

COVID - 19 Challenges

Challenges and Management in Italy and Lessons Learned, *M. Cecconi*

From Hydroxychloroquine and Remdesivir to Plasma Administration, *JL Vincent*

Adaptive Strategies for Intensive Care: The Brussels Experience, *E. De Waele et al.*

Tracheal Intubation in the ICU, *A. Higgs, M. Udberg, G. Hopkin*

An Adaptive Response, *J. Nosta*

Ultrasound in Times of COVID-19, *A. Wong, O. Olusanya, J. Wilkinson, C. McDermott*

Nutrition for Critically Ill Patients with COVID-19, *L. Chapple, K. Fetterplace, E. Ridley*

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Immersive Virtual Reality in the Intensive Care Unit, *C. Lynch, G. Jones*



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COVID-19 CHALLENGES

Coronavirus disease (COVID-19) continues to spread. While nations that were hit early are now seeing a flattening of the curve from mitigation strategies, countries that have been hit more recently continue to suffer. It is true that the majority of the population experiences mild symptoms of the disease, but age, comorbidity, and male sex are important risk factors that are still resulting in poor outcomes in patients who get severely ill with COVID-19.

Clinicians have learned quite a bit regarding the course of the disease, its clinical characteristics, and supportive treatment. But questions still remain regarding vaccines, potential drug treatment, immunity, and when mitigation strategies could be relaxed, if at all.

Our cover story, **COVID-19 Challenges**, talks about the response to COVID-19 by critical care workers across the world - from China to Italy to the US and UK, Belgium, South Africa, and Switzerland. We include input and observations from critical care experts around the globe.

In an exclusive interview with ICU Management & Practice, Prof. Maurizio Cecconi talks about the COVID-19 critical care response in Italy while I discuss the various treatment strategies that are being proposed and why caution must be exercised, and scientific evidence must be given priority.

Prof. Elizabeth De Waele and colleagues discuss adaptive strategies for intensive care during the spread of COVID-19 in Brussels, and John Nosta also highlights the need to develop an adaptive response to manage the COVID-19 crisis.

Andy Higgs, Martin Udberg, and Gethin Hopkin explain how tracheal intubation can be made safe for both patients and healthcare providers while Adrian Wong, Olusegun Olusanya, Jonathan Wilkinson, and Cian McDermott discuss the clinical utility of ultrasound modalities in the COVID-19 patient.

Emma Ridley, Lee-anne Chapple, and Kate Fetterplace talk about the nutritional implications for COVID-19 critically ill patients while Armin Quispe Cornejo and Ana Alves Cunha discuss masks and the most effective strategies that healthcare workers can use to protect against airborne particles.

Chunyao Wang shares his experience about daily care and supportive therapies for COVID-19 used in Wuhan, China, while Kuban Naidoo, David Kloeck, and Lufano Mathivha share their COVID-19 intensive care experience from South Africa.

Hatem Ksouri and colleagues highlight the importance of keeping collective intelligence intact when facing stressful and challenging situations in the ICU while Joanna Poole shares her experience from the UK and talks about the lessons we can learn from similar diseases over the last few centuries. Adrian Wong also shares his experience while battling COVID-19 in the UK.

The world is going through a terrible healthcare crisis - a crisis that has stunned most healthcare systems around the globe. Amidst the numerous flow of patients, we have seen healthcare workers rise to the occasion and delivering essential healthcare services despite the risk of transmission and infection. We have seen clinicians around the world connect and collaborate, and a display of team spirit never seen before. These are challenging times, but the healthcare community has shown that together they can surpass any challenge. The COVID-19 pandemic will pass, but with it, healthcare systems will learn how to become stronger and how to be more prepared if such a thing happens again.

As always, if you would like to get in touch, please email JLVincent@icu-management.org.



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COVID-19: Challenges and Management in Italy and Lessons Learned

Prof. Maurizio Cecconi is the President-Elect of the European Society of Intensive Care Medicine (ESICM). He is also the Head of Anaesthesia and Intensive Care Department at Istituto Clinico Humanitas and a full professor of Anaesthesia and ICU at the Humanitas University. Prof. Cecconi has worked in different healthcare systems, including the UK NHS & Private and Italy NHS & Private. He has a strong background in research and has been an active voice in the field of Anaesthesia and Intensive Care, clinical research, clinical trials, and health policies and guidelines. ICU Management & Practice spoke to Prof. Cecconi about his experience during the COVID-19 pandemic in Italy.



a message to others because we realised that perhaps we had underestimated this, and maybe the world was underestimating this. The European Society of Intensive Care Medicine sent out a letter telling everyone to get ready because this was not the regular flu.

What, in your opinion, is the danger to the general population? We know it affects the elderly, and people with a low immune system, but what about the risk to the general population?

It is a mistake to think that this is affecting only the elderly population. COVID-19 can affect all parts of the community, but the older people are the ones that are getting the disease in a worse way. If you're older, you are more likely to get very sick from this compared to if you're younger. But in a society when you're facing something that does not have a specific cure or a vaccine, every citizen is responsible not just for themselves, but also for other citizens. If we believe that we're working in a society that is taking care of each other, we cannot just accept that this is dangerous only for older people and let them become infected. Overwhelming the capacity of hospitals is dangerous for everyone. This disease is indeed affecting more older adults in terms of becoming very sick and dying from this disease, but that should not be an

Doctors say that if they had known about the seriousness of COVID-19, they could have been better prepared, and the world would not have wasted the three weeks China gave them to prepare. What is your opinion?

We could probably have used the time that China gave us to prepare a better surge response. We were still tracing contacts. Nobody was ignoring this, and people were being quarantined, and there was contact tracing. Despite that, clearly something skipped through the filter. The World Health Organization (WHO) has to be praised for the work they were doing

in telling us to be careful because these epidemics can become a pandemic, and that is what happened with COVID-19.

We were surprised by the magnitude of sick patients that could come to our healthcare systems during an uncontrolled cluster. That is what we were fighting day and night. From the moment we realised there were patient clusters in the area, we had to make new beds. We had engineers in the hospital building new units. It is true that if we could forecast, we could have increased our capacity earlier. And indeed when we realised this in Lombardy that the numbers are so high, we sent out

excuse not to control the virus transmission. Nobody benefits from a system that is reaching saturation, whether you're young or old. It was very responsible for all countries that decided to control virus transmission. You can argue that some countries were a bit faster or a bit slower compared to others. Still, the majority understood the message that you're not going to win this by only increasing your capacity in hospitals. You have to control the virus transmission. Therefore, we have to protect the young and the old, and we need to protect the old from getting the disease.

South Korea was very aggressive with its testing and contact tracing. Do you think other countries should have done the same?

I'm not a public health expert. I've been in the middle of this pandemic now for a couple of months. After speaking with public health experts, I can tell you that one recipe cannot be applied to every country, and the same strategy cannot be applied for the same moment on where you are during the pandemic. Even in Italy and in Europe, before we had these clusters, we were doing PCR swabs and aggressive quarantine on specific cases that were COVID-positive. In the beginning of February, there were three cases in Italy, one case in Germany, etc. These were not huge numbers and you could put a whole organisation around those cases to contain them. You have to be very aggressive with that, and if your strategy is controlling the transmission that way, you should carry on doing it.

But in Italy, at least in Lombardy, our cluster is very different from what was happening outside China up to that moment. I remember it was the 20th of February in one of the intensive care units in the region, and a young patient in his 30s tested positive for coronavirus. This patient had no risk factors for having been to China or for having been in contact with somebody from China. There was

no reason to think that the patient could have been a coronavirus patient, but he was not responding to typical pneumonia treatments. The intensivist conducted the PCR swab test, and the patient tested positive. Up to that moment, we were using the same strategy used by South Korea and other countries, but we realised that the filter had not stopped the transmission and that we had a big problem because there was a patient in his 30s in intensive care. We know from data coming from China that the case fatality rate for young people was very low, and we know that it was affecting more older people. But when your first patient that you cannot trace back to other patients is young and in intensive care, you realise that you have a bigger problem. Of course, you try and trace it back and quarantine people, but your strategy has to change. It cannot be the same when you only have a few cases, or when you have a lot of cases.

We are now at the peak of the pandemic here, and we are moving towards Phase two. We cannot have the same strategy of Phase one. Hence, it's important to apply different strategies to contain and control the virus transmission, depending on where you are on the disease. The ideal situation is that you don't have any transmission at all. But we know that for a virus that doesn't have a vaccine, this is probably not possible in Europe. Public health measures have to be in place to try to control the transmission as much as possible. If you cannot suppress it and have a cluster, you may have to use different strategies and choose to lockdown. It's a very painful strategy for society and the economy, but it would not have been possible to do anything else at this stage because the number of cases was high.

Should deaths in hospitals in patients with comorbidities, and with COVID-19 be classified a COVID-19 death? Is that a safe assumption?

People are saying that a patient may have died with COVID-19 and not because of COVID-19. I would argue that you can refer

to that only if you have an asymptomatic patient that dies, as in a car accident, but by definition if you're dying of a clinical deterioration and if your clinical deterioration is due to respiratory symptoms, I really don't care if you started with heart failure or chronic kidney disease. You are now getting a chest infection out of COVID. We know that you're starting from a very low baseline over the physiological reserve. However, I would argue that you're still dying because of COVID even if you're 90 years old and have a lot of comorbidities. That's exactly why society has to protect its old people; otherwise, we run the risk of making these assumptions that because you're old and frail with comorbidities, if you get COVID, maybe you were dying anyway. It is possible, but if you're dying with some symptoms that are traceable to COVID like respiratory symptoms or failure, I think it will be a big jump to say that you've died with COVID and not because of COVID. This assumption that people are dying with COVID and not because of COVID is not correct. If you die in a car accident, and you were having COVID, then you're not dying because of COVID. But if you're dying with a chest infection, and you had comorbidities, you're old, and this chest infection is because of COVID, I would argue that you're dying with COVID even if you have a lot of comorbidities.

Should chances of survival be the criteria for allocating life-saving resources in case there is a shortage?

As an intensive care doctor in Italy and as the President-Elect of the European Society of Intensive Care Medicine, I believe we must give intensive care to anyone who needs intensive care. This is true when you have one free empty bed and when you have 1000 free empty beds. We don't want to reach a situation where we don't have enough beds and have to make choices that we don't want to make. It is important to realise that this virus is something that you don't win just in hospitals, but you

win with citizens, with self-isolation, with lockdowns, with suppression, and with mitigation manoeuvres. We're asking the help of citizens because we want to give intensive care to whoever needs intensive care. This is what we've done in Italy, and this is what doctors are trying to do worldwide. We need the help of citizens to make sure that we don't get an uncontrolled wave of sick patients coming into our hospitals. If they don't help us, we could reach a stage in which hospitals are overwhelmed.

Our hospitals have been stretching. We made an enormous effort in Italy to increase our capacity in ICU. In Italy, age was not the risk factor to come to intensive care. Our median age was 63 years, which means that half of the population was older than 63 and half was younger. But to admit everyone that we thought would benefit from intensive care, we had to increase our intensive care beds. We had to bring intensive care outside of the wards. This is not just being done in Italy. I speak with colleagues from Spain, from France and America. Everyone is trying to increase the intensive care beds where you can do invasive mechanical ventilation, and provide CPAP and non-invasive support.

In the region where I work, we started with 720 beds for intensive care for about ten million people. When we reached the peak of intensive care COVID-19 positive patients' occupancy, we had 1500 intubated COVID-19 patients, and we treated nearly 4000 patients. Outside the intensive care walls, we created a high dependency unit - a level two intensive care - to provide CPAP and respiratory support, non-invasively in which we worked together with internal medicine doctors and pneumologists. That accounted for another 2000 beds approximately. Therefore, we moved from 720 beds for respiratory support in the region to 1500 mechanically ventilated for COVID, and another 300 for other pathologies and another 2000 for CPAP. If you do the math,

we increased our capacity from 720 to 4000, which is five-six times our pre-ICU capacity. This is the effort that people have made to treat every emergency in the region. This is the only choice that we decided to make. However, this would not have been enough if there had not been containment manoeuvres and lockdown in the region.

My two messages to everyone around the world is to increase your ICU capacity and hospital capacity because we want to give intensive care to whoever needs

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intensive care. But don't expect this solution to work only by increasing your capacity by four or five times, which is already an incredible number. You also need to work with public health authorities, and citizens have to work with us to allow everyone to receive treatment. This virus is something we've never seen in our career. It can give you severe respiratory symptoms and can be transmitted easily from person to person. If you don't control the transmission outside of the hospitals, you can really overwhelm any healthcare system in the world.

Different treatment strategies are also being proposed, and many of them are not backed by any clinical evidence. Do you see any strategy that would be effective?

The strongest evidence that we have at the moment is supportive care. We've learned

over the years how to provide ventilation and oxygen to our patients in a way that protects their lungs. We do not cure with our machines in intensive care but rather buy precious time for patients to get better. We are giving time that those patients would not have without our work and without being connected to a machine that we have to know how to use. I would really like to stress this. Everyone talks about ventilators and shortages. The biggest drama is not the lack of ventilators. The biggest problem is finding a way to bring competencies that are required in ICU by intensivists and ICU nurses to so many new ICU beds and patients. You have a much larger team of people that have never worked with these devices and these patients. You have to try to teach them, supervise them, and work with them as a team. Everyone has gone the extra mile around the world. There were doctors and nurses who have never worked in intensive care and who came to help. We were very grateful to these people, but we had to find ways to teach them in a very short period of time how to use these machines and how to have our expertise for a large group of patients. That has been the biggest challenge, much more than any machine shortages. Don't expect that just by bringing 3000 ventilators, you will solve the problem. People, as always, are the most important resource in any crisis. Healthcare workers have been the most important resource that we have had to find in this crisis.

We have to buy precious time by giving support - what we call protective lung strategy. This means giving time on the ventilator but avoiding the ventilator to cause harm. Imagine the ventilator as a machine that brings air with pressure and oxygen to the system. It could be like a caress or like a punch. We don't want to punch the lungs - we want to caress the lungs so that they don't get damaged from the ventilator. It requires a very fine balance to do that. Also, every



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patient is different. We have to find ways to individualise the therapy in a large volume of patients. By providing supportive care, we're giving the best chances for patients to recover. We are also giving them nursing care, mobilisation, sedation, nutrition - everything that we can do in terms of support.

Many drugs are being tried, but so far, no drug has proven to be effective and safe. An important thing to remember is that when we use treatment, everyone focuses on efficacy. But we need to think about safety as well. You may hear people say this patient is sick, and we should give this drug. If it works, the patient gets better, but if it doesn't, we have nothing to lose. I'm not so sure about that. We don't know if the drug, when it is not effective, could actually be unsafe. It's a very dangerous assumption to give something just because it's available without studying the profile of these drugs. It's very difficult during a pandemic. You get a large number of patients that you didn't know before, in terms of disease, and there is pressure from the system to try to do the best for these patients. But we have to be very careful. We may do harm if we use treatments for everyone without trying to be precise in what we're doing. The last decades have been all about precision medicine, whether in oncology, haematology, or intensive care. We have also talked about characterising phenotypes. But what we need to do is to understand who the patient is in front of us and understand the physiology and using supportive care in the most precise way. When it comes to drugs, we have to be very careful. We have to find ways and not lose time, but we have to do it scientifically. We can't start using drugs without testing these drugs against a control group and without seeing if there is a cause and effect of what we are doing. It can be very dangerous. We need to find the right balance between doing and learning. It's

not just about the efficacy but also about safety and we need to balance these two things when we try new treatments in our patients.

How close do you think we are to developing a vaccine?

I'm not an expert on vaccinations. There is a lot of research going on in different parts of the world. I suspect it would be unrealistic to believe that we could have a vaccine so soon. It will take a few months, maybe a year. We don't have time to lose because we don't know how long this virus will stay with us. Different countries are preparing for Phase two, and we have to see if we have to manage secondary peaks. We have to assume that this is something that could stay with us a bit longer. I do hope not, but we have to be ready, and this means that we have to carry on working on a vaccine, and other strategies. We need to study new drugs, and we must accept that it could take months before we have something proven to either prevent the disease or treat it. We have to be fast, but that doesn't mean that we have to be faster than what's necessary to develop our strategies in a safe way.

Do you think that there could be a second wave?

We don't know but we cannot afford to be unprepared the second time. I don't think we can afford that for our citizens, our patients, and our healthcare workers. We have to prepare for a second peak. Hopefully, we will not have it, and hopefully, we will do things better, control the virus transmission, and hope there are no secondary peaks. But we need to be prepared to manage these secondary peaks. We have no excuse now. You were asking me before if we wasted time when the virus hit China. If I could go back, we would try to prepare better. I'm sure that is something that every doctor and every healthcare system will tell you now. But if

that was true in February, I don't think we can afford not to be prepared when we release lockdowns.

Do you think the healthcare system has failed healthcare workers and could have provided better support?

It's a very difficult answer to give because the principles are worldwide principles that the WHO is sending out to everyone in terms of which masks to use, which gloves to use, which protection to use for different situations. But in any protocol or guidance, it is the local leadership that puts these things in place. When I realised that there would be a wave of patients in my hospital, I called the simulation team of the University to put together simulation in-situ to train everyone. We trained 80 people in 48 hours about donning and doffing procedures, protective equipment, proning, and incubations before we got the wave of patients. So far, in my team, no one has an infection while working in the COVID-19 ICU units, because we are using a high level of protection. Not in my hospital, but some doctors have died. They seem to be a bit older, and maybe they had been in contact with infected patients without knowing. It is a tragedy, and we are very sad for all the colleagues - not just doctors but also nurses and other healthcare workers. We've all been scared to get the disease. We've been scared to pass the disease to our families and to our parents. It's not been easy, but I would say the recommendations are out there.

You need strong leadership in your country, but you also need strong leadership locally to make sure that you protect your team and that hospitals protect healthcare workers. Speaking for my team, I felt very protected from my management. They worked very closely with me and accepted all my recommendations on how to protect healthcare workers. We've all been very stretched, but because I was focused on protecting my team and the team of the emergency areas where the most invasive

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procedures take place, we decided to put an extra effort. We monitored the people that are helping in the most difficult areas. It is important to feel protected in your own hospital and to see that there is that passion and that effort to protect healthcare workers. The recommendations are out there, but how effectively you apply them in your practice is down to local leaders. We need to use simulation for training as much as possible. There's not enough training for this because no one can get used to working with this protective equipment and with these suits. It's a completely different way of working. We cannot afford to have healthcare workers that become sick because of the work that they're doing. It's very important to use as much training and simulation as possible.

In Italy, doctors have also developed a Coronavirus ICU network. What's the goal of this network? What are the experiences or lessons?

There are different networks. I can talk for the COVID-19 Lombardy ICU Network. This network is probably one of the reasons that allowed us to buy extra time in the first two or three days. When we realised we have a cluster and secondary transmission, we knew there was a big problem. No one had prepared isolated units. This network was in place before COVID-19 for providing VV-ECMO and VA-ECMO. It is a network that was put in place by Antonio Pesenti of Policlinico and Alberto Zangrillo from San Raffaele. The network was created to help each other if we have a patient with a severe respiratory failure that requires VV-ECMO or admission that requires cardiac support for VA-ECMO. We coordinated in less than 24 hours from the first case to immediately identify hospitals that could manage the initial surge of patients. Every time there was a positive case in one hospital, we would bring them into the isolated unit. This gave hospitals the time to get organised because containment is important not just in the community,

but also in hospitals. We cannot afford for hospitals to become clusters.

It is important to separate the COVID-19 pathway from the non-COVID-19 pathway because other emergencies are still going on. The network allowed us to have space for whoever needed intensive care. The mission was to create beds for intensive care. It was not just for COVID-19 but to manage all emergencies. We reorganised our emergency network into hubs and

the biggest drama is not the lack of ventilators. The biggest problem is finding a way to bring competencies that are required in ICU by intensivists and ICU nurses to so many new ICU beds and patients

spokes so that we could still care for every emergency, whether it was trauma, stroke, cardiac surgery, myocardial infarction, and so on.

The network is really the most important thing that we had in place to help each other. Patients that were coming to a cluster hospital with no beds were still receiving intensive care by being transferred to a unit that had space. Every time we had space, we were calling back the coordinating centre to inform them in case they had a patient that needed a bed.

I am also a part of this network, and I am in the clinical and technical Scientific Committee of the region. I'm helping and working very closely with Giacomo Grasselli, and Antonio Pesenti, and we advise and help each other.

How can quality research be conducted in times of a pandemic?

We should not forget the basics. We have so

much to learn from a new disease by just observing it. The ICU Network has put a huge effort in disseminating the results and sharing data. Also, the clinical community is doing the same through journals that have decided to open full access. Data is being shared across the world by health authorities and by doctors through social media. It has been a very unifying moment for the clinical and scientific community. Sharing information about what we are observing is very important, but we have to be careful that we don't forget the scientific methods of observations. Epidemiological observations are equally important now, and to know the rate of mortality for intensive care patients. This can inform you about policies and planning. The immunological and inflammation profile of the patient is also important. The more we know about the virus, the more we can find a way to do precise tests and research in an effective way. Despite the stress on the system and the emergency, we must not lose sight of a good scientific method that starts from observation, from realising which phenotype may have a possibility for treatment and then to test the efficacy and safety of this treatment. Some ongoing trials in the UK and America are very interesting, especially the new trials with an adaptive design. We have the tools; we just have to decide how to use them.

Do you think this will be over soon?

In life, you cannot decide what is happening to you, but you can decide how you react. I hope we are managing COVID better now, but we have to be prepared in case it stays with us for longer. We cannot afford to be surprised twice by COVID. We all got a surprise once, but if we release the lockdown and something happens, we need to be in control to protect our citizens, our patients and our healthcare workers. ■

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COVID-19 Experts Dialogues

- [1. China with the World: COVID-19 Experts Dialogues - The 2nd Talk Transcript](#)
- [2. China with the World: COVID-19 Experts Dialogues - The 4th Talk Transcript](#)
- [3. China with the World: COVID-19 Experts Dialogues - The 6th Talk Transcript and Video](#) 

China with the World:
COVID-19 Experts Dialogues





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COVID-19: From Hydroxychloroquine and Remdesivir to Plasma Administration

Clinicians are faced with a serious disease with no effective therapy. Several options are being considered to treat COVID-19, but how promising are these drugs?

A number of colleagues and friends from outside the hospital have asked me whether they should take hydroxychloroquine for their COVID-19. A friend asked me whether he should take lopinavir-ritonavir even though he is not HIV-positive. A hospitalised patient requested administration of remdesivir regardless of the cost involved, and another patient even requested transfer to another hospital to receive the tocilizumab that she had heard about, but that we did not want to prescribe in the absence of a recognised indication. These drug names and miraculous cures are widely discussed on social media and various internet sites, which seem to take precedence over scientific publications! Nevertheless, it is easy to understand an individual's frustrations when faced with such a potentially serious illness and no effective therapy.

Faced with this pandemic, everyone is of course, trying to find a treatment. A large number of studies are currently ongoing, involving more than 60 drugs. **Table 1** is only a partial list.

The topic of hydroxychloroquine is particularly hot for two reasons: the first is that the drug is cheap, can be obtained quite easily, and seems "safe" because it has been widely used for many years in

the prevention of malaria. The second reason is that its administration was promoted by Professor Didier Raoult, an internationally recognised expert who can be very convincing when he appears on screen. However, his clinical data are unconvincing: the "famous" study included only 26 patients and had serious

the most exciting news is the very initial promising data on the effects of administration of plasma from convalescent patients to those who are critically ill

methodological problems, the principal one being exclusion from analysis of six patients in the treated group who did not improve. Current recommendations are, therefore, to reserve administration of hydroxychloroquine in the hospital to severely ill patients receiving cardiac monitoring.

The results of a study on lopinavir-ritonavir were recently published in

the New England Journal of Medicine. Interpretation of the data is difficult. The conclusion of the manuscript states no significant difference with treatment, but the data did show some benefit, including a decrease in mortality from 25 to 19% in the treated group. We also give this medication in severe cases in the hospital.

Remdesivir, an anti-viral agent developed against Ebola, is more promising. It prevents the replication of viral RNA in the laboratory. Remdesivir was administered to some American patients from the famous cruise ship in Japan, possibly with some success. The FDA has just authorised the introduction of this drug in the US but in the category of drugs for orphan diseases (is COVID-19 so rare?) so that it will be very costly. A recent randomised double-blind placebo-controlled study was undertaken at ten hospitals in Hubei, China. 237 patients were enrolled and randomly assigned to a treatment group and placebo. Findings show that patients treated with remdesivir had a faster time to clinical improvement compared to those treated with placebo. However, the difference between the two patient groups was not significant. While these results are optimistic, the difference is still not that significant and

more research is required. The Gilead-initiated SIMPLE trials are also evaluating the safety and efficacy of remdesivir as is the U.S. National Institute of Allergy and Infectious Disease (NIAID). Early results of a federal trial show that treatment with remdesivir can speed recovery. These findings are being considered very optimistic by Dr. Anthony S. Fauci, the director of the NIAID.

From the many possible therapies under investigation, some people would like to select one, or even several in a sort of cocktail. Some Chinese colleagues warmly recommend the use of Chinese herbs, considering that they were an effective treatment contributing to control the infection in China. Extracorporeal purification techniques have also been proposed in severe cases, and a small Chinese study gave promising results. Preliminary data on tocilizumab are also promising.

The search for a new effective therapy

requires the appropriate clinical trials, i.e., prospective, randomised, controlled trials comparing treatment and control groups. Unfortunately, there has been little coordination or collaboration in the way in which such trials are being conducted worldwide. There are some large studies, for example, Discovery in France or Solidarity (World Health Organization), aimed at randomising patients to several possible treatment options, using an adaptive design.

It is difficult not to take any medication. The use of ibuprofen and other anti-inflammatory agents for fever is controversial. Even the use of paracetamol may not always be a good idea, because fever can have a protective effect.

The most exciting news is the very initial promising data on the effects of administration of plasma from convalescent patients to those who are critically ill. The technique is quite an old method and has been used effectively in previ-

ous viral outbreaks, including Ebola, and is thus an attractive approach. While awaiting larger trial results, the FDA has approved its use for single patients with serious or immediately life-threatening COVID-19 infections. Let us hope that this new therapeutic strategy will be shown to be successful rapidly. ■

Possible Therapeutic Interventions in COVID-19

Lopinavir/ritonavir
 Remdesivir
 Chloroquine/hydroxychloroquine (with or without azithromycin)
 Anti-JAK (baricitinib)
 Tocilizumab
 Methylprednisolone
 Stem cells
 IV immunoglobulins
 Convalescent plasma
 Favipiravir
 Carrimycin
 Bromhexine
 Thalidomide
 Favipiravir (Avigan)
 Oseltamivir (Tamiflu)
 Umifenovir (Arbidol)
 Angiotensin
 Thalidomide
 Sildenafil
 Traditional Chinese medicines: yinhu qingwen, haaier

Key Points

- A number of drugs are being investigated for COVID-19 including hydroxychloroquine, lopinavir-ritonavir, remdesivir etc.
- These drugs are widely discussed on social media and seem to take precedence over scientific publications.
- Hydroxychloroquine should be used with caution because of risk of QT prolongation.
- Results of a study with lopinavir-ritonavir shows no significant difference with treatment.
- Recent findings with remdesivir seem promising but require more investigation.
- Convalescent plasma seems more promising and could be an attractive approach once trial results are available.

Table 1. Ongoing drugs being investigated for COVID-19

Vasoactive Agent Management for Haemodynamic Support in COVID-19 Patients - The Surviving Sepsis Guidelines

An overview of the Surviving Sepsis Guidelines for the vasoactive agent management of COVID-19 patients with septic shock and the use of arginine vasopressin in this patient population.

The SARS-CoV-2 has caused a global health crisis. Thousands of people across the globe have been affected by COVID-19. Clinicians are in urgent need of guidance and recommendations to treat patients and improve outcomes. The Surviving Sepsis Campaign COVID-19 panel has issued 54 statements, which include four best practice statements, nine strong recommendations, and 35 weak recommendations.

Guidelines on the management of critically ill adults with coronavirus disease also include recommendations for vasoactive agent management and haemodynamic support in COVID-19 patients with septic shock. As per the WHO categorisation of clinical symptoms associated with COVID-19 in adults, septic shock is defined as patients with a clinical construct of sepsis with persisting hypotension despite adequate volume resuscitation, and vasopressors are needed to maintain MAP \geq 65 mmHg, and serum lactate level $>$ 2 mmol/L (WHO Interim Guidance 2020).

According to the Surviving Sepsis Guidelines, the following recommendations should be followed for vasoactive agent management of COVID-19 patients with septic shock (Alhazzani et al. 2020):

1. Norepinephrine should be used as the first-line vasoactive agent in adults with COVID-19 and septic shock (SSC Guidelines Recommendation 16).

2. If norepinephrine is not present, vasopressin or epinephrine should be

used, and preference should be given to these drugs over other vasoactive agents. Both agents have been assessed in RCTs without any clear evidence of harm. The choice between the two should be based on availability and contraindications to the two agents. With vasopressin, digital ischaemia may be a concern while with epinephrine, tachycardia and excess lactate production may occur (SSC Guidelines Recommendation 17).

▶▶ early combination of arginine vasopressin helps reduce norepinephrine dose and may lessen risk of further increase in catecholamine induced pulmonary artery hypertension ▶▶

3. Dopamine should not be used in COVID-19 patients with shock if norepinephrine is not available (SSC Guidelines Recommendation 18).

4. Vasopressin should be added as a second-line agent instead of over-titrating norepinephrine dose if mean arterial pressure (MAP) cannot be achieved by norepinephrine alone. In a recent clinical practice guideline, the use of vasopressin

and vasopressin analogs in critically ill adults with distributive shock was assessed and high certainty of a reduction in atrial fibrillation and moderate certainty of an increased risk of digital ischaemia with the addition of vasopressin or its analogs to catecholamines was observed (SSC Guidelines Recommendation 19).

5. Vasoactive agents should be titrated to a MAP of 60–65 mmHg. Anything higher is not recommended in COVID-19 patients with shock (SSC Guidelines Recommendation 20).

6. If there is a presence of cardiac dysfunction and persistent hypoperfusion despite fluid resuscitation with norepinephrine, dobutamine should be used instead of an increased dose of norepinephrine (SSC Guidelines Recommendation 21).

7. In the case of refractory shock, low-dose corticosteroid therapy should be used instead of no corticosteroid therapy (SSC Guidelines Recommendation 22).

