein in it.

And we and others are looking at other heart diseases to see if those heart diseases are also ACE2 accentuating heart diseases, whereby more ace 2 receptor means easier access for viral penetration, viral load, viral infiltration into those tissues. And we think that probably correlates, kind of a dose response curve. Easier access into those tissues that have more ACE2 receptors on it, going to be more tissue damage. Les, what do you think?

LESLIE COOPER: So ACE2 is clearly expressed on cardiac myocytes. But the other protein that's required for viral entry, TNPRSS2, is not expressed on cardiac myocytes, but maybe in macrophages. The electron microscopy from northern Italy showed that macrophages are infected, and there's also a paper from Germany, from Berlin, that also suggests macrophages or fibroblasts can be infected.

Inducible pluripotent stem cells induced to have a cardiac phenotype can be infected with the SARS-CoV-2 virus. That's been demonstrated by Jay Schneider at Mayo Clinic in Rochester, as well as a group in Cedars-Sinai in California. But we don't know the clinical significance of that yet. So the short answer is, there is evidence that you can have a viral infection, but it isn't clearly that that's really a myocarditis.

This actually leads well, Mike, into a question that we just received from Kyle Claritch. What kind of myocarditis do we see in COVID-19, lymphocytic or otherwise? And the answer is, we don't see much in the way of lymphocytic infiltrate. There are a few specimens-- one autopsy, one from Germany that I've seen-- where you see scattered, very-- not very much lymphocyte infiltration. There are a few that have a bit more macrophage inflammation.

But I think the more important story is, is there a direct viral effect that doesn't involve an immune-mediated mechanism. So it would be more of a viral cardiomyopathy. You could call it a myocarditis, but it wouldn't directly involve lymphocytes like T and B cells.

MICHAEL ACKERMAN: And Les, I think what's interesting there in follow-up is that Cricket Seidman at Brigham Mass General showed that the ACE2 that's present in heart muscle is actually probably not in the ventricular cardiomyocytes, but actually in the pericytes. And the pericytes is where the macrophage and the interleukin in the cytokine storm is all probably coming from. So the viruses are probably not stealing entry into the heart muscle contractile cells themselves, but the adjacent pericytes, and that's where all of the cytokine storm havoc is happening, rather than gaining direct access into the heart muscle cells themselves.

LESLIE COOPER: I think that's exactly right. There's a bit more science to be done, particularly translational science, on human heart tissue, to be certain. But at this point, that would be what I would think.

We've got quite a few more questions. Let's go onto the next one, which is for Gury. How do you clinically assess a patient with a high clinical suspicion of an MI?

GURPREET SANDHU: This is a great question. This is something we struggle with all the time. So realistically, anyone with all the classic risk factors-- hypertension, diabetes, previous coronary artery disease-- those patients presenting with a typical appearing story-- ST elevation, ST depression-- and if there's no other confounding factor, we have a very low threshold of taking them to the cath lab and treating them immediately. And this, again, is entirely clinically based for the STEMIs.

For the non-ST elevation MI, there are still a little bit of time, but you can get the troponin back and help that guide you. And also if you can get an echo, give them a bedside echo, that would be helpful. But clinically, we have to rely upon the story for the STEMIs. And that's pretty much all we have to guide us in a majority of cases.

LESLIE COOPER: So we've received a whole group of questions which I'm going to group together. I think, Gury, let's continue with a group of questions here focused on MI management. There is, from Dr. Curenzizia, please outline when to take patients to the cath lab with the protective measures, focusing on a hospital with one cath lab. And then further down, I think, cardiogenic shock. Dr. Okafor asked, please manage-- how would you manage cardiogenic shock? I guess we could talk about Impella and other potential devices in that setting.

GURPREET SANDHU: Yeah. So thanks for the question. I'll start with the outline of how to take a COVID patient to the cath lab and all the protective measures involved, focusing on hospitals but just one cath lab. So within the Mayo system, we've got six hospitals with cath labs. And we do have some hospitals where they only have two cath labs and only two interventional cardiologists.

So in terms of how we bring a patient in safely, I'll stick with the STEMI pathway. So with the STEMI pathway, if somebody comes in and is otherwise stable, you're taking them to the cath lab, putting a simple face mask on the patient would reduce the risk somewhat of droplet transmission.

