

**American College of Cardiology**

**CCA-ACC Communication**

**Conference of COVID 19**

**March 18, 2019**

**(Video shown)**

MODERATOR: Good morning, Harlan. Good morning, the governance of ACC and their colleagues from the United States of America and also colleagues from China. Professor Cao and all of the colleagues. First of all, welcome to this webinar organized by the Chinese Cardiovascular Association and the American College of Cardiology.

Since last nearly three months, since the outbreak of this novel Coronavirus-19 was initiated, the first case in Wuhan, up to now, we have had a very difficult in the early period, especially in last December and January of this year. Because at that time, no one knows what it is. We get - the hospital and the government were not prepared for this outbreak. Therefore, in the early phase, we were really confused by this epidemic.

Afterwards, under the organization of our General Secretary, President Xi, we sent 42,000 medical personnel to Wuhan. Among this, 28,000 were nurses. You have merely seen from the news that now, today, we have only 21 cases all over China, but only one from the Hubei Province, three from Shanghai, 14 from Beijing. All of those cases were travelers or passengers that just came from abroad.

It seems to be now the situation is becoming

better and better. This is, therefore, why our teams from - out of Beijing, Shanghai, and Anhui(?), they now came back.

Today, we try to share our experience, the last three months what we had, what we have been undertaking, and what experience on evidence we got. We have tried to help our colleagues from American College of Cardiology to shorten the mistakes we had in China, especially for the patient with multiorgan damage, with complications. It is hard to handle this kind of patient and hard to screen or diagnose the patient.

Today, we are really delighted to have - I would like to give a brief introduction of all of the members who attend this teleconference. First of all, the person talking, he is President Elect of Chinese of Chinese Society of Respiratory Disease and also Vice President of China-Japan Friendship Hospital. He is the top physician who evolved from the beginning of this epidemic in Wuhan. He is today still in Wuhan. He connected and upload his slides to give an introduction regarding the therapeutics of this disease.

We have from CCA, Professor Huo Yong, the Chief of the Department of Cardiology of Peking First Medical College and Professor Xu Yawei, the Director for the

Department of Cardiology from the Tenth People's Hospital in Tongji University, Shanghai, and Professor Chen Yundai. She is the Chief of - Director of the Department of Cardiology from the Military General Hospital. And, of course, Ma Yi-Tong from way northwest China, from (?), Xinjiang Medical University, affiliated with the hospital, the Chief of the Department of Cardiology.

We have from the ACC, the governance. We have our guest of honor and also our old friend, Harlan Krumholz. We knew him very well. I think every cardiologist in China knew him well, except I think Professor Cao Bin. Maybe you don't know him. Every year, he traveled to China to deliver lectures to help us to do research. He is the professor of medicine and professor in the Institute for Social and Policy Studies at Yale University. He is also the director in the Center for Outcomes Research and Evaluation at Yale University, New Haven Hospital. He has published numerous original articles, which really influenced the direction of cardiology, especially for the policy making in the last few years. Harlan, I thank you very much.

First off, I would like to invite Professor Cao Bin to give his presentation because Professor Cao, he has to leave a little bit earlier. Following his presentation,

we have a short discussion. We start afterwards with the second presentation. Professor Cao Bin, he will deliver the first presentation regarding the interpretation of the Guidelines of Diagnosis and Treatment of COVID-19, Version 7.

In the last two months, from the first version to the seventh version. We know this virus more clear. Professor Cao, please deliver your lecture. Thank you very much.

DR. CAO: Thank you. Thank you for the kind invitation. It is my great honor to introduce the Chinese Guideline of Diagnosis and Treatment of new Coronavirus disease. Now, this is called COVID-19.

Can I have the slide, please?

Thank you very much. As introduced by Professor (Moderator), I have been working in Wuhan for more than two months. I came here on the last day of 2019. I drafted the first version of the Guideline on the day of January 1<sup>st</sup>. We got to know the disease step by step. Now, we can see that China has the seventh version of the guideline.

Now, everyone knows that it is a new disease. The disease is caused by a virus. The virus is Coronavirus-2 now. When we look at the genome sequencing, we find that

the SARSC-2 shares about 80 percent identity with SARS and shares only half of the identity with MERS. Because the virus is sensitive to ultraviolet and heat in hospitals we also use ethanol to do the disinfection.

Now, the disease has spread to the world and is not a Wuhan disease. It is not a China disease, but also a global disease. Everyone knows that the number of cases, over 10,000, include Italy, Germany - and it will be no surprise that the Americas will face increased cases. Now, I have a number of more than 5,000. Maybe the number will increase to 10,000 during the next days.

The academicians and the pathologist in China have investigated the pathological changes of the lungs. We can find that - from the H&E stain, we can find that there is a hyaline membrane formation and interstitial mononuclear inflammation. Also, there is some thrombus. Later, I will show in details of the clots of the small vessels of not only lung, but also other organs, including the heart, the liver, and the kidney.

Here, from the electron microscopy, you can find that the typical virus particles. So, you can imagine that it is really a viral disease because there are lots of viral particular in alveolar type II cells. This is the

main reason or the cause of the disease.

It is bad for the lungs. We also find that there is some damage to other organs, including the heart, including the liver, and include the kidney. There is a predominant phenomenon of the severe or critical COVID-19 that we find decreased number of lymphocytes. We are not clear about the underlying reasons of the lymphopenia. It is maybe due to the direct damage of the virus to lymphocytes or maybe due to the immune modulating cell damage of the lymphocytes.

I am going to introduce the diagnostic criteria of COVID-19 used in China. The latest WHO guideline also follows the Chinese guideline. When we look at the suspected cases, we use both the epidemiology data and the clinical symptoms.

During the early days, when we drafted the first version, maybe the epidemiologic histories were located in Wuhan. Now, it is not only located in Wuhan, but other areas. So, maybe we can find that via the Wuhan travel or surrounding areas or contact with a COVID-19 patient or contact with patients with fever or respiratory symptoms or with the COVID-19 confirmed. Maybe there are cases with the clusters. When they have such epidemiologic history and one

or two of the clinical symptoms, the patient will be diagnosed as a suspected case.

When we look at the confirmed case, we have to - first, is a suspected case. Second, he or she will have the etiology evidence. According to our latest China Guideline, we use both nucleic acid testing or antibody testing. So, either RNA testing or antibody positive would be diagnosed as confirmed cases.

Here is our recent data. We can show the dynamic changes of the antibody response. You can find that the IgM responses comes very soon, but later followed by IgG. During the two months from the onset of illness, the IgM titers decrease, but at the same time, the IgG titer increased.

It seemed that the COVID-19 can transmit very successfully between human to human. The arrow is about - from 2 to 2.9. It is an etiology concept, which means that it is estimated that one COVID-19 patient can transmit at least to another patient if the situation is there. The median incubation period is around five days and usually no less than 14 days. Another bad news, even patients infected but with no symptoms can transmit the virus from human to human. Because of this, it is very difficult to isolate



patients. Some of them infected have no symptoms. We don't know who has the potential to transmit the disease.

The most important route of transmission is from the respiratory droplets and close contact. Today, I got a message from a physician in U.S. She told me that in her hospital the authority to not allow them to use N95 mask, but only allow them to use the surgical mask. I think in that hospital it is very dangerous for all of the healthcare workers because they are in high risk of this virus and high risk of getting infected. We have to keep in mind that I am not only talking about infection. I am also talking about death. Doctors and nurses get infected and died in Wuhan City. In my ward, there are two surgeons in very critical condition. Both of them are on ECMO and at risk of mortality.