Use of Arginine Vasopressin in COVID-19 Patients

Arginine vasopressin, also known as vasopressin, argipressin, and anti-diuretic hormone, is a naturally produced human hormone used for raising blood pressure and inducing water retention. The vasoconstrictor effects of arginine vasopressin are due to the activation of V1a receptors. This is different to catecholamines, which activate adrenergic receptors with possible

pro-inflammatory and pro-arrhythmogenic potential. The difference in mode of action justifies addition of arginine vasopressin, when increasing mean arterial pressure with norepinephrine alone is not possible, a condition known as catecholamine refractory septic shock. Arginine vasopressin's mode of action also offers a norepinephrine sparing effect.

Norepinephrine increases pulmonary artery pressure and pulmonary vascular resistance, a possible disadvantage for patients with underlying lung disorders such as pulmonary arterial hypertension, (Annane et al. 2018). Early combination of arginine vasopressin helps reduce norepinephrine dose (Russell 2011) and may lessen risk of further increase in catecholamine induced pulmonary artery hypertension. Current experimental evidence indicates that arginine vasopres-

sin does not seem to constrict pulmonary arteries (Currihan et al. 2014; Chan et al. 2015; Holmes et al. 2004).

For mechanically ventilated patients, cumulative dose of norepinephrine is associated with the development of ICU-acquired weakness (ICU-AW). For every 1 µg/kg/d dose of norepinephrine a patient received, the odds of developing ICU-AW increased by 1%. This relationship was not seen with arginine vasopressin (Wolfe et al. 2018) and with the norepinephrine sparing effect of arginine vasopressin, ICU-AW maybe reduced (Russell 2011).

In addition to that, early combination of arginine vasopressin can reduce the incidence of atrial fibrillation and ventricular tachycardia (Dünser 2003; McIntyre et al. 2018; Reardon et al. 2010). In patients with septic shock who are at an increased risk of renal failure (1.5x serum creatine

based on the RIFLE criteria), additive treatment with arginine vasopressin can reduce the progression to renal failure and the need for renal replacement therapy by 55% (Gordon et al. 2010).

AMOMED Pharma is the only company in the European Union that has approval for marketing and distributing arginine vasopressin for catecholamine refractory hypotension in septic shock to raise mean arterial blood pressure. The use of arginine vasopressin in the treatment of COVID-19 in septic shock has now been included in the Surviving Sepsis Guidelines.

Arginine vasopressin is marketed by AMOMED under the following brand names: Empressin®, Embesin®, Embesyn®, Empesin®, Empressine® and ReverPleg®. For more information regarding the product, please visit amomed.com. ■

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Surviving Sepsis Campaign:

Guidelines on the Vasoactive Management of Adult COVID-19 Patients with Septic Shock Recommend: Add arginine vasopressin as a second-line agent over titrating norepinephrine dose, if target mean arterial pressure (MAP) cannot be achieved by norepinephrine alone, or use it as first-line vasopressor, if norepinephrine is not available.¹





EMPRESSIN[®]
ARGIPRESSIN



Benefits of Empressin[®] for COVID-19 Septic Shock Patients

Empressin[®] is the only arginine vasopressin (AVP) in Europe labeled and approved for the treatment of catecholamine refractory (resistant) hypotension following septic shock in patients older than 18.²

-  Increase mean arterial pressure³
-  Decrease norepinephrine dose⁴

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NAME OF THE MEDICINAL PRODUCT: Empressin 40 I.U./2 ml concentrate for solution for infusion. QUALITATIVE AND QUANTITATIVE COMPOSITION: One ampoule with 2 ml concentrate for solution for infusion contains argipressin acetate corresponding to 40 I.U. argipressin (equating 133 microgram). 1 ml concentrate for solution for infusion contains argipressin acetate corresponding to 20 I.U. argipressin (equating 66.5 microgram). Excipients with known effect: Each ml contains less than 23 mg of sodium. List of excipients: Sodium chloride, glacial acetic acid or pH adjustment, water for injections.

Therapeutic indications: Empressin is indicated for the treatment of catecholamine refractory hypotension following septic shock in patients older than 18 years. A catecholamine refractory hypotension is present if the mean arterial blood pressure cannot be stabilised to target despite adequate volume substitution and application of catecholamines (see section 5.1 of the published SmPC). Pharmacotherapeutic group: Vasopressin and analogues, ATC code: H01BA01

Contraindications: Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the published SmPC. Nature and contents of container: Clear glass ampoules (Type I, with a broken ring on the narrow part of the ampoule) with 2 ml concentrate for solution for infusion. Pack sizes: 5 and 10 ampoules. Not all pack-sizes may be marketed. MARKETING AUTHORISATION HOLDER: Orpha-Devel Handels und Vertriebs GmbH, Wintergasse 85/1B, 3002 Purkersdorf, Austria DATE OF REVISION OF THE TEXT: 02 / 2018 Prescription status/ Delivery by pharmacies: Prescription only medicine/ Pharmacy-only.

For information on undesirable effects, special warnings and precautions for use, interaction with other medicinal products and other forms of interaction, use in pregnancy and lactation and impact on fertility please refer to the published SmPC.

COVID-19 CHALLENGES

WHAT IS CORONAVIRUS

- The coronavirus is **one** of many viruses that cause respiratory tract infections in humans.
- While typically mild, these infections have seen more **severe forms** such as SARS, MERS and now COVID-19.
- Novel coronavirus (nCoV) is a **new strain** that has not been previously identified in humans.
- COVID-19 is **spread through** droplets which survive 2-3 hours on most surfaces and 2 days on metal and plastic.

COVID-19 SEVERE INFECTION

- 1** Pneumonia
- 2** Severe acute respiratory syndrome
- 3** Kidney failure
- 4** Death

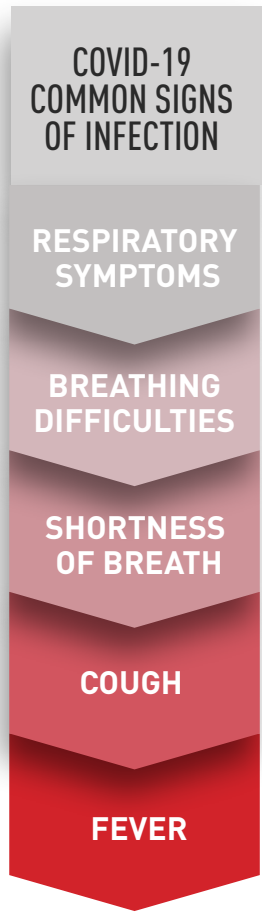
Source: <https://www.esicm.org/resources/coronavirus-public-health-emergency/>



MYTHS VS. FACTS

#1 Myth	Hydroxychloroquine can cure or prevent COVID-19	Fact	There is no proof that this is true and misuse of hydroxychloroquine can cause serious side effects.
#2 Myth	Heat can prevent or cure COVID-19	Fact	Temperatures higher than 25°C do not prevent or cure COVID-19.
#3 Myth	Antibiotics are effective against COVID-19	Fact	COVID-19 is a virus and cannot be treated with an antibiotic. Antibiotics are only given to hospitalised patients to prevent bacterial co-infection.

Source: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public/myth-busters>



KEY FACTS

- Total Cases Worldwide **4,181,077**
- Total Deaths Worldwide **283,868**
- Total Countries affected **212**

DEMOGRAPHIC TRENDS: COVID-19

Nearly **80%** of those who have died **were over the age of 60**. However, COVID-19 can infect people of all ages.

Approximately **75%** of those who died had **pre-existing health conditions** such as cardiovascular disease, diabetes, asthma etc.

More men have been **infected** compared to women.



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Adaptive Strategies for Intensive Care During the Spread of COVID-19: The Brussels Experience

This article describes the approach of the COVID-19 crisis at a tertiary Intensive Care Unit in Brussels, Belgium. Structured interventions and bottom-up initiatives are highlighted, and practical examples given.

Introduction

Optimisation of medical response to no-notice events has been an important focus of research in the field of disaster medicine (Debacker et al. 2016). However, evidence-driven development of medical response protocols in novel domains of hospital medicine is time-consuming, and time is lacking in unforeseen circumstances. The respiratory disease COVID-19 (CO-rona VI-2 rus D-isease 2019), caused by the novel severe acute respiratory syndrome (SARS) coronavirus (CoV), named SARS-CoV-2 or 2019-nCoV, has resulted in thousands of infected patients and deaths worldwide since the end of 2019 (Livingston and Bucher 2020). Countries have adopted their own timeframe of risk-reduction strategies at the level of their health service, reflecting their differential risk assessment strategies.

In response to the COVID-19 outbreak, the structure and organisation of health care at the hospital level had to be reconsidered and action plans had to be developed and implemented as new challenges kept emerging.

This article describes the approach of the COVID-19 crisis at a tertiary Intensive Care Unit in Brussels, Belgium. Structured interventions and bottom-up initiatives will be highlighted, and practical examples given. More specifically, internal reshaping

of the ICU management as an intuitive response to the urgent challenge of the COVID-19 pandemic led to the development of seven building blocks that constitute the functional organisation of the ICU, with specific responsibilities assumed by seven dedicated members of ICU staff. This novel structure was established following a senior staff meeting on March 9, 2020, before the admission of the first COVID-19 patient in ICU. During that meeting, several unmet needs were identified. Seven specific building blocks were identified and one single member of staff was appointed to take responsibility of each element, with no interference of responsibility across different elements. Crisis unit meetings were held on a daily basis, with room for feedback and discussion although ownership of responsibilities was maintained to reduce overlap of expenditure of time, energy and resources. The reshaping of the ICU management into a structure with seven key elements led by seven single commanders is depicted in **Table 1**.

Macro Level

In line with hospital rules, the head of the department has final responsibility for the ICU. Alerted by the situation in other countries, mainly Italy, the head of department had reported the status of

Macro level	Operational management	Communication and staff well-being	Non-ICU environment (Coronary Care Unit, recovery room)
Internal and external stakeholders contact	Medical and organisational command	Communication strategies Staff physical and psychological well-being Patients Family Care	Management of ICU structure and medical support in remote ICUs
Head of Department	Senior Staff Member	Senior Staff Member	Staff Member with Combined Profile
Management of non-COVID patients	Communication support	People management and training procedures	
Medical and practical management	Back-up Members Crisis Unit Confidential Counselor	Management Nursing Department Logistics, Material, Drugs	
Senior Staff member	Non-medical	Head Nurses	

Table 1. Organisational structure

Meetings Macro level

Timing	Meeting
9u.	UZB Crisiscel Covid - fixed
14u.	UZB working group patient flow
17u.	UZB Crisiscel - fixed

Table 2. Meetings Macro Level

capacity and infrastructure at the ICU and transmitted the specific needs to the CEO of the hospital, to the medical management, the head of nursing and other hospital directors, before the first patient arrived in need of critical (or invasive) treatment due to COVID-19 disease (Table 2). He had preliminary discussions with stakeholders outside the ICU to pave the way for the dynamic adaptation process of the ICU department, with an important focus on enhancement of capacity and expansion of medical and nursing staff. Additional beds were created by restraining non-urgent surgical procedures, which typically result in 600 cardiac surgery and 400 brain surgery or brain trauma patients admitted to ICU each year. This was in line with the hospital's medical emergency plan where all non-urgent medical care, including out-patient clinics and non-urgent out-patient and in-patient interventions were downscaled.

A nationwide direct line with peers from other ICU's across Belgium was set up in order to exchange ideas and materials, both medical and non-medical. The national society of Intensive Care was contacted and the website of the society (siz.be) was activated as a platform of information.

Daily information regarding the number of COVID-19 positive patients treated in ICU, patients requiring mechanical ventilation, ICU capacity and number of available respirators had to be communicated to the Belgian Government and daily briefing sessions, chaired by the head of department, were held to discuss the latest updated information provided by the seven building blocks of the reshaped ICU and



Image 1. Briefing



COVID-19 positieve patiënten op IZ UZB

Opvang en behandeling

Concept protocol versie 4.2 - 12-03-2020



Image 2: Protocol

to share this information with the entire ICU staff (**Image 1**).

In view of the need to enhance the ICU capacity, the development of a strategy to create additional ICU beds was a primary goal; indeed, further to the scenario in Italy where the impact of the spread of the disease was massive, we learnt that tripling the number of ICU beds would potentially be required. A capacity expansion algorithm was developed based on a “Phase 1 to 5 Approach” in line with a growing number of patients to treat: accordingly, it was decided to enter a higher-level phase with every series of 5 ICU COVID patients admitted to ICU, which entailed the creation of a new 6 beds ICU unit with each phase, dedicated to the treatment of critically ill COVID-19 patients. So once 5 out of 6 beds were taken, the next unit was put into action.

It was first decided to partially transform the 6 bed CCU (Coronary Care Unit) to an almost full capacity ICU: mechanical ventilation and monitoring were installed,

and invasive procedures such as percutaneous tracheostomy were introduced in this accessory ICU. The operational lead of this ICU/CCU unit was delegated to an ICU member of staff with a combined cardiology/intensive care medical profile. Within two days, the novel ICU/CCU unit was fully operational and the first patients were transferred to this remote ICU. These were non-COVID ICU patients with chronic critical illness or lower need of care. One ECMO-treated Influenza A patient was not moved to this ICU/CCU because the high complexity of care could not be guaranteed in a ‘new’ remote ICU. Expansion of ICU beds was created on this macro level in agreement with other departments. In the recovery room of the operating theatre, a COVID zone was designed for infected surgical patients, and 3 ICU beds were created. This enabled the transfer of non-COVID critically ill patients to this new ‘remote ICU.’ Mixed ICU/recovery staff was foreseen. A Medium Care unit was created when the first ICU patients were ready for step down or did not fulfill indications for full ICU therapy.

The tasks at macro level continued to evolve with new challenges during the COVID crisis.

Operational Management

The primary aim of redesigning the structural framework of the department was to provide high quality, evidence-based medicine to critically ill patients, including those suffering from COVID-19. When compared with standard care, three key differences can be identified: 1) specific evidence-based medicine is largely lacking due to the novel aspect of the disease and lack of time for a ‘traditional’ RCT driven research approach. 2) The harsh bed-side working environment (risk of viral contamination by patients with very high viral load which necessitates extended protective clothing) with priority to the safety of health-care practitioners does not allow certain ‘high-end’ medical procedures.

3) In view of the risk of work overload due to the high number of patients for a limited number of specialised health care providers (HCP), short and lean medical management is mandatory.

Two days after the initiation of the ‘COVID-19 Plan,’ the chair of operational management finalised a 15-page COVID-protocol that was made available for bedside use by HCP. Within this operational protocol, treatment strategies in patients with respiratory failure were described, including nasal oxygen therapy, ‘optiflow’ approach, the decision not to use non-invasive ventilation because of too high viral aerosolisation and rapid crush intubation, and ventilation in prone position. Other aspects of this protocol included (**Image 2**):

- Sedation strategies;
- Haemodynamics failure (drug management);
- Medical drug treatment, antivirals and antibiotics, drug interactions;
- Nutritional treatment including enteral nutrition in prone position and supplemental parenteral nutrition;
- Physiotherapy.

Standard Operating Procedures (e.g. endotracheal intubation) were developed to facilitate standard procedures and to reduce bedside time for HCP in a high-risk environment with high exposure manoeuvres. Paper versions of these documents, easily readable through plastic goggles and screens, were provided in the closed COVID-19 treatment zones.

Medical decision making on the use of resources (ICU units and medical and nursing staff) was the responsibility of the operational manager. Dedicated areas for confirmed COVID-19 patients, patients with uncertain COVID-19 status, and for patients who tested negative for the virus were created to ensure secure individual patient care (**Image 3**).

Non-COVID ICU patients were transferred to newly created remote ICUs to create a ‘buffer zone’ in the main ICU. In the absence of COVID-19 positive infants,

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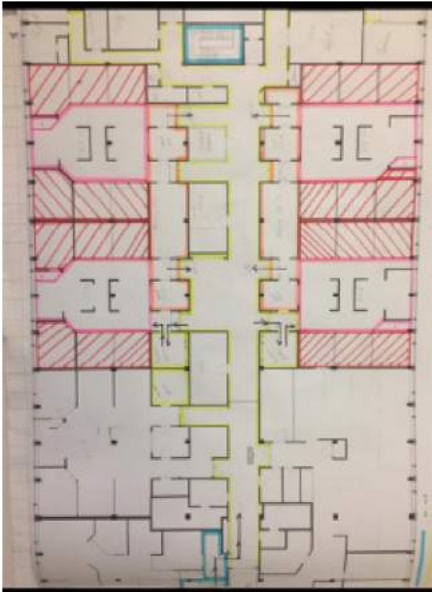


Image 3: Units

paediatric ICU was moved to a ‘clean’ part of the hospital, more specifically the operating theatres and recovery rooms of the ART (Assisted Reproduction Technologies) department.

The operational manager took the responsibility to continuously screen the literature for newly available medical information on the treatment of COVID-19 critically ill patients and to adapt the COVID-protocol where appropriate. The COVID protocol was continuously adapted & updated.

The Ethical Committee of UZ Brussel drew up a guideline that determines who will be admitted to the ICU in case of over-capacity. Triage of patients was based on the chance and quality of survival and was carried out by a team of experts consisting

of senior ICU medical staff, an emergency physician and a specialist depending on the condition.

Communication and Well-being of ICU Staff

An Intensive Care Unit is a 24/7 staffed work environment with a very broad multi-disciplinary nature. Medical doctors and highly qualified paramedical staff including nurses, physiotherapists and dieticians collaborate in an environment that is kept safe and lean by logistic personnel and cleaning staff. At Universitair Ziekenhuis Brussel, the ICU counts approximately 200 staff in total.

In an acute, rapidly changing setting, communication within this group is of cardinal importance. A dedicated communication base was set up in the main waiting area of ICU, strategically positioned and liberated as family members were not allowed during COVID crisis. Correct social distancing was ensured by barring seats, and floor marks were made to discourage staff from gathering too closely during briefing sessions.

Communication Base

Full responsibility for the building block of communication was given to a single member of staff, who physically manned the communication base during regular daytime working hours to gather questions and provide answers to other members of staff. Patient related communication was developed besides communication related to the “adaptive strategy” of the ICU. Paper flipcharts were present and all crucial information and procedures were schematised on a single-page leaflet, to make all ICU staff familiar with the new series of interventions and rules, including those staff whose knowledge of Dutch as the official language in the hospital was poor.

As emerging information had to be shared in a rapid and efficient manner, the smart phone application WhatsApp® was chosen as the communication platform for



Image 4a. Communication Base



Image 4b. Visuals

all people active in the ICU department. This represented a portable mode of communication where new information could be shared instantly within a multidisciplinary team (Nikolic et al. 2018). Visuals were attached to the ICU walls and posted on the WhatsApp platform. (Images 4a and 4b).

Positive feedback from all different levels of HCP confirmed the usefulness of this communication strategy. A laptop was made freely available to all staff to check their emails or consult the hospital's information channels. This strategy was copied to the two remote ICUs (CCU and Recovery Room).

Two days after setting up the COVID-protocol at ICU, a specific WhatsApp group named "IZ COVID" ("Intensive Zorgen COVID," intensive care COVID) was created to include every ICU staff member.

WhatsApp Information shared in "IZ COVID" included:

- Reallocation of ICU Units;
- Recordings of daily ICU briefing (Movie);
- Daily report on number of treated COVID patients;
- Educational movies on how to wear protective clothes in which areas.

Examples of WhatsApp Feedback posted within this group included:

- Practical callouts (urgent need of anti-fog spray for plastic helmets in COVID zone)
- Temperature in COVID ICU rose to 26°C: urgent question if it was allowed to open the windows.

A second WhatsApp group was created for senior medical staff only, and a third group was created in which humorous corona related jokes could be posted. This served as a 'mental break out' for ICU practitioners (Amici 2019). More than 200 jokes were shared between the members of the group in less than 10 days.

Call Centre

Critically ill patients already hospitalised in the ICU before the start of the pandemic were reallocated to newly created remote

ICUs when possible. To ensure that family members were able to keep track of their beloved ones, a dedicated Call Centre was set up on day three. Volunteers from a non-ICU department, more specifically midwives from the ART department, were recruited to man this Call Centre. For every patient who was admitted to or discharged from the main ICU department, a separate communication line was opened. As patient numbers increased, all Digital Enhanced Cordless Telecommunications (DECT) in the ICU were redirected to this Call Centre from 8 am to 8 pm so medical and paramedical staff could focus on patient care.

Examples of communication with patients' relatives through this Call Centre include:

- "Your father/mother/child/relative is present in ICU n° 13, 14, 15, 16, CCU, PACU, ...;"
- "You can call up to three times a day to the following phone number for a short status update;"
- "The medical doctor will call you between 2 and 3 pm or in case of emergency";
- "We will call you with an information summary (stable situation, worse, better) two times a day;"
- "Who is the single contact person please, what is the link with the patient and on which number can we reach him/her?"
- "Do you have any other questions? If we cannot answer them now we will get back to you."

Soon after the activities of the Call Centre had been announced through the communication base, the first calls were made. A dedicated internal phone number '9080' was provided and shared.

The Call Centre rapidly expanded to count five members of staff who manned the call centre seven days a week in shifts. After one week, eight call takers operated in two shifts with one medical coordinator and one link to remote ICUs and non-critical COVID-19 units. Members of staff

who were proficient in foreign languages were also recruited to the call centre in view of the ethnic background of our patients. Medical doctors from non-ICU departments in the hospital were relocated to join this group, to liaise between ICU physicians, the members of the Call Centre and the patients' relatives.

Psychological Support

Because of the novel and invisible nature of COVID-19, this acute challenge put a psychological strain on health care practitioners in the acute care setting of ICUs, where the background patient mortality rate is already 14%. In view of this and other factors, ICU belongs to the top three of work environments with a high burn-out susceptibility (Pastores et al. 2019). The harsh physical circumstances (double layers of protective clothes, face masks that injure nose and face, high temperature and difficult bedside manipulations of critically ill COVID positive patients) all contribute to this mental pressure, even in a skilled ICU crew. A Chinese cross-sectional study suggests that health care workers exposed to COVID-19 have a high risk of developing unfavourable mental health outcomes (Jianbo et al. 2020).

Therefore, the head of the ICU psychologist department was contacted, and a 'psychological support plan' for HCP was established. Two times per day, psychologists were present in the coffee room where medical doctors, nurses and other HCP took a break from work in COVID positive ICU's. Although mainly small talks were done, several colleagues had to be isolated with these psychologists because of sudden crying or panic attacks. A specific email address for psychological support was made available for all hospital staff, with optional support outside the hospital.

The psychiatric department was also contacted, but because of a high number of sick colleagues, they were not able



Image 5. Breathe



Image 6. CCU/ICU

to contribute. Relaxation and breathing exercises were demonstrated and shared on the communication platforms (Image 5).

Upgrading of Coronary Care Unit

The increasing patient flow and need for separation of COVID positive patients urged the need for extra ICU beds. A cardiologist with intensive care accreditation took the lead of this key element and created three ICU beds in the former CCU, which were supplemented with three quarantine beds at a later stage. Signposting and logistics were provided.

To be able to supervise ICU patients in this remote area, additional staff was

recruited: cardiologists and nephrologists were given crash courses in mechanical ventilation, inotropes and vasopressors and correct use of protective gear. A 24/7 surveillance was ensured, with direct liaison with anaesthesiologists and ICU physicians in case of specific technical procedures or questions (Image 6).

Non-COVID-19 Critically Ill Patients

A single senior staff member was made responsible for the medical care and supervision of medical treatment by clinical fellows and junior medical directors. Quality of care for these patients was not altered by the COVID-19 crisis.

Team Spirit

At the start of the pandemic, the senior management of ICU was assisted by a specialist in communication techniques and change management. This person proved to play an important role in communication between members of staff, because diplomacy might cease to exist in such a stressful situation. The professional approach of daily briefing sessions and follow-up of the activities of different working groups appeared instrumental in reducing the risk of potential conflicts among staff.

People Management

The head nurses of the ICU were engaged to fulfill the following responsibilities:

- Management of day and night shift of nurses, with attention to a fair spread of the work load in the harsh environment of the COVID-19 'war zones.'
- Incorporation of non-COVID ICU nurses in the pool, to reduce workload and to be prepared for drop-outs of ICU nurses because of illness.
- Supervision and liaison with the logistic department, facility care etc.
- Creation of new logistic areas where drugs, disposables and other material can be reached by HCP working in COVID and non-COVID zones.

The availability of medical ICU staff was optimised: the rotation of clinical fellows and junior medical directors to other departments was discontinued, which enhanced their presence in ICU. Cardiologists and nephrologists were recruited and were provided basic ICU knowledge. Clear algorithms were made with regard to when to reach out for assistance from medical ICU staff.

Anaesthesiologists, as a second in line medical specialist group, were invited to reorganise their organogram in order to be of assistance where needed. At a later stage, surgeons who volunteered to help were enrolled in the ICU step-down medium care to supervise critically ill

patients in the post-acute rehabilitation stage of disease.

The organogram of medical staff was profoundly changed, with days off scheduled randomly, in order to keep a 7/7 medical staffing present. Higher level in-house medical staff at night was organised, with three medical doctors at central ICU, one cardiologist and one resident at the remote CCU/ICU and three anaesthesiologists to cover the operating theatre and the remote recovery room – ICU. A junior staff member made daily adaptations to the medical staffing in terms of need.

Further assistance was offered spontaneously by medical doctors from various disciplines, who saw their own clinical activities downscaled. Non-medical assistance was highly appreciated too. An otorhinolaryngologist acted as supervisor for the call centre and assisted with practical issues. Medical doctors from the ART Department were in charge with supervising the Call Centre and with liaison. A urologist reached out and was added to a list of volunteers. She was subsequently relocated to the out-patient clinic for sick HCP.

A professor emeritus of oncology took over the scientific work: ongoing studies at ICU were put on hold, contacts with sponsors were made and administrative paperwork carried out by the data nurses. Prospective data registration of COVID positive patients was launched.

Conclusion

The approach of the COVID-19 pandemic at the ICU of Universitair Ziekenhuis Brussel was characterised by reshaping the structure of the department and assignment of different novel responsibilities. The design of the new structural ICU framework comprised seven specific building blocks, each chaired by a single dedicated ICU member of staff, who was made responsible for one of the following elements: macro level management, operational management, communication and psychological

support, creation of remote ICUs, non-COVID management, communication support and people management/logistics. Capacity of ICU beds was raised from 30 to 66 with a medium care up to 29 or 49 beds, medical and non-medical staff was recruited and crash course trained to occupy relevant work slots, medical management provided treatment protocols and Standard Operating Procedures, internal and external communication with patients' relatives was established, newly developed logistic algorithms were developed and the care for non-COVID ICU patients remained optimal. This narrative overview can serve as a template for other ICU departments worldwide confronting no-notice events such as the COVID-19 pandemic, to check their current practice, develop new ideas and copy whenever useful.

The writing of this article did not go at the expense of valuable clinical work as the first author, an ICU physician, wrote the manuscript while suffering from active COVID-19 disease and text editing was done by helpful non-ICU colleagues. Acknowledgements go to the colleagues of all kind who work and suffer in the ICU department of Universitair Ziekenhuis Brussel and all HCP facing their duty in these devastating times.

Conflict of Interest

Elisabeth De Waele is an occasional member of the medical advisory board of Baxter Healthcare and consults for Baxter Healthcare, Fresenius-Kabi, Nutricia. She receives research grants from the Belgian Government, KCE, and unrestricted grants for clinical research. She is an Executive Board member of the European Society of Metabolism and Clinical Nutrition ESPEN. She declares no conflict of interest to this paper. Manu Malbrain is co-founder, former President and current Treasurer of WSACS (The Abdominal Compartment Society, www.wsacs.org). He is also co-founder of the International Fluid Academy (IFA,

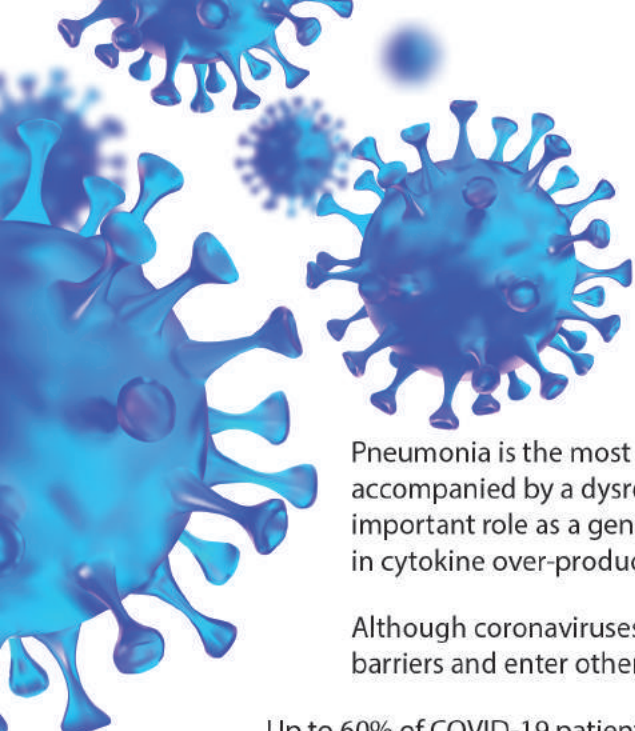
fluidacademy.org), and is integrated within the not-for-profit charitable organisation iMERiT, International Medical Education and Research Initiative, under Belgian law. He is also a member of the medical advisory Board of Getinge (Pulsion Medical Systems) and Serenno Medical, and consults for Baxter, Maltron, ConvaTec, Acelity, Spiegelberg and Holtech Medical. The other authors have no potential conflict of interest with regard to the content of this review paper. ■

Key Points

- A tertiary Intensive Care Unit in Brussels, Belgium shifted to a COVID-19-centric ICU by developing seven building blocks: macro level management, operational management, communication and psychological support, remote ICU's, paediatric care, non-COVID management, and people management and logistics.
- A single dedicated staff member had final responsibility over one block.
- The ICU was optimally prepared for the arrival of a yet unknown number of severely ill COVID-19 patients, ready to upscale the care as patient numbers increased and ready to keep all staff involved, well informed and in the best possible shape to face the threat.

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PATHOPHYSIOLOGICAL ASPECTS OF COVID-19

Patients with SARS-CoV-2 infection may present with mild, moderate, or severe illness; the latter includes severe pneumonia, ARF, ARDS, AKI, endothelial damage, coagulopathy, sepsis and septic shock¹⁻³.