And while the cath lab is activated, normally most cath labs are up and running within 20 minutes, 24/7. With the current situation, it takes us additional 10 minutes to do all the donning and doffing. So our practices, we get the cath lab personnel in. People put on their N95 masks, the face shields, the gowns, the double gloving. As soon as we ready, the lab will call the emergency department and say, send the patient up. And at that point, the patient is brought in.

We do the procedure as it's normally done. And when the procedure is completed, previously our hospital teams, ICU teams, would walk right into the cath lab and take the patient from inside the lab. Here, if we've had an aerosol-generating event such as chest compressions or CPR, it is not safe for people to come in wearing surgical masks until you've had at least about seven air exchanges completed in the room, and that varies a lot from room to room and place to place.

So once the procedure is done, patient is still masked or intubated. And even with the intubation, the ventilators have to have the proper filters in place to avoid aerosolization risk. At that point, we basically deliver the patient and do the handoff in the hallway outside the lab so that external personnel don't come inside the room and get exposed. And so this has been working reasonably well. But again, our numbers are very low at this point because of the flattening of the curve.

And then the second question was about hemodynamic support devices. So here I'm going to back up a little bit. So someone coming in, in shock, and is unstable. What we have as a practice currently is to try and intubate the patient where they are, which would be in an emergency department room or in the ICU, as opposed to rushing them off to the cath lab are doing all the intubation and everything else in the lab because that simply spreads the aerosolization risk and infection risk amongst groupings versus one.

So once they're intubated, stabilized, they come up to the cath lab. And at that point, if someone has significant hemodynamic instability, then we reduce our standard Impella as our frontline, but we're also very comfortable with putting people on ECMO, especially those who need oxygenation and are not on a ventilator. Or even if they're on a ventilator, they're not fully being oxygenated, we would go with ECMO at that time. Thanks.

LESLIE COOPER: There are several questions related to the QT interval measurements and hydroxychloroquine. Mike, would you take those?

MICHAEL ACKERMAN: Absolutely. And this is another great set of questions. I love this format. So thanks to all the participants. I hope you're enjoying as much as we are.

Lali is asking about the hydroxychloroquine benefit. Our role as cardiologists is the safety of these drugs, especially when the drug has a QT risk factor signal, a sudden death potential signal. Treating a COVID-19 patient is not like treating rheumatology patient with stable lupus. It's comparing apples to watermelons, really. So what may be completely safe in that population, completely safe for antimalarial prophylaxis, it's not directly translatable to somebody who is sick with a virus that involves the heart directly.

And so on the benefit side, it's not looking so good, is it? At least for sick COVID-19, there is not an obvious strong signal of therapeutic efficacy emerging, and we should have seen that signal by now. So I'm bearish on hydroxychloroquine for inpatient sick COVID-19.

I'm still quite optimistic about the current clinical trials that are looking at hydroxychloroquine in the post-exposure prophylaxis setting. We might see an efficacy signal there. And if we do, it's going to be really important to do QT monitoring, although those kind of patients who would be getting hydroxychloroquine at that time point are much, much healthier patients. So it'd be a much safer time period and with a much greater therapeutic safety window.

In terms of those while we're using it-- and we still are using the corona cocktail a lot in hospitals all over the country and the world-- know the QTC. Assess the QTC by ECG, by telemetry, by smartphone-enabled devices. And to that, one, is asking, well, how do we correct it? We use the Bazett formula. That is the heart rate dependency correction formula for which we know green light go, yellow light pause, and red light stop.

And a QTC corrected by a different formula-- Fridericia, Hodges, Framingham, those formulas-- we would need different thresholds because a QTC 500 by Bazett's doesn't have the same meaning as a 500 by Fridericia. So that's why we use Bazett still is because it's been around since the 1920s, and it hasn't been beaten well enough.

Amar is asking, could we use a QT countermeasure so that we could keep using these drugs if they work? So let's say the corona cocktail works and works well in different settings. What if we're seeing the QTC rise? What could be our countermeasures? And that's a great question because there are several.