When we look at the disease spectrum, 80 percent have mild illness. No pneumonia or mild pneumonia. 80 percent of them recovered spontaneously. But there were 14 percent with severe condition, which means they have low oxygen level and they need oxygen support. Among all of them, about five of them were critically ill status. They need mechanical ventilation or ECMO or septic shock. Those five percent of patients require ICU admission.

Here are the typical clinical features of the COVID-19 patient. Fever is the predominant symptom followed by cough, myalgia. But there are less patients that have sputum. Some friends in America asked me, what is the difference between influenza and the COVID-19? I told him that COVID-19 symptoms are dry, which means that they have less of the sputum production. And COVID-19 comes more silently compared with influenza because influenza comes acutely in the high grade level of fever and headache. It seems that COVID-19 comes a little silently. So, it is a small difference between influenza and COVID-19.

We have to keep in mind that the more severe and critical cases, they will have the acute cardiac injury. Some of them may be complicated with myocardial infection. We will have to keep in mind that for patients with the cardiovascular underlying diseases or hypertension, we will have to keep a close eye on those patients because these patients are a risk to have the cardiac complications.

Here is a paper published in Lancet one week ago. You see the clinical course of the disease. The upper picture shows the survivors. The lower picture is non-survivors. It seems that the duration of dyspnea was 13 days for survivors, but 45 percent of survivors still had

cough at discharge. The median duration of viral shedding is as long as 20 days and could be as long as 37 days. It is the first time we find that for acute response to the viral infection, the virus can last so long distance.

Lymphocyte count was lowest on day seven. For survivors, lymphocytes can increase to normal. For non-survivors, the lymphopenia will continue until death.

When we look at the severe disease, we will have the inflammation. From our first paper in Lancet about one month ago, we have noticed the increase of the cytokine and chemokine, such as IL-2, MIP-1, and IFN interferon-gamma, which show that the inflammation may be one of the manifestations of a severe COVID-19. Could show that maybe the host-directed therapy may have some potential therapeutic.

Here is our recent paper, submitted and under revision, to our knowledge that for severe and critically ill patients it is not only a local disease. So, we cannot call COVID-19 is a pneumonia disease, but also a sepsis disease. In severe and critical cases, we will find not only pneumonia and ARDS, but also the acidosis and the internal environmental disorders, also acute kidney injury and acute cardiac injury. When we look at the multi-organ

damage we recall these conditions is viral sepsis.

Another common - abnormal finding is that the coagulation anomaly. You can find that there is - this picture shows that for survivors, the D-dimer has remained very low level. But for non-survivors, we can find that the huge increase of the D-dimer, even more than 70 or 80 - maybe later. I put later. Yes. For our recent Lancet paper, we had strong evidence that the D-dimer is an independent risk factor for in-hospital death.

So, there was a reason. When we published the paper, yes, many readers sent me emails asking me that Dr. Cao, what is the reason underlying the increase of D-dimer. Yes, when we look at the COVID - the SARS-2 virus, the receptor is E2. The most common E2 receptor is on the alveolar epithelial cells followed by endocytes. For severe cases, the virus invades the lung and from the lung to the blood vessels and to spread all over the body. The virus can bind to the endocytes. They may cause damage to the blood vessel, especially the microcirculation of the smaller blood vessels.

So, as soon as the endocytes is damaged, there will be a platelet and the coagulation around the damaged blood vessels. You should imagine it is not a mycotic

infection. It is not a (indiscernible). It is clots. It is clots all over the body. You can imagine why the high level of D-dimer. It is because of the widespread of normal coagulation all over the body. It is a problem of the disease. So, maybe for severe cases, we recommend anticoagulation therapy for those patients if otherwise contraindicated.

We can find that because it is not a lung disease, it is a whole-body disease. So, we can detect SARS-2 RNA not only from the upper respiratory tract secretions and the lower respiratory secretions, but also from the feces, from the urine, and also from the blood. So, when virus is - viral RNA is detected from blood, we call this patients is viremia. It is not strange that we have viremia in severe or critical cases. This disease can spread from the lungs to other organs, including the heart.

Here is typical features of the CT scan of all patients. You can find that the typical CT scan is ground-glass opacity of both lungs, from the early beginning to the later stages. We can find there is a rapid increase of the lung infiltrates from the local patchy to the bilateral distributed ground-glass opacity.

Now, here is a beautiful paper published in

Lancet ID. You can find that from the beginning, there is only ground-glass opacity. When the disease has progress to the second week kind of to the third week, we find that the consolidation and reticular CT scans of the patients.

We also have encountered many patients with rapid deterioration on CT scan. You cannot imagine how fast. In the morning, you go around the patient and the patient seems good condition. In the afternoon or in the evening, there is rapid deterioration to respiratory failure and a need for mechanical ventilation. Some of them may die because there is no rapid intubation for them. The downside is rapid deterioration can occur within 24 hours.

Here is a 70-year-old man. The first CT scan is taken on day nine. After four days, we can find a rapid increase of the ground-glass opacity of both lungs. The patient died two weeks later.

Here is another 62-year-old male, also manifestation with ground-glass opacity. You see the rapid increase to the consolidation. So, that is the typical scan of ARDS. The patient unluckily died 15 days later.

Now, I will introduce the isolation and support treatment because at the beginning there is no effective antiviral therapy for this new disease. So, how can China

control the disaster?

Yes, I think the two key points is - the first is isolation. We opened over 10,000 beds for those suspected and confirmed cases to stop the transmission between human to human transmission.

The second that we used is supportive treatment for those patients. For severe patients, they have been admitted to hospital and critical patients are admitted to ICU and close monitoring and given the optimal supportive therapy. Most of them recovered from the illness.

Here is a picture to show what we used to treat these patients, including the respiratory support, circulatory support, renal replacement therapy, convalescent plasma, and the other therapeutics.

I think the most issue I want to talk is antiviral because it is a disease because by a virus. It is easy to understand that these patients need an antiviral. Unfortunately, so far, there is no solid evidence-based medicine data to show a specific antiviral therapy.

I have been leading three clinical trials. One is the Lopinavir/ritonavir monotherapy. Now, we have a Chinese name for this trial. It is LOTUS China trial. The trial has been completed and our paper was accepted. I am happy that

you can find this paper tomorrow morning. The data shows that this drug has some promising results, but I will not show you the details at this time. You can read my paper in I think about 12 hours.

I am also leading another two trials. They are the CAP China Remdesivir 1 for mild-moderate pneumonia cases and the CAP China Remdesivir 2 for severe and critical care pneumonia patients.

This flow shows the CAP-China Remdesivir trials for COVID-19. So, I will not go into the details of this trial. I only want to show you that the - I know that in America and other countries, Remdesivir have already used the severe or critical care patients with good outcome. What we, in China, sought to do is to provide the solid evidence to show the accuracy and safety of Remdesivir.

Other options including the interferon, Ribavirin, Chloroquine, and the Arbidol and Convalescent plasma and the Favipiravir. But all of the other options also have no solid evidence of the accuracy and safety.