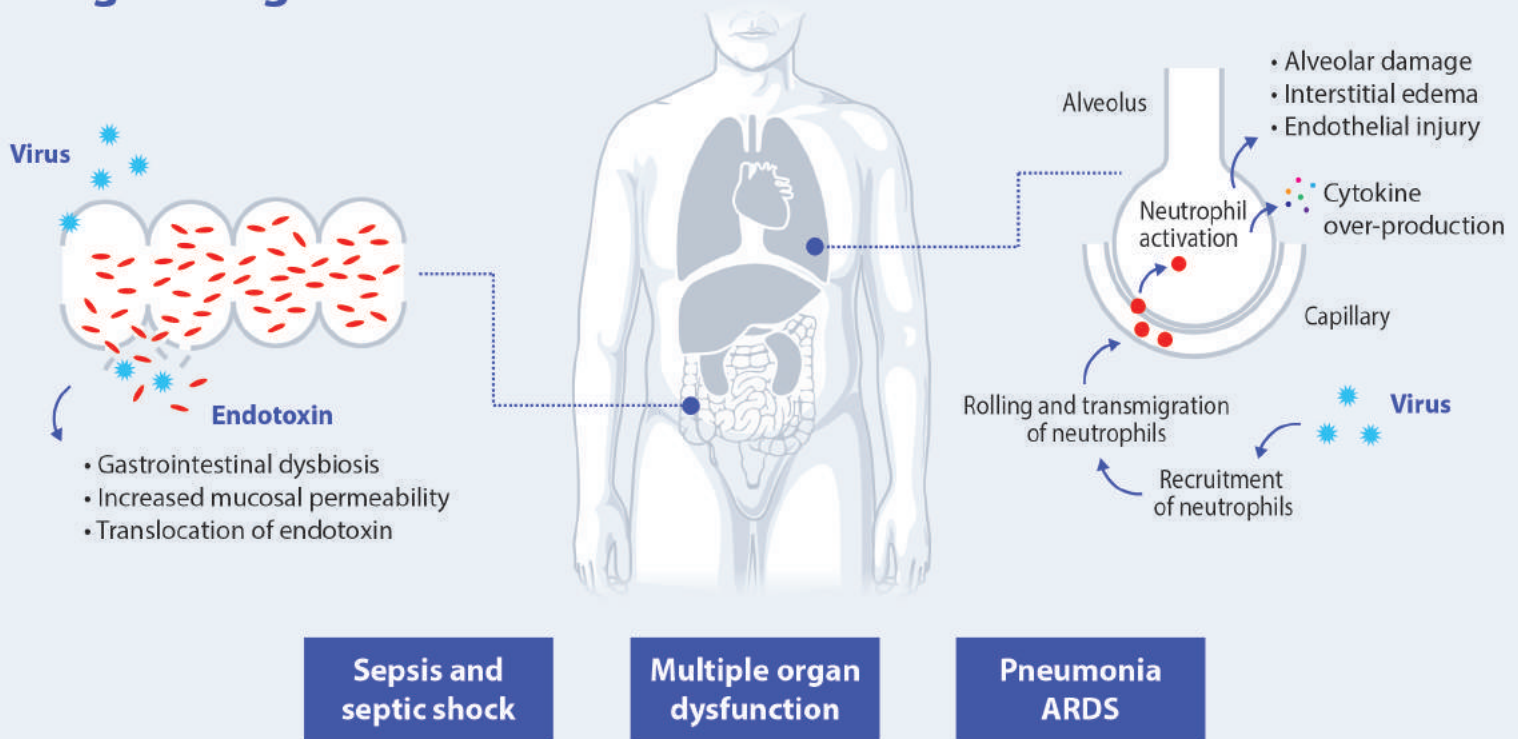
Pneumonia is the most common complication in COVID-19 patients. In severe cases this may be accompanied by a dysregulated immune response. Neutrophils have been found to play an important role as a generator of this response⁴ and rolling of neutrophils is one of the key factors in cytokine over-production⁵.

Although coronaviruses are known as respiratory pathogens, they clearly have an ability to cross barriers and enter other organ systems⁶. One example of this is the gut-lung axis.

Up to 60% of COVID-19 patients have gastrointestinal symptoms at admission or developed during hospitalization and viral RNA was found to be present in the faeces in 48% of patients⁷. Gastrointestinal dysfunction may lead to increased mucosal permeability and leakage of endotoxin.

Patients who are hospitalized for extended periods in an ICU are more prone to superimposed infections⁸. Gram-negative infection and/or direct mucosal gut translocation lead to the circulation of endotoxin (**endotoxemia**)⁹.

The gut-lung axis



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POLYMYXIN B HEMOPERFUSION IN SEVERE CASES OF COVID-19

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The US Food and Drug Administration (FDA) has approved an investigational device exemption (IDE) for Toraymyxin® in COVID-19 patients with septic shock and high level of endotoxemia (EAA™ = 0.6-0.9).

Health Canada has approved the use of Toraymyxin® in COVID-19 patients with severe ARF.

Toraymyxin® has been used to treat severe unresponsive COVID-19 patients in Europe, Russia, Asia, and U.S.



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Introduction

COVID-19 is a newly recognised viral infection which first appeared in Wuhan, China in late 2019. It is caused by a novel Coronavirus, Severe Acute Respiratory Syndrome-CoronaVirus-2. For the most part it results in a mild, self-limiting flu-like illness but unfortunately, severe type one respiratory failure complicates between 14-17% of confirmed cases (Huang 2020; Chen 2020). At present, there is neither a proven specific anti-viral treatment nor a vaccine. Management is largely supportive. It is spread principally in droplets from the upper respiratory tract and fomite (surface-contact) transmission, but crucially, also by the kinds of aerosols generated during airway management procedures (Wang 2020; Van Doremalen

Tracheal Intubation in the ICU During the COVID-19 Emergency

Making tracheal intubation safe for both patients and their health care providers.

2020). Consequently, airway operators are particularly vulnerable to contracting COVID-19 (Wax 2020). This article discusses how tracheal intubation is best performed in these patients using techniques which are safe for both patients and their health care providers. We do not address ethical considerations arising during an overwhelming pandemic. This article references the open access UK and Australian guidelines for airway management in COVID-19 patients (Cook 2020; Brewster 2020) and we commend these to the reader seeking a more detailed exploration of this vital area of practice.

Background

The impact of any infectious disease is a function of its transmissibility and case fatality rate. This single-stranded RNA virus has been fully sequenced and is genetically similar to both SARS-CoV-1 and the Middle East Respiratory Syndrome (MERS) coronaviruses. The latter two pathogens have fatality rates of approximately 10% and 40% respectively. By comparison, the highly contagious 2009 Influenza H1N1 organism had a case fatality rate of only 0.026% (Christian 2020; Majumder 2020). SARS-CoV-2 combines high infectivity (perhaps up to 80% of the European population will be infected in the next 12 months ([bbc.co.uk/news/uk-51730686](https://www.bbc.com/news/uk-51730686))

with a case fatality rate of approximately 2%. Consequently, substantial numbers of critically ill victims need advanced respiratory support and the World Health Organization has declared a global health emergency (WHO 2020).

SARS-CoV-2 Modes of Spread

SARS-CoV-2 is contained in coughed droplets which immediately settle from the air less than two metres from the patient and on the surfaces of objects touched by infectious individuals; it may also be airborne, suspended in aerosols which are very small particles (down to 300 microns). The latter remain in the atmosphere for some time. Virus particle-containing aerosols are created during coughing, sneezing, expectoration and various upper airway interventions referred to as aerosol generating procedures (AGPs). These include bag-mask or supra-glottic airway (SGA) ventilation (without an adequate seal), High Flow Nasal Oxygenation (HFNO), Non Invasive Ventilation (NIV), and extubation. Laryngoscopy, tracheal intubation, tracheostomy, cricothyroidotomy, bronchoscopy and CPR (without a protected airway) may all create aerosols in the presence of high gas flows. About half of all SARS-CoV-1 victims in the 2003 Canadian SARS outbreak were health care workers (HCWs) (PHE 2020) and as many

as 9% of those who performed intubation of these patients contracted the disease; several died (Caputo 2006).

Personal Protective Equipment

These considerations inform what Personal Protective Equipment (PPE) should be worn during intubation of patients with this high consequence infectious disease. Appropriate AGP PPE includes a full-length waterproof long-sleeved gown, double gloves, hat, washable shoes, eye protection (wrap-around defog goggles or visor) and a correctly fit-tested high-grade filtered face piece (FFP3) N95 respirator (Cook 2020; Brewster 2020). All staff should undergo systematic training in donning and, crucially, doffing (removing) this PPE. Self-contamination is common during doffing. HCWs should always have a PPE buddy to ensure compliance with best practice. Thorough handwashing with a lipid solvent like soap is mandatory (PHE 2020).

Intubation - Overall Philosophy

The highest concentrations of SARS-CoV-2 particles are found in the sputum and upper airway. Intubation thereby exposes the operator to high viral loads which are associated with more severe disease. To diminish this risk it is important that airway management is rapid and smooth, without being hurried. Operators should aim to achieve their best effort in as minimal a number of attempts as possible. Simulated training in full PPE using a well-designed COVID-compliant guideline & algorithm (Figures 1 & 2) together with a cognitive aid such as the Vortex approach (Figure 3) and specific COVID-19 intubation checklist (Figure 4) is required to achieve prompt and complication-free intubation under pressure.

When, Where and Who

Plotting the trajectory of physiological decline is demanding and experienced intensivists are required at the bedside.

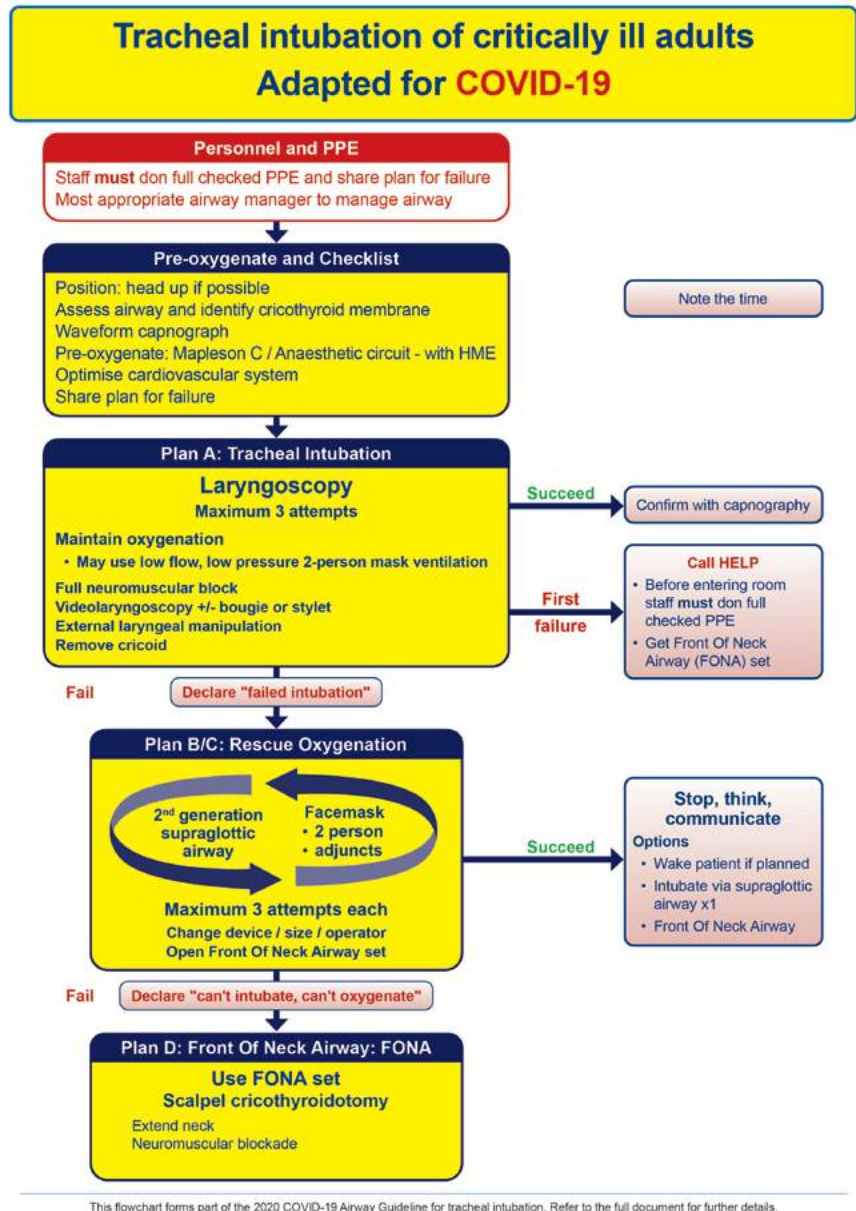


Figure 1. COVID-19 airway management consensus guideline. Cook et al. 2020, with permission.

Whenever possible, intubation should be done before patients are in extremis. Persisting with NIV, CPAP or HFNO when a patient is not responding to these modalities is associated with poorer outcomes. Delayed decision-making may precipitate crises which entice staff to accept inadequate preparation and planning in situations fraught with logistical challenges - which in turn make it difficult to rectify oversights easily or quickly.

To minimise the risk of nosocomial infection of HCWs, intubation should ideally be performed in a cleaned negative pressure isolation room with at least 12 air changes/hour. Failing this, a neutral pressure room with the doors closed (Wax 2020). If it has been used before for AGPs, it should have been cleaned after no less than 20 minutes (PHE 2020). Wherever it occurs, efforts must be made to reduce the number of staff exposed to aerosols,

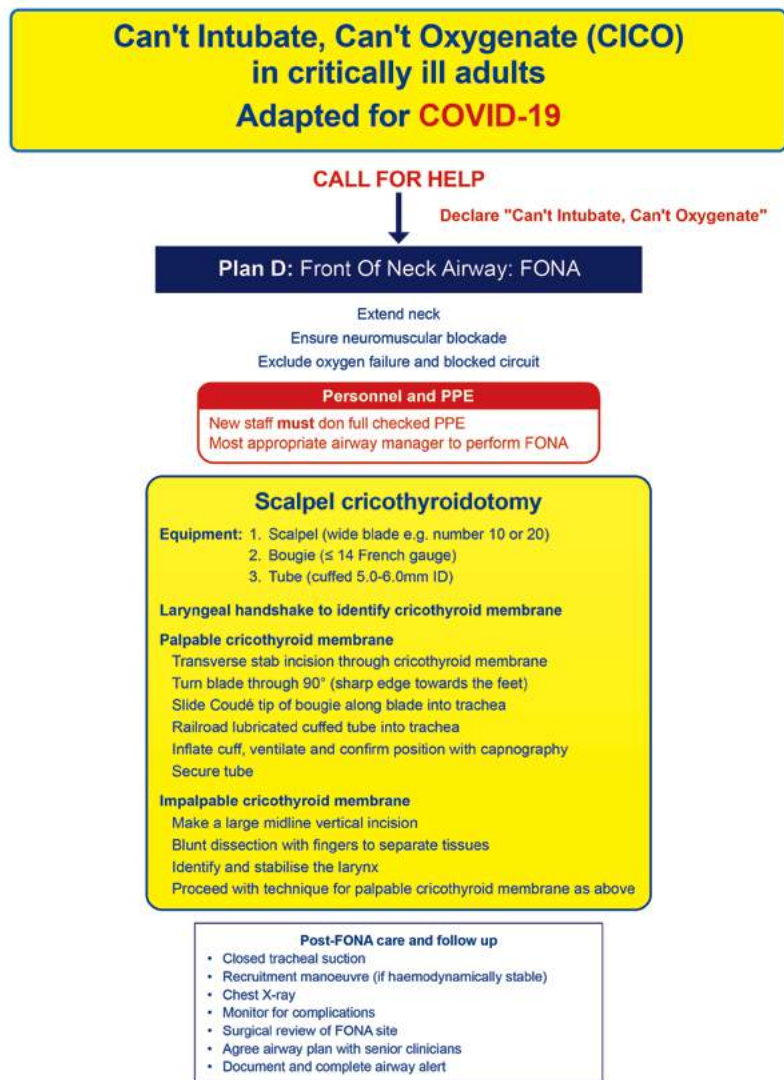


Figure 2. COVID-19 eFONA consensus guideline. Cook et al. 2020, with permission.

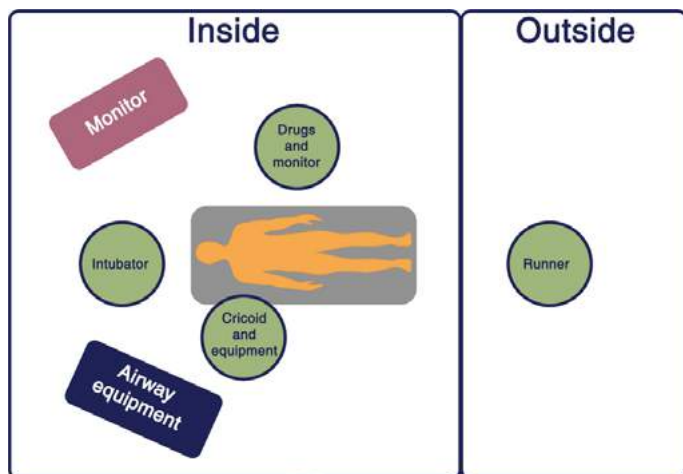


Figure 5. COVID-19 airway team. Cook et al. 2020, with permission.

droplets and fomites by deploying the lowest number of personnel consistent with safe airway management. The airway team can be reduced to an operator, an assistant and one other - who administers drugs, checks monitors and coordinates. A fourth member acts as an immediately available runner outside the room (Figure 5). As these patients admit no margin for error, the operator must be experienced in critical care intubation, be reasonably expected to achieve first pass success and able to work without immediate back-up. If it is believed a second operator could be needed, that person should be immediately on hand just outside the room wearing full AGP PPE.

Preparation & Checklist

A well-designed airway strategy such as that described in 2018 (Higgs 2018) is crucial. This has been modified for COVID-19 patients (Cook 2020). An intubation checklist modified for this patient population optimises the team's performance (Figure 4). The specific airway strategy should be agreed before entering the room and the algorithm and a cognitive aid such as the Vortex (Figure 3) (Chrimes 2016) should be visible in the room to act as aide-memoires if difficulty arises. The team should familiarise themselves with each other (identification is difficult when wearing PPE) and write their names on their gowns for easy communication. Every team member should be empowered to raise concerns before, during and after the procedure – a major safety feature of modern airway management performance (Shorrock 2017).

Intubation Sequence and Maintaining a Safe Apnoea Time

We recommend a modified RSI, aiming to minimise aerosol generation and exposure of the operator to viral particles.

Preoxygenation

Thorough preoxygenation is vital. We

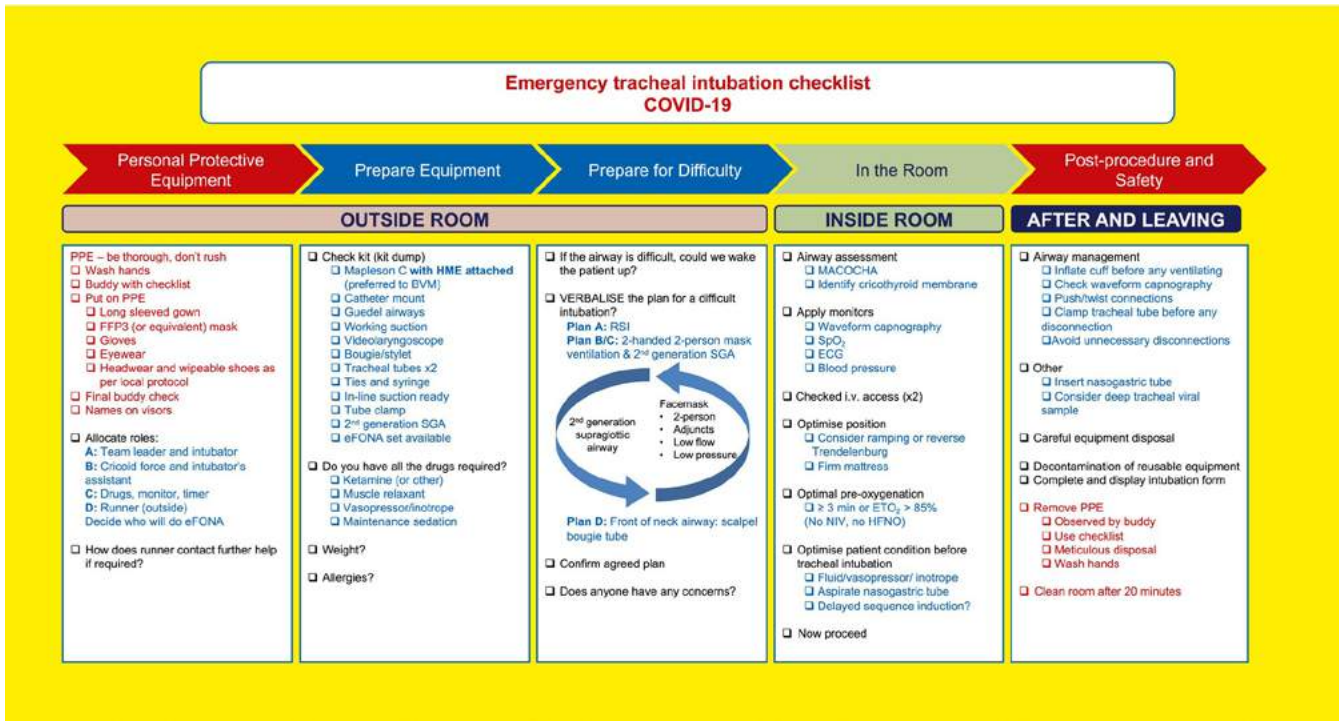


Figure 4: COVID-19 Intubation checklist. From Cook et al. 2020, with permission.

support the recommendation to use closed circle-type circuits or re-breathing Waters circuits (Mapleson C) as these do not expel unfiltered gas into the room. A heat moisture exchanger (HME) with high efficiency viral filter is positioned between the catheter mount and circuit. PEEP can be applied via a tight-fitting anaesthetic face mask and gentle, manually assisted ventilation timed with the patient's inspiratory effort provides an element of pressure support. This helps reassure the operator that the face mask is an appropriate size for the patient. If not, this is the time to swap to a better-fitting mask interface. End-tidal oxygen > 85% is the target but these monitors are rare in the ICU and in their absence, perform preoxygenation for 3-5 minutes.

If the patient is already on a CPAP circuit, this may be used for preoxygenation but the early opportunity to check the fit of the face mask you may later rely on to maintain oxygen saturation is lost. Using this technique also means that formal MACOCHA-based airway assessment

(e.g., mouth opening etc.) is not done (De Jong 2013). In the absence of studies

the highest concentrations of SARS-CoV-2 particles are found in the sputum and upper airway. Intubation thereby exposes the operator to high viral loads which are associated with more severe disease

excluding transmission of viral particles by HFNO (an AGP which provides only low-level PEEP), it is not recommended for preoxygenation. Of note, HFNO also consumes inordinate quantities of oxygen and en masse may jeopardise a hospital's oxygen supply.

Induction & intubation

COVID-19 patients are often dehydrated and septic; ketamine 1-2mg/kg IV is an appropriate induction agent. Coughing must be avoided at all costs and rapid-onset neuromuscular blockade is essential. Rocuronium 1.2-1.5 mg/kg is ideal and is likely superior to suxamethonium, as the latter can wear off equally rapidly and make difficult, prolonged airway management even more demanding. Cricoid pressure is used if appropriate and released promptly if difficulty is encountered. This includes difficulty with facemask ventilation, laryngoscopy, tube insertion, when an SGA is inserted or if active vomiting occurs.

Severe COVID-19 pneumonitis may cause precipitous and life-threatening desaturation. The safe apnoea time can be extended by applying gentle CPAP using an anaesthetic face mask with a good seal. This is best achieved using a two-handed technique. Only use facemask positive pressure ventilation if required to prevent/treat hypoxaemia. A leak risks

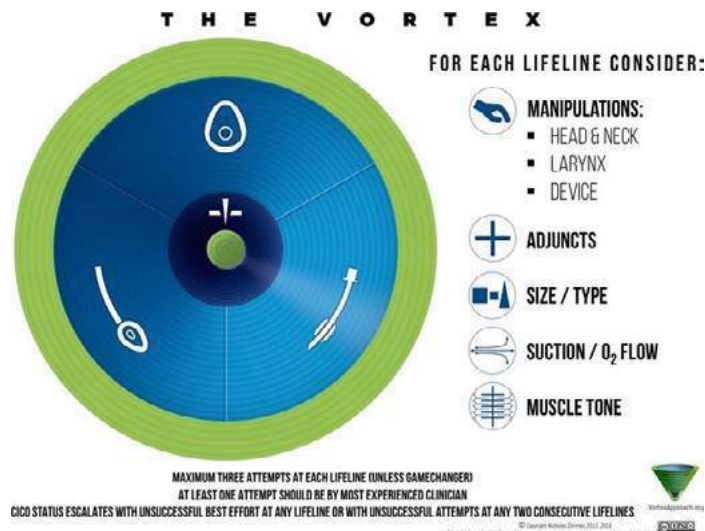


Figure 3. The Vortex cognitive aid. Chrimes 2016, with permission.

aerosolisation. Use low inflation pressures and low fresh gas flows to reduce this hazard. Sensible use of a Guedel airway, after full paralysis, helps overcome any upper airway obstruction which may be contributing to high inflation pressures. Nasal oxygen at low flow (6L/min) is favoured by many, but the operator must be prepared to use positive pressure ventilation if apnoeic oxygenation fails in these patients with significant V/Q mismatch.

Ventilation using a second generation SGA is an alternative but involves instrumenting the upper airway directly (AGP) and if high pulmonary inflation pressures are necessary to recruit alveolar lung units, a leak at the larynx may occur which is more difficult to control than when using a meticulous face mask technique. The operator should make this choice based on their own skill-set and the post-induction behaviour of the patient's upper and lower airways. Prior experience of airway management in critically ill patients is a substantial advantage in this regard.

The same is true of minimising the number of laryngoscopy attempts as repeated instrumentation risks desaturation and increases HCW exposure. Videolaryngoscopy (VL) in experienced hands offers the best chance of first pass

success because the view is better but also because direct laryngoscopy necessitates the operator coming very close

▲▲ a well-designed airway strategy such as that described in 2018 is crucial.

This has been modified for COVID19 patients. An intubation checklist modified for this patient population optimises the team's performance ►►

to the patient's upper airway. VLs with a remote screen allow the operator to keep their arms relatively straight such that their own airway is distant from the patient's mouth and nose. Disposable VLs are preferable as cleaning reusable devices may contaminate HCWs.

Inflate the cuff to 20-30 cmH₂O BEFORE any ventilation occurs. Confirm endotracheal intubation with waveform capnography. Auscultation is difficult when wearing PPE. Consider ultrasound or early chest radiography. It is important

to record the depth of the tube as partial dislodgement is common and gas leaks are aerosol-generating. It is our practice to insert a naso-gastric tube immediately after securing the tube to minimise upper airway interventions and to take a (closed) tracheal suction specimen in patients in whom COVID-19 is not yet proven. Dispose of all devices as soon as they are no longer required. It is important that the tracheal tube (a) is long enough to enable it to be clamped (see later) and (b) allows for bronchoscopy if this becomes necessary.

It is wise to ensure a bolus vasopressor is immediately available as sepsis, high intra-thoracic pressures and occasional SARS-CoV-2 induced cardiomyopathy may precipitate haemodynamic collapse at induction.

Unanticipated difficult intubation

It is important to plan what the airway manager will do should difficulty arise. This should follow a familiar standard approach such as the DAS Critically Ill intubation algorithm, modified for COVID-19 patients (Cook 2020). As discussed above, this may include sealed face mask or second generation SGA ventilation. It is imperative to achieve a best effort with these techniques in the fewest number of attempts to minimise staff contamination. If an emergency front-of-neck airway (eFONA) becomes necessary, we recommend the scalpel-bougie-tube technique. Cannula techniques using high flow oxygen generate significant aerosols and are contraindicated. Efforts to continue oxygenation via the upper airway during an eFONA crisis are likewise contra-indicated as this too will cause aerosol contamination.

Post-Intubation Airway Management

All airway interventions, including even emergent reintubation, require all staff to be fully donned in AGP PPE. Tube displacement is potentially disastrous when the

trachea contains high concentrations of virus. The initial insertion depth should be recorded and checked at least every shift and whenever respiratory deterioration occurs. The cuff pressure should be monitored regularly: ensure there is no leak. Inflation to at least 5 cmH₂O above the peak inspiratory pressure is advised. This also applies during recruitment manoeuvres. This may result in mucosal ischaemia, but is acceptable as it is crucial to protect attendant staff. If the cuff is damaged, prompt reintubation taking the same precautions as above is required. Aerosol contamination can be minimised by occluding the throat with a wet pack pro tem until the faulty tube is replaced.

Closed suction apparatus is mandatory. During planned circuit disconnections (e.g., to turn, prone or transfer the patient, blocked HME changes, etc.), or inadvertent disconnections which cannot be rectified immediately, the tube should be clamped and the ventilator paused.

Anticipated Difficult Intubation in COVID-19 Patients

There are many techniques which are used in this extremely hazardous situation. Most, especially awake methods, generate voluminous aerosolisation. The risk-benefit can only be weighed on an individual basis but COVID-19 status lowers the threshold to resort to asleep techniques like hyperangulated VL or intubation through an SGA (Higgs 2005) with, for instance, an Aintree Intubation Catheter.

Disclosures

Andy Higgs co-authored the UK and Australian guidelines (Cook 2020; Brewster 2020) and is Treasurer of the Difficult Airway Society. He is Chair of the joint Difficult Airway Society – Intensive Care Society- Faculty of Intensive Care Medicine- Royal College of Anaesthetists committee on intubation of the critically ill adult. ■

Key Points

- COVID-19 is a newly recognised viral infection caused by a novel Coronavirus, Severe Acute Respiratory Syndrome-Coronavirus-2.
- Severe type one respiratory failure complicates between 14-17% of confirmed cases.
- Airway operators are particularly vulnerable to contracting COVID-19.
- All staff should undergo systematic training in donning and, crucially, doffing (removing) personal protective equipment (PPE).
- It is important that airway management is rapid and smooth, without being hurried. Operators should aim to achieve their best effort in as minimal a number of attempts as possible.
- Whenever possible, intubation should be done before patients are in extremis.
- To minimise the risk of nosocomial infection of HCWs, intubation should ideally be performed in a cleaned negative pressure isolation room with at least 12 air changes/hour.
- Every team member should be empowered to raise concerns before, during and after the procedure – a major safety feature of modern airway management performance.
- There are many techniques which are used in this extremely hazardous situation. Awake methods generate voluminous aerosolisation. The risk-benefit can only be weighed on an individual basis.