We could make sure the potassium is normal, high normal. That helps with repolarization. We could give magnesium. That helps protect. We could remove any other QT-aggravating medications that the patient might already be on, that they came in on, if we have room to safely remove them. There is a lot of medications that are QT aggravating.

And we might be able to use medicines like mexiletine or even lidocaine to help shorten the QT interval in sick or heart muscle cells. No proof of that yet, for IV lidocaine, but those would be potential QT counter countermeasures. Les, those were great questions.

LESLIE COOPER: They absolutely were, Mike. Thank you so much. We've received more questions. There are a couple that I'll take. Drs. Arujo and Farasat asked, when would we begin elective clinic visits? And the second question is, and when do you accommodate employees who have a reason to be at higher risk for infection?

For the first question, we are slowly, state by state, increasing our elective clinic visits. We started with the people who were sickest first, beginning-- those people who had very active need for monitoring or cardiovascular testing, and we're slowly increasing. Now, we never fully closed our clinic because there were people with severe aortic stenosis, unstable angina, who still needed to be seen.

But we are now gradually opening it step by step while we maintain safe social distancing. Everyone's wearing masks. If a patient can't wear a mask for physical reasons, we wear goggles. And it seems to be going well. We have no documented cases at Mayo Clinic in Florida of any patient-to-physician or physician-to-patient in the outpatient setting transmission.

The second is when to accommodate. Every institution may have their own guidelines for this. The Mayo Clinic has a tiered system where patients who are employees who are over a certain age threshold, for example, 65, or people have immunosuppression or underlying disorders, medical disorders, that would limit their ability to cope with infection, have a ranked tiering system.

There are accommodations for some people who care for people who are immunosuppressed or have been under cancer chemotherapy recently. And we work with employee health and our legal department to determine when it is safe to come back. It is actually individualized, and so I can't give you really more specific information about that.

And perhaps, Mike, you and I might have-- this next question is about obesity and the association of obesity with poor outcome. The question asks, is that really mediated by ACE2 increase expression in adipocytes? As you were saying, it's the pericytes. It's the macrophages, the cells that are surrounding the myocytes, that may be primarily affected by this virus.

And so it's not unreasonable to think that other cell types like adipocytes, which express ACE2, could be mediating that kind of inflammation. It would be interesting to hypothesize whether you might see, because of pericardial fat, more pericarditis or pericardial effusions in those people who had adipocyte-mediated inflammation in the heart, but no human data that I'm aware of.

MICHAEL ACKERMAN: I like that. But I think that the question also means it gives us all a good reminder that I think all of us as cardiovascular specialists, cardiologists, we need to do a much better job in preventative cardiology. Those who are obesity are not doing as well. Those who are smoking are not doing as well. So once we get to the other side of COVID-19 pandemic, it's time to get our patients in shape again.

We need to be stopping smoking. Do it now. We need to be losing weight. Do it now. None of these things have any health value whatsoever, and the cost is tremendous.

LESLIE COOPER: Absolutely. There are a few other questions I'll touch on, but I don't think we have a definite answer. The next, from Dr. Martin, why do African-Americans have worse outcomes? Is it due to electrical complications or something else? I don't know that we know the mechanism, but I-- do we know?

MICHAEL ACKERMAN: No, we don't. I think, Patricia, the reason I love the question-- I wish I could give you a full answer. But stay tuned. We have an embargoed paper that's coming out early next week that suggests one potential explanation as to the why it's been so much worse. Obviously, there's health care disparities in minority, in certain ethnicities, and we know about that.

But there may be more than just health care disparities. What if there is genetic predilection? What if there is genetic vulnerability? And there is one particular long QT syndrome-associated gene where African-Americans have a much higher frequency of a pro-arrhythmic polymorphism. And you could envision that being an element of the perfect storm, even without hydroxychloroquine, that the cytokine storm itself in a black individual, and the hypoxemia, could interact in an environment gene way to make black individuals much more at risk of lethal ventricular arrhythmias in the setting of COVID-19 than, say, Caucasians, for example, where this genetic marker is almost completely absent.

So stay tuned. That's not going to be the whole story. But I'll put a nickel or so when we look back at the data-- and if we could genotype those black individuals who are succumbing-- that they're going to have a much higher burden of this genetic susceptibility marker.