The corticosteroid is still controversial. Although, I have shown you there is - the over-inflammation is one of the phenomena of the severe cases. But in China, we only used corticosteroid with patient with rapid



progressive deterioration of oxygen, especially for those with the rapid degeneration of the CT scan. In our China (indiscernible), I am the corresponding of the China corticosteroid (indiscernible). We have listed the contraindications, such as allergy to corticosteroids, uncontrolled diabetes, uncontrolled hypertension, GI bleeding, severe immunosuppression, and so on - and the severe bacterial or fungal infection.

We recommend low to moderate doses and the short-term use of corticosteroid. There is still some controversy of the steroids. I have published a comment in Lancet to introduce what the Chinese doctor thinks about the use of corticosteroid and the contraindications.

During the last week, after we had published the paper in Lancet, I received many letters. Most of them - most of the letters come from primary physicians, but some of the letters come from cardiologists. Here is a letter from Professor Giovanni. He is the Chair of the Council on Hypertension at the European Society of Cardiology. His question is about the ARB and ACEi for hypertension patients. His concern is that the anti-RAS, of course, reduce the angio-II activity, which maybe is good for lung inflammation response. But another concern is too much

inhibition of angio-II might increase ACE2. I had mentioned that the virus will bind to ACE2 receptors in the COVID disease.

So, it is a dilemma. Use or not use ARB or ACEi? Another side of the scientific question is for those with this hypertension already receiving ARB or ACEi, who would be more at risk to develop severe or critical illness? The answer - I have no clear answer to this question.

In my response to Professor Giovanni, I told him that in our cohort, for non-survivor, 48 percent of them had hypertension. Only 23 percent in survivors. The OR for hypertension is 3.05. Is it that hypertension is really a severe complication of COVID-19? We need more research and even the animal model has not answered the question of ARB and ACEi.

Last, I will show you the discharge criteria of COVID-19. In China, we use the criteria of body temperature is normal and respiratory symptoms improve. Pulmonary CT scan shows obvious absorption. And they list two consecutive negative RNA testing for respiratory specimens.

So, at least, I appreciate the contributions of my colleagues at Friendship Hospital. Also, I appreciate my friends Fred Hayden, Peter Horby, and Liu Liang for the

pathological findings. I also appreciate our cooperators in Wuhan City and all of the healthcare workers involved in the diagnosis and treatment of patients, especially for those who have lost their lives during the last few months. Also, I appreciate WHO and National Natural Science Foundation of China, and also CAP-China Network. Thank you very much.

MODERATOR: Thank you. Thank you very much for the talk. This is the first time I have had such a complete overview of all of the information you shared with us. Any questions? Do you have any comment or questions?

DR. KRUMHOLZ: Yes, first of all, I just wanted to express our deep appreciation for all of the panelists today and to you for organizing this and for all who are participating. As you know, we all have deep respect for the service that you provided to your country, but also the ways in which you have spread information and taught us all, all of you and all of your colleagues in China. You have been so committed to trying to help us - and help us prepare.

Who knew that this was coming and that you were going to be the first, but that you were going to help us learn quickly and were so generous in sharing what you were

learning in the midst of working so hard. Having to see so many patients, but still recording and learning and applying scientific principles so that we could get smarter fast so that we could help to confront this. So, I think on behalf of colleagues around the world, we are deeply appreciative of our Chinese friends, colleagues. We are all in this together.

The other thing is that in medicine, we know no borders. We work together. We are one family in medicine. We work together on behalf of our patients to do everything we can to ensure their best outcomes and to work together to share knowledge so that we can all do our best. What one person learns can be transferred to others.

I can think of no better example than what we just heard from your presentation. It is a terrific summary. But also, the fact that you were on the frontlines. You have seen more people directly than any of us in the United States and many others around the world. You have seen. You have been there. You know what they have done.

I wanted to ask you when you started caring for these patients what surprised you the most? What did you think was most unusual or different about this? How did you

know that this was more than just a usual bad season of influenza? What was it did you learn? You have given us a lot of knowledge. In your heart, when you saw this, what made you say this is different? What was the most important things that you thought were different?

DR. CAO: Thank you for your kind words. I think it is a good question. During the early stage of the COVID-19, during the influenza season, yes. At the beginning, when I first came to Wuhan on the last day of December 2019, yes, in my mind, I am thinking of influenza viral pneumonia. But the RNA testing told me that isn't active.

It takes Chinese scientists about one week to find the truth. It is a special viral pneumonia caused by a normal virus. Now, it is called the new coronavirus.

Yes, you are right that in Wuhan City we do find the co-infection, a mixed infection with the influenza virus and then Coronavirus. During the last two months, we have more COVID-19 cases compared with the influenza viral pneumonia.

I think the nature is very special. Usually, in the flu season, we will have many influenza viral pneumonia. During last season, we have less influenza viral pneumonia. It seems that the two viruses - as if they have

discussed they will not come together. I don't know. I don't know the underlying reasons, but it seems that the two viruses will not come together. If they had come together, I believe that more and more people would die from the disease.

DR. KRUMHOLZ: Let me ask you one other question while we have you. I want to make this important point as the United States prepares for this. We do hear from some voices in the U.S. that we are over preparing, that this will not be as bad as we think. You have been on the frontlines. Can you reflect on what you saw in Wuhan and speak to the public and to the professional people in the U.S.

People all over the world are listening to this. Some people are not yet seeing what you have seen. You have seen it up close. We would like to hear from you what was the experience. Do you think anyone is over preparing?

DR. CAO: I think there is no story of overreaction, only less reaction. Because - yes, not only China, Italy, Iran, Korea, and now Germany and Spain, they have encountered the problem. I think the most dangerous thing is that the people are infected and can transmit virus between human to human transmission, but these people

only have mild illness or no symptoms. I think it is the most dangerous.

For example, yes, you are sitting together with your friend. The friend seems okay. But maybe he has been already infected. You have a dinner with him and you will be getting infected. Here, it is - it is a most terrible thing. You can imagine there will be 1,000 or 10,000 people getting together, such as music, such as the basketball game or TV show maybe, a lot of people getting together. One person - as I mentioned, at least one infected patient can transmit the disease to two or more. This is very dangerous.

You cannot imagine how fast the virus can spread from human to human. I will tell you that some of them - of course, 80 of them will be recovered without consequence. We will look at the data from Italy. About five percent of them died from the disease - not only elderly patients, but also the young end and even doctors and even nurses.

We don't know all of the numbers, all of the knowledge. You can answer the question of overreaction. There is no overreaction.

MODERATOR: I fully agree. Unless you see the hospital from the ophthalmology even hospital - my

hospital, four colleagues died during this epidemic. I think even though we see the total mortality is not very high. It is roughly three percent according to the statistics now. But I think really - because no people has immunity against this virus. If you see the influenza, maybe you have a proportion of our people will get infected. If you get contact with colleagues or friends and close enough, you will get infected. I think no one has immunity to this new virus. No one can see this overreaction.

DR. KRUMHOLZ: Can I ask one more question? I can tell you just because I am representing I think a lot of interest in the U.S. about this. Can you tell us something about what it was like in the hospital and how you managed the surge in cases? What was the spirit like? What were the strategies that were best that enabled you to manage this kind of unanticipated need that occurred and also the shortage of materials, often, including ventilators, but maybe also masks and other protective gear?

We are experiencing that now. We haven't yet escalated in cases. But can you comment on what life in the hospital in healthcare areas were like and how you best coped with that?