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A COVID-19 Dashboard: Data Analytics to Aid Resource Allocation in Intensive Care Units

In this article, we focus on clinical and practical application of current available cloud-based data analysis to track and benchmark in real-time suspect and confirmed COVID-19 cases, resource use and availability.

Introduction

The COVID-19 pandemic represents an unprecedented challenge to intensive care units (ICU) due to the surge of severe cases of pneumonia posing great stress to hospitals and healthcare systems (Phua et al. 2020). The fast occupation of ICU beds by these severe cases has exceeded any possibilities of organisation and planning making ICU beds and ventilators a scarce and valuable resource (Phua et al. 2020). The possibility of monitoring case-load, local and regional trends as well as the current use and availability of resources in ICUs has become even more important in the present scenario (Phua et al. 2020; Salluh et al. 2018).

In the present article we describe the characteristics of a COVID-19 dashboard for ICUs and its deployment in 1100 ICUs.

Methods and Results

We used as a base the Epimed Monitor ICU system (epimedolutions.com), a cloud-based quality improvement (QI) software that allows near-real time

monitoring of case-mix, performance metrics and benchmarking for adult, paediatric and neonatal ICUs (Zampieri et al. 2017). The solution is currently

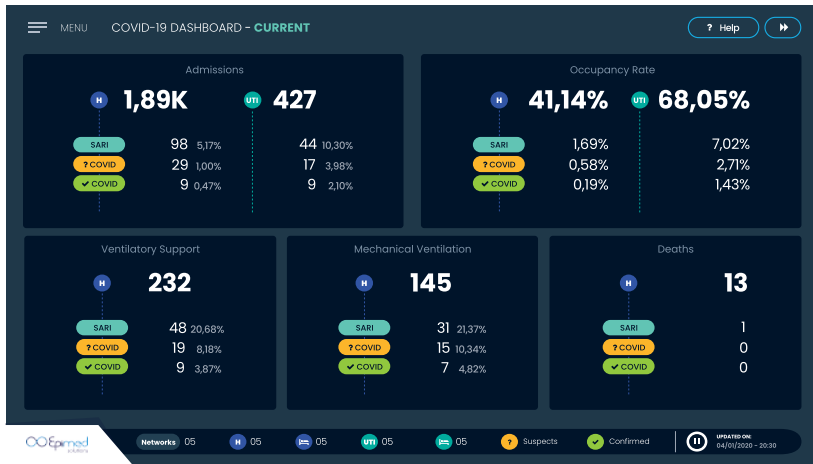
the Epimed Monitor ICU system cloud-based quality improvement software allows near-real time monitoring of case-mix, performance metrics and benchmarking for adult, paediatric and neonatal ICUs

implemented in 1100 ICUs in Belgium, Brazil, Chile, Colombia, France, Portugal and Uruguay. Data from this platform is also publicly available (beyond the scope of QI) in National projects (Belgium- micaproject.be, Brazil- utisbrasileiras.com, Uruguay- ucisuruguayas.com

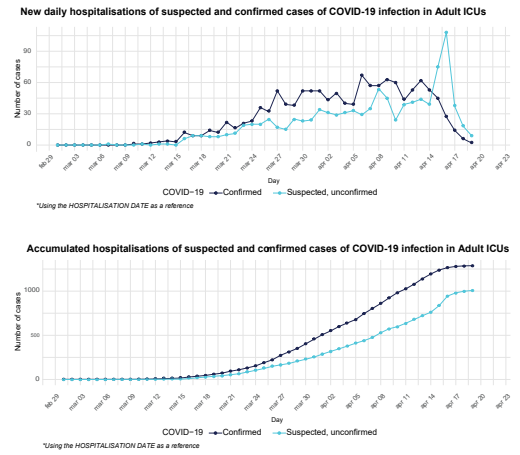
and the international project LOGIC – icubenchmarking.com). As of February 2020, we incorporated the diagnosis of COVID-19 pneumonia in the diagnostic/coding of Epimed. We subsequently developed an online platform that was seamlessly integrated with the Epimed Monitor database and allowed the near real-time surveillance of suspected and confirmed COVID-19 cases in the ICUs, its occupancy rates, use of mechanical ventilation (MV), outcomes (mortality) as well as the availability of ICU beds and ventilator support resources remaining (ventilators, NIV, ECMO) in the hospital (**Figure 1**). Through the benchmarking all users of Epimed can track the cumulative cases in their hospitals and region, including the outcomes and resource use. Thus, ICU managers can use near real-time data on the availability of the combined local and regional data to better inform the planning on resource allocation and use. In large hospitals with multiple ICUs or in a hospital network, such information would be a part of the routine evalua-

COVID-19 ICU Dashboard

Real-Time covid-19 patients, resource use and availability



SARI, Suspected and confirmed Covid-19 cases



Daily trends and cumulative data

Epimed solutions

tion of ICU status and therefore would improve the transparency of decision-making process of ICU admission of COVID-19 cases as well as serve as a platform to evaluate where to admit or transfer a patient within an ICU or hospital network.

In addition, the present pandemic represents a unique condition leading to ICU strain. Strain is defined as discordance between available resources and demand to admit more critically ill patients while continuing to provide the highest quality of care (Hussain et al. 2019). During a pandemic or a disaster management, it is fundamental to check the ICU strain. As an ICU manager it

is possible to evaluate the ICU strain integrating all this information cited above and evaluate the contingency risk and eminent crisis in almost real time. Moreover, it is fundamental to develop a framework to triage and adequate resource allocation (Christian et al. 2014) and the availability of reliable and timely data is an important part of it.

Conclusions

The implementation of a specialised COVID-19 dashboard with near real-time information of suspected and confirmed cases as well as resource use and availability is feasible and was delivered in two weeks for 1100 ICUs

in 7 countries. Information technology and clinical data may be used to help improve resource allocation in ICUs for the COVID-19 pandemic.

Data-driven management applied to COVID-19 patients in the ICU allows not only evaluation of ICU performance but may help the planning and resource allocation for these patients.

Conflict of interest

Dr. da Silva Ramos reports no conflicts of interest. Dr. Salluh is co-founder and shareholder at Epimed Solutions®, the provider of a cloud-based healthcare analytics and performance evaluation software. ■

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An Adaptive Response to COVID-19

John Nosta is the founder of NostaLab, a digital health think tank. He is regarded as one of the top global strategic and creative thinkers in digital health. He's also a member of the Google Health Advisory Board and a technology expert for the WHO. John is a contrarian with a sharp focus on the future, and it is this quality that makes him a defining force in dissecting and deliberating global events and trends. He has built his career on the science of innovation. *ICU Management & Practice* spoke to John Nosta on how the healthcare system has handled the COVID-19 crisis and the role data modelling, technology, and collective effort has played and will continue to play in combating this pandemic.



an adaptive response, I'm saying we need to be smart, but we might also need to be agile. We may need to look at modelling and medicines and be able to adapt as things come in through a clearer lens.

With respect to clinical information, we're seeing that COVID-19 may not be like a traditional nosocomial or a community-acquired pneumonia; it may be a systemic scenario that might be more akin to something like altitude sickness. The condition may reflect changes in damage to haemoglobin and oxygen transport. One of the manifestations of this is that the nature of the respirator settings, the force with which air is pushed into the lungs or settings, such as positive end-expiratory pressure (PEEP), may have to be modulated to accommodate some of the tissue damages in the lungs. Hence, for me, the key word is not only 'adaptive' but also 'agility' - the ability to be agile and modify in a circumstance that is evolving as we speak.

You've talked extensively about the need to develop an adaptive response to manage this crisis. What do you mean by this?

Developing an adaptive response has become even more important as time goes on, and we recognise a few central facts. Originally, I looked at the adaptive response as being a function of social distancing and risk evaluation to establish more personal, social, and economic freedom. Today, I think that we need to look at our response in an adaptive way. This applies to some of the modelling that's been done, as well as our clinical perspective in terms of patient management, and therapeutic modalities. We have to be adaptive as new knowledge comes to bear. Modelling is

difficult; when we look at statistical models of large systems, we see it's made on many assumptions. Sometimes those assumptions are slightly off target, sometimes they are exactly right, and sometimes they are completely off the mark. This can push our modelling in ways that can cause significant changes in the projections. For example, if we look at the numbers out of New York state, where the initial projections are significantly higher than the current clinical need, this is a red flag. When we talk about social concern, psychological concern, stress, social isolation, and other important issues, we need to understand that the models have social and intellectual consequences. Therefore, when I talk about

What about your two-pronged strategy? We all hear recommendations on flattening the curve, but is there another approach?

We all know the expression "flatten the curve" and flattening the curve is important. It talks about, in essence, what social distancing and social isolation can do to decrease the transmission of the disease.

But in certain instances, that really doesn't change the total number of people infected. In fact, what it does, it flattens the curve and the area under the flattened curve is similar to the area under the higher peak curve. It looks at the amount of patients getting sick relative to the capacity of our healthcare system. That's an important dynamic. But the other side of that equation (and this is where the wonderful global ingenuity of the life science industry is coming into play), is not only social isolation, but treating the curve and being able to use clinical practices such as having patients prone and face down to increase oxygenation when they're in the intensive care unit to drugs that treat the immune response. That could be Interleukin 6 (IL-6) or natural killer cells that can help destroy the virus in our bodies, and also the utility of hydroxychloroquine, as well as azithromycin and remdesivir. While there's a lot of controversy about that, the anecdotal evidence is very interesting. In those instances, p stands for patient, and what we need is p to stand for p less than .05. One of the greatest tools we have to combat COVID-19 is the ingenuity of the life science industry to treat the disease and to treat the curve. Among the therapeutic modalities that are entering the clinic today, probably the most important one is the use of vaccines.

When I talk about a two-pronged approach, there's a flattening of the growth from social isolation in some of the traditional modalities but, treating the curve, whether it be with hydroxychloroquine, IL-6, convalescent serum or with other treatments, is the essence of the two-pronged strategy. I would argue that therapeutic modalities may become the most important tool we have in our clinical armamentarium. Testing - for the virus and immunological status - is also critical.

I would also argue that the matter of hydroxychloroquine has become a political as well as a clinical discussion. I think in the U.S., it's distressing that we are arguing a therapeutic choice on the basis of a

presidential election. Hydroxychloroquine can be a dangerous drug, as it certainly has an association with QT prolongation. But the drug has been around for fifty years, and it's being used extensively in patients with Lupus and Rheumatoid Arthritis. Where is the QT prolongation with this patient population, and why isn't it a tremendous public health issue that people are dying from ventricular arrhythmia when using hydroxychloroquine? I think that the data will speak loudly. There are many, many hundreds, if not thousands, of patients in a variety of double-blind controlled clinical trials so that information will be out soon. Further, because this is a short course of treatment, we may be able to see a clinical benefit sooner than later. I am hopeful that again, the p -value will switch from p equals patient to p is less than 0.05.

How close do you think we are to developing a vaccine against COVID-19?

The genome was determined almost instantly, and we have the methodology in place to create vaccines. But that's the short side of the equation. The longer side of the equation is dosage, safety evaluation, and clinical efficacy, and moving into phase-three trials. This could take a year. It's being explored extensively by pharma and being funded by governments and the Bill Gates Foundation which is donating a lot of money to drive this idea forward. Probably the solution with regard to vaccines may not be for this pandemic; it may be a modality for the recurrence of this virus at another time.

What we've seen in European countries like Italy and Spain and what we see in the U.S. is that most global healthcare systems were not prepared. Why do you think this has been the case?

This is a very complicated question because it touches on everything from clinical preparedness, to financial capabilities and even human nature. Number one: I think people are optimistic, and they tend to

look the other way. I also think that the economic constraints put upon countries have also let us reprioritise preparation for more current or urgent needs. The question is, how do you pick the issue that you need to be prepared for? Pandemics are reasonably high on the list. But there can be many others. How do we pick the appropriate emergency to begin to build readiness? As a first responder, we've always done drills, we've always tried to be ready. Prioritising is a difficult job, but I think our first job is to prioritise what represents an urgent risk. This involves a little bit of science and a little bit of guessing.

The interesting thing is when you look at dollars spent, and we look at the EU in particular, Italy had one of the highest healthcare spends per capita than any of the other countries in the EU. It wasn't an impoverished country. It was a country that had a reasonably robust and qualified healthcare system. So even some of the best systems can be overwhelmed in certain instances. Was it multi-generational living that caused things to get out of control in the northern region of Italy? Is it the economic relationship that Italy had with China in terms of manufacturing, particularly associated with the Wuhan district, and tremendous travelling back and forth? Or was it some other unknown factor?

If you look at the U.S., using one data set is sub-optimal. The U.S. has many regions. We're looking at New York, California, Washington, and New Orleans as well as some of the Midwest states that are not as populated and have a much lower occurrence of the condition. We also see a younger population in Spain, a similar hotspot. This is an epidemiologist's dream. We are generating so much data, and it is going to be extraordinary. I predict that we'll find some surprises. We may find that certain drugs worked or didn't work; we may find that some elements of social distancing were more effective than others, or wearing masks was extraordinarily effective or completely inappropriate.

What do you think is the most important lesson that we should learn from COVID-19?

That is a tough question because we're seeing things change on a daily basis, and we're seeing the models themselves change by tens of thousands of people. We're seeing curves shift, and we're seeing a peak or flattening in a variety of countries. I think the lesson learned is to be open-minded, follow the data, and recognise that in today's data-based, analytical driven AI world, we have a tremendous opportunity to advance human civilisation in new, important, and exciting ways.

Do you think that virtual reality could have any role in combating such a pandemic?

We are seeing the empowerment of technology from areas as functional and practical as telemedicine to eLearning in schools. I believe that a new human connectivity will emerge, and whether it will be traditional chat-based, or something richer, virtual reality, is certainly going to play a role. I think that virtual reality is probably at the wrong spot in the continuum for today. Six months ago, virtual reality was relevant. It drove a sense of empathy. It allowed a caregiver to understand what macular degeneration looked like for another person. It allowed someone with a movement disorder to walk in a patient's shoes. I think that today, we're taking a step back and looking at some of the functional realities of video conferencing and telemedicine, but the expanded world of virtual reality might have actually been a bit compromised at this stage of the game.

Could there be a second wave of COVID19?

Yes. It is important to question whether the virus is going to be eradicated. Will the virus develop a seasonal nature? What is the nature of the mutation or mutations? It was originally assumed to be a slow mutating virus that bodes well for vaccines, but if

there is a second peak, the question is, how high will that peak be? Is it regional? Are there local hotspots? Is it a pandemic? We may get a hotspot in Italy or New Orleans, or we may find local areas where the virus emerges. But I don't think it's fair to apply the vast global response to that wave. I think that again, we have to be adaptive and agile. The recurrence of this virus may occur on a regional and local level but we might be better prepared to manage it and to implement social distancing quickly in ways that are highly effective. Maybe we'll have drugs that we can use and other treatments. I think that any second wave would have to be looked at in the context of the first, but also how, where, when, and why it's happening.

■ ■ we live in a unique time in human history. Never before have we had the opportunity to have scientific, technological, and manufacturing opportunities to rise to the occasion ■ ■

We've seen different countries using different approaches to containing COVID-19. Do you think that the strategies are sufficient or effective? Do you have any examples that could have been more successful?

Let me ask that question rhetorically. Are the strategies we're using to treat cancer effective? Are the strategies and tactics we're using today to treat high blood pressure appropriate and effective, recognising that most patients don't stay on drugs or aren't even diagnosed? I think that, in the context of human nature and clinical medicine as it exists today, it is difficult to say that what different countries are doing is enough or is appropriate. The answer would be no,

they're not. The question is, where does it fit on the continuum that will often find countries doing a variety of strategies and tactics? Some might be experimental; some might be optional. There may be a cultural dynamic; others might be absolutely fundamental. The use of quality care insights around respiratory care when these patients are severely ill and hospitalised in the intensive care unit and the use of certain drugs or therapeutic modalities certainly can be a checklist. But unfortunately, in today's world, I think that there are a lot of question marks in boxes versus hard and fast checklists.

We can talk about countries like New Zealand and South Korea squashing the curve, but what drugs have come out of these countries and what is the contribution to global health provided by them? From my perspective, these are almost cultural issues. When you look at the South Korean population, it's easier to align them with a social goal. It's the nature of their society. Now, when we look at other countries where they have a greater spirit of independence or entrepreneurship, you may have a harder time getting people to adopt social distancing at the snap of a finger. If you look at the curves in New York City, it has been doing surprisingly well in relation to the predictions. Look at Sweden and the emergence of the idea of herd immunity, and how it may or may not be working. Clearly, Sweden took a more contrarian approach - and that in itself is very interesting. It's easy to point to success stories when the underlying factors are complex. Successful models make many assumptions. That being said, I tip my hat to South Korea, It has taught us some very important things that if we can act collectively, we could get on top of the COVID-19 spread.

For how long do you think it's practical and feasible to implement social distancing?

This goes back to your first question, which I think is really at the heart of what we're

doing now. The notion of an adaptive response, as was originally articulated, was the notion of reopening life, of reestablishing some level of social and economic connectivity. If there was a recurrence of the disease, we would have to go back to more controls and more constraints. It's a balancing act between suppressing the disease and returning to normal societal activity. Society is a complex structure and to look at the clinical implications, without looking at social, economic, financial implications, will not do the problem justice. Prioritising health, safety and wellness is extraordinarily important, but we have to prioritise it in the context of running the country, of our businesses, and of our livelihood.

How long can it go on? That's a really interesting question. What I'm seeing is in terms of the curves, flattening of peaks, of decreased deaths, decrease in admissions into the ICU, decrease in hospitalisations makes me optimistic. I put my hope in what society is doing and what our brave and bold healthcare providers are doing, and what the life science industry is doing in terms of therapeutic treatment choices.

If the pandemic continues, how should healthcare decide who gets what resources if there is a shortage?

We have a lot of what-if questions to be answered. We could wonder if you have a shortage of respirators, say where you have 100 patients in a hospital, and you only have 50 respirators, what happens? Well, first, as a mechanical engineer, we know that we can split respirators, and there are options where we can use respirators in other interesting, effective ways. I see extraordinarily interesting opportunities for Tesla, for Dyson, to build respirators. Yet we cling to the notion of catastrophe as a defining element. When we plot the curve, we have to make assumptions that are aligned with the data. Some people plot the curve, and then they fill in the data, because they have pre-existing notions about where it's going. But what we're finding is, after

we draw the curve and we plot the data, we're seeing significantly different scenarios. I think that the potential issues of not having enough medicines, or enough respirators are going to be handled on local levels. Number one: I think that problem is not as big as it has been suggested. Number two: I believe in the technological ingenuity of many people to repurpose respirators in a two-to-one modality or someone squeezing an ambu bag for a few hours until we can get the technology in place. Again, I tend to be optimistic and am driven by the data rather than emotion. It's important to recognise that all these ideas need some strategic focus. We need to channel our intellectual capacity to key areas of need and future need.

Let's look at both perspectives. If we look at the negative perspective, we could potentially have hundreds of thousands of people in the intensive care unit with 20,000 respirators. From a U.S.-centric perspective, I have seen an extraordinary amount of effort going into moving respirators, using stockpile, driving corporations to make new devices, whether it be Tesla or the auto industry or Dyson. I think this is a human miracle that is rising to the occasion. We live in a unique time in human history. Never before have we had the opportunity to have scientific, technological, and manufacturing opportunities to rise to the occasion. If you go back to the Spanish Flu (1917 to 1918) and look at the data from that time, you will see some very different modalities. It's a very different time, whether it be the ability to communicate through the internet or the ability to sequence a genome to test drugs and develop technology like respirators.

Are we doing enough to protect brave healthcare workers?

Healthcare workers are heroes. The Person of the Year in Time magazine should be the healthcare worker. The Nobel Prize should be the healthcare worker. They walk into danger every day when they go to work and

then they go home and bring that danger with them. When a soldier comes home, he or she is embraced with a hug. But when a healthcare worker comes home, they very well may be bringing the danger into their own house. For me, they are at the forefront of this physical and psychological war.

Are we doing enough? I think that we are struggling to understand this in the context of a new global pandemic. Healthcare workers are overwhelmed, the system is overwhelmed, medicine is overwhelmed, and society is overwhelmed. I think that we have to push forward with an adaptive response. If we can decrease viral shedding, if we could decrease the likelihood of hospitalisation or the need for intensive care or the need for respirators, then we can shift the burden off the healthcare system. That comes right back to the idea of flattening the curve, the ability to lower the clinical need to match the capacity of the healthcare system. This may be the most important way that we can help our healthcare workers. I believe that they can manage an appropriate caseload. It's when the caseload supersedes capacity that errors occur. I'm overwhelmed personally by the sacrifice that these people are making for the system.

Is there anything else you would like to say?

What bothers me is that these issues have become political. I believe that there are some people who wish that the system could be reset to accommodate their political and social perspectives. I think that there is a sense of social responsibility and that we have to be fair. Sometimes I'm criticised by trying to look at issues more broadly but my voice is one of my perspectives, and it's by far from definitive. Some voices have positioned themselves behind a set perspective and they can't see outside of that box. We need to change that. ■

Continuous Monitoring of Urine Flow in COVID-19 and Other Critical Care Patients: Why and How

Acute Kidney Injury (AKI) develops in over 55% of ICU patients (Hoste et al. 2015). As infections and the need for mechanical ventilation are known to be among the high-risk factors for the development of AKI (Bellomo et al. 2017), the incidence may be even higher in the COVID-19 era.

For ICU patients with COVID-19 or other complex conditions, essential physiological functions such as cardiac output, respiration rate, blood pressure, body temperature, and blood gases are routinely electronically monitored and displayed around the clock, alerting the staff of irregularities and enabling them to provide minute-by-minute, life-saving care. However, despite the fact that real-time urine monitoring can provide critical information regarding impaired renal function and/or fluid balance (Kaddourah et al. 2017), urine output is still being recorded manually and intermittently.

The importance of continuous urine flow monitoring for AKI and fluid management in critically ill patients has been emphasized by leading nephrologists and critical care experts. In a retrospective study of close to 16,000 ICU patients, intensive monitoring of urine output (UO) was associated with improved detection of AKI and reduced 30-day mortality in patients experiencing AKI, as well as less fluid overload for all patients (Jin et al. 2017).

Manual urine flow measurements are time-consuming, requiring manipulation of urine meters, visual assessment and painstaking data recording. These difficulties in measuring, monitoring and accurately

recording urine output bring into question the reliability of urine bag readings, in terms of frequency, regularity, and accuracy (Macedo 2015).

The availability of electronic, real-time urine flow information can facilitate early AKI risk assessment, staging and early intervention, as well as improved monitoring of fluid balance and assessment of response to diuretics in patients with fluid overload.

In addition, "no-contact" data transmission can reduce the risk of cross-infection for COVID-19 and other ICU patients in isolation.

With a urine monitoring system like the Clarity RMS® by RenalSense, real-time urine flow data and notifications of fluctuations are automatically transmitted to the medical staff on a 24/7 basis, similarly to other vital signs, providing an early sign of acute kidney injury (AKI) risk and facilitating rapid intervention. This enhances monitoring

of treatment efficacy and management of fluid balance. The system's patented electronic sensor can be used with any existing, indwelling Foley catheter, and patient data is displayed graphically on a cordless, battery-operated bedside monitor. It is currently in use in leading medical institutions in the US and Europe. ■



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Ultrasound in Times of COVID-19

The potential clinical utility of ultrasound modalities in the COVID-19 patient, the limitations, evidence base and governance over point of care ultrasound images during a pandemic and a discussion on whether the hype surrounding Lung Ultrasound (LUS) is justified.

Introduction

The use of ultrasound outside radiology has already become well established within many of the acute specialties, such as critical care and emergency medicine. Critical care ultrasound (CCUS) takes place at the point of care. It has many advantages:

- Non-invasive
- Negates the need to expose the patient to ionising radiation
- Associated with minimal logistical disruption, being performed at the bedside
- Repeatable (Huang et al. 2020)
- Quick to perform
- Low cost

Many of these qualities have become particularly relevant in the current climate of the COVID-19 pandemic we are facing, where moving patients with COVID-19 around the hospital, in order to perform imaging studies, comes with significant risks. Sending patients elsewhere in order to perform other imaging studies removes them from a place of isolation/infection quarantine, to non-infected areas. This places other staff, patients and the general public at significant risk of contamination.

There has been much fixation with COVID-19 being a disease solely affecting the lungs. In this article, we will discuss the potential clinical utility of the other ultrasound modalities in the COVID-19 patient. We will also discuss the limitations, evidence base and governance over point of care ultrasound images during a pandemic. Indeed, is all of the hype surrounding

Lung Ultrasound (LUS), justified, as it has certainly received the limelight?

What is the Advantage of Ultrasound in Times of Pandemic?

During the Ebola outbreak, Henwood describes ultrasound as being fairly pivotal to patient care and assessment (Henwood 2019). It assisted them in the support of the pregnant patient, as well as in the assessment of respiratory status. Moreover, it aided them in volume assessment, which is always a contentious issue in febrile states. They state that it narrowed down their differential diagnosis list and also allowed them to piece together the clinical puzzle in resource-limited settings where they lacked other diagnostic imaging tools—essentially utilising whole body ultrasound as their 5th pillar of clinical examination (Narula et al. 2018).

Interestingly, and a point we make on many occasions, they state that it helped them to conserve valuable PPE, as they could utilise even relatively unskilled sonographers to perform the examinations. They placed an expert user outside of the clinical area on standby to interpret the images; the first form of telemedicine if you will. Handheld ultrasound devices were used (presumably due to affordability within resource constrained areas), and linked to Wi-Fi in order to send images to providers in low-risk zones. The chosen devices could be cleaned easily between patients, so minimising the spread of infection.

Adapted from Peng et al.	Adapted from Volpicelli et al.
<p>Thickening of the pleural line with pleural line irregularity. B-lines in a variety of patterns including focal, multifocal, and confluent.</p> <p>Consolidations in a variety of patterns including multifocal small, non-translobar, and translobar with occasional mobile air bronchograms.</p> <p>Appearance of A lines during recovery phase.</p> <p>Large pleural effusions are uncommon.</p>	<p>Intermediate probability of COVID-19</p> <p>Small, very irregular consolidations at the two bases without effusion or with very limited anechoic effusion.</p> <p>Focal unilateral interstitial syndrome (multiple separated B-lines) with or without irregular pleural line.</p> <p>Bilateral focal areas of interstitial syndrome with well-separated B-lines with or without small consolidations.</p> <p>High probability of COVID-19</p> <p>Bilateral, patchy distribution of multiple cluster areas with the light beam sign, alternating with areas with multiple separated and coalescent B-lines and well-demarcated separation from large “spared” areas. The pleural line can be regular, irregular or fragmented.</p> <p>Sliding is usually preserved in all but severe cases.</p> <p>Multiple small consolidations limited to the periphery of the lungs A light beam may be visualised below small peripheral consolidations and zones with irregular pleural line.</p>

Table 1: Summary of sonographic characteristics of LUS in COVID-19 infection

How Does LUS Compare to Plain Chest Radiography (CXR) and Computed Tomography (CT)?

Chest imaging is important for diagnostic and prognostic reasons. The ideal test would be quick, reliable, reproducible, deliverable at the bedside and have a high sensitivity and specificity. Currently, the main modalities used are CXR, CT and in some centres, LUS. Small studies have looked at the sensitivity and specificity of CT compared to RT-PCR, and CT currently has the highest sensitivity of any test for COVID-19 (Fang et al. 2020).

Almost all patients will receive a chest radiograph, but plain chest radiography has a poor sensitivity as compared with CT and LUS. Plain radiographs may miss up to 40% of confirmed COVID-19 cases. One reason why plain radiography has a reported low sensitivity is that virus particles are small and lodge in terminal alveoli close

to the pleural interface. These areas are well visualised on CT and LUS, but are more difficult to see on plain imaging (Huang et al. 2020; Tian et al. 2020).

Thoracic CT imaging has been proposed as a primary screening tool for COVID-19 detection, since it performs better than PCR. Lung abnormalities on CT may precede physical symptoms of COVID-19, thus allowing early detection, isolation and management of infected patients.

However CT is a finite resource and may not be available in some healthcare settings. Decontamination protocols are not well defined and are time consuming. The practicalities of moving critically ill patients to CT are difficult and thus a risk benefit approach has been taken by some clinicians, reserving this technology for patients with complications of COVID-19 infection or when other causes of illness such as pulmonary embolism are suspected.

LUS has been recommended by Italian

emergency physicians as an ideal form of imaging for evaluation of suspected COVID-19 infection. The authors discuss portable and inexpensive handheld US devices, ease of use by the treating clinician at the bedside and reduced movement of patients to the radiology department and reduced exposure of other healthcare workers (HCW).