LESLIE COOPER: And while we're on genetic susceptibility, is there any evidence for a sex difference? The last couple questions from Dr. Al-Akshar relate to estrogen and the influence of the virus.

MICHAEL ACKERMAN: I know from our paper, Ammar, that in our hypertrophic cardiomyopathy collection, our biorepository of the frozen myocardial specimens, ACE2 levels, protein levels, were higher in every sample, regardless of the genetic driver for the HCM, regardless of gender. But what we did observe and is that the women, the female samples, their levels of ACE2 were 30% higher than the males.

So there may be that. I haven't seen that in the other forms of heart disease that have reported higher levels of ACE2, but it was a pretty convincing signal of a difference in ACE2 levels in the female samples compared to the male samples. Besides that, I haven't seen anything on gender. Have you, Les?

LESLIE COOPER: No. No. The first papers didn't-- I don't remember a sex difference in the early ones. There are a lot of more recent ones. Good question for Gury here on endothelial dysfunction. Is it important-- I'll paraphrase the question-- to know whether endothelial dysfunction versus myocyte dysfunction is causing cardiac injury? And that's obviously something we can measure in the cath lab with our pharmacological interventions.

[INTERPOSING VOICES]

GURPREET SANDHU: Thanks, Les. Yeah, that's a great question. That is something which we have been debating internally, what is a contribution of endothelial dysfunction. At this time, we truly don't know, and we really have no way of testing in acute phases because then some of the markers are not quite right, and the information we get with CFR, FFR, may not be accurate.

So there are many theories in terms of what's causing ST elevation-- combination of myocarditis, combination of DIC, just generalized inflammation with those patients also showing up with Kawasaki-type of lesions in younger patients. So right now it's pretty much an unknown.

LESLIE COOPER: Yep. Mike, we have several questions that have come in related to QTC assessment between the EKG versus telemetry or other methods. That's a general question, and another above that on QTC differences between races.

MICHAEL ACKERMAN: Great. Things, Les, and thanks, Mansoor, for the question. And I think you can-- we all can measure the QTC off of telemetry. It's good enough. So and you know, if you walk in the room and you see on telemetry that the QT interval is less than half of the proceeding RR interval, you know that the online calculator will tell you that the QTC is under 460 without even entering it. So that's a quick, on the fly, green light go assessment on what's the state of the QTC health.

The smartphone-enabled technologies are giving very good signals. Right now there's only two companies that have FDA approval for QTC monitoring. One is AliveCor. And just recently, Mayo Clinic and AliveCor signed an agreement where virtually all of the QTC measurements being made off of the AliveCor device right now are being overread for a QTC measurement from the Mayo Clinic ECG laboratory that is directed by Dr. Peter Noseworthy.

So we can assess the QTC off of any of those modalities, which is great for our patients and great for our ECG technologists. We don't have a 12-lead ECG being wheeled into the room with an ECG professional using up their PPE equipment and having a machine getting contaminated and so forth. So I think on the other side of COVID-19, we're also going to have these advances in how do we assess the QTC and how we incorporate the QTC as a vital sign in the care of our patients.

LESLIE COOPER: Thank you. Before we finish-- and we're almost at the top of the hour-- I think Dr. Sandhu has one more comment.

GURPREET SANDHU: Thank you, Les. I basically wanted to talk a little bit about elective procedures versus the non-elective ones. In cardiology, in general, a majority of things that we do in terms of procedures, both invasive as well as noninvasive, if not done in a timely manner, there will be an impact on the morbidity and mortality of the patient. So I would basically say, a majority of things are not truly elective.

But in terms of elective procedures, what Mayo Clinic did very early on in alignment with all the local, state, and national guidelines, we shut down all elective procedures completely. So here in Minnesota, we still have restrictions. So in Rochester, we are not doing any elective procedures. But other states have more relaxation on elective procedures, especially in areas where there is less prevalence of COVID-positive patients, and there elective procedures will slowly start being offered in the near future.

LESLIE COOPER: Great. Gury, thank you so much. And I'd like to thank everyone for joining us today. I hope that you've enjoyed this webinar as much as we have. Thank you so much.