DR. CAO: Thank you for the question. The answer is diagnosis. The answer is diagnosis. The third answer is also diagnosis. If you do not know who is infected, you can do nothing. Diagnosis is the key point.

So, the recommendation to the American doctor and American hospitals that at least you will have the capability to do diagnosis. I think the most important is RNA testing, followed by antibody detection. As soon as you make the diagnosis of a patient, you have to keep in mind that the patient maybe will not go to the department of respiratory medicine. The patient will go to the cardiac clinic. The patient will go to the diabetes clinic because these patients have such underlying diseases. They will go to the hospital for the capabilities. The danger is that maybe he has already been infected. Here is a lesson that we have.

So, you have to be very, very careful about the patient not only to the respiratory clinic, but also to the cardiac clinic, to the diabetes clinic. If there is any suspicion, you will do the RNA testing immediately. As soon as you make the diagnosis, you will keep the patient in isolation.

I think it is very easy to understand. If we do

this, it is not overreaction. I think it is a normal reaction. It will help the patient. It will help the relatives of the patient. It will help your colleagues because your colleagues, doctors and nurses, you will be at high risk of infection.

MODERATOR: Thank you very much. I think that gives a very clear answer. I think because of different philosophy, Asia, especially in Japan, a lot of people have allergies. They are used to having a mask. This time, also, we ask to wear mask when you go outside, when you get together, and so on. As I heard in Europe and the United States, people there do not like if anyone wears a mask walking on the street or in a walking area. In this situation, you should really change this philosophy or this habit. To protect is very, very important.

So, thank you very much for the talk. We will continue to the next -

DR. KRUMHOLZ: I just have one other last question. When did you wear protective gear in the hospital? Were you wearing N95s all day or only when you entered rooms of people in isolation? When did you use this protective gear and what was the most effective strategy?

Sorry, but it is on our minds a lot. In some

ways, we have a shortage of these. I think there is a lot of interest in the States about how did you protect yourself. What was your approach within Wuhan? Sorry, just last question.

DR. CAO: I will give you the quick answer. If you are working in the isolation ward, if you are taking care of COVID-19 patients, you have to wear the N95 mask. If you leave the isolation ward - for example, you are staying in the office, you go to the café, then a surgical mask is enough.

DR. KRUMHOLZ: But you were wearing surgical masks all the time?

DR. CAO: Yes. In the hospital. In hospital. I have to remind you - I remind the American doctor that normal life is changing. If you are still - if you still think that you should live your normal life, it is not true. Normal life is changing not only in China, but also in America, in other countries. You have to think about it. It is not a normal life. It is a COVID-19 life. It is a pandemic life now. Thank you.

MODERATOR: Thank You very much. We will continue to the next presentation, delivered by Professor Chen Yundai, the director of the Department of Cardiology of the

Military General Hospital. She will deliver a presentation regarding the clinical characteristics of COVID-19 patient with cardiovascular disease. Professor Chen, please.

DR. CHEN: Good evening. Also, everybody, I think a very excellent presentation from Professor Cao. Something is quite clear for everybody, but I want to just share some information about this kind of disease combined with cardiovascular disease.

As you know, it is an epidemic. It is a problem. Now, it is quite severe globally. Also, it is a fatal threat to the global public health. The mortality I think it is not only 2.3 percentage, but is from China early stage. In Italy, outside of China, maybe it is a little bit higher. As mentioned by Professor Cao, mortality might be five percent in Italy.

Anyway, it is lower - the mortality is lower than SARS and MERS. For the recent cardiac injury, and also its underlying implications, some information. From the early stage data, shows it is 60,000 subjects, the data. You can also find this kind of disease combined with cardiovascular problem with a little bit higher mortality, almost 10 percentage. It is a problem. This kind of virus also is quite homologically to the SARS and MERS. Also integrated

package is very ACE2 and also is quite targeted about the (indiscernible) and also others.

From the autopsies, some issues. Also shows inflammatory change in heart. Jst as Professor Cao mentioned in Lancet and others explained - but anyway, for the heart, we also find there generally is an inflammatory change. You can find interstitial mononuclear inflammatory infiltrates. Also, some endothelial shedding. Until now, (indiscernible) couldn't find some REA(?) about this kind of virus inclusions in the heart.

For what we can find for the cardiac injury in clinic situation, this very early stage paper showed us some troponin I and troponin T biomarkers, cardiac injury biomarkers, a little bit higher. Generally, very high elevation of the CK-MB or troponin I generally in the severe cases. But in more general amount and also normal cases, only shows some tachycardia and also a little bit higher troponin.

When we find the - have some hypotheses of the cardiac injury, maybe from some literature, find maybe the three hypotheses. First of all, some ACE2-mediated direct damage just like the - shows increased affinity to the ACE2 and reduced ACE2 expression and dysregulated RAS system.

And also very severe hypoxia induced-myocardial injury. Also we can find intracellular acidosis and oxidative stress, which can cause the myocardial injury.

Also, cardiac microvascular damage. This is also vessel hyperpermeability and angiospasm.

Also, systemic inflammatory response syndrome. Just, generally, we call cytokine storm. Also, we can find some thrombosis microvascular damage. So, this also can be found from the pathology.

This is just to mention the current diagnosis. I do want to say a little bit more about that.

For the mortality, we generally find it to be quite related with this kind of disease and combined with cardiovascular problem. Cardiac injury occur in severe patients. Mortality, generally, in the severe cases accounts for more than higher - 49 percentage. So, this kind of infection maybe is an initiating factor. Maybe the preventing the transition to severe cases is crucial.

From the seventh version, we need to pay attention to some cases from the amount of normal cases and change to the severe cases. So, we can follow the lymphocyte levels and the inflammatory cytokines. Also, to pay attention about pulmonary lesion progresses.

In my team, I also want to find some new imaging index. We use 41 consecutive patients in Beijing's YouAn Hospital to find some issues. This is decreased pericardial adipose tissue is positively associated with the severity of the disease. You can find some CT threshold attenuated value of the pericardial adipose tissue decrease in the critical and severe issue. Confounders is inflammatory degree, but it is not quite clear whether or not with the cardiac injury.

This is a management - it is not special.

For this kind of disease combined with CVD, we just need to pay attention to some drugs used for this kind of patient. Just now, Professor Cao mentioned about the RAS system problem. Actually, for the ACEi or ARB, whether patients should continue taking this also remains controversial. Some Chinese cardiologists think that maybe for this kind of case, also with coronary heart disease and all hypertension and heart failure patients, generally, if no special issue, it is generally recommended to give the standard therapy - follow the standard CVD guideline. Also, for the antiplatelet drugs, also we can continue to use some antiplatelet therapy drugs.

Also, monitoring the liver function closely. So

also use of statin, we need to test the liver function.

For some critical patients or severe cases, also we can find some monitoring EKG. We can find some tachycardia cases. Generally, the heart rate is almost to 100 or 120 beats. So, it is quite dangerous for some initiated - some acute coronary syndrome or acute myocardial function. So, also to pay attention for this.

For some cardiovascular drugs, interaction between the antiviral drugs and also cardiovascular drugs I think is - also should pay attention. To be learned, we just want to show two cases from - my colleagues sent me. I think they are very interested. Because when we focus on cardiac events - this case is Coronavirus also with myocarditis. This is a male, 77-years-old. The chest pain and dyspnea for three days. X-ray shows just like the - shows enlarged of the heart. You can show that is SER(?). Chest CT indicated pulmonary infection. EKG - I'm sorry it is that small - shows it is very definitely inferior wall ST segment elevation. Also, we performed a coronary angiography. It looks normal. The troponin T is quite high and also CK-MB. Echo also shows ejection fraction is very lower.