Clinical Utility

The radiological appearance of patients with COVID-19, using traditional chest imaging techniques such as CXR and CT, have been described in the literature (Inciardi et al. 2020). Indeed, radiological changes are thought to precede the onset of the symptoms themselves. Compared to these modalities, lung ultrasound (LUS) has many advantages. It reduces the dependence on CT and improves risk stratification, while maintaining isolation protocols. This minimises contamination of staff



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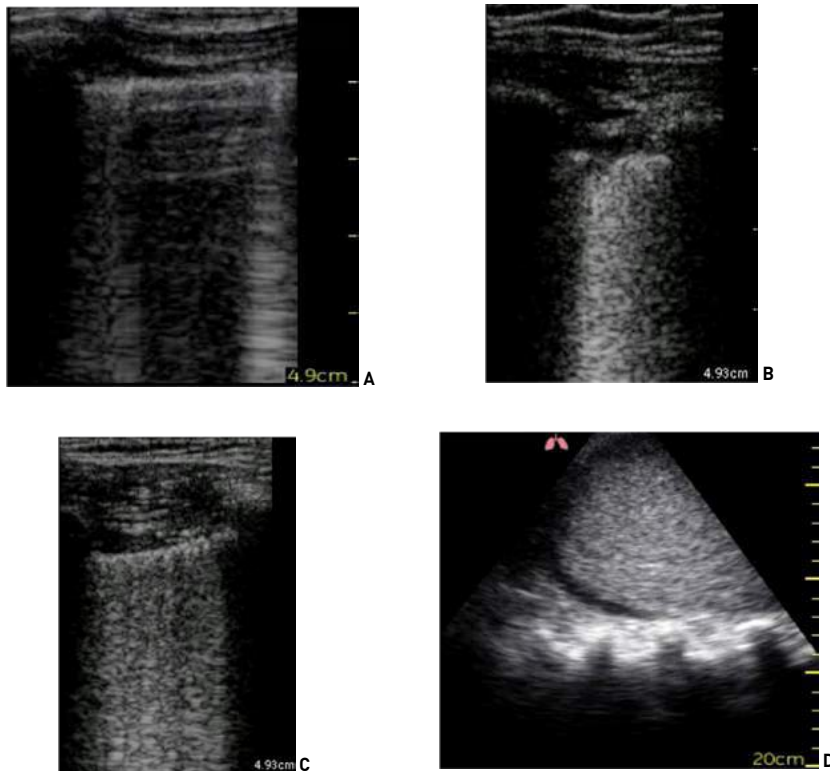


Figure 1: a) Linear view LUS, with skip B-line profiling and preserved A-line profiling in early COVID-19 pneumonitis; b) Confluent B-line profiling, sub-pleural consolidation and irregular thickened pleura in medium severity COVID-19 pneumonitis; c) Confluent B-line profiling and obliteration of all A-lines in severe COVID-19 pneumonitis; d) Basal consolidation, paraneumonic effusion and spine sign seen at the base of a COVID-19 patient with severe pneumonitis.

and equipment.

Broadly speaking, ultrasound has 3 main uses:

1. The initial diagnosis of COVID-19
2. Assessment of disease severity along with history and other clinical examination
3. The ongoing management of the disease

LUS in COVID-19

LUS is the primary imaging modality for COVID-19 as respiratory symptoms are the herald of the disease (shortness of breath and exertional dyspnoea). However, gastrointestinal and neurological symptoms have also been reported in the literature. Early experience with LUS amongst colleagues in China found the following characteristics (Peng et al. 2020a; Volpicelli et al. 2020). The LUS features of patients with COVID-19 are summarised in **Table 1**.

Overall, the characteristic changes in COVID-19 infection are similar to other viral pneumonitis (Yousef and De Luca 2018). Examples of the findings are shown in **Figure 1**.

The sonographic appearance depends upon the time course of the illness and the presence of other pre-existing or superimposed conditions. Clinical deterioration can be investigated using the other ultrasound modalities. These may include acute cardiomyopathy, acute pulmonary embolism, evidence of secondary or superadded infection, pleural effusions and pneumothorax.

Figure 2 shows the Focussed Ultrasound for Intensive Care pathway (FUSIC) pathway.

Two broad divisions or phenotypes have been proposed by Gattinoni et al. (2020); the “L”- and “H-” type.

H-Type

This phenotype is characterised by high

lung elastance, low lung compliance and a significant accumulation of lung water. Similar to more traditional forms of ARDS, these patients are more difficult to ventilate and the use of PEEP may be beneficial during significant refractory hypoxic periods.

L-Type

Characterised by low lung elastance and higher compliance, such patients are ‘easier’ to ventilate. Hence, high PEEP levels may be detrimental during hypoxic episodes, with patients potentially benefiting from early proning.

Whilst it is tempting to discuss the phenotypes as two separate entities, it is likely that they represent ends of a continuous spectrum.

Lung ultrasound to direct ventilatory strategies

POCUS may differentiate the two lung patterns mentioned above:

1. Bilateral, diffuse, anterior, multiple B-lines with pleural abnormalities (H-type).
2. Normal anterior lung (or anterior lobar consolidation) with postero lateral basal atelectasis consolidation (L-type).

As the lung goes from aerated to non aerated, lung ultrasound appearances progress from A lines → a few B-lines → lots of B-lines → coalesced B-lines → consolidation. Performing a PEEP or prone trial while monitoring lung appearances in real time could potentially give a guide to lung “recruitability,” similar to studies performed in the early 2000s (Volpicelli et al. 2020), however there is no COVID-19 specific data on this technique.

Lung ultrasound to monitor extravascular lung water

PICCO studies have demonstrated that these patients have an increased amount of extravascular lung water (EVLW; Personal communications, April 2020). B-line density has been shown to correspond with increased extravascular lung water



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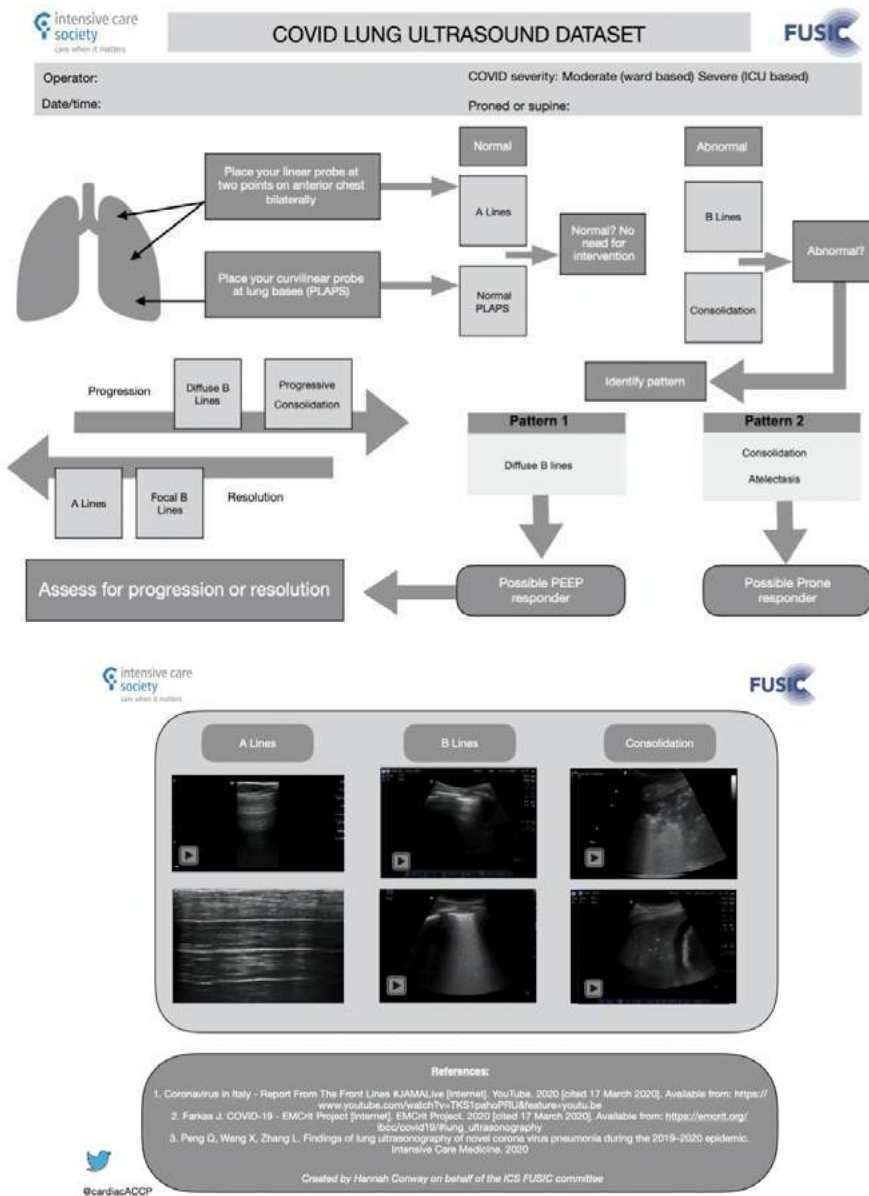


Figure 2: Focussed Ultrasound for Intensive Care pathway (FUSIC) pathway

in ARDS. LUS thus provides an attractive non-invasive monitor of such changes and can be used to assess the need for, and response to, diuretic therapy.

In patients with cardiovascular instability, fluid administration can be monitored by assessing the lungs for the appearance of increase in B-lines following a fluid bolus (Lichtenstein 2013). This is challenging in COVID-19 patients, as most will have B-lines already. Combining LUS with echocardiographic measures of stroke volume

and fluid responsiveness can potentially increase the diagnostic accuracy and safety threshold of fluid therapy, but data on this approach is sparse.

Cardiac Ultrasound in COVID-19

Although predominantly affecting the lungs, COVID-19 can affect the cardiovascular system through several mechanisms. There are indirect effects on myocardial function, secondary to heart-lung interactions; this can be observed when high PEEP adversely

affects the right ventricular afterload (Peng et al. 2020b).

There are also direct cardiotoxic viral effects; the virus has been isolated from myocardial tissue in case reports (Tavazzi et al. 2020). This has anecdotally manifested as an acute deterioration 7 to 10 days into the course of the illness. The sequence of events seems to be in keeping with a generalised hyper-inflammatory process, with corresponding rise in laboratory biomarkers such as CRP, ferritin, D-dimers etc. This inflammatory response can cause myocardial injury with focal or global myocardial inflammation, necrosis and ventricular dysfunction. A recent case series from Wuhan suggested a 19.7% incidence of myocardial injury in a cohort of hospitalised patients with COVID-19 (Bonow et al. 2020).

CCUS is perfectly suited to monitor these effects at the bedside. Heart-lung interactions can be monitored using LV and RV size and function, in time with the respiratory cycle, as previously described. Fluid status, ventilation, and PEEP can then be tailored to optimise cardiac function.

The downstream effects of severe LV or RV dysfunction on systemic organ perfusion can also be monitored using CCUS. Profound RV dysfunction can manifest as hepatic and renal dysfunction, visible on CCUS as abnormalities in hepatic, portal and renal blood flow (Beaubien-Souligny et al. 2020). Management of a congestive phenotype of organ failure would include fluid removal, inotropic support, pulmonary vasodilators, and venovenous ECMO.

Vascular Ultrasound in COVID-19 Vascular access

COVID-19 patients who are critically unwell will require central venous access either for drug administration, renal replacement therapy or ECMO. Ultrasound guidance has been proven to increase first pass success rate while reducing complications during vascular access.

Ultrasound guidance also facilitates

access in the prone position, where the usual anatomy becomes distorted (Chen et al. 2017). Post placement, line position can be confirmed using an ultrasound only technique, minimising the use of CXR (Saul et al. 2015).

Thromboembolic disease

Patients with severe COVID-19 are immobile and have a hyper-inflammatory state. These, in combination, lead to a hypercoagulable state. There is also the possibility of endothelial cell activation/damage due to binding of the virus to the ACE2 receptor. Hence, it seems obvious that they are at increased risk of developing deep venous thrombosis and subsequently pulmonary embolus. Optimal thromboprophylaxis in COVID-19 patients is unknown. The use of ultrasound by the bedside clinician to assess for DVT is quick, easy and sensitive; there may be a role for monitoring these patients for the development of VTE and changing anticoagulation strategy as felt appropriate (Hunt et al. 2020).

Airway Ultrasound in COVID-19

Patients with COVID-19 can present in severe hypoxic respiratory failure where intubation is performed as an emergency procedure. Previous data has shown that intubation outside the theatre environment confers a higher risk of morbidity and mortality with an increased incidence of difficult airway scenarios (Cook et al. 2011).

Upper airway ultrasound is a convenient, cost-effective and reproducible tool. The integration of upper airway ultrasound to complement pre-intubation airway screening may be the way forward, and a future standard of care.

The use of ultrasound has 3 main advantages:

1. The assessment of upper airway anatomy
 2. Confirmation of appropriate airway device placement
 3. Aiding in placement of tracheostomy
- It is beyond the scope of this article to

describe the sonoanatomy of the upper airway.

Assessment

Ultrasound may permit appropriate risk assessment and hence airway management strategy formulation. Various scoring systems have been described to formulate a more consistent and robust approach to this strategy.

On a related matter, in the 'cannot intubate, cannot ventilate' scenario, timely identification of the cricothyroid membrane to facilitate emergency front of neck access is lifesaving. This is even more advantageous if the identification is done under controlled circumstances preemptively (You-Ten et al. 2018).

Airway device placement

Ultrasound can be used to confirm appropriate placement of the endotracheal tube. This is especially important in resource limited environments, where the availability of capnography is not universal.

Tracheostomy

Further down the patient clinical time course, it is expected that a proportion of patients recovering from COVID-19 will require tracheostomies. Traditionally, the use of bronchoscopy to guide percutaneous tracheostomies have been advocated. However this is recognised as a high-risk, aerosol generating procedure which exposes the operator to significant risk. The use of ultrasound to replace bronchoscopy-guided PCT has been described and should be considered if appropriate expertise be available (Ravi and Vijay 2015).

Abdominal Ultrasound

Hepatic complications of critical illness include portal vein thrombosis, cholecystitis, biliary stasis, and hepatic congestion as a result of right heart failure. These can be readily detected by CCUS.

Data from the UK has shown that 20% of patients have required renal replacement

therapy (20- ICNARC data). Ultrasonography is useful for ruling out obstructive uropathy in these patients. More advanced applications involve using doppler imaging techniques for detecting alterations in renal arterial and venous flow; there is currently very limited COVID-19 specific data on this modality.

Haemophagocytic lymphohistiocytosis (HLH) is a recognised complication of COVID-19, and manifests as multiple cytopenias, a high ferritin, and hepatosplenomegaly. CCUS can be used to monitor and detect organomegaly if it were to occur (Tveiten et al. 2020).

Intra-abdominal free fluid, ileus, NG tube position, and free intraabdominal air can be detected with CCUS. It would seem prudent to utilise CCUS expertise, where available, as the first line imaging modality in these patients, reserving CT for where there is diagnostic ambiguity or inadequate imaging. This has been the practice of the Chinese Critical Ultrasound Group (Personal communications, March 2020)

Learning and Research During COVID-19

During the COVID-19 pandemic, there are two compelling (and competing) priorities: treating patients and learning new knowledge including skills and treatment.

Exploiting existing knowledge or beliefs is helpful in the short-term, but not in the long-term. Conversely, learning something new is risky in the short-term, but essential in the long-term. In this uncertain situation, we need to try and do both simultaneously.

Like any other skill, there is a learning curve associated with CCUS and the various accreditation programmes available require a period of mentorship as well as assessment (Smith et al. 2020). Many regulatory bodies are pausing formal training programmes in ultrasound during this period; however, abbreviated focused training pathways for very specific subsets of CCUS have become available, most noticeably with lung ultrasound.

The decisions on how to deploy CCUS should be taken on an institutional or indeed national level. An example is the UK's Intensive Care Society National COVID-19 Point-of-Care Ultrasound Evaluation exercise (FUSIC 2020).

Governance

CCUS is a diagnostic modality and as such should be subject to quality assurance, similar to any other diagnostic modality in the hospital (laboratory tests and other forms of radiology). A system should be in place to assess the quality of both individual sonographers and the interpretation of these images.

The authors suggest that any images used for clinical decision making are stored, ideally on a patient archiving system. A minimum dataset should be suggested and maintained. Individual sonographer case review should be regularly undertaken to ensure standards are kept- this could be in the form of a monthly audit or case presentation. Units should align themselves with national policy for each diagnostic modality used wherever possible, such as recent guidelines on the use of POCUS written by EFSUMB, the Intensive Care Society, and BMUS.

The individuals who will perform governance will likely vary from institution to institution - the authors would suggest a mix of radiologists, cardiologists, and acute physicians would cover all bases of CCUS.

Cleaning & Disinfection Protocols

Decontamination strategies are vital to prevent patient-to-patient COVID-19 transmission as well as patient to healthcare worker COVID-19 transmission.

Several international bodies have described US machine specific COVID-19 cleaning and disinfection protocols (BMUS 2020; CPoCUS 2020).

The following (Table 2) are best practice summary points drawn from international standards and should be considered when using US with suspected COVID-19 patients

(ACEP.org).

Place a dedicated US machine in the COVID-19 examination area of your Intensive Care Unit
Use disposable single-use gel packets rather than gel bottle
Wear standard personal protective equipment when performing LUS and wear gloves when moving the machine from cubicle to cubicle
Strip away all leads, gel bottles extra buckets, straps from your machine
Clean cables, screen, legs, wheels
Cover the transducer with plastic sheath
Use a touchscreen device to minimise keyboard, knob handle handling
Wait for up to 3 minutes 'dry time' after using disinfectant wipes before you use the machine again
Use your machine in battery mode - precharge at all times, remove all cables
Use a handheld device eg. Lumify or Butterfly systems with the advantage that images are uploaded to the cloud for remote reviewing

Table 2: Best practice summary points

This material has been 'crowdsourced' or extrapolated from shared knowledge of global expert user groups. There are many practical and innovative approaches to US machine decontamination available on social media, collated under the hashtag #POCUSforCOVID (ultrasoundtraining.com.au/news/covid-19-pocus-resources).

Conclusion

COVID-19 is a novel disease and hence our understanding of the entire disease pathology, management and imaging features are still evolving. There is much that remains unknown and hence the evidence base for the use of ultrasound in the pandemic is weak. When considering the use of any intervention or investigations, the practicalities and logistics need to be taken into consideration.

Conflict of Interest

Adrian Wong has received speaking honorarium from the industry. Olusegun Olusanya has received honoraria to teach ultrasound. Jonathan Wilkinson has received honoraria from GE Healthcare. Other authors declare no conflict of interest. ■

Key Points

- LUS has been extensively discussed in the literature.
 - It is a well established tool in the diagnosis of acute respiratory failure.
 - It demonstrates clear patterns in COVID-19 infection, many of which are very similar to other patterns of viral pneumonitis.
 - CXR is a poor screening test for COVID-19 compared with CT. CT may be better used for screening for the complications arising from COVID-19 infection.
- Cardiac, abdominal and vascular ultrasound complement LUS and allows for a holistic, whole body approach in the assessment of patients with COVID-19.
- With the conveniences ultrasound affords, it is a highly useful decision support tool in COVID-19.

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Noninvasive Hemodynamic Check to Guide Educated Decisions in the Management of COVID-19 Patients

The rapid global distribution of COVID-19 is challenging healthcare systems worldwide. In many countries hospitals and ICU departments are overloaded or fear a potential collapse - the optimal allocation of healthcare resources is required. Healthcare professionals are forced to treat severely ill patients with limited access to ventilation equipment, qualified intensive care personnel or protective patient monitoring devices. The effort to prevent COVID-19 patients from deterioration and ICU admission is huge.

The World Health Organization (WHO)¹ identified challenges and summarized recommended measures in the different disease stages.

During the initial screening phase, when patients present to emergency services, the early recognition of patients at risk for severe disease or mortality due to cardiovascular comorbidities is very important. In older patients even mild symptoms can exhibit a high risk of deterioration, therefore these patients should be sent to designated units for close and continuous cardiovascular monitoring.¹

In order to avoid deterioration and progression of symptoms in severely ill patients, a regular monitoring of vital signs utilizing early warning scores is considered essential. Conservative fluid management may help at an early stage as fluid overload may lead to insufficient oxygenation and respiratory complications that would require mechanical ventilation and admission to an ICU. For the critically ill patients in the ICU, among other measures, the monitoring of dynamic indices of fluid responsiveness remains an indispensable tool to guide life-saving

volume administration in order to fight fluid overload, Severe Acute Respiratory Infection (SARI) or septic shock, as well as acute kidney/cardiac injury or organ failure due to hypovolemia².

Further, the WHO clearly states the need for “the application of timely, effective and safe supportive therapies” as the cornerstone of therapy for COVID-19 patients¹ with severe manifestations in order to support the course of recovery from the virus.

To date, blood pressure, cardiac output and other hemodynamic parameters can easily and noninvasively be measured using the patient’s fingers to support educated decision making in the management of COVID-19 patients. The cardiovascular status can be monitored more completely than with blood pressure monitoring alone. This enables a better control of fluid management in situations in which the methods of classic advanced hemodynamic monitoring either cannot be used due to limited resources of

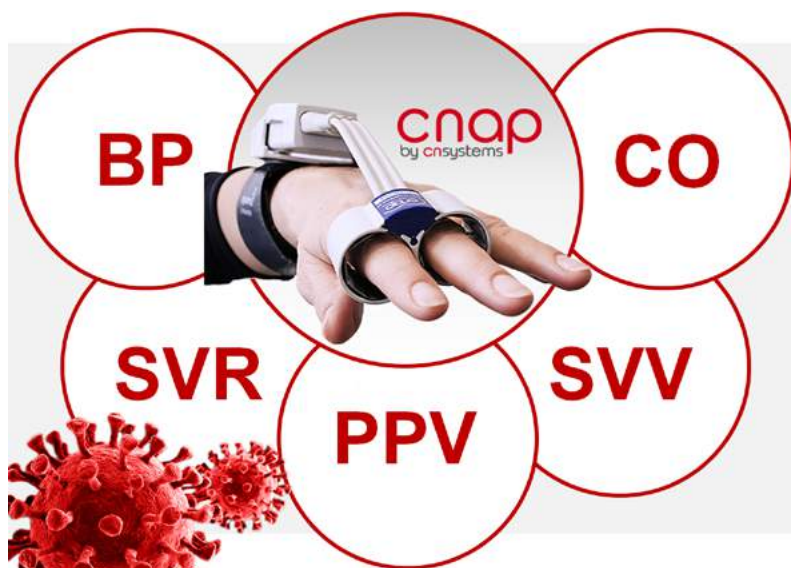
time, equipment or qualified personnel or are simply not indicated. A quick and simple non-invasive monitor is comfortable for patients, saves valuable time, and allows for better allocation of personnel.

In addition to oxygenation the immediate and accurate feedback on cardiovascular status can help to maintain adequate blood pressure levels (MAP > 65 mmHg). Identifying patients with impaired cardiac output to direct fluid management from the emergency departments to intensive care units is important especially when invasive monitoring is not applicable or time and resources are limited.

Noninvasive technologies have been established as reliable and accurate tools for Fluid Optimization in surgical patients.^{3,4} To date, they also demonstrate a high value in the time-efficient cardiovascular management of COVID-19 patients. ■

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Introduction

The global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is predicted to result in 5-10% of infected patients requiring admission to intensive care (Grasselli et al. 2020a; Poston et al. 2020). It is likely that patients will be at significant nutritional risk, as a result of catabolism and significant nutritional deficits, which may result in poor functional recovery if not well managed.

This review provides perspective on the nutritional implications and management of coronavirus disease 2019 (COVID-19), the resulting illness from SARS-CoV-2, by drawing on available clinical data for patients with COVID-19, as well as the literature from Acute Respiratory Distress Syndrome

Nutrition for Critically Ill Patients With COVID-19

This article discusses the nutritional implications for critically ill patients admitted to intensive care for the management of COVID-19, and considers the inflammatory metabolic processes, nutrition-impacting symptoms, medical therapy, and the impact of a pandemic on staff resourcing and remote practice.

(ARDS). It considers the implications of a global pandemic on caseload, resourcing, supply chain shortages, and the logistics of managing highly infectious patients.

Clinical Characteristics, Medical Therapy and Nutritional Implications

Risk factors for ICU admission

Patients most likely to require ICU support tend to be older (~60 years) (Guan et al. 2020; Livingston and Bucher 2020), ~25-40% have at least one comorbidity such as hypertension, diabetes, heart disease, or chronic obstructive pulmonary disease (Guan et al. 2020; Huang et al. 2020; Zhou et al. 2020), and almost 75% are overweight or obese (ICNARC 2020). The most common reason for admission to ICU is respiratory failure, with around two-thirds of patients meeting criteria for a diagnosis of ARDS (Wang et al. 2020; Murthy et al. 2020). Additionally, data suggests that patients are admitted to the ICU approximately 10 days after the onset of initial symptoms (Huang et al. 2020) and; therefore, patients may have sustained nutritional deficits prior to admission.

Metabolic processes

COVID-19, as a respiratory condition, has

a number of metabolic sequelae that may influence nutritional care. Around 95-98% of patients present with fevers (Guan et al. 2020; Huang et al. 2020; Zhou et al. 2020), with case series data suggesting temperatures of between 37.5-39.0 °C are common (Guan et al. 2020). This may have implications on metabolic rate, with an increase in metabolic demand of ~10-13% per every 1°C increase in body temperature due to heat production (Del Bene 1990). An aggressive pro-inflammatory immune response is also expected, leading to an increase in glucocorticoid and catecholamine production, increased insulin sensitivity, poor glycaemic control and protein catabolism (Prompetchara et al. 2020).

Medical therapy

Critically ill patients with COVID-19 present with declining respiratory function and in severe cases can have shock, respiratory and multi-organ failure. The highly transmittable nature of COVID-19 means that intermediate therapies to support lung function, such as non-invasive ventilation, are aerosol-producing and hence are not recommended (ANZICS 2020). There is general international consensus that patients should be intubated early (where

Clinical features and medical management	Nutritional implication	Nutrition management strategies
Clinical Features		
Metabolism alterations	Insulin resistance Protein catabolism	Blood glucose control Higher protein EN
Highly transmittable virus	Bedside practices limited Staff sickness Impact on food service and menu selection	Remote consults Team planning Upskill non-ICU dietitians
Medical Management		
High flow nasal oxygen therapy	Dry mouth Shortness of breath Fatigue Fasting for potential intubation	High energy/high protein diet Oral nutrition supplements Early escalation to EN
Deep sedation	Delayed gastric emptying Non-nutrition calorie contribution from propofol	1.25-1.5kcal/ml EN Prokinetics for GI intolerance Post-pyloric feeding or PN Account for propofol calories in nutrition prescription if >110% is being provided by nutrition and non-nutrition calories
Prone	Delayed gastric emptying Increased regurgitation and vomiting Feeding interruptions	Lower GRV threshold 1.25-1.5 kcal/ml EN Post-pyloric feeding or PN
Respiratory failure	Restricted fluid input	Energy-dense formula Potential compromised protein intake

Table 1: Clinical features and medical management, nutritional implications and suggested nutrition management strategies for patients with COVID-19 in intensive care. EN: Enteral Nutrition; ICU: Intensive Care Unit; GI: Gastrointestinal; GRV: Gastric Residual Volumes; PN: Parenteral Nutrition

required) (Poston et al. 2020; ANZICS 2020). In patients admitted to ICU, rates of mechanical ventilation have varied internationally from 47% in China (Wang et al. 2020), 69% in the UK (ICNARC 2020), 71% in the US (Arentz et al. 2020), and 88% in Italy (Grasselli et al. 2020b), with a median duration of 7 (IQR 4, 11) days (ICNARC 2020). Additionally, in patients who develop ARDS or those with ongoing hypoxaemia, despite optimising ventilation strategies, high levels of sedation are common and the use of neuromuscular blocking agents (NMBAs) is recommended to facilitate protective lung ventilation (Poston et al. 2020). The use of deep sedation and NMBA may have significant effects on gastrointestinal (GI) function (Deane et al. 2019) and muscle wasting (Puthuchery et al. 2012).

In addition, patients are responding well to management strategies such as periodic prone ventilation (12-16 hours) (Murthy et al. 2020; Poston et al. 2020; ANZICS 2020) with around 27-50% of patients receiving this therapy (Grasselli et al. 2020b) in an attempt to promote equitable air distribution through the lungs and improve oxygenation (Scholten et al. 2017). One of the nutritional consequences of proning is the increased prevalence of delayed gastric emptying and risk of vomiting (Reignier et al. 2004). Therefore, nutritional strategies are required to appropriately manage delayed gastric emptying due to risks to both the patient and staff (airborne virus).

COVID-19, similar to ARDS, is associated with acute renal failure (possibly due to dehydration associated with ongoing pyrexia, shock or multi-organ failure) with

~20% receiving renal support (ICNARC 2020). Conservative fluid management practices are recommended as a means of reducing extravascular lung water (Murthy et al. 2020; Zhou et al. 2020; Poston et al. 2020; ANZICS 2020). As part of this strategy, enteral formula volume restriction may be required but sometimes compromises the quality of nutrition provision and may exacerbate dehydration and hypernatraemia.

Nutrition-impact symptoms and oral intake

COVID-19 presents a number of unique physiological symptoms likely to impact oral intake including a loss of taste and smell, and GI symptoms in around 10% of cases such as diarrhoea, nausea, and vomiting (Guan et al. 2020; Wang et al. 2020). Further, 62% of general ICU survi-

Recommendation	British Dietetics Association	Australia/New Zealand	European Society of Parenteral and Enteral Nutrition	American Society of Parenteral and Enteral Nutrition
Nutrition screening				
Nutrition screening	No recommendation	-High nutrition risk criteria stated	-Use MUST or NRS 2002	No recommendation
Nutrition prescription				
Calorie prescription	-As per current local practice	-No IC -Algorithm first 5 d (approximately 20-25kcal/kg) -25-30 kcal/kg/d after 5 d	-IC if safely available -Hypocaloric (<70% of EE) with increments to 80-100% after day 3	-No IC -Hypocaloric feeding progressive to 15-20 kcal/kg/day (~70-80% caloric requirements)
Protein prescription	-As per current local practice	-≥1.2g/kg/d	-1.3 g/kg/d delivered progressively to target by day 3-5 -Actual weight or adjusted body weight in obesity	-1.2-2.0 g/kg/d
Formula	-Consider protein supplements if unable to meet targets -Volume restricted/low electrolyte EN if fluid restricted -Consider 1.3/1.5 kcal/ml feeds if prone	-1.25-1.5 kcal/ml -Avoid 2 kcal/ml EN	No recommendation	-Standard high protein (> 20% protein) polymeric isosmotic enteral formula -Fibre can be considered once stable
Body weight used in equations	-Use actual body weight or ideal weight if unavailable	-Use actual weight or adjusted weight if overweight/obese	No recommendation	-Actual body weight
Nutrition delivery				
Timing	No recommendation	-Commence within 24h -Goal rate within 5 d	-‘Early phase’ feeding- not further specified -Goal rate within 3-5 d	-Commence within 24-48 h of ICU admission -Goal rate within first week
Route of feeding	-Gastric -Post-pyloric if poor tolerance -PN if post-pyloric not available	-Gastric -Post-pyloric or PN if not tolerating	-Gastric -Post-pyloric if not tolerating or at high aspiration risk -PN if not tolerating for 1 week	-Gastric -PN if gastric contraindicated

Gastrointestinal management	-GRV monitoring as per usual practice, or GRV cut-off <300ml, monitor 4 hourly if prone -Early/prophylactic prokinetics in patients with high GRVs	-GRV cut-off <300ml, monitor 8 hourly. Cease measures if GRVs <300ml for >48h in patients who are not prone	No recommendation	-No GRV monitoring -Prokinetics -Post-pyloric feeding if all other measures not successful
Proning	-Gastric feeding -Early/prophylactic prokinetics in patients with high GRVs -Consider post-pyloric feeding if poor tolerance 48-72hrs	-Gastric feeding -GRV cut-off -Consider post-pyloric feeding if poor tolerance -Pause EN and aspirate stomach prior to re-positioning	-Gastric feeding	-Gastric feeding -Elevated head of the bed to at least 10 to 25 degrees
<i>Additional considerations</i>				
Nutrition assessment and monitoring	-Close monitoring recommended	-Within 24-72h in high risk patients -3-5 d in lower risk patients	No recommendation	No recommendation
Population specific recommendations	-Non-invasive ventilation	-Obesity -Non-ventilated patients -Post-ICU	-Non-intubated patients -Post-extubation -Dysphagia -Post-ICU	-ECMO
Dietetic practices/resourceing	-Remote reviews -Upskill non-ICU dietitians -Stock levels of EN formula, pumps & ancillaries -Review communication pathways	-Remote reviews -Consider team structure -Train on PPE -Utilise Allied Health Assistants -Review food service systems -Stock levels of EN formula, pumps & ancillaries	No recommendation	-Bundling clinical care -Remote reviews -Stock levels of EN formula, pumps & ancillaries

Table 2: Comparison between different guidelines and recommendations for nutritional management of patients with COVID-19

ECMO: Extracorporeal Membrane Oxygenation; EE: Energy Expenditure; EN: Enteral Nutrition; GRV: Gastric Residual Volume; IC: Indirect Calorimetry; ICU: Intensive Care Unit; PN: Parenteral Nutrition; PPE: Personal Protective Equipment

vors experience dysphagia (Zuercher et al. 2019). These symptoms have particular implications for patients that are attempting to eat orally. These are coupled with nutrition-impacting symptoms typical of a respiratory illness, including extreme fatigue, dyspnoea, dry mouth and loss of appetite (Wang et al. 2020; Huang et al. 2020). Additional operational barriers to oral intake may impact menu selection, limitations with meal delivery, and feeding assistance, including fewer nursing staff,

restrictions on family visitations, the need to conduct dietetic consultations remotely and less frequent reviews due to staffing levels, and restrictions on food service management systems.

