

COVID-19 in Outpatient Settings: Expert Insights on Identifying Patients Who Remain at Risk for Severe Outcomes and Complications

Introduction

Dr Cristina Mussini (University of Modena and Reggio Emilia): This is COVID-19 in Outpatient Settings: Expert Insights on Identifying Patients Who Remain at Risk for Severe Outcomes and Complications.

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Faculty and Disclosures

I am Cristina Mussini. I am a full professor of infectious diseases at the University of Modena Reggio, and I am the Chief of the Department of Infectious Diseases at the Modena Hospital.

These are my disclosures.

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Learning Objective

So the learning objective of this activity is to identify patients who continue to be at high risk for severe COVID-19 outcomes, despite the widespread availability of a vaccine. We all know that availability as a recommendation, does not mean that the people who are at risk are really undergoing the vaccination, and this is something that we have to investigate while we see someone with some symptoms.

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Timely COVID-19 Diagnostic Testing

The first thing to do if we have to have an early treatment is to diagnose, and now we have very rapid testing, and if it is at home, we have a rapid antigen test for symptomatic individuals and close contacts, while at the hospital we use PCR.

For example, in my hospital we have a combined test for flu and COVID-19. If the antigen test is negative and the patient continues to have symptoms, we have to repeat it in 3-5 days. If it is positive, since the specificity is very high, it should be interpreted as definitive.

The problem is that at the beginning of the pandemic we kept the patients in isolation until the test was negative. We know now that if the antigen test continued to be positive after 10 days, it just represents noninfectious viral particles. This is really true for immune competent people. For immune compromised patients, this is not really true because the problem is that when you do not have the defense, the immunological defense to protect against SARS-CoV-2, the risk of having a replicating virus even after 10 days is something that is absolutely possible.

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Burden of COVID-19 Severe Disease

What is the burden of severe COVID-19 disease now, 5 years after the beginning of the pandemic? Obviously, we can have an exacerbation of underlying medical conditions if someone has some risk despite the fact that new variants, they do not replicate in the deep lung, but mostly in the upper respiratory tract, making this virus now more transmittable but less severe. If you have some clinical problem, clinical issues in your respiratory tract, like if you have COPD, if you have asthma, if you underwent a lobectomy for cancer, or something like this, COVID-19 could be like the cherry on the top, and there could be an exacerbation of an underlying medical condition.

And then you have an advanced infectious process because you can have persistent viremia, long COVID, secondary bacterial infection, you can have a superinfection with bacteria. And also, persistent viremia is something that could be very relevant in the immune compromised because, in a way, it will postpone the chemotherapy and could have an impact on the prognosis of patients affected by these diseases. And then we know that with hospitalization, we have an increased risk of morbidity and even mortality because we are talking about very fragile patients who, just because they are admitted to the hospital, they could be affected by hospital-acquired infection. So it could be really something that changes the prognosis of a patient.

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Determining Outpatient Management of People With Proven SARS-CoV-2 Infection

So in determining outpatient management of people with proven SARS-CoV-2 infection, we have to evaluate if there are risk factors for severe disease, yes or no.

If risk factors for severe disease are present, but the patient's current symptoms are not severe and symptoms started less than 5 days ago, we can consider an oral antiviral or just schedule a telehealth follow-up. Or, if symptoms started more than 5 days ago, oral antivirals are not an option, but we can consider IV remdesivir. One thing to note is that if the patient starts using nirmatrelvir/ritonavir, we have to take into account all the comorbidities and all the drugs for comorbidities because there are many potential drug-drug interactions with ritonavir.

And our management will change because if we have severe symptoms, we should refer the patient to the emergency department for evaluation.

So I think that what should be the take-home message is to evaluate the symptoms, and on the basis of the symptoms and of the date of the onset, evaluate which antiviral should be prescribed if the patient is at risk of developing a severe disease.

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Why Is it Important to Assess Risk of Severe COVID-19?

Why is it important to assess the risk of severe COVID-19? Obviously, because it determines the hospitalization status.

As I said, can patients be managed at home? I mean, I am not a huge fan of telehealth, especially in someone who has symptoms. So I prefer to monitor them as an inpatient for a couple of days, and then they can be discharged. But at the beginning, I would like to admit the patient to the hospital and to provide IV treatment with remdesivir if there are drug-drug interactions or if the symptoms date back more than 5 days.

And when we have to think about antivirals, we really have to evaluate when the patient received their last shot for the vaccine, which comorbidities this patient has. So what is the risk of this person to develop severe disease, and which among the antivirals is the most appropriate?

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Patient Case 1

So let us think about the case. So this is a 78-year-old man that reports to his primary care physician with fever and cough.