The treatment, according to the myocarditis. So,



one week later, you can find the x-ray shows normal size of the heart. Echocardiography shows - the ejection fraction has gone to the normal. So, it is quite an interesting case.

Another case is just a recent STEMI case. It is a male 60-years-old and a dry cough for one week and chest pain for 26 hours. You can show this EKG is quite - ischemia disease. Also with a history of hypertension and smoking. This case is troponin T quite high. BNP also shows heart failure. Also, the echo lower - ejection fraction is lower.

For this case, because the situation is not allowed to go to the (indiscernible). Also, no thrombolysis. Generally, give the IABP and also incubation therapy. Quite unfortunately, three weeks later, he looks no better. Also, shows severe ischemia in inferior wall.

Just for my personal view, we need to with this kind of disease combined with cardiovascular disease, early self-management and also diagnosis in time. Therapy for severe cases. Also, for this kind of case, it is quite important.

So, also, until now, for the cardiac injury also we have this kind of problem and also it is not clear for

the pathophysiology. Also no effective treatment yet. For the severe case, we need to pay attention to some patients combined with cardiovascular disease.

Just we want to show a thank you much.

MODERATOR: Thank you very much Prof Chen. I think we first invite Professor Xu's group to give his presentation regarding the diagnosis and treatment of acute myocardial infarction and protection of cardiologists in this COVID-19 outbreak. We will put the discussion at the end. Thank you.

Professor Xu, please give your presentation.

PROF. XU: Good evening, distinguished Professor (Moderator). On behalf of our Clinical Chief, Professor Yawei Xu, I am Dr. Yi Zhang from Shanghai Tenth People's Hospital. I am so glad to take this great opportunity to present to you some Chinese experience on the diagnosis and treatment of acute myocardial infarction and prevention of cardiovascular disease in this outbreak of the COVID-19.

What we are facing today actually is a pandemic. On March 13<sup>th</sup>, WHO Director-General said that we have, therefore, made an assessment of the COVID-19 can be categorized as a pandemic. It is true that this virus has been widely spread all over the world. Until March the 16<sup>th</sup>,

more than 153,000 cases of COVID-19 have now been reported from 146 countries and territories with over 5,000 deaths.

So, if we get a chance to compare the situation in the previous outbreak of SARS in China in 2003 and this outbreak, we will see that Chinese people really get lessons from the previous outbreak. Now, we respond very rapidly to this outbreak. Until now, we can see that this Coronavirus in China has been gradually controlled.

If we take a look at the clinical future of this previous 72,000 patients, we see all of the (indiscernible) very susceptible to this disease with about five percent of the cases actually critical cases. We also can see the overall mortality for the infected people at 2.3 percent. It is increased in the elderly population. For severe cases, the mortality is as high as 49 percent. We also can observe there are about 3.8 percent of the healthcare providers actually infected by this disease. It is all workers in the previous stage and many in Wuhan with five deaths.

If we take a close look at the daily unique confirmed case among the health providers, then we see that the peak of the incidence happened in February the 1<sup>st</sup>. After that, the incidence decreased gradually. That is

because within about 50 days we released seven versions of the Chinese Guidelines for the Diagnosis and Treatment of COVID-19 as Professor CAO previously mentioned. Also, under the work from the CC-CP(?) led by Professor Jing-Bao Gu(?) that we totally published five guidelines of the expert consensus on the management of the patients with cardiovascular disease, including the protection of the cardiologist strategy and also the treatment and diagnosis strategies of acute myocardial infarction. Today, we will focus on these two topics.

As I mentioned, the situation in China is gradually controlled. The peak of the incidence or we say the newly confirmed cases, the peak happened February the 13<sup>th</sup>. They decreased gradually until now. Daily, we would have only 10 to 20 newly diagnosed cases. For the cumulating or the remaining confirmed cases, it decreased dramatically in a couple of weeks until now we have totally 9,900 cases - remaining cases, many in Wuhan.

As I mentioned, the Coronavirus has been widely spread in the world. If we do the comparison, the red line indicated the daily newly diagnosed cases in China. The orange line indicated the newly diagnosed cases outside of China. We now totally get the number is 92,000 cases with

the confirmed cases in the countries outside China.

So, we think that we can share some experience. Maybe it is valuable and helpful to our colleagues overseas. Today, we will focus on the two topics. The first is diagnosis and treatment of acute myocardial infarction because it is our duty. As cardiologists, we need to treat the severe case and emergency case like acute myocardial infarction patients. Also, we need to focus on the protection of the cardiologist because we need to protect ourselves. So, there are some general principles that we want to show.

As for the AMI treatments, there are five general principles for treatment. The first, nearby treatment. We encourage AMI patients to seek and receive medical treatment at the nearest medical institute, minimizing the patient transfer.

And safe protection. Patients with fever and other respiratory symptoms should have their first consultation at the fever clinic. I think the fever clinic is very useful to control this disease.

Third, the thrombolysis first. In the case of suspected or confirmed COVID-19 infection, patients with STEMI should be admitted to an isolation room. The

thrombolysis should be performed for those without any contraindications.

Fourth, the designated transfer. If the pathogenic test is positive for the COVID-19, AMI patients with severe respiratory symptoms should be transferred to the designated hospital.

Lastly, we encourage cardiologists to do the remote consultation or to guide the team to make the future treatment plan.

Here is the flow chart for the diagnosis and treatment of STEMI patients. If the STEMI is diagnosed, the first question we need to check is we need to check the patient's history like the travel history or the contact history and also the body temperature, the ECG, the chest CT scan, and also the routine blood test. If it is a suspected or confirmed case, we will ask the second question, if the patient is stable or not.

If the patient is not stable, if because of the pneumonia or the cardiac issue - if it is a cardiac issue, then we will assess the STEMI onset time. If it is within 12 hours and without any contraindications of the thrombolysis, then we prefer to do the thrombolysis first. If it works - if it does not work or we - the treatment

window has exceeded 12 hours that we were to weight the benefit from the PCI and the risk of the further infection. So, if the benefit has over-weighted the risk that we suggest to the primary PCI in the designated catheter lab - the isolated catheter lab. But it is better to do it in an active ventilation catheter lab, but it is really (indiscernible) in China. We can choose the designated catheter lab for this kind of treatment.

So, this is several questions for the STEM patient treatment.

Second, we are talking about some strategies for the protection of cardiologists. There are also five general principles. The first is house quarantine. We need to - for the patient with stable cardiovascular disease, just to persuade the patient at home or the elective procedure intervention just to avoid unnecessary hospitalization. To save our bed capacities in the hospital, it is very important.

Second, for the confirmed patients with severe cardiovascular diseases, they are supposed to be isolated in situ. The hospital needs to organize a cardiologist consultant to make the treatment plan.

For the patients with suspected COVID-19 combined

by the acute cardiovascular diseases, these patients should be transferred to a designated hospital with a designated catheter lab.

For the patients with fever, first, they need to go to the fever clinic at first and then invite a cardiologist to do the in-hospital consultation, maybe a remote consultation.