Post-ICU nutrition

While mortality rates have been higher than in non-COVID-19 respiratory illness, approximately 50% of COVID-19 ICU patients are expected to survive (Wu and McGoogan 2020). Patients admitted with

ARDS lose an average of 18% bodyweight by hospital discharge, with reduced functional outcomes and poor quality of life that persist long after ICU discharge (Herridge et al. 2003). A potential contributing factor is a reduction in intake during the post-ICU period; previous data suggests nutritional deficits after ICU discharge are greater than in ICU, particularly via the oral route (Chapple et al. 2016; Ridley et al. 2019; Merriweather et al. 2014). In addition, in periods of high ICU admission

numbers and competition for ICU beds, early discharge to the ward is inevitable, and the potential reduction in physical and nutritional interventions due to resource shortages, may worsen long-term recovery of patients with COVID-19.

Resourcing

A further complicating aspect of a global pandemic is the large number of patients that will be affected, and hence admitted to intensive care. In addition, the potential spread of COVID-19 to healthcare workers leads to a reduction in trained clinicians. Given critical care nutrition is a specialist skillset requiring an in-depth understanding of nutrition support within the context of medical care, up-skilling of non-ICU trained dietitians should occur early, with prioritisation of patient complexity to clinician expertise. For nutrition support the influx of ICU patients combined with limited healthcare resources means the clinician roles, scope of practice, and ways of working will need to be carefully reviewed. Consideration should be given to the use of an algorithm-based feeding protocol early in the ICU admission, prioritised care to high nutrition risk patients, and utilisation of Allied Health Assistants where possible.

Clinical Nutrition Guidelines for COVID-19

A number of nutrition recommendations and guidelines for use in patients with COVID-19 have recently been made available. These recommendations are summarised below and in **Table 2**, highlighting important differences and similarities between the recommendations.

Nutrition prescription

Calorie targets

Indirect calorimetry (IC) is recommended as the gold standard to determine metabolic needs in critical illness (McClave et al. 2016; Singer et al. 2019). However, conducting IC requires disconnection of the ventilator circuit thereby potentially exposing staff

to the airborne virus if attempted in a patient with COVID-19. For that reason, the majority of COVID-19 nutrition guidelines recommend against the use of IC (Chapple et al. 2020; Martindale et al. 2020; Bear and Terblanche 2020) or only where it can be conducted safely (Barazzoni et al. 2020).

In the absence of IC, caloric targets are similar to those recommended for critically ill patients, aiming for 20-25 kcal/

▶▶ patients who are admitted to the ICU with COVID-19 are at high nutritional risk, due to their presenting condition, the intensive care management strategies required to treat the disease and the likely course of the treatment ▶▶

kg/day (Barazzoni et al. 2020; Chapple et al. 2020; Martindale et al. 2020). The Australian/New Zealand guidelines also suggest up to 30 kcal/kg/day for those that are severely unwell or those with an anticipated length of MV >7 days (Barazzoni et al. 2020), and the American guidelines suggest initially providing less for those at risk of re-feeding (Martindale et al. 2020).

Protein targets

Protein recommendations are similar between the guidelines, aiming for at least 1.2 g/kg bodyweight/day should be provided as per international recommendations for the general ICU population (Singer et al. 2019; McClave et al. 2016), keeping in mind that less than this is often provided in routine care.

Nutrition delivery

Route

For critically ill adults, nasogastric tube (NGT) feeding is considered best practice which is consistent across all COVID-19 recommendations. Consideration to safety concerns of placement of NGTs in patients with COVID-19 and expose of staff to virus-containing gastric secretions is documented in two of the guidelines (Chapple et al. 2020; Martindale et al. 2020). In these, parenteral nutrition (PN) is recommended if a feeding tube cannot be safely inserted. For patients that are unable to meet calorie and protein targets over 5-7 days, alternative feeding methods, such as post-pyloric feeding or PN are recommended in all guidelines (Barazzoni et al. 2020; Bear and Terblanche 2020; Chapple et al. 2020; Martindale et al. 2020).

Delivery

In keeping with a slow introduction of nutrition in the acute early phase of illness, hypocaloric nutrition (~70% of requirements) is recommended for the first 3-7 days, with commencement within 24-48 hours. This is supported by international recommendations and large randomised controlled trials that suggest early hypocaloric enteral nutrition has no associated harms when compared to full nutrition provision in the first 5-7 days (TARGET Investigators et al. 2018; Singer et al. 2019; National Heart, Lung and Blood Institute et al. 2012).

Enteral formula

Three of the four nutrition guidelines provide recommendations on the type of EN formula to be prescribed, recommending energy-density (1.25-1.5 kcal/ml) for volume control (Bear and Terblanche 2020; Chapple et al. 2020) or a standard high protein polymeric formula (Martindale et al. 2020). The use of a concentrated enteral formula (i.e. 2 kcal/ml) is not recommended due to the increased osmolality and higher fat content likely exacerbating

delayed gastric emptying (Kar et al. 2016; Chapple et al. 2020; Bear and Terblanche 2020).

GI tolerance

Current critical care nutrition guidelines provide different recommendations regarding monitoring of gastric residual volumes (GRVs) in critically ill patients (Singer et al. 2019; McClave et al. 2016), which may reflect differences in recommendations in COVID-19 nutrition guidelines. The American guidelines recommend not monitoring GRVs (Martindale et al. 2020), keeping in line with their recommendations for general ICU patients (McClave et al. 2016), and the European guidelines do not contain a specific recommendation on GRVs (Barazzoni et al. 2020). Viral content of gastric contents is not known and therefore GRV conduct may pose a risk if appropriate precautions are not used. Both the British and Australian/New Zealand guidelines; therefore, recommend a lower GRV threshold of <300ml to reduce the risk of vomiting (Bear and Terblanche 2020; Chapple et al. 2020), with less frequent monitoring recommended in the Australian/New Zealand guidelines, using appropriate PPE for airborne precautions (Chapple et al. 2020). Post-pyloric tube placement should also consider these risk/benefits.

Prone

Across all four COVID-19 nutrition guide-

lines, gastric feeding is recommended as the starting route for prone patients. If GI intolerance is observed, then early prokinetics or post-pyloric feeding is recommended, weighing up the risks/benefits (Chapple et al. 2020; Martindale et al. 2020; Bear and Terblanche 2020).

Oral intake

There is a growing appreciation of the nutrition risk in critically ill patients who are not receiving MV and eating orally, with 3 of the 4 COVID-19 nutrition guidelines including recommendations following extubation or for non-intubated patients (Barazzoni et al. 2020; Bear and Terblanche 2020; Chapple et al. 2020). For those able to eat, the recommendations suggest early intervention or close monitoring providing oral nutrition supplement prescription as soon as oral intake is commenced are recommended, with a lower threshold for escalation to EN (Bear and Terblanche 2020; Chapple et al. 2020) or supplemental PN (Barazzoni et al. 2020). For those patients who have a nasogastric in place, it is recommended that this is maintained where possible as it is recognised that oral intake is likely to be poor following extubation (Chapple et al. 2020).

Conclusion

Patients who are admitted to the ICU with COVID-19 are at high nutritional risk, due to their presenting condition, the intensive

care management strategies required to treat the disease and the likely course of the treatment. Alteration in metabolism and gastrointestinal function, coupled with nutritional deficits during critical illness and following, are all likely to contribute to a decline in nutrition status and poorer functional ability.

Optimal nutrition therapy may help to minimise deficits and manage complications such as poor glycaemic control and delayed gastric emptying, with the aim of optimising recovery. The four nutrition guidelines for the management of patients with COVID-19 recommend providing early enteral nutrition support via the gastric route, use of algorithms or hypocaloric nutrition in the first 5-7 days, protein delivery of at least 1.2 g/kg/day, and consideration given to pandemic nutrition resourcing and planning. ■

Key Points

- Alterations in metabolism (including increased energy demands), catabolism, and insulin resistance, as well as alterations in normal gastrointestinal function are all features of COVID-19.
- The medical management of critically ill patients with COVID-19 may have nutrition implications (including deep sedation, early mechanical ventilation, conservative fluid management and the prone position).
- Contingency planning to prepare staff resources, services and stock is critical.
- Four nutrition guidelines for the management of patients with COVID-19 exist, with all recommending early enteral nutrition via the gastric route.

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Precise Automated Resuscitation With RESPIRA

An innovative solution to ventilator shortages has been found in Spain – a relatively simple and cost-efficient alternative named RESPIRA.

One of the major problems for hospitals fighting the COVID-19 pandemic has been the lack of emergency ventilation devices. GPAINNOVA, a multinational company from Spain, has a simple and efficient solution to this – RESPIRA.

Novel Approach

RESPIRA is an ICU ventilator based on AMBU automation for assisted ventilation. It has been designed specifically for the needs of intensive care doctors involved in the COVID-19 treatment, and its performance is comparable to that of high-class ventilators from top brands.

RESPIRA automates manual resuscitation devices (BMV or AMBU) with sensors for remote real-time monitoring of parameters, such as frequency, tidal volume, flow, Ratio I:E and pressure of air supplied to the patient (maximum/PPI, minimum/PEEP and plateau). These parameters can also be fine-tuned thanks to an automatic system with PLC and an actuator – the two main components of RESPIRA that enable the precise piston movement and air insufflation. It also incorporates an FIO2 sensor with external display to monitor oxygen supply while a smart module allows for parameter adjustment based on pressure and tidal volume.

Such adjustability is achieved with advanced sophisticated software PLC

developed in cooperation with top engineers of Siemens Digital Industries. This world-class partnership is what distinguishes RESPIRA from other projects, open-source and non-homologated for medical device data transmission. For the high-quality components, which ensure safety and reliability, the RESPIRA project has the technical support of SMC, TEG and MAM.

Major hospitals in Spain including Hospital Clínic of Barcelona, Sant Joan de Déu and the Institute for Health Science Research Germans Trias i Pujol have participated in developing RESPIRA and running validation tests.

Upholding Standards

In Spain RESPIRA has passed all technical examinations for both the machinery and documentation, including those from Agency of Medicines and Health Products for Spain (AEMPS). This means that the device standards are similar to those of professional ventilators.

The first phase of the clinical trial is now completed. At this point RESPIRA is approved for use in all hospitals in Catalonia, and 45 of those already have it onsite. The device is currently in the second phase of the clinical trials, which means it has been approved by AEMPS to be used in several patients affected by COVID-19.

For other hospitals in Spain and other

countries, the device can be used during the COVID-19 emergency with an authorisation by the health authorities. An exemption from CE-marking requirements for medical devices in limited circumstances was approved by the European Parliament on 17 April, 2020, to cover shortages during the pandemic, with only local authorities' permission needed. GPAINNOVA has also applied for CE and FDA certification and is trying to fast-track the EU certification of RESPIRA as emergency medical equipment.

Work in Low-Resource Settings

GPAINNOVA is already in contact with several humanitarian organisations and plans to donate RESPIRA units to fight the COVID-19 pandemic in Africa. The device will be practical there, as it is very compact, light and portable. It can run on battery and has its own Wi-Fi, which allows to manage up to 16 units through one control station – a big advantage, considering the limited number of physicians in African countries. All this makes RESPIRA an attractive alternative to more complex ventilators, which hospitals there may not be equipped to install.

Manufacturing, Delivery and Support

RESPIRA is a locally manufactured product, with all the facilities located in Spain,



and can be quickly delivered globally. So far, GPAINNOVA has received orders for over 21,000 units. It is upscaling its production to 300 units per day and has the capacity to increase further if needed.

GPAINNOVA has branches in the U.S, China and Hong Kong, and distributing partners in every other country of the world. This ensures not only fast delivery but also efficient technical support and maintenance. There is a 24/7 hotline for any kind of technical enquiries from hosting hospitals.

For health professionals, GPAINNOVA has created comprehensive training videos like this [one](#), which complement a very detailed manual. In addition, another 24/7 hotline is operated by Hospital

Clínica de Barcelona to provide assistance to clinicians who work with RESPIRA across the world.

The device is relatively simple, assembled mostly from standard parts. It runs on dynamic and complex software and even though the technology is quite superior, RESPIRA's advanced features are still being offered at a very competitive price, even more so with large orders. It is portable and can be operated onsite or remotely, with an accessory incorporating Wi-Fi. This makes RESPIRA a cost-efficient alternative to standard ICU ventilators. Post-pandemic, in ambulances or emergency care the device can be used instead of manual resuscitation bags.

About GPAINNOVA

GPAINNOVA is a multinational company based in Barcelona, Spain. It specialises in surface metal finishing machinery and runs a water drones innovative project. With a turnover of €5.9 million in 2019, the company has received an EU Horizon 2020 grant under the SME Instrument Programme (phase 2 – innovation project). It has also been ranked 76th in the '1,000 fastest growing European companies in 2020' list compiled by the [Financial Times](#). ■



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Introduction

The COVID-19 pandemic caused by the novel severe acute respiratory syndrome Coronavirus-2 (SARS-Cov-2) has wrought havoc on hospitals throughout the world. As of 25th April 2020, the burden of disease in South Africa remains relatively low with just over 4220 confirmed cases and 79 attributable deaths (sacoronavirus.co.za/). Nevertheless, cognisant of the extent of disease which has manifested in many countries around the world, the Department of Critical Care together with various other stakeholders at the Chris Hani Baragwanath Hospital (CHBAH) have set about preparing for the expectant “surge” of serious COVID-19 cases, many of whom will predictably require critical care.

CHBAH is a 3200-bed academic hospital located in Soweto, Johannesburg ([# The Calm Before the Storm](http://chrishani-</p>
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Preparing intensive care capacity for the COVID-19 pandemic at a tertiary hospital in South Africa.

baragwanathhospital.co.za). CHBAH is the fourth largest hospital in the world, serving an immediate population of at least 1.5 million people in surrounding Soweto while simultaneously serving as the tertiary referral centre for much of the Gauteng (11.4 million) and North West (3.7 million) provinces (statssa.gov.za).

The Main Intensive Care Unit (MICU) at CHBAH is a combined Adult and Paediatric unit comprising 9 paediatric beds, 9 adult medical and surgical beds, 9 trauma and 6 adult surgical post-op high care beds. Additionally, neurosurgical and burns patients are managed in dedicated ICUs. Adult ICU beds represent less than one percent of total beds while paediatric ICU beds (excluding neonatal ICU) are closer to two percent. These numbers are considerably lower than the number of acute care beds designated for intensive care in European high-income countries (Rhodes et al. 2012).

Despite the limitation on beds, the ICU offers mechanical ventilation and continuous renal replacement therapies which necessitates a one nurse per patient ratio. The shortage of ICU trained nurses in South Africa has placed further restrictions on the availability of critical care services at hospitals like CHBAH. Given these factors, it is unsurprising that the demand for critical care beds, both adult and paediatric, far exceeds the resources available under usual circumstances. The constant pressure for ICU beds represents a mismatch which has in time led to the development of a set of triage principles designed to optimise the utility of these scarce resources. As such, patients requiring intensive care are denied

access on a daily basis by the attending intensivists with full appreciation of the dire consequences of these decisions. The patients negatively affected include both in-patients at CHBAH as well as referrals received from outside hospitals.

It is against this background that the discussion regarding the need for additional critical care capacity for the COVID-19 pandemic needs to be framed.

COVID-19 ICU Preparation

The team tasked with leading the preparation at CHBAH has been drawn from the departments of Internal Medicine (particularly Infectious Diseases), Critical Care, Anaesthesia, Infection Control, Microbiology and Paediatrics with oversight from the senior management of the hospital. Additional support to initiate testing for COVID-19 was sought from the Infectious Diseases Research Unit located on the CHBAH campus. Given the transmission risk posed by COVID-19 patients and the current R0 in excess of two, the first challenge was identifying the optimal physical flow of these patients into the hospital. Consensus quickly determined the need for rapid separation of respiratory and non-respiratory patients. A triage tent has been set up modelled on the immigration area of an airport to rapidly screen the risk of COVID-19 among new patients entering the hospital. For those requiring admission, dedicated wards have been established within the pre-existing Medical and Paediatric departments to nurse those patients with COVID-19 and thus allow isolated co-habitation.

For those requiring critical care, the first

and most important consideration was the impact that COVID-19 patients would have on existing capacity. Given the pre-existing burden on the ICU, it was determined that additional, physically separate, capacity would have to be created to address this problem. This would allow both for the continuation of routine critical care to non-COVID-19 patients and simultaneously reduce the risk of nosocomial transmission of the virus to this vulnerable group given what was known about mortality risk factors associated with COVID-19 at the time.

To this end, the ward which had been designated for possible Viral Haemorrhagic Fever patients has been re-tasked as the temporary COVID-19 ICU. This area is quite distant from the MICU and has the physical ability to be cordoned off from the general hospital, thus limiting the mixing of general human traffic around the hospital and the staff specifically assigned to the management of critically ill COVID-19 patients. The critically ill present the highest risk of nosocomial transmission given the increased frequency of aerosol inducing procedures routine to the management of these patients. Another significant benefit stems from the presence of a negative pressure ventilation system within the unit. Nineteen separate cubicles have been established within the ward, 15 for adult patients and four dedicated to paediatric patients, excluding neonates. The neonatal patients will be managed within the neonatal department.

A significant drawback in this repurposed ward, however, is the space constraints imposed by an environment not specifically intended for intensive care. The cubicles are approximately five square metres, which allows for a patient bed, basic monitoring, a group of infusion pumps, a mechanical ventilator and very little else. This physical constraint has created an intensive care unit limited primarily to the provision of cardio-respiratory support with limited access to the full gambit of intensive care

interventions including continuous renal replacement therapy. CHBAH currently does not provide extracorporeal support so this is a moot point.

The limitation of space impacts other crucial activities and procedures. In order to transfer intubated patients to this unit, they would have to be carried in on a “scoop stretcher.” Moving of the patient beds requires manipulation at various angles which poses a challenge when trying to optimise the position of medical staff attempting to undertake tasks such as intubation, placement of central lines, echocardiography and CPR.

The physical characteristics of the designated ICU, the limitations of both human and physical resources to service additional ICU capacity and reports of the early experiences from other countries have combined to inform a set of triage criteria which will be utilised specifically at CHBAH during the pandemic. Indeed, the offer of 15 adult and four paediatric intensive care beds may at first glance seem a paltry attempt at addressing the expected tsunami of cases. However this represents an increase in capacity of 83% and 44% respectively, which is considerable given the challenges inherent in public health care in South Africa. At a pragmatic level, the limited availability of critical care trained nurses means that the patients will be nursed by less experienced individuals at a much lower nurse to patient ratio, further limiting the ability to offer multi-organ intensive care support.

Early experience in the use of mechanical ventilation and associated mortality rates has been astonishing. Chinese clinicians reported rates of 86% and 97% (Yang et al. 2020; Zhou et al. 2020), the Intensive Care National Audit and Research Center (UK) reported 66% mortality (icnarc.org) and most recently a preliminary report of 2634 patients from New York found 88% mortality (Richardson et al. 2020). Of particular concern was the clear increase in case fatality rates with advancing age,

notably above the age of 60 years (Grasselli et al. 2020) and the obvious detrimental association of medical co-morbidities (Zhou et al. 2020; Grasselli et al. 2020). These factors clearly informed the COVID-19 triage criteria recently published by the Southern Africa Critical Care Society (criticalcare.org.za) which have been further adapted by the CHBAH critical care team (**Table 1**) in an attempt to navigate the ethical dilemmas inherent to the process of attempting reasonable allocation of life saving measures to only the few.

These triage criteria may seem excessively stringent to many intensivists around the world but are not that different from those applied at CHBAH before the pandemic. The crucial difference has been the inclusion of very specific cut-offs such as an age greater than 65 years. While older patients are not usually viewed favourably in terms of ICU admission, the lack of a cut-off allows for decisions to be made on a case by case basis. The thinking around the pandemic necessitated much clearer criteria to allow for all the various teams involved to sing from the same hymn page per se. Interventions such as inappropriate intubation are not helpful for the patient, utilise additional resources and creates unnecessary risk to the staff. The exclusion of so many categories of critically ill children was aimed at keeping potential ICU stays to a minimum to facilitate rapid turnover times of patients, thus increasing the access to critical care to higher numbers of patients.

Additional preparation has involved the development of local guidelines and protocols to assist various levels of staff to manage these patients. The need to enhance safety around intubation has seen the Department of Anaesthesia create a specific roster for a COVID-19 intubation team. The advantages of video laryngoscopy have been recognised and new equipment has been procured, necessitating additional staff training. Staff to manage the patients within the “COVID-19” ICU has been seconded from Internal Medicine and Paediatrics.

Triage exclusion criteria CHBAH (March 2020)

The following patients should not be considered for ventilation:

1. Patients over the age of 65 years
2. Patients with severe underlying lung disease e.g. COPD, Bronchiectasis, Ca lung
3. Advanced malignancies
4. Multiple co-morbidities e.g. metabolic syndrome
5. Multi-organ failure
6. Neurological devastation (from whatever cause)
7. Significant malnutrition
8. Chronic renal failure
9. Post cardiac arrest
10. HIV positive per se is not an exclusion criteria at this stage, however severely immune-compromised patients will not be considered.
11. Prolonged oxygen therapy

In addition to the above, the following paediatric patients will not be considered for mechanical ventilation:

1. Severe malnutrition and failure to thrive (Weight-for-age score < -2)
2. Chronic respiratory diseases including proven Pneumocystis & Cytomegalovirus pneumonia
3. Congenital heart disease
4. Chronic renal failure
5. Congenital syndromes and metabolic disorders
6. Malignant and haematological disease
7. Predicted “long term PICU patients” e.g.: severe Traumatic Brain Injury

Table 1: Current working triage exclusion criteria at CHBAH for COVID-19 ICU admission

Perhaps the greatest source of ongoing staff anxiety has been the question of the adequacy and ongoing supply of personal protective equipment (PPE). CHBAH has never faced such a demand previously, with current estimates of 1200 packs of PPE required on a daily basis. It seems an amount beyond the realm of our reality. Both departments and individuals have

resorted to sourcing PPE independent of the usual process. The unfortunate shortage created by increased worldwide healthcare demand compounded by public stockpiling of PPE has seen equipment purchased from non-medical suppliers. The visors and suits which may have to be used by the intensivists have come from the local hardware store!

The potential impact of COVID-19 on a population with high rates of both HIV and Tuberculosis remains to be revealed. The influences of higher ambient temperatures, pollution and malaria are probably less relevant in the South African context.

These are unprecedented times and the uncertainty is difficult to bear. Much preparation has been done. The government's response to the pandemic has been lauded and the response from our leaders at a hospital level has been heartening. CHBAH awaits its first COVID-19 ventilated patient with bated breath. ■

Conflict of Interest

The authors declare no conflict of interest.

Key Points

- Chris Hanani Baragwanath Hospital (CHBAH) is the fourth largest hospital in the world, located in Soweto, Johannesburg and serving a population of 1.5 million people.
- The demand for critical care beds, both adult and paediatric, far exceed the resources available under usual circumstances.
- A triage tent has been set up modelled on the immigration area of an airport to rapidly screen the risk of COVID-19 among new patients entering the hospital.
- The ward for Viral Haemorrhagic Fever patients has been re-tasked as the temporary COVID-19 ICU.
- The COVID-19 triage criteria recently published by the Southern Africa Critical Care Society has been further adapted by the CHBAH critical care team to navigate the ethical dilemma of reasonable allocation of life saving measures.
- The government's response to the pandemic in South Africa has been lauded and the response from leaders at a hospital level has been heartening.

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Personal Experience With Severe COVID-19 After 66 Days in Wuhan

COVID-2019 has become a worldwide pandemic. After working in Wuhan as intensive care physicians for 2 months, we have gained significant experience and would like to share our experience about daily care and supportive therapies for severe COVID-19 patients with our colleagues all over the world. The goal is for all of us to gain victory over COVID-19.

Oxygen Therapy: Divided by Phenotypes or Stages?

According to the SSC guidance (Alhazani et al. 2020), respiratory support for COVID-19 patients included non-invasive support and invasive mechanical ventilation. As mentioned in Gattinoni et al. (2020), COVID-19 was divided into two different phenotypes factitiously. For type L, the respiratory mechanics showed high compliance, low V/Q ratio and was less recruitable, while type H showed low compliance and was more recruitable. Thus, oxygen therapy, according to the author, was different in these 2 types: for type H, the strategy was similar to severe ARDS, while for type L, the main principle was to maintain adequate CO₂ level rather than to facilitate low tidal volume method, or just follow the ventilation strategy for patients with interstitial lung disease, since the CT scan showed interstitial lesions.

However, we noticed in our daily practice that the two phenotypes may be just different stages of the same disease. Since we worked in a special ICU for COVID-19, we admitted patients from other general wards and high dependency units. After reviewing the CT scan in other teams, we noticed the process from type L to type H. Daily images other than x-ray should be performed to access the exact process.

Lung ultrasound, including the PLAPS (posterolateral alveolar and/or pleural syndrome-point (Lichtenstein 2016), might be a useful choice. According to Rouby et al. (1998), the learning curve of the lung ultrasound seemed to be flat, and the skill was easily grasped, thus it was quite suitable for daily monitoring during the outbreak of such a disaster like COVID-19.

We agreed to utilise different oxygen therapies for different radiological manifestations in different stages rather than different phenotypes of COVID-19, and bedside lung ultrasound might be an alternative to CT scan for daily monitoring of COVID-19 process.

Intubation and ECMO: More Aggressive, More Efficient?

Almost all the guidance about the treatment of severe COVID-19 recommended unhesitating alteration from non-invasive oxygen therapy, such as high flow nasal cannula or non-invasive ventilation, to intubation. However, we noticed the median days between onset of respiratory failure to intubation is about two weeks in our patients, while the duration of NIV usually exceeded 10 days. The exact indication of intubation was not published as a consensus, but we suggested less than 24 hours for investigation. If no improvement was

observed within 24 hours, intubation should be performed immediately with adequate personal protective equipment. According to one meta-analysis in the period of SARS (Tran et al. 2012), after intubation, the risk of airborne spreading by sputum aspiration decreased, and OR dropped from 13.8 to 0.6.

After intubation, though some centres suggested not routinely performing recruitment manoeuvre and prone ventilation in COVID-19 patients, we found improvement of oxygenation after prone ventilation in patients with consolidation in dependent zones. Xu et al. (2018) reported in patients with acute exacerbation of interstitial lung disease, prone ventilation could also improve oxygenation. For interstitial lung disease-mimic type L phenotypes, prone ventilation might be also a choice.

However, we titrated PEEP by compliance rather than oxygenation, and found some patient's optimal PEEP was 4-6cmH₂O, although recruitable. Thus, daily monitoring of respiratory mechanics was suggested in patients with intubation, and if available, oesophageal pressure and transpulmonary pressure should be monitored, since we also noticed cases of pneumothorax could occur even when tidal volume was less than 350 ml.

According to ELSO guidance (Bartlett et

al. 2020), when meeting one of the following 3 criteria: $\text{PaO}_2/\text{FiO}_2$ (P/F) < 80 mmHg for more than 6 hours, P/F < 50 mmHg for more than 3 hours or $\text{pH} < 7.25$ with $\text{PaCO}_2 \geq 60$ mmHg for more than 6 hours, ECMO was recommended. In our practice, we noticed the ECMO was also delayed according to those criteria. Thus, the weaning of ECMO seemed impossible, especially for elderly patients. The causes of delay were multilingual; shortage of device supply was one of the major reasons. In our unit, we utilised ECCO2R operated by CRRT. Although current issues showed controversy on minimal-flow ECCO2R (Moerer et al. 2019; Schmidt et al. 2018), some of our patients benefited from the manoeuvre; further result of minimal-flow ECCO2R in severe COVID-19 patients was reported by our colleagues and is currently under review.

Although less is more for an unknown disease such as COVID-19, individually aggressive utilisation of currently available methods should be of great importance in daily practice.

Hyperinflammation, Peaceful Coexistence or Vigorous Intervention?