He is currently receiving chemotherapy for prostate cancer. He received 1 COVID-19 vaccination 5 years ago. Which risk factors for severe COVID-19 does this patient have?

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Age Is Strongest Risk Factor for Severe COVID-19

Age is really the strongest risk factor for severe COVID-19. This was very clear from the beginning, especially from data from Italy, because we are an old country and so many, many older patients were affected by the pandemic. And you see that there is really a growth in the risk of death with the increase in age. There is an increase with the comorbidities, but not as high as with age.

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Medical Conditions That Increase Risk for Severe COVID-19

So there are medical conditions. As I said, the comorbidities could increase the risk of severe COVID-19.

But which one? Cancer. The vast majority of patients who were admitted to the hospital with COVID-19 now have cancer. And in this case, the patient was also on chemotherapy, so he was immune compromised.

I'll list the other medical conditions that increase risk for severe COVID-19: Cardiac disease, chronic kidney or liver disease, chronic lung disease, dementia, diabetes type 1 or 2. Diabetes and obesity were the 2 main comorbidities in the literature. HIV infection, but only in untreated or very advanced immune compromised. And then mental health conditions, people with disabilities, physical inactivity. But more than physical inactivity, I would say someone who is really overweight. Pregnancy, sickle cell disease, or thalassemia, smoking, solid organ or stem cell transplant, stroke, substance use disorder, and tuberculosis.

So obviously, if patients have these diseases, they also have to take many medications. And when we have to evaluate which antiviral we have to prescribe, we have to go to the Liverpool website in order to see the drug-drug interaction.

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How Do Medical Conditions Increase the Risk for Severe COVID-19?

How could medical conditions increase the risk for severe COVID-19? They reduce immunity. They are all immune compromised. But also, many conditions that increase risk, even obesity, are characterized by chronic inflammation.

Impaired organ function, we have seen either respiratory, but also kidney, also liver. Vascular dysfunction because there is this hypercoagulability. We know that during COVID-19, we also have to prescribe prophylaxis for inpatients for thrombosis and metabolic dysregulation.

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Assessment of Severe COVID-19 Risk

When we have to assess for severe COVID-19, as I said, we have to evaluate the vaccination status because everybody is so stressed and so shocked by the pandemic that nobody wants to talk about COVID-19 again. Also, there are some people everywhere in the world who are criticizing the vaccine and trying to discredit the efficacy of the vaccine.

And you see that if we consider COVID-19, the risk of death increases with the number of comorbid conditions.

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Patient Case 1: Risk Assessment Is the First Step

So the first thing that we have to do for this patient, we have to do the risk assessment, and we obviously have to evaluate his advanced age, his lack of COVID vaccine (because being vaccinated 5 years ago is too long ago), his cancer, and his immune suppression with chemotherapy.

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Risk of Severe COVID-19 Is Impacted by Varying Processes

One thing to keep in mind is that risk of severe COVID-19 infection can change over time and can be impacted by the infectious disease process itself. So the patient who is immunosuppressed, who is unable to clear viremia, is at higher risk for negative outcomes of COVID-19. But severe COVID-19 can also impact other diseases and contribute to decompensation of underlying conditions, such as lung disease, COPD, asthma, or treatment delays with, for example, chemotherapy. This can result in a feedback loop where comorbidities contribute to risk of severe COVID-19, and severe COVID-19 contributes to risk of exacerbation of comorbidities.

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Patient Case 1: Key Points

So there are others impacts to patient health. If the patient cannot clear a replicating virus, there could potentially be a delay of chemotherapy. By being hospitalized for COVID, they could be exposed to other infections (bacterial or viral, or it could be a healthcare-associated infection). Then, there could be decompensation of the underlying disease or a more severe infectious disease process itself.

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Change in COVID-19 Variants Limits the Use of Certain Therapies

Here are the data from the Italian Ministry of Health on COVID-19 variants. And you see in a few months, from May to October, a change in the variants. They all belong to the Omicron lineage. But what we have to say is what we have seen since the beginning of the pandemic that there is a complete substitution of the new variants compared to the old ones. So XFG started in May, and then there was an increase in June, July, August, September. And in October, it has become the only variant that is circulating. These are variants, as I said, that belong to Omicron, and so they are very infectious because they replicate in the upper respiratory tract, so they circulate a lot. And this is a risk factor for the immune compromised, but on the other hand, they do seem to lead to severe picture of pneumonia, unlike Alpha and Delta did.

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Key Points

Key points of this activity.

Patient risk factors impact the risk of severe COVID-19. Advanced age increases risk and is the most significant risk factor. But you need to consider other risk factors in order to determine the true risk. COVID-19 disease can be associated with other non-infection-related sequelae, because we may have to postpone, for example, chemotherapy. The ideal management of COVID-19 is early diagnosis and prevention through vaccination.