For the patients who really need an intervention for the operation consent need to be signed by a family member who has no history of close contact with this patient. It is also very important to avoid the unnecessary contact.

There are also some specials for the fever clinic. I think fever clinic was useful during the SARS outbreak in 2003. Normally, it is set at the entrance of the hospital. Patients with fever and respiratory symptoms are set for the fever clinic. We need to check the routine blood test, assess the contact and travel history, and also the chest CT scan. If the cardiovascular disease has priority, remote consultation from a cardiologist is recommended. Otherwise, the cardiologist should be well protected with the personal protection equipment.

If an urgent surgery or intervention is needed,



cardiologists should report the case to the infection control department and medical affair department of the hospital. If the patient is excluded from the COVID-19, transfer them to outpatient or emergency.

So, that is all I want to share with you. Thanks for your attention. With all of our will, we will surely win the final victory. Thank you for your attention. Thank you.

MODERATOR: Thank you very much. Now, I think we have finished all of the presentations. We have nearly three-quarter for discussion and for questions. Any questions or comments, please?

PARTICIPANT: Yes. I just heard a very excellent lecture from Professor Cao. Really experienced on the COVID-19. I really struggle about the high elevation about D-dimer, especially in the severe cases or even the death(?) patient.

My question is about how to imagine what is the mechanism of - like the thrombosis, the whole body - is there any clinical evidence for that? It really is people with thrombosis - it is from clinical aspect, you find the difference, the general case of myocarditis compared to the severe case. So, is there any answer to mechanism or other

clinical manifestation?

MODERATOR: I think Professor Cao, he left. I will give some comment regarding your question. I think we do see a considerable proportion of patients they have elevation of troponin. They have elevation of CRP, elevation of BNP, and also elevation of LDH. Also, we see a considerable proportion of patients with elevated D-dimer. The underlying mechanism we are still - just like Professor Cao mentioned, we do not know why.

If you analyze the patient with the virus and not the virus, you see the patient with severe inflammatory storms have a worse outcome. This is why I think in my hospital we use the Interluken-6 antibody. In the patient with elevated interluke-6 and with elevated inflammatory infections, we have benefit from that specific group of patients, but not for all.

I do believe this is a mechanism - underlying mechanism is because of the systemic inflammatory storm, not by specific anything. I believe it is because maybe of this like DIC or the conception of platelets or the virus taking the bone marrow, but we do not have evidence. If you have the elevation of the D-dimer, we get the recommendation from the consensus - from the Guideline that

you have to give the anticoagulation no matter what the underlying mechanism.

PARTICIPANT: Thank you. Is there any indication for the severe patient with a high D-dimer we should give a patient the anticoagulation. Do you think it is reasonable for that? If we found maybe a really high D-dimer, if we found some thrombosis in some part of the body (indiscernible), is it reasonable for that? Do we use the anticoagulation for this kind of patient?

MODERATOR: To my mind I think it is reasonable because elevated D-dimer indicates no matter - large or micro-thrombosis event, I think it is reasonable to use anticoagulant.

DR. KRUMHOLTZ: I will say my opinion about this. Sorry, I was on mute. I think what is most important for us is to develop the means by which we can study rigorously what we do. So, I think there will be many plausible approaches to the care of these patients.

That is a very good thought about the anticoagulation. And it is one that - but we should test it. We need to be able to deploy rapid trials within our institutions in situations where there is a high level of uncertainty, where we could be doing benefit or harm. I

think we need to be able to not have a research infrastructure separate from our clinical infrastructure. We need to be able to funnel into our clinical care immediately in situations like this, the means by which we can rigorously test and learn from our experience.

We need to get smarter every day. That smarter means that we are able to test different approaches and then feedback to the group. These are also adaptive in nature in the sense that we need to be able to test and then refine what we are testing rapidly.

I think one of the things about this crisis is maybe it will help us to rapidly change our systems in that way. At least in the U.S., we are not configured to do that very well. We tend to take a long time putting together protocols. We take a long time getting approvals. Trials are expensive and take a lot of time. Increasingly, people are thinking about how do we build these into our workflows. Some of the work like what was done in Sweden where they were able to do the thrombectomy trials within the context of a registry, they were able to do that relatively rapidly. But we need to be able to do this.

I would love to test that idea. People come in with high D-dimer, what happens if we put them on

anticoagulation? How do we compare them with those we don't? We need to admit where we are ignorant. We need to run to try to throw light on that area and to learn fast and well.

I have a question or two that I think American colleagues would want to know. One is - so, Professor Chen, are you recommending that people have troponins routinely who are testing positive? When is this screening occurring? You gave examples of people with chest pains. Naturally, we would be thinking about the heart.

Our Chinese colleagues are reporting to us a very high rate of cardiac involvement. I think most cardiologists in this country, in the U.S., are still thinking this is not a cardiac disease. This is something else. A group is publishing in JAC soon a review that we have done with colleagues across the country trying to distill a lot of lessons from China, saying to our colleagues this is actually something that does involve the heart. I think that is one of the central messages we are hearing today.

But how are you suggesting we manage screening for that? How are you doing it in China? Can you tell us something about that, any of you, and Professor Chen, in

particular?

PROF. CHEN: Thank you for your question. I think for the biomarker testing for the case I think are quite important for the diagnosis of the cardiac injury. When we review some literature from some of the clinical investigations, it shows for the minor cases or some normal cases, the troponin I or CK-MB generally is normal or very minorly elevated. So, this is the level of the troponin-I for the majority of the cases, almost 80 percent of the cases. It is generally from the normal range to maybe several times elevated level.

So, generally, for the very severe cases or critical cases in the ICU for this kind of case, the CKmi or troponin I is dramatically elevated.

At this moment, from our seventh version recommended for the testing/screening, generally it is not very focused about CK-MB or troponin-I. But, you know, when you want to check the creatinine or some other liver function also you can check CK-MD or troponin-I. So, generally, I think that is the point.

Another one, generally, if we want to find from the mild or normal case to the severe case, just like Professor Cao mentioned, we need to pay attention about the

inflammatory testing, some CRP, but it is not very typical index. Interluken-6 or -8 and also just like Professor Cao mentioned, it is a new index, D-dimer, just as Professor (Moderator) mentioned, the D-dimer. I think there is enough emphasis in the seventh version, diagnosis and the treatment.

I think for the cardiac injury I think it is a quite important issue because just as Professor Cao mentioned, from the pathology's phenomenon, you also find vascular endothelium inflammation. It is quite popular. You can find it in the lung, heart, liver.

So, that is - I just reviewed his presentation. Just to mention, maybe the mechanism is vascular endothelium cell express high level of the ACE2. So, maybe that is why we can find vascular endothelium inflammation extensively. So, also we think maybe from the pathology find some point necrosis in myocardium. So, maybe that is the reason. We need to pay attention to the cardiac injury.

DR. KRUMHOLZ: Thank you. I have another question that was sent to me from Dr. Mary Walsh, the former president of the ACC. She asked me to ask you all what were you doing with the routine patients at the time when you were anticipating that this could grow? Were you changing

the outpatient visits? How did you change the structure of the way in which you were caring? Did you employ more telemedicine and remote for the routine patients? Do you have anything to share about your experience preparing for this and changing the outpatient practice?