Increased level of serum interleukin-6 (IL-6) and C-reactive protein suggested hyperinflammation during the process of COVID-19. Thus, anti-inflammatory drugs such as steroid, chloroquine and tocilizumab were utilised in different centres, while the results were also controversial. Theoretically, IL-6 can cause macrophage activation-mimic syndrome in COVID-19 patients (McGonagle et al. 2020), and some histological autopsy samples from patients who died from COVID-19 showed bilateral diffuse alveolar damage including oedema, proteinaceous exudate, focal reactive hyperplasia of pneumocytes with patchy inflammatory cellular infiltration, and multinucleated giant cells (Xu et al. 2020), which suggested inflammatory cytokine storm. The block of IL-6 receptors seemed possible to block the pathway of

the storm, and therefore might decrease the severity of COVID-19.

Hyperinflammation was common in sepsis patients (Yadav and Cartin-Ceba 2016). However, anti-inflammatory therapies in septic patients had never shown any improvement. The immune reaction during the process of sepsis consisted of two phases: cytokine storm and immune exhaustion, and the exact boundary of those was difficult to determine, thus theoretical therapy always failed in the real world.

Almost all patients admitted to our unit received steroids in general wards. The average dose was about 1 gram methylprednisolone/kg body weight daily, and the duration was 5-7 days. However, we did not find any improvement in those patients, but due to admission bias, steroids might help in mild to moderate COVID-19 patients.

Interestingly, we had three special cases of immunocompromised patients, including two patients who had received renal transplantation and one with myasthenia gravis. All those patients received tacrolimus regularly before the outbreak of COVID-19, and this was discontinued after diagnosis of COVID-19. Their respiratory manifestations were less severe than other patients, and serum IL-6 remained low-level during the process of COVID-19. The same process was also reported in a patient with systemic sclerosis regularly treated by tocilizumab, and the last dose was given four weeks before being diagnosed with COVID-19 (Mihai et al. 2020). Perhaps prophylactic anti-inflammation rather than post-infected utilisation of anti-inflammatory drugs might be more efficient.

We also noticed different autopsy discoveries from different centres. Autopsy report from Ohio (Barton et al. 2020) showed heterogeneity in two patients, which suggested individualised therapy should be applied, if we could perform lung biopsy during the process of COVID-19.

The beneficial effects of reducing inflammation should be reconsidered when comparing with the potential of immu-

nocompromising effects. Thus, we did not suggest routine use of anti-inflammatory drugs in severe COVID-19 cases.

Since we were focused on severely ill patients with COVID-19, the experience seemed only focused on such patients. Further studies are needed to verify the exact effect of certain therapies like mechanical ventilation or ECMO. Antiviral therapies and anti-inflammation therapies might also have their roles in certain patients or certain conditions, for example, early stage of COVID-19 within two weeks. We believe we can deal with this disease and meet the victory in the near future. ■

Key Points

- An overview of our personal experience in Wuhan from the intensive care unit at Peking Union Medical College Hospital in China.
- COVID-19 was divided into two different phenotypes factitiously but we noticed in our daily practice that the two phenotypes may be just different stages of the same disease.
- We noticed the median days between onset of respiratory failure to intubation is about two weeks in our patients, while the duration of NIV usually exceeded 10 days.
- We found improvement of oxygenation after prone ventilation in patients with consolidation in dependent zones.
- Almost all patients admitted to our unit received steroids in general wards. The average dose was about 1 gram methylprednisolone/kg body weight daily, and the duration was 5-7 days.
- The beneficial effects of reducing inflammation should be reconsidered when comparing with the potential of immunocompromising effects. Thus, we did not suggest routine use of anti-inflammatory drugs in severe COVID-19 cases.

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COVID-19: Masks in Intensive Care Units

With the number of COVID-19 cases increasing in the intensive care units, there is a high risk of infection for healthcare professionals. What kind of masks can be used and what are the most effective strategies to protect against airborne particles?

Currently, there is an increasing number of patients in the intensive care units (ICUs) due to COVID-19 all over the world (some more than others). Since there is a high risk of infection for healthcare professionals (HCP), it is necessary to pay attention to their protection, starting with masks. N95 filtering face piece respirators and surgical masks are commonly used to protect the human respiratory system against fine airborne particles (WHO 1999).

What is the Evidence Behind Masks?

Viral particles are one of the smallest known bioaerosol agents, with a diameter of 20 to 300nm, that can easily penetrate through the human respiratory system (Reponen et al. 2001). Small particles of < 5 µm and < 10 µm diameter readily penetrate until the alveolar space and below the glottis, respectively (Tellier 2019). Previous studies (Oberg et al. 2008; Lee et al. 2008) showed that particles of up to 3,1µm in diameter are not adequately filtered by surgical masks, what may include SARS-CoV-2, assuming that its size is similar to SARS-CoV

[0,08-0,14µm] (Ksiazek et al. 2003).

Surgical masks started to be used to prevent wound infection in the surgery room from staff-generated respiratory bacteria since the early 1900s (Lipp and

■ surgical masks as respiratory protection devices are not National Institute for Occupational Safety and Health certified ■

Edwards 2002; Belkin 1996). Its application has evolved into the prevention of employee exposures, including respiratory viral transmissions (Johnson et al. 2009). Nevertheless, there is an ongoing debate about the use of surgical masks as respiratory protection devices. They are not National Institute for Occupational Safety and Health (NIOSH) certified (Balazi et al. 2006), and it remains uncertain whether they can prevent the transmission of SARS-CoV-2 (Feng 2020; Oberg and Brosseau 2008).

On the other hand, the NIOSH lists nine categories of respirators (N95, N99, N100, P95, P99, P100, R95, R99, and R100). Among these, N95 respirators, with a filtration efficiency of at least 95% a particle size of 0.3 µm (NIOSH 1996), have been recommended by the Centers for Disease Control and Prevention (CDC) for HCP to protect them from infectious diseases potentially spread through the air.

In the ICU setting, we found only one study about COVID-19 related to masks, published the 16th of March: a case report of 41 health workers in contact with the same COVID-19 patient during at least 10 minutes, closer than 2 metres, performing an aerosol-generating procedure (AGP) (endotracheal intubation, extubation, noninvasive ventilation, and open circuit exposure) that used either a surgical mask or an N95 mask (respirator). After two weeks of isolation, they presented neither symptoms nor positive swabs (Ng et al. 2020).

Indeed, the panel of the Surviving Sepsis Campaign for COVID-19 (Alhazzani et al. 2020) makes recommendations and suggestions of whether to use surgical masks or respirators for AGP, non-AGP and for usual care for non-ventilated

COVID-19 patients, purely based on evidence extrapolated from other viruses to SARS-CoV-2. Besides, if we search for studies after the time point when the virus appeared (December 2019) we find not more than two studies, and unrelated to COVID-19 (Radonovich et al. 2019; Long et al. 2020).

Regarding cardiopulmonary resuscitation, as an AGP, all staff should wear airborne personal protective equipment (PPE) including an N95 mask or similar (according to local indications) before commencing chest compressions, and if available, an automated compressor device should be used to minimise required staff and exposure (Alhazzani et al. 2020; Edelson 2020).

What are Public Health Institutions’ Position?

WHO (WHO 2020) states that HCP should:

- Wear a medical mask when entering a suspected or confirmed COVID-19 patient’s room.
- Use a particulate respirator at least as protective as a US NIOSH N95, EU standard FFP2, or equivalent in settings where AGPs are performed.

CDC (Center for Diseases Control and Prevention 2020) states that HCP should:

- Wear a facemask at all times while they are in the healthcare facility.
- Put on an N95 respirator (or higher-level respirator) or facemask (if a respirator is not available) before entry into the patient room or care area.

Moreover, other institutions and organ-

isations recommend the respirators over surgical masks for protection, together with the rest of the PPE [cloth masks are not PPE (Center for Diseases Control and Prevention 2020)] and precaution in the performance of procedures to guarantee the staff safety (Matos et al. 2020; Nicola et al. 2020; Abi Saleh et al. 2020).

What About the Resources?

Low-middle income countries are also dealing with the pandemic, and there is a high concern in their ICUs about the staff protection and the limited resources they might face in this situation.

Supported by the Oxford University Press for the Infectious Diseases Society of America (IDSA), Bahl et al. write: “the ability of countries to respond effectively depends on the safety and confidence of the health workforce, especially in low-income countries with low ratios of HCWs [Health Care Workers] per head of population, and protective measures are crucial to ensure a functional health workforce” (Bahl et al. 2020).

This reasoning led to proposals of alternatives to overcome the scarcity of PPEs (Table 1) (Bong 2020).

Hitherto, the CDC states that standard respirators and facemasks should be removed and discarded after using them, and reusable respirators must be cleaned and disinfected according to manufacturer’s reprocessing instructions prior to re-use. Meanwhile, other institutions are testing other decontamination procedures to allow the reuse of respirators (FDA 2020).

In brief, it is inevitable to pay attention to our world as a whole helping the less privileged to have fatal outcomes, and indeed prevention and protection might be the answer (Bong 2020).

Do we Need RCTs to Prove the use of Masks?

There is only a randomised controlled trial registered in ClinicalTrial.gov

Minimise contamination during AGP	Use transparent plastic drapes or clear box for bag and mask, intubation and extubation.
Use face-shields to prevent contamination of masks	Face-shields can be easily made from common inexpensive materials, including plastic bottles.
Creative solutions to make PPEs using everyday materials:	
• Masks	-In the absence of N95 masks, consider DIY options -Standard anaesthesia facemask or scuba diving masks with viral/bacterial filter
• Eye protection	- Any waterproof material that protects the front and side of the eyes will be adequate -Consider safety goggles obtained from hardware stores, swimming or diving goggles
• Protective gowns	-Any splash-proof or water-proof material will do -Consider plastic aprons, plastic bags, garbage bags, raincoats, ponchos.

Table 1. Alternatives to PPEs

(NCT04296643) in which nurses will be randomised to use either medical masks or N95 respirators when providing care to patients with COVID-19. This Canadian multi-centre randomised controlled trial will assess whether medical masks are non-inferior to N95 respirators when nurses provide care involving non-aerosol generating procedures.

Since this an important issue for health-care workers and patients, it is crucial to clearly understand the role of masks in the ICU. ■

Key Points

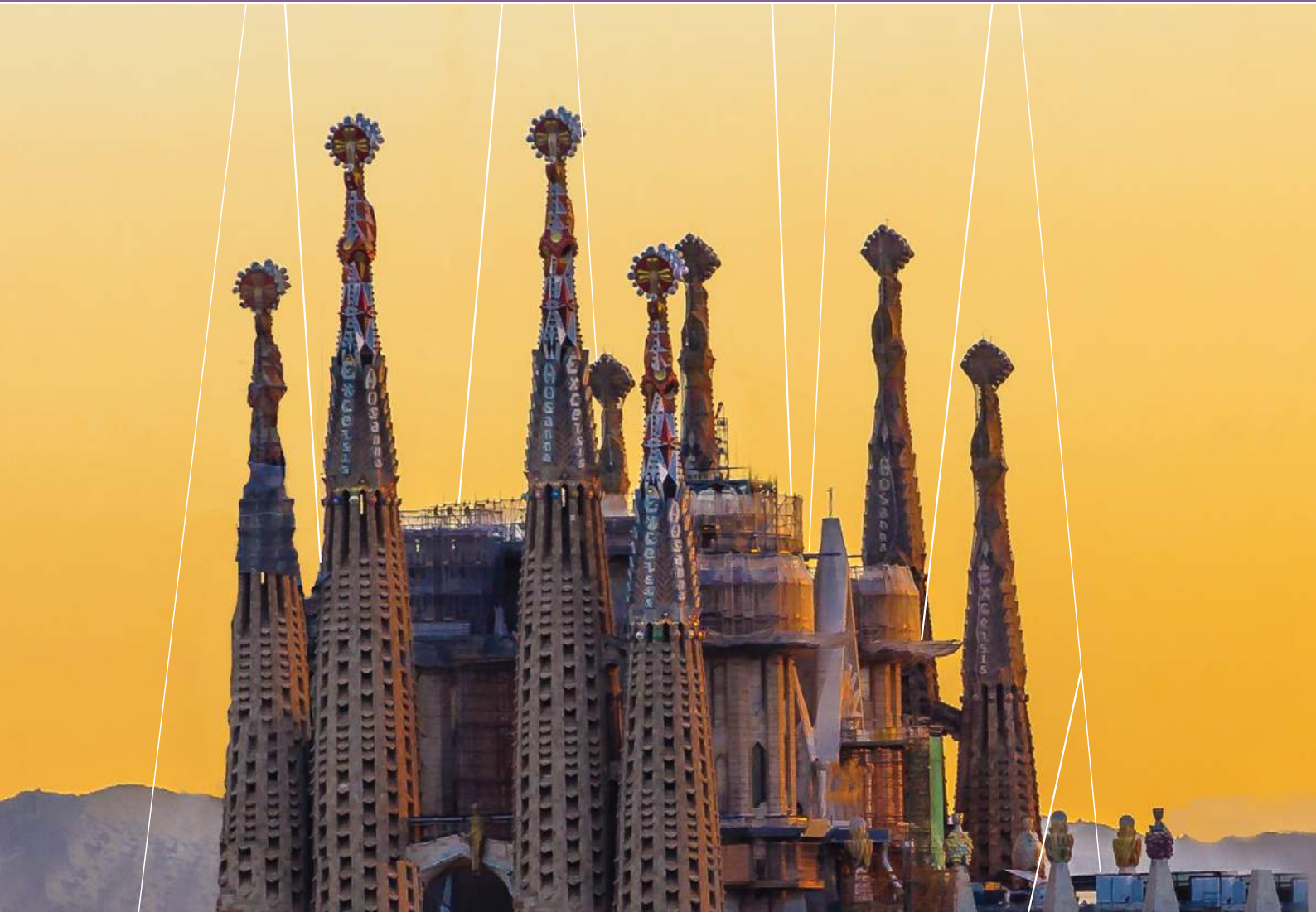
- It is necessary to pay attention to protection of health-care workers, including use of appropriate masks.
- N95 filtering face piece respirators and surgical masks are commonly used to protect the human respiratory system against fine airborne particles.
- Viral particles are one of the smallest known bio-aerosol agents, with a diameter of 20 to 300nm, that can easily penetrate through the human respiratory system.
- Particles of up to 3,1µm in diameter are not adequately filtered by surgical masks, what may include SARS-CoV-2, assuming that its size is similar to SARS-CoV.
- The WHO recommends medical masks when entering a COVID-19 patient's room and a particulate respirator when performing aerosol generating procedures.
- The CDC recommends wearing a facemask at all times while in a healthcare facility and an N95 respirator or higher before entry into a patient room or care area.

Abbreviations

AGP: Aerosol-generating procedure
 CDC: Centers for Disease Control and Prevention
 DIY: Do it Yourself
 EU: European Union
 FDA: Food and Drug Administration
 HCP: Healthcare professionals
 HCWs: Healthcare workers
 ICU: Intensive Care Unit
 IDSA: Infectious Diseases Society of America
 NIOSH: National Institute of Occupational Safety and Health
 PPE: Personal protective equipment
 RCT: Randomised Controlled Trial
 WHO: World Health Organization

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COVID-19 and the History of Pandemics

How are we dealing with the COVID-19 pandemic and the lessons we can learn from similar diseases over the last few centuries.

The face of human history has always been pockmarked by disease, in more ways than one. In our current privileged world of technology, gene sequencing and micro RNA, the possibility of a new disease that kept us inside our houses seemed an impossible dystopia. However it has proved inevitable and recurrent across Europe and the wider world, for disease to bring disaster in a sudden and unwelcome wave. Mass graves silently bear forensic evidence of societies past, as they will this one.

The novel coronavirus COVID-19 was first presented to the world in the embers of December 2020 (Wang et al. 2020), and the world looked on, intrigued as China drafted in the military, barricaded the city of Wuhan and built new hospitals. From February through March 2020, the domino effect left Italy, Spain, France, the UK and the US reeling, with their own medical services drowning, a significant lack of ventilators, new hospitals and vast re-organisation of services required, such as cancelling elective operations and outpatient clinics. This was all accompanied by an enemy vanguard of PPE shortages, amidst ever-fluid guidance from public health bodies.

What do we know about this version of coronavirus? It belongs to a family of viruses that have often infected mammals, especially bats, and is known to cause a mild respiratory illness such as the common cold in humans. This particular strain however, can prove lethal. It seems to

have originated in Wuhan, China, possibly from a live animal market (Wang et al. 2020). It shares many convincing genomic features with bat coronaviruses, and this animal host is known for fairly virulent, highly mutating viruses due to a rather impenetrable immune system, which the host can withstand potentially due to anti-oxidant and mitochondrial adaptations that have arisen for the necessities of flight (O'Shea et al. 2014).

In humans it was first described as a highly contagious airborne and droplet-spread pathogen causing fever, dry cough and pneumonia in some, but not all, afflicted individuals.

From an epidemiology standpoint it seemed to have an R0 number of 3 (in contrast to SARS which was less), affect men more than women (Sun et al. 2020) [consistently 60-80% for UK ICU data (ICNARC 2020)], possibly because of gendered behaviour or X-chromosome conferred immunity (Schurz 2019), for the main part did not produce symptoms in children [which remain less than 1% of cases and minimal fatality (Kelvin and Halperin 2020)] and could be carried asymptotically (Sun et al. 2020). Although it can attack the young and apparently healthy, the majority of victims are >65 years when it comes to mortality rates. Those with diabetes and hypertension seem to be particularly affected, as do smokers (Jordan et al. 2020). There have been cautious questions of whether non-Caucasian ethnicities seem to be a

greater risk for lethality, however this remains hypothetical and the reasons are unexplored as yet (Science Media Center 2020). Postulates are socioeconomic, urban living probability – at least in the UK, and potentially genetic/MHC subtypes, as MHC class has significant variability on antigen presentation/strength of T cell activation (Wieczorek 2017).

It is from the family coronaviruses, and contains a particular spike protein for invasion. Though it bears resemblance to past MERS and SARS viruses, it uses the ACE2 receptor to enter cells (Wang et al. 2020). ACE 2 is, in many ways, the yang to ACE's yin; it is a separate receptor, unaffected by traditional ACE inhibitors, that has a vasodilatory effect on vasculature. COVID-19 then goes on to replicate inside cells as all viruses have a wont to do, and has been found in both lung and capillary epi/endothelium, alongside biopsy findings of pulmonary oedema, pus, hyaline surfactant disruption, microthrombosis and pulmonary infarction (Xu et al. 2020).

COVID-19 originally was said to present with a cough and fever, and potentially GI upset, leading towards pneumonia. Now we are further into the outbreak (3-4 months), we are aware of presentations such as rashes (Recalcati 2020), ophthalmic complications (Wu et al. 2020), anosmia (Iacobucci 2020), neurological complications (Mao et al. 2020) and peri/myocarditis (Fried et al. 2020). Critically ill patients appear to have a high rate of mortality [50% of ICU admissions in

ICNARC data (2020)], suffering from cytokine storm, haemodynamic collapse and a significant proportion have renal failure. In the UK roughly 1/5 of hospital admissions require critical care, but without mass testing it is unclear what the true fatality rate is, given the likely presence of asymptomatic infection. Whilst initially focus was on an ARDS like development of pneumonia, which some do yet display, it was clear there were different phenotypes of disease when it came to lung pathology (Gattinoni 2011). Some do not have the classic stiff, wet lung characteristic of bacterial ARDS, though biopsy findings have described very similar features shared by both (Xu et al. 2020).

It is of particular note that the microthrombosis and hyper-coagulable state of COVID-19 patients is a rather novel component of its natural history. D-dimer was early on reported as a poor prognostic marker in these patients (Jordan et al. 2020), representing clot turnover. This fits with the clinical picture that is consistent with widespread microthrombosis such as renal failure, apparent pulmonary shunting, and certain skin changes. If heparin yields little effect in some, it suggests that part of the pathology is related to platelet dysfunction, a feature of other viruses (Lope da Silva 2011) such as dengue (Rossi et al. 2010) ADAMTS13 is a molecule that affects the cleavage of vWF. Auto-antibodies against it are commonly provoked by numerous viruses, and defects with it are the cause of complaint in thrombocytopaenic thrombotic purpura, which has a similar constellation of coagulopathy signs, including renal failure (Zheng 2013). Clotting is very much married to the immune cascades both evolutionarily, for example a species of snail secretes immunoglobulins that are attached to fibrinogen (Janeway 2001). This enables trapping and scavenging of pathogens. In humans too, we are aware of the effect of cytokine activation on clotting and recognise DIC for example as a consequence of

profound sepsis. Even the 1665 physician Nathaniel Hodges, recognises DIC in bubonic plague (Hodges 2012). Other significant issues in these patients are the high rate of adverse cardiac features (Fried et al. 2020), arrhythmias and right heart failure. It is unclear if this is secondary to cytokines, direct viral attack on ACE2, viral myocarditis, hypoxic vasoconstriction causing right heart failure and so on.

Investigations obviously are testing – both antigen PCR and antibody testing are available, although of limited sensitivity

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and specificity. FBC shows lymphopaenia, U&Es may show renal dysfunction, LFTs are often elevated, and a high D-dimer is a poor prognostic sign.

X-ray/CT imaging (Soldati et al. 2020) will show bilateral opacities, concentrating predominantly in the peripheries, and CT describes bilateral ground glass opacities and consolidation. ECHO may demonstrate any of a hyperdynamic circulation, Takotsubo-like cardiomyopathy, reduced cardiac function and in particular, right ventricular dysfunction (Peng et al. 2020). Lung ultrasound reveals consolidation, subpleural thickening and less frequently, effusions (Soldati et al. 2020). These patients can in some circumstances, be notably hypoxic without appropriate respiratory distress.

Management of COVID-19 typically involves supplementary oxygen and CPAP, ideally prone which improves VQ mismatch

(Gattinoni 2011). These patients respond to proning rather well. Their fluid balance should be managed to avoid exacerbating either pulmonary oedema or AKI; dehydration from febrile illness can cause them to be underfilled on presentation. They may require renal replacement therapy. NIV is used with appropriate staff precautions such as filters, negative pressure rooms and staff PPE. HFNC is not globally advised given the high oxygen demands and potential aerosol dangers, although it is popular in the US (Poston et al. 2020). Ventilation strategies appear to be causing controversy given ventilator associated lung injury and the fact these patients have compliant lungs in some phenotypes, however these patients can be profoundly hypoxic, deteriorate fast and can be hard to extubate, so naturally intubation and ventilation is a step that must be taken in some patients, abiding by lung protective strategies such as low tidal volumes and minimal oxygen titration to limit iatrogenic exacerbation of disease (Gattinoni 2011).

Antibiotics should be given for secondary infection and be guided by biomarkers, potentially procalcitonin, and clinical features. Anti-coagulating these patients may extend renal filter life, and potentially assist disease recovery (Tang et al. 2020). Heparin infusions are the most commonly used. ECMO is an option for countries with available beds (Poston et al. 2020).

Multiple agents are in use with respect to trials – hydroxychloroquine, azithromycin, kaletra, remdesivir, vitamin C, IL-6 antagonist agents, convalescent plasma and steroids are all under trial surveillance, with some nominally interesting results, none of which have robust RCT evidence. Registered trials in Europe are available on the clinical trials register (EU Clinical Trials Register). Steroids have been used to attempt to control the cytokine storm, however there are concerns they could enhance mortality/viral progression and enable secondary infection. Randomised

trials are awaited. Many trials are compassionate use-based.

Most measures have focused on public health interventions such as hand-washing, isolating the afflicted, limiting travel, shop and public space closure, social distancing, working from home/furloughing staff and school shut down. There have been and will be profound economic effects, with secondary health consequences. COVID-19 truly is the plague of our time.

As we do with law, in our own personal lives, we find ourselves reflecting on precedent to predict the future in medicine. The medical response throughout past epidemics has proved both predictable, humorous and sorrowful at once. As a profession we have witnessed Ebola, Influenza, Cholera, Typhus, Syphilis, Malaria, Dengue. Our bones have joined those of patients, riddled with the same disease. Some have chosen to assist, head on, others have chosen to direct from the rear. We can all sympathise with everything the ghosts of history experienced, and wonder how they coped, acted, and died. In many ways, infectious disease was a more familiar creature to the medics of the past and perhaps more bearable. Alternatively lack of explanation, the wrath of religious figures, and the inevitable socioeconomic chasm led to dissolution of order that was only partly bridged by the moral conscience of individuals. You will recognise shut downs, rationing and neighbourly kinship in the narratives of plague history.

When it comes to how our forebears managed the moral maze of self preservation amidst epidemics, I have sourced material from literature, diary entries, and commentators at the time, including information published by the Church and clergy concomitant with outbreaks. Plagues have been a perpetual shadow over human societies – whether it be the Justinian plague in 542 BC, the Black Death between 1348 AD and the late 17th century, or others such as those mentioned

in Ancient Greece and Egypt, for which we have less information. I will start by explaining the role of medical practitioners within their historical framework.

Traditionally, the identifying feature of physicians was a university degree (Mellinger 2006). There was much time dedicated to studying the liberal arts – theology, philosophy, logic, rationality – and even astrology, in addition to basic sciences. This forms the basis for the Oxbridge science degree as a Bachelor of The Arts accreditation. Anatomy was something more prevalently studied in the Middle East. Much of European early study focused on Galen and Hippocrates, however there were limited translations available of Greek texts during the Middle Ages. Indeed, many Islamic texts were more accessible, and Ibn Sina (Avicenna) around the 9th/10th century had a lot of influence over European medicine.

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Most theories focused on the idea of humours as we are familiar with – but uroscopy (Eknayan 2007), in compact with astrology, was often used. Uroscopic kits were actually rather popular! The consistency, appearance, odour and even taste of urine was examined. The pulse too, was a source of information for the ancient physician. Descriptions were rather poetic - gazelle, worm or ant-like pulses are described (Boylen 2007).

Universities therefore generally managed medicine, as they do today. One of the first putative medical schools was in Salerno,

Italy (originating in 9th Century AD, formally recognised in 1231). Ideas from Greece and the Middle East, generally spread across to Italy, France, and England, although various cultures flavoured the exact form of medicine that was applied, and of course religious direction cultivated certain theories. Again it is notable that anatomy and physiology flowed from the Middle East (Mellinger 2006).

In fact, the universal physician philosophy, which had tended to focus on prevention rather than cure through agency via a good diet, and avoidance of certain foods or behaviours (usually sexual ones), was that flight was the only method of managing plague (Wallis 2006). To flee, flee far, and return late (Bocaccio 1886). This was a consistent approach, and their rational one – in an era whereby death was common and cures minimal, this was not considered morally inept. However for the clergy and the churchmen – flight was not considered appropriate and edicts from the Church authorities stated this. This was partly due to the fact that an early death, though tragic, was not as eternally damning as death before confessing one's earthly sins (Wallis 2006).

Bishop of Gloucester and Worcester, John Hooper, wrote, there were 'such officers of trust ... [who] for no cause may flee:' the bishop, parson, vicar, and curate... Such also as have places and offices of trust for the commonwealth, as the captains of soldiers in the time of war, judges and justices in the time of peace" (Wallis 2006).

Physicians therefore were often absent from plagues, tended chiefly the rich, and left a vacuum for plague doctors. These varied from 'second rate' unsuccessful physicians, apprentices, barbers, herbalists... right through to fruit salesmen (Mellinger 2006). The characteristic beaked appearance of a plague doctor did not really represent a traditional physician. Practitioners were those, without a university degree, who had dabbled, or

received a little training, and doubtless varied in their efficacy.

Two popular commentators, Martin Luther and Beza had opposing views on flight (Wallis 2006). Luther argued it was immoral to desert one's family/leave the poor in harm's way, whilst Beza felt people had a moral obligation to leave and not 'tarry' recklessly, where they might tempt the condemnation of God. Indeed most commentary towards the end of the pandemics did not oppose flight, although charity and concern for one's kin was highly regarded, there was no 'state obligation' for the greater common wealth (Wallis 2006). Flight discussions were targeted more towards clergy and other public offices, and frankly physicians earned little notice, at odds with commentary of today. A lot of discourse swirled around the state of people's souls, poverty, social inequality, dissolution of order and the physical consequences. Magistrates and governance were heavily scrutinised.

The only exception to the absence of physician scrutiny was specifically employed 'city physicians' who were employed for the purpose of the epidemic, and swore an oath. Which suggests that magistrates should provide the common wealth "of Phisitions, Chirurgians, and such as they commonlye call Apothecaries, such as for yeares, fame, experience, honestie of manners, virtue, and the feare of God, they shall iudge to bee best liked and fitte." Furthermore such individuals 'should be 'hyred for a convenient stipend, & bound by oath unto the common wealth, that they take no occasion to start away, for feare of the sickness greatly increasing' (Wallis 2006).

What is interesting is that in such times, to be a physician was a rather ordinary calling, but had little spiritual overtone, so the weight of moral obligation was perhaps not quite so profound – either by the standard of society, or by personal conscience. One commentator,

a vicar called Balsmsford, rather meekly attempted to criticise physicians with the argument that their ability to do good, fortified their duty to provide it. He was, of course, criticised for not visiting the sick himself (Wallis 2006).

It is notable that in 1630, members of the College of Physicians were criticised because they "did not go out in their gowns in the street" to avoid public recognition (Wallis 2006). I'm sure we can all draw our own parallels to contemporaneous behaviour.

It would be remarkably improper not to use the diary of our favourite naval officer, Samuel Pepys to help us reflect on this time. I managed to find this incredible passage:

management of COVID-19 typically involves supplementary oxygen and CPAP, ideally prone which improves VQ mismatch

"Dr. Goddard did fill us with talke, in defence of his and his fellow physicians going out of towne in the plague-time; saying that their particular patients were most gone out of towne, and they left at liberty; and a great deal more, &c. But what, among other fine discourse pleased me most, was Sir G. Ent about Respiration; that it is not to this day known, or concluded on among physicians, nor to be done either, how the action is managed by nature, or for what use it is. Here late till poor Dr. Merriot was drunk, and so all home, and I to bed." (Pepys 1666)

Physician's own musings on the subject also favoured flight, whether mentioned in books such as 'The Touchstone for the Physik' by William Walwyn, and "The Chymical Galenist" by George Castle, or by individual physicians. A supporter of the College of Physicians, Kemp stated firmly "Think well then of your Doctor,

and oblige him whilst you are in health, to venture his life to preserve you when you are sick" (Wallis 2006), meanwhile the head of the College, Nathaniel Hodges, was very clear that when duties to neighbours and existing patients disbarred, many of whom had indeed left, flight was advisable. It was felt however, that the College had also ever been reluctant to provide city physicians during epidemics.