MODERATOR: Yes. Because we nearly closed all of the routine outpatient clinics. I called all my colleagues of the Chinese cardiovascular physicians to give internet consultation for all patients, especially with chronic disease, with hypertension, with antiplatelet therapy, and so on. By the emergency - of course, the emergency room is still open. Ordinary patients, we are encouraging them to do the consultation on the internet. We have called many, many of our colleagues. They are doing on duty every day to answer the questions and try to give advice on patient medications and so on.

Secondly, we - a patient, for example, with emergency myocardial infarction, we announced that our consensus for the five items. Get the patient to the nearest hospital for the protection. We encourage thrombolysis. For example, with a patient with very risk situation, we have to shut down our essential air condition to do the primary PCI. We also encourage remote



consultation through (indiscernible).

We have one question to ask. What was the criteria for doing echocardiogram? In Wuhan, we have 10,000 patients. We are accumulated to every hospital. It is not possible to do echocardiogram for the patient even in suspected cases because in the early phase, all of the doctors, they are from respiratory disease, from ICU, from the infectious disease department. The cardiologist not got involved in the early phase. Only afterwards we sent 42,000 medical personnel to Wuhan. Among them, some of them from the department of cardiology. We began to pay attention to the heart problems.

This disease is a respiratory disease. The main issue is hypoxemia. A patient with hypoxemia, if he is afflicted with coronary artery disease, the myocardial ischemia is becoming more severe. Therefore, through remote consultation, I met several patients with myocardial infarction, but the myocardial infarction was - the diagnosis was established one week after. At the beginning, we do not record the ECG.

The piece we do see rarely - patient with the fulminant myocarditis. The case that Professor Chen Yundai just reported - we see also another case also with the

acute fulminant myocarditis. This kind of patient we need, for example, early initiation of an ECMO.

Because I saw Professor Yi-Tong Ma is on the screen. His group published the paper, the initial review of cardiology regarding how to use - how to manage hypertension in patients with or without ACI and AIB. Do you have any comments or your group has any comment?

PARTICIPANT: Yes. Please, Professor Ying-Ying, give us a comment about cardiac injury.

PROF. YING-YING: Okay. It is my honor to be here to present to the ACC. I will make a brief introduction of our articles on behalf of Professor Yi-Tong Ma.

COVID-19 and cardiovascular disease. We all know that in December 2019, an outbreak of pneumonia caused by a novel coronavirus occurred in Wuhan and spread rapidly throughout the country, with an ongoing risk of pandemic. After that, over 7,000 died around the world.

As we know, ACE2 is involved in heart function and the development of hypertension and diabetes mellitus. ACE2 has been identified as a functional receptor for coronavirus, including SARS-Coronavirus and SARS-Coronavirus-2. ACE2 is expressed in lung type I and type II alveolar epithelial cells, of which type II epithelial

cells are more strongly expressed.

In SARS-virus induced acute lung injury mice, the level of angiotensin II was also significantly increased. The level of ACE2 was down-regulated. The use of ARB effectively reduced the acute lung injury, reduced the pulmonary edema, and improved the lung failure.

With acute cardiac injury, SARS-Coronavirus and MERS-Coronavirus have similar pathogenicity. A recent meta-analysis suggested cTnI values were significantly increase in patients with severe SARS-Coronavirus infection. Up to date, several publications discussed cardiac injury. Accumulated evidence suggests that patients with severe symptoms often have complications involving acute myocardial injury.

As a mechanism of acute cardiac injury and as Professor Chen has introduced, the mechanism first the myocardial injury caused by SARS-Coronavirus-2 infection may be related to ACE2. The impairment related to oxygen supply-demand imbalance and (indiscernible) maybe the cardiac causes. (Indiscernible) direct injury. A cytokine storm triggered by an imbalanced response by T helper type 1 and type 2 cells.

For chronic cardiovascular damage, 12-year

follow-up survey of 25 patients who recovered from SARS-Coronavirus infection found that 68 percent had to have hyperlipidemia, 44 percent had cardiovascular system abnormalities, and 60 percent had glucose metabolism disorders. However, the mechanisms by which SARS-Coronavirus infection leads to disorders of lipids and glucose metabolism and chronic damage to the cardiovascular system are still unclear. Given that SARS-Coronavirus-2 has a similar structure to SARS-Coronavirus, this novel virus may also cause chronic damage to the cardiovascular disease system.

The patients with pre-existing cardiovascular disease, in one study, among the patients with severe symptoms of COVID-19, 58 percent had hypertension, 25 percent had heart disease, and 44 percent had arrhythmia. According to mortality data released by NHC of China, 35 percent of patients with SARS-Coronavirus-2 infection had a history of hypertension and 17 percent had a history of coronary heart disease.

Therefore, in patients with SARS-Coronavirus-2 infection, underlying cardiovascular disease can aggravate the pneumonia and increase the severity of symptoms. For patients with cardiac insufficiency who have underlying

heart disease, SARS-Coronavirus-2 infection may act as a precipitating factor to worsen his condition and lead to death.

The drug-related heart damage. In a study of 138 patients with COVID-19, almost 90 percent were given antiviral drugs. The antiviral drugs may cause complete heart block and dilated cardiomyopathy. It also increased the blood lipid levels and may accelerate the progression of coronary<sup>6</sup> heart disease. Arbidol may increase the incidence of heart failure. Interferon is also toxic to the heart and can cause disorders in the cardiac conduction system. Therefore, during the treatment of COVID-19, especially with the use of antivirals, the risk of cardiac toxicity must be closely monitored.

In conclusion, SARS-Coronavirus-2 is thought to infect host cells through ACE2 to cause COVID-19, while also causing damage to the myocardium, although the specific mechanisms are uncertain. Patients with underlying cardiovascular disease and SARS-Coronavirus-2 infection had an adverse prognosis. Therefore, particular attention should be given to the cardiovascular protection during treatment for COVID-19.

That is all. Thank you for your attention.

MODERATOR: Thank you very much. It is a very nice overview regarding the COVID-19 and the cardiovascular disorder. Thank you very much. Any question or comment?

DR. KRUMHOLZ: I just got a few that I am getting. I just wondered if I could share them with the group. From Martha Radford, who is organizing the response for cardiologic care at Hackensack in New Jersey, she asked do mildly ill and asymptomatic individuals develop immunity as suggested by the IgG response? That is one of the questions.

So, are you seeing that - we have heard even from Japan there was a case where somebody was negative and then came back positive. What is the experience in China? If you have had this, are you seeing people come back or are they not immune and we can consider them will not be infected again? What is your experience so far?

MODERATOR: Very good question. We also asked ourselves for the last several days. Two weeks ago, our group we developed a kit for testing IgM and IgG. Try using this kit for patient screening. Because to confirm the diagnosis of the COVID-19, we normally are using the swab to test the nucleic acids to confirm the diagnosis. The negative - the false negative is too high. Therefore, we

develop a kit to test the antibody. Normally, the (indiscernible) of the infection, you have activation of IgM and followed by the level going down and followed by the elevation of the IgG.

If we only test the IgM, sometimes you also get - you get also a negative. If you combine these two antibodies, you get - no matter if it is in early phase or later phase. We test 1,000 patients, we get the sensitivity. It is about 98 percent. We do see two percent with false positive. The patient has steroid overtake. We do see the two lines of the IgM. This was afterwards confirmed. It is a false positive. But if you test the IgM and IgG, it is really improved (indiscernible).

The question is do we have the patient with the negative nucleic acid and the patient is discharged. A week after, the patient came back with a positive again. We do not - we are not able to give you an explanation for this specific patient. We do see cases of the nucleic acid becoming positive again after discharge.

DR. KRUMHOLZ: Very helpful. Another quick question is this issue has been raised in France and the UK about ibuprofen and non-steroidal anti-inflammatory drugs. I just wonder if any of your experience aligns with that.

You know in France they are saying move over to acetaminophen instead of using non-steroidals. Do you have any experience with that to share with us?

MODERATOR: Yes, I would probably suggest - give you the consensus and the guidelines just issued by the WHO just yesterday or the day before. We do not have experience - because ibuprofen is not very commonly monitored regarding this. I searched today the literature. Only one paper was published several years ago regarding ibuprofen and Coronavirus, but not specifically with the Coronavirus COVID-19.

This brings the concern. They probably said that ibuprofen may worsen the infection of the COVID-19. I cannot give any comment regarding this. I don't know if any other colleagues could comment on this. I only read from these guidelines from the WHO.

DR. KRUMHOLZ: Let me ask one more question and maybe colleagues can respond. I am just channeling a lot of things that I am getting - people are asking me. So, you all have commented a lot about the lack of data about ACE and ARB. Also, many people here want to know when you are faced with someone with heart failure and also with severe multi-organ damage as a result of COVID-19, what have



Chinese doctors been doing? Have you been recommending stopping, leaving alone, you just continue what they are on?

Is there any - you quoted the national guidance about it, but is there even any anecdotal experience about what has happened? Are you studying this with what experience you have had so far in ways that we can learn from?

I think certainly for American cardiologists, this is a very big issue. Even in my own institution, one day we were saying we should stop. Then the guidance came out. We are relaxing that probably. But there is a lot of uncertainty. So, anything we can learn from you is useful.

MODERATOR: According to Version 7, the latest version of the treatment - diagnosis and treatment of COVID-19, we do not recommend to stop the ACEI and ARBs for this group of patients.

DR. KRUMHOLZ: Great. It is good to have your clarity on that. I think even as you - many people mentioned before, there was still some uncertainty.

PROF CHEN: Actually, it is quite a hot point for this issue. At the early stage, we are not clear about what is the clinical characteristic for this disease. Also, we

know it is an integrated packet point is SAE2. Generally, the first reaction for (background noise) is to want to stop the ACEi or ARB. Because, also, with the hyperemia and also tachycardia and the higher blood pressure (background noise) we think maybe is an ACEi or ARB problem.

After that, the majority of the cardiologists think - we did not have some evidence for this issue, just like the Professor mentioned. So, especially for some COVID-19 combined with coronary heart disease and also hypertension is special for the heart failure, heart dysfunction case. So, ARB or ACEi is most important management for this issue. We don't recommend fully the stop use. Generally, we recommend you continue to use.

Individually, the management issue if at risk for some hypertension or other issues, maybe it depends.

DR. KRUMHOLZ: That is great.

PARTICIPANT: If I can add something, I think there are heated discussions about the use of ACEi and ARB during the outbreak of the COVID-19. After the heated discussions, I think the cardiologists got some consensus. I think February 20<sup>th</sup>, the first - the European Society of Hypertension released a statement on the use of the ACEi. Later on, I think two days ago, the European Society of

Cardiology and International Society of Hypertension also released some statements to suggest the continued use of the ACEi and ARB.

In some serious individual case that we need to - based on the situation, I think. Thank you.

DR. KRUMHOLZ: Maybe I can ask a broad question as we sort of come to the end. So, in the U.S., we are seeing measures that we have never seen before, measures that you have instituted in China already, where we are restricting people, making social distancing - asking people to stay home, doing remote work. What is happening in China now? Are you relaxing what you did? Are you seeing any - you have said cases are quite low right now in China. So, you have been successful in slowing the spread, in fact, maybe stopping even to the moment.

What is happening in the society now? Are the restrictions being relaxed? Are you going back to where you were? What is happening? Can you give us a sense of how China is moving now and what is going on? A lot of anxiety in this country as we have adopted these measures.

MODERATOR: Professor (indiscernible), would you please give us some comments regarding this?

PARTICIPANT: (Indiscernible) From the very

beginning of our outbreak of COVID-19, we don't know how to stop the disease, except with isolation, with early diagnosis, and also with stopping the city transportation. I think that is very effective so far.

Now, we continue to follow-up this policy I think for a longer time. It is not about risk inside China. Now, it is the risk outside China. Maybe with you. Even for Wuhan, for the Hubei Province, they are now quite stable. Only 2,000 patients in the hospital. No new cases. We face a very important influence from outside China. So, we still have a high risk, two weeks, three weeks, even one month (indiscernible) protection so far. Thank you.

MODERATOR: I have here several questions regarding the patient with myocarditis and ST elevation. Do they get the thrombolysis. If not, how did you decide between and thrombolysis and coronary angiography. Dr. Chen, could you please answer this question regarding this patient with myocarditis?

PROF CHEN: For this very young patient, he suffered the chest pain. Also, when we admitted to the hospital clinic, generally find the EKG is elevated. Meanwhile, also find the troponin I and the CK-MB is quite higher. So the patient go to do - perform the angiogram -

coronary angiogram.

After that, check with the CT - yes, lung CT finds some problems. That is - and also the nuclide testing is positive. Also, we find the coronary angiogram is no stenosis. It is normal. Also, the management is after one week later, the ejection fraction is from very poor go into the very well. So, that is a very definite diagnosis of the myocarditis.

I think for this case, he is very lucky. If the story - if the just initiated symptom is a cough or fever, then we find there is Coronavirus disease, maybe I think the story will be changed. We don't have the ethylated cath lab even in Peking, maybe Shanghai. So, generally, we just recommended for this kind of issue, even we quite suspected STEMI case, generally, thrombolysis is the first recommendation for this.

MODERATOR: I think we have another three minutes. We have a lot of questions. I think I will leave it to Harlan for tomorrow. Tomorrow evening at the same time I invited our colleagues from the frontline, they are handling the patients in Wuhan. We will discuss several cases during - of COVID-19 with myocardial infarction or with myocardial damage. Followed by how to interpret the

guidelines of ECMO use in the severely or critically ill patients.

We publish our consensus of ECMO use because we do believe it is very important for the very critically ill patients, especially with heart disease and COVID-19. We will discuss a case-based study tomorrow. I hope to see you tomorrow evening at the same time at eight o'clock. I have to here close the session. I thank all of the colleagues who were involved in this event this evening, (speakers listed). We will see you tomorrow evening. Thank you very much.

DR. KRUMHOLZ: Let me just say one thing to say this. I am getting so many messages from so many people expressing such deep gratitude to our Chinese colleagues, to your generosity and willingness to share this knowledge, and for paving the way and helping us to be able to be better prepared. Our deep appreciation to all of you for doing this.

It also highlights - I think it makes everyone feel better to know we are all in this together. We are connected. We are one family within medicine. It also makes everyone feel better to see how connected we are. Again, a great appreciation to you. Thank you so much.

MODERATOR: Thank you very much, Harlan. Thank you, all of the governance from ACC and colleagues from the United States. We believe this could offer help for your practice for identifying this new virus infection. If we can be of any help, any assistance, or for supplying information and our data, we would be more than happy to do that and see you tomorrow evening. Thank you.

(Webinar ended.)