Nathaniel Hodges, this erstwhile head of the College, wrote a book called "Loimologica: An Historical Account of the Plague in London" published in 1665. I am hard pressed not to quote all of it, simply for the writing.

"Disputes are raised about the use of Alexipharmicks, Fumigations, Fires and other general Topics, which have little Foundation, than a wilful misapprehension, for it cannot be imaged, that these are either good or bad in all Circumstances but that they require the Conduct and Discretion of able Judges, as Particular Occasions or Symptoms demand them."

These words are not unwholly foreign to any of us who have attended many a discourse on new treatments. By the time of publication of his book in 1665, he was rather annoyed by people 'of mean thought' using astrology, and could not imagine that any conjunction of Saturn or Mars, had any bearing on the matter, other than to sink spirits and reduce resistance to 'the contagion.' He also goes into a great explanation about comets, for though they seem intimidating he states 'there is nothing strange about the ascension of heterogeneous particles into flame.' It is also notable however, that he laments a surfeit of cherries and grapes, which may have contributed to the pestilence and the body's disposition to it.

He himself does appear to have tended patients, for he describes that during Christmas Holy days he attended a young man with a fever, and risings on each thigh the size of a nutmeg, who had caught the plague. This patient recovered. He had received a two day course of Alexiterial medicines.

What is very heavy, throughout all accounts, is the reliance on neighbours for charity and aid. This is naturally a very biblical concept, but one commented upon even by the College of Physicians. Nathaniel Hodges in his accounts, expresses worry over magistrates shutting people in their houses and painting a red cross – he feels, though trying to be impartial, that this doesn't work and drives the neighbours away, who could otherwise deliver food and medicine. He feels more died than necessary, due to the abandonment of neighbours. Curiously in his reflections, he strongly advocates for accommodation to be made outside the City Walls for those with infected families, as he finds it 'abhorrent to religion and humanity' to shut up the sick and unafflicted together. I am not sure, this is something even now, we have quite grasped.

It is clear in many ways, that although flight is somewhat less acceptable now that it was to the people of the 17th Century, many of the ethical problems we address about the role of healthcare workers in epidemics were actually less problematic and also better solved, in a historical reference frame. I have drawn heavily on concepts from an incredible reference by Malm et al. (2008) for understanding 'moral theory' in relation to the role of medics in plagues. Please attribute most of the following concepts to their paper, although I have tried to apply their principles to the current pandemic.

Firstly, moral theory argues there are at least two categories of good deed. One is a General Good – helping someone frail with shopping or rescuing someone trapped, with an obvious answer and little skill required, and we all as people are morally obligated to do so. The other is a Special Good – one has skills or training to be of particular benefit, such as a trauma surgeon. Lots of arguments through history, including during plagues, have suggested that doctors do have a duty to perform 'Special Good' deeds. An easy example

is a call to aid on public transport for a deteriorating patient, and even the GMC have a position on this. Other Special Good deeds might relate to the position between carer and dependent – parent and child. Moral decency extends to slightly more investment in action.

However, Special Good does not always logically conclude that we must risk life, to save life. We would expect a lifeguard to save a drowning person. We would not necessarily expect them to get in and fight a shark, unless trained or equipped to do so. And this comes down to five key arguments regarding 'duty to treat' at risk of harm. This is a seriously topical subject, given the nature of not only an infectious corona epidemic, but the call to arms from retired and potentially vulnerable health care workers.

1. **Consent:** We are all familiar with consent, and many of us sign job contracts. None of us have signed a contract to say we accept we are risking our life, and have not necessarily got any compensation for doing so – unlike someone in the armed forces for example. Gaining a medical degree and working in the NHS is not informed consent for pandemic office. The magistrates in the plague epidemics therefore specifically hired city physicians in these outbreaks, who took oaths, who acknowledged the danger and CHOSE employment.

2. **Implied consent:** Many of us are familiar with implied consent. There is an argument (although it is not very strong) that by choosing to be doctors or nurses or allied professionals, we accept this risk, and by continuing to be employed, we implicitly accept it. But this is not necessarily true, and also does not hold up vigorously in law. After all, consent relies on being able to weigh up information, be it on risks or mitigations such as PPE, that not all of us possess.

3. **Special good:** Here is probably the most prominent argument for me as an individual. Some of us, by dint of fortune or training, have special skills that either have special benefits for the situation or reduce the risk to ourselves. This is sacrifice for the greater good or common wealth argument.

4. **Reciprocity:** The above argument becomes particularly strong when we consider whether special skills have arisen due to public investment. For example whilst private physicians weren't much commented on during epidemics, city physicians (funded by magistrates) were. In the NHS certainly, we are mostly publically funded, although with the position of bursaries and loans etc, this may vary between professions, individuals and nationality. This argument is that society gives us special skills, training and equipment, including PPE (in some, not all hospitals of course!) and therefore we are morally obliged to give back to society.

5. **Oaths and codes:** There is no medical oath, or Hippocratic oath, performed at graduation in the West, that addresses the situation of risk to one's own life. "First do no harm" or *primum non nocere*, is the prevailing wind. This quote moreover, is not directly attributable to Hippocrates, despite assiduous efforts, although a similar vein is present in original texts. The closest I could find is "But I will keep pure and holy both my life and my art." In the context of biblical teachings in plague times, charity was very much salient, however suicide was not. Moreover, today, we are meant to consider separate our religious ideals and treatment of the unwell. Again, during plague outbreaks, magistrates used physicians who had sworn a very specific oath.

Overall it can be concluded that there is no obvious and easy moral answer to

the dilemma of medical assistance during epidemics. However I think many of us possess unease regarding the exposure, particularly of susceptible colleagues, to contagion. This is particularly prominent in the setting of insufficient PPE. Moral arguments regarding the continued provision of healthcare clearly vary by consent process, degree of training and protection, public investiture into funding and equipping healthcare, and one's own moral position on duty to treat – be it spiritual or otherwise. Is it a moral role to become a medic, or a scientific one? Do we have a public office that helps to sustain order? Even if these are true we also possess a moral obligation to our own families and neighbours, indisputably, to reduce harm to them.

As fascinating as historical precepts are – scientifically and sociologically, our knowledge now far exceeds that of the

plagues of the past. Early 17th Century scientist Van Leeuwenhoek discovered 'animalcules' in dental plaque and onwards from there appeared discoveries about the agents and methods of infection, throughout the 17th-21st centuries. Our approach will have to evidentially differ from our forebears.

"The dogmas of the quiet past are inadequate to the stormy present. The occasion is piled high with difficulty, and we must rise with the occasion. As our case is new, so we must think anew and act anew." Abraham Lincoln

Absolutely. And with respect to one other controversy during this period – the onslaught of less-than-rigorous but rapid-turnover research, Nathaniel Hodges had very pointed suggestions about any perceived quackery, which he termed "Trash with pompous Titles" (Hodges 1665). ■

Key Points

- The novel coronavirus COVID-19 was first presented to the world in the embers of December 2020.
- From February through March 2020, the domino effect left Italy, Spain, France, the UK and the US reeling, with their own medical services drowning, a significant lack of ventilators, new hospitals and vast re-organisation of services required.
- COVID-19 originally was said to present with a cough and fever, and potentially GI upset, leading towards pneumonia. Now we are aware of presentations such as rashes, ophthalmic complications, anosmia, neurological complications and peri/myocarditis.
- Multiple agents are in use with respect to trials - hydroxychloroquine, azithromycin, kaletra, remdesivir, vitamin C, IL-6 antagonist agents, convalescent plasma and steroids are all under trial surveillance.
- Most measures have focused on public health interventions such as hand-washing, isolating the afflicted, limiting travel, shop and public space closure, social distancing, working from home/furloughing staff and school shut down.

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What COVID-19 Has Taught Me...

A personal narrative of Adrian Wong's experience while battling COVID-19 at King's College Hospital. These are the author's personal opinions and do not represent the views of the institution and professional societies to which they belong.

The global COVID-19 pandemic has changed healthcare throughout the world and the specialty of Intensive Care Medicine has never been under such scrutiny. The events in China and Italy in particular sharply focus healthcare professionals at all levels to work together and prepare for the inevitable.

I work in a tertiary-level, teaching hospital with five critical care units spread across two hospital sites. In total, we had approximately 75 beds pre-pandemic (it is a well known fact that the number of ICU beds in the UK is the lowest in Europe for its population size). We have more than doubled the number of ICU beds; there was also a concomitant expansion in the number and size of high-dependency areas staffed by colleagues from non-ICU specialties.

COVID-19 has taught me the importance of teamwork and colleagues, which have been central to the care of our patients in the various healthcare facilities.

The Successes

Excellent colleagues

Unsurprisingly, despite the best-laid plans, goalposts for patient care during this pandemic have changed frequently - the number of admissions, the number

of staff available to work, resource availability etc.

To increase the capacity of ICU, several areas of the hospitals had to be converted to accommodate ventilators and other equipment. In addition, we managed to open our brand new, state-of-the-art critical care unit ([youtube.com/watch?v=jgHkToeEHSw&t=11s](https://www.youtube.com/watch?v=jgHkToeEHSw&t=11s)). However, we all know that an ICU is not just about ventilators and monitors - it relies upon the skill and dedication of healthcare professionals to look after these patients.

I work with an incredible team of healthcare professionals in the department of critical care at King's College Hospital. The doctors, nurses, physiotherapists, cleaners, porters, administration staff, pharmacists, ACCPs are steadfastly committed to delivering the best possible care under such challenging circumstances. Colleagues with previous ICU experience have come back to work in the ICUs. Outside of critical care, colleagues in other specialties have redesigned their workflow, with some having to upskill to work in the ICU. Staffing rotas were rapidly redesigned to provide increased cover on the floor and continue to be refined in response to changes in demand. Staff health, wellbeing and sustainability of these staffing models are carefully

considered at every juncture.

Planning of operational issues requires significant coordination, with colleagues taking on board various workstreams. Ensuring appropriate supply of equipment, staff and medication in the face of an international pandemic is challenging to say the least. Issues such as working out the maximum oxygen delivery capacity of the hospital and regular supply of Personal Protective Equipment require organisational and leadership prowess.

The leadership team had to find the balance of keeping staff updated versus communication overload. Due to physical distancing, new ways of working had to be explored.

Technology to the rescue

Our institution has an established Clinical Information System for both the general wards and the ICUs; this was rapidly reconfigured to support the new clinical areas. High-quality data has allowed us to collectively learn from and reflect on the patients across the hospital. Access to these platforms was facilitated through the use of Virtual Private Networks (VPN).

Team meetings whilst observing physical distancing meant that teleconferencing and virtual meetings became the normal mode of communication; software such

as Microsoft Teams and Zoom allowed for colleagues to discuss operational and clinical issues remotely. Evolving clinical guidelines were then developed to be shared with the relevant teams.

On a wider scale, the pandemic has forced the cancellation/postponement of several major medical conferences. In their place, professional societies have organised regular online webinars to educate and discuss clinical issues. As an example, the European Society of Intensive Care Medicine organised a #COVIDmarathon which comprised online talks by numerous experts discussing various aspects of COVID-19 management ranging from public health issues to ventilatory strategies. It attracted thousands of colleagues and ran for nearly 10 hours. The recordings from this virtual conference have been made freely available on the ESICM website and its blog (esicm.org/blog) provides summaries with educational links.

When the pandemic ends, will we expect to see an evolution in the format of workplace meetings and medical conferences?

Learning

It is a strong personal belief that front-line practice and experience should be shared in a timely manner, so that lessons can be learnt and clinical management strategies adjusted accordingly. Traditional sources of information such as journals and professional societies have had to swiftly adapt their practice. Medical journals have made articles related to COVID-19 mostly free and open access; the submission process has been significantly streamlined to fast-track publication. These well-intentioned changes do raise the issue of quality of the material, resulting in considerable debate and strong opinions for both sides of the argument. Fundamentally, the individual practitioner retains responsibility for critical examination of the evidence, and

should acknowledge that the emotive desire to try a novel treatment is a strong source of bias.

The pandemic has also highlighted the importance of social media in communicating this new knowledge and sharing front-line practice throughout the world. There has been widespread use of Twitter, Facebook and WhatsApp to instantaneously disseminate information

When will things go back to normal, and how? Should things revert to their original state? These legitimate questions will need to be discussed and answered at societal level

across geographical boundaries. This is especially useful when considering that healthcare teams in different countries are likely to be dealing with different temporal stages of the pandemic, where earlier experiences may inform the management strategies of latterly affected populations. It is important to remember the risk of miscommunication and misinformation as discussed above, and there needs to be particular emphasis on professional scrutiny of the evidence and news.

Going Forward

We are not yet at the end of the pandemic although several countries have started discussing easing social distancing rules. When will things go back to normal, and how? Should things revert to their original state? These legitimate questions will need to be discussed and answered at societal level.

The pandemic has compelled us to

revisit the way we deliver critical care, healthcare and indeed work as a whole. The ability to work and learn remotely has been pushed to the forefront and will likely continue on its own trajectory, hopefully with beneficial effects on resources and efficiency.

Conclusion

The pandemic has focused attention on intensive care, and in particular, the ability to provide advanced respiratory support. However, as time goes by and increasing numbers of patients are treated in ICUs internationally, it is clear to me that the key factor is not the fancy machines and monitors, but rather, the dedication of healthcare professionals. I have never been more proud of and humbled by the tireless efforts of colleagues in my institution, the critical care specialties, and the healthcare profession as a whole. There are still challenging times ahead with an unclear outcome but we will deal with it together. We are far stronger in collaboration with one another - after all, no ICU is an island. ■

Key Points

- COVID-19 has changed global healthcare, in particular, the specialty of Intensive Care Medicine as it has never been under such scrutiny.
- King's College Hospital more than doubled the number of ICU beds and expanded the number and size of areas staffed by colleagues from other specialties.
- Colleagues in other specialties have also had to redesign their workflow, with some having to upskill to work in the ICU.
- Access to patient data was facilitated through Virtual Private Networks; team meetings were conducted through Microsoft Teams and Zoom.
- Social media has played an important role in communicating new information and sharing front-line practice with colleagues working elsewhere.
- Despite the challenges, COVID-19 has shown the dedication of healthcare professionals around the world and has proven that we are far stronger in collaboration with one another.



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Intensive Care in the Coronavirus Era: Keep in Mind Your Collective Intelligence

Above and beyond the logistical and organisational aspects, shaken by the COVID-19 pandemic, here is an overview of our experience as an intensive care team in Switzerland.

We will not parade the efficient measures implemented in our institution in preparation for welcoming COVID-19 patients; rather, we will discuss the impact of this epidemic on the clinical and emotional intelligence of intensivists.

Our usual pragmatic and evidence-based practice of medicine was shaken by the COVID-19 assault before we found our footing about two weeks after the first COVID patient had been admitted to our ICU. At the beginning of the pandemic, we were overwhelmed by fear-based medicine and we fell into its trap. This fear-medicine was triggered by the ignorance that leads to anxiety and aggravated by several factors:

- First of all, before the arrival of the wave, the massive influx of COVID patients and mortality were the central subjects in scientific exchanges with Chinese and Italian colleagues and in the media through the images conveyed.
- The anticipation of an overwhelming surge of critical care patients led us to organise ourselves to treat more than triple the number of patients we usually admit to our ICU, by doubling staff and searching for solutions for beds and materials. This particular situation increased uncertainty and anxiety about admission or therapeutic withdrawal decisions. Our emotions have not been attenuated by the published recommen-

ations of the Swiss Academy of Medical Sciences for the triage at admission and during the stay in ICU of COVID-patients according to the availability of resources. Indeed, on the one hand, we faced an unknown disease complicated by an expected single organ failure (ARDS) requiring an invasive approach of mechanical ventilation, based on publication of articles of sometimes questionable scientific quality. On the other hand, as we are usually bound to reduce the number of deaths, we had to make difficult ethical decisions especially regarding withdrawal when an additional organ failure set in. Thus, the automatic and logical thought was: we are going to have a high mortality, is it worth engaging in a fight lost in advance and at the expense of non-COVID patients (collateral victims)?

• Our emotional stress was amplified by the portrayal of deceased patients in the media and the high mortality among mechanically ventilated patients reported during the initial scientific exchanges with Chinese and later Italian colleagues (Zhou et al. 2020; Yang et al. 2020). They impressed in our collective unconscious a feeling of helplessness in the face of this virus.

• Intensive media coverage of a highly complex debate on experimental approaches for management of SARS-

CoV-2 (antimalarial and antivirals) massively increased the pressure on healthcare workers. We have been overwhelmed with proposals for these experimental approaches coming from inside and outside of our institution, and even from patients and their families influenced by all kinds of media. This led to prescribing treatments not based on scientific evidence and at the risk of causing harm. Our desire to save our patients, combined with a lack of effective treatments, distracted us from evidence-based medicine and the principle of “do no harm” and “less is more” (Zagury-Orly and Schwartzstein 2020; Rice and Janz 2020). This generated fear-driven reactions (contempt, blame, disappointment) which are worsening an already very complex situation.

- The discrepancy of the recommendations on protective measures for health workers and the shortage of personal protective equipment with its reported consequences: contamination and death among doctors and nurses in China, Italy and Spain have also increased our anxiety and fear of contagion.

This whole cascade of factors affected our stressability (internal reaction to stress) which reached a critical threshold causing our brain to switch from intentional conscious functioning, where results determine our actions and vice versa (learning loop) to an automatic functioning where the funeral context, audiovisual stimuli and ignorance determine the action.

At the outset of the pandemic, all these factors led for a short time to a medicine based on fear and emotional stress rather than clinical intelligence. It was invasive and degraded: less contact with patients, less auscultation, less chest X-ray, less transport to CT scan, no aerosol-generating procedures (administration of nebulised treatment, non-invasive ventilation, high flow oxygen therapy, and bronchoscopy). All of this might have contributed to the initial high mortality rate among critical

care patients exceeding 50%, observed in our service and in other centres (Richardson et al. 2020).

Fortunately, we rapidly became aware of these misguided influences, thanks to daily exchange within our medically team about our first experiences with this new disease. In the light of the relevant published data, we realised that COVID-19 was a complex multi-system disease that required our usual comprehensive and scientific approach to critical care. In parallel, we could once again rely on the availability of personal protective equip-

our desire to save our patients, combined with a lack of effective treatments, distracted us from evidence-based medicine and the principle of “do no harm” and “less is more”

ment and we could observe an excellent rate of protection among our staff thanks to the applied measures.

Our collective awareness of the ineffectiveness of our invasive and degraded approach during our first experiences with COVID-19 patients, and the plethora of published scientific data led us to collectively rethink: change tack and go back to reasoned and reasonable medicine based on the endeavours obligation and not of result.

Nevertheless, the result is right on time and it's gratifying. In our ICU, during the first pandemic weeks, mortality dropped down dramatically, from 67% for patients admitted during week 1, to 33% in week 2, and 15% in week 3, leading to an overall mortality during 7 weeks of 22% (12 out of 54 patients).

We can summarise this experience by saying: COVID-19, a hell of an attack on the system!

Conclusion

The COVID-19 pandemic stripped bare our vulnerability when we were ignorant in the face of "an unknown enemy." However, it also brought us back to the essential question: what do we do when we do not know what to do? We mobilise our collective intelligence by sharing our emotions and our experiences, thereby reinforcing our teamwork. ■

Conflict of Interest

The authors report no conflict of interest.

Key Points

- During the COVID-19 pandemic, intensivists could fall prey to cognitive error and unconsciously rely on anecdotal experiences, whether their own or others, instead of scientific evidence.
- In the face of great uncertainty, we believe that intensivists should rely on clinical and collective intelligence as a safeguard mechanism.
- The frantic race for publication should not make us lose sight or critical thinking.
- The media noise on experimental treatments must not pollute the scientific debate.

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Thoughts on COVID-19 from the International Fluid Academy

An overview of what has been published on fluid strategies in COVID-19, guidelines available and reflections on personal practice.

by frontline colleagues in China and Italy, who have had to deal with the pandemic before the other countries were affected, are hugely invaluable. In this paper, we summarise what has been published on fluid strategies in COVID-19, guidelines available and provide some reflections on personal practice. Importantly we ask colleagues to rally around this important issue and review their own practice with regards to fluid therapy.

to hospital later in the illness may be hypovolaemic due to increased losses from fever and tachypnoea. Whilst most cases primarily present with respiratory symptoms, gastrointestinal symptoms such as vomiting and diarrhoea are not uncommon. Hence it is important to take a concise history (paying particular attention to symptom onset), clinically assess the patient and individualise therapy.

In general, a judicious fluid strategy whereby fluid is cautiously administered only after pre-load responsiveness has been assessed as preferable (Silversides, 2019). Given the incidence of myocardial dysfunction in a subset of patients (Zheng, 2020), early use of vasopressors/inotropes alongside regular assessment via echocardiography would be prudent.

Introduction

The global COVID-19 pandemic has sharply focused the attention of the world onto critical care as a specialty. At the moment, there are no proven treatments for COVID-19, although several trials and case series extolling the merits of various agents have been published. As always, good intensive care practice is founded on a strong understanding of physiology and doing the basics well.

Whilst issues such as staffing, resources and ventilation strategies are undoubtedly important when considering a holistic approach to treating COVID-19, fluid management remains a cornerstone of intensive care.

Unsurprisingly, given that it is a novel virus and illness course, published data and guidelines on how best to treat patients with COVID-19 are continually evolving. The experiences and data shared

What do we Know?

There is little doubt that fluid therapy, either too much or too little, can adversely affect patient outcome (Malbrain 2018). As a novel disease, the general principles of fluid management in critical care provides the foundation for fluid therapy in COVID-19, but the shared experiences of colleagues add to and refine this. The goals of resuscitation and management are therefore constantly evolving.

As an example, during the early stages of the COVID-19 pandemic, it was common advice to aim for a negative fluid balance. More recently, a higher than expected occurrence of acute kidney injury requiring renal replacement therapy has been observed, prompting calls for a more liberal fluid strategy.

A particular challenge is the fact that patients are presenting at different stages of their illness. Those that are admitted

What Guidelines are Available?

Several organisations and professional societies have published guidelines on the management of patients with COVID-19. With regards to fluid therapy, the core recommendations stem from the initial Surviving Sepsis Campaign guidelines along with its COVID-19 specific update (Alhazzani et al. 2020). However, no direct evidence exists for patients with COVID-19 and shock, therefore indirect evidence from critically ill patients with sepsis and ARDS was used to formulate these recommendations. A selection of

these guidelines with emphasis on fluid management is summarised below.

Surviving Sepsis Campaign

The Surviving Sepsis Campaign group has suggested the following in their COVID-19 specific guidelines for acute resuscitation of adults with shock:

- Measuring dynamic parameters to assess fluid responsiveness (weak recommendation; low quality of evidence [QE]),
- Using a conservative fluid administration strategy (weak recommendation; very low QE),
- Using crystalloids in preference to colloids (strong recommendation; moderate QE),
- Balanced crystalloids preferred over unbalanced crystalloids (weak recommendation; moderate QE).

As shown, these recommendations are based on low quality evidence.

World Health Organization

World Health Organization guidelines recommend that patients with COVID-19 in respiratory failure should be treated cautiously with intravenous fluids, especially in settings with limited availability of mechanical ventilation.

- Use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion.
- In resuscitation for septic shock in adults, give 250–500 mL crystalloid fluid as a rapid bolus in the first 15–30 minutes and reassess for signs of fluid overload after each bolus.
- If there is no response to fluid loading or if signs of volume overload appear, reduce or discontinue fluid administration.
- Consider dynamic indices of volume responsiveness to guide volume administration beyond initial resuscitation based on local resources and experience. These indices include passive leg

raises, fluid challenges with serial stroke volume measurements, or variations in systolic pressure, pulse pressure, inferior vena cava size, or stroke volume in response to changes in intrathoracic pressure during mechanical ventilation.

- Starches are associated with an increased risk of death and acute kidney injury compared to crystalloids. The effects of gelatins are less clear, but they are more expensive than crystalloids. Hypotonic (vs isotonic) solutions are less effective at increasing intravascular volume. Surviving Sepsis also suggests albumin for resuscitation when patients require substantial amounts of crystalloids, however this conditional recommendation is based on low-quality evidence.

UK Joint Anaesthetic and Intensive Care Guidelines

- Conservative fluid management strategy in ARDS.

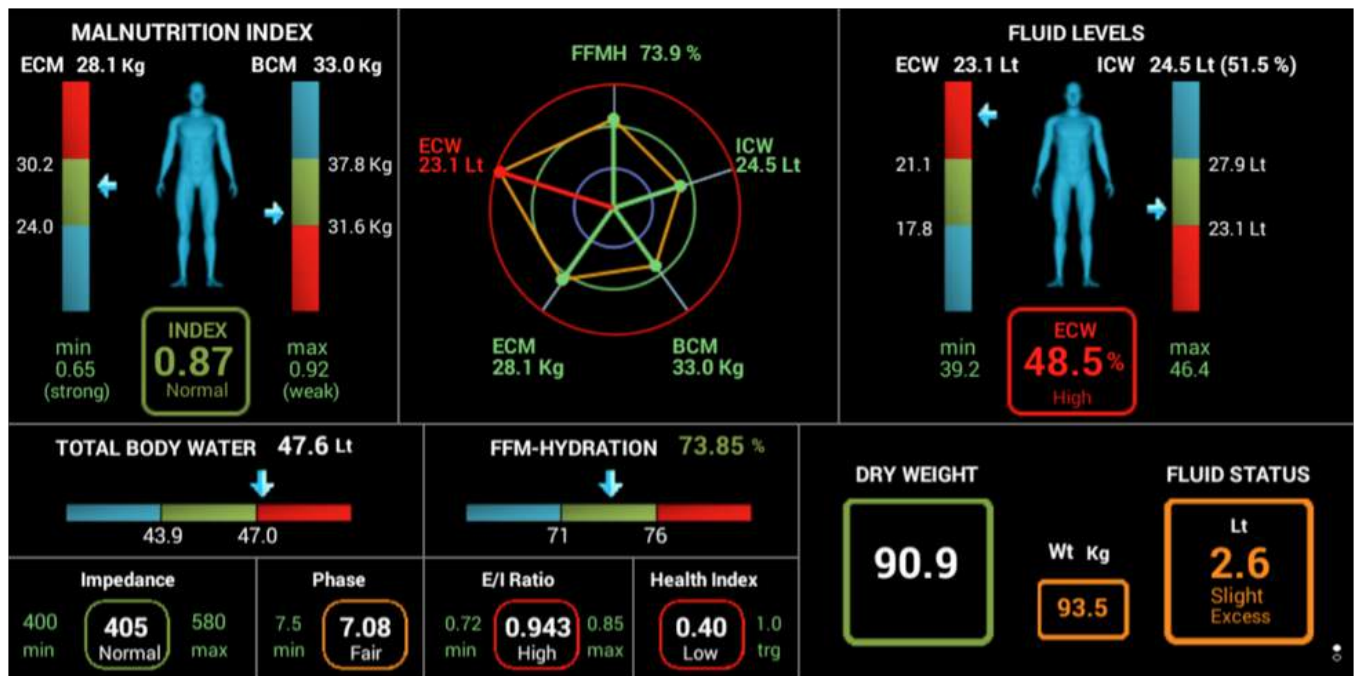


Figure 1. Sample screenshot with results obtained via full body, multifrequency bioelectrical impedance analysis (BIA) with touch i8 device (Maltron, UK) showing a volume excess of 2.6 litres and an increased ECW:ICW ratio of 0.943 indicating capillary leak. The patient’s fluid composition is monitored with BIA separating intra- and extracellular water and estimating the volume excess [Source: Myatchin et al. 2020].

System	Identifiable structures	Measurable parameters	Potential indication in COVID-19
Airway	Tracheal rings Cricothyroid membrane Thyroid cartilage Hyoid bone	Distance to structures Diameter of trachea Presence of oedema or external compression	Plan for difficult intubation and extubation
Thoracic	A-lines B-lines Consolidation Collapse Effusion Diaphragm	Number of B-lines Volume of effusion, depth to effusion Extent of pneumothorax (lung sliding, lung-point) Diaphragmatic function	Assess degree of lung involvement Diagnose any concurrent conditions
Cardiac	Right atrium and ventricle Left atrium and ventricle AV valves Pulmonary valves Aortic valves Inferior vena cava	Size and dimension Valvular pathologies Systolic and diastolic dysfunction Presence of mass/vegetation Regional wall motion abnormalities	Assess cardiovascular function Assess response to therapy e.g. fluid bolus
Abdominal	Free fluid e.g. ascites, blood Aorta Inferior vena cava Gastric content	Size of organs Size of vascular structures Doppler analysis of vascular flow to organs Volume of free fluid, depth to free fluid Calculation of gastric residual volume (GRV) Inferior vena cava collapsibility index (IVVCI)	Assess cause of liver dysfunction Part of haemodynamic assessment
Renal	Kidneys Ureter Bladder	Size of kidneys Doppler analysis of vascular flow to kidneys (renal resistive index) Volume of bladder	Assess cause of renal dysfunction
Vascular	Thrombosis (clot visualisation) Dissection	Doppler analysis of vasculature Compression of veins	Aid vascular catheter placement Diagnose venous thrombosis

Table 1. Potential ultrasonographic assessments

• In cases of significant hypotension or circulatory shock, standard circulatory assessment (fluid responsiveness, cardiac output assessment) and administration of an appropriate fluid and/or pressor

(where appropriate) should occur.

- Balanced electrolyte solutions are preferred to 0.9% saline and colloids.
- While fluid overload should be avoided and more conservative administration

may help improve respiratory function, this should be carefully balanced against the risk of inducing acute renal impairment.

- Care should be exercised in ‘running

4 Questions	4 Indications	4 Ds	4 Stages	4 HITs
When to start IV fluids? When to stop IV fluids? When to start removing fluids? When to stop removing fluids?	Resuscitation Maintenance Replacement Nutrition	Drug Dose Duration De-escalation	Resuscitation Optimisation Stabilisation Evacuation (de-escalation)	1st HIT: initial insult (e.g. COVID with sepsis) 2nd HIT: ischaemia and reperfusion 3rd HIT: fluid accumulation and GIPS (global increased permeability syndrome) 4th HIT: hypoperfusion during de-resuscitation

Table 2. Rules of Fours

patients too dry' in an effort to spare the lungs, as there are increased insensible fluid losses.

Guidance and Recommendations from the International Fluid Academy

The following are some suggestions and best practice recommendations taking into account those mentioned above.

Assessment and monitoring

- The patient's fluid balance is assessed on admission in the hospital and on a daily basis with cumulative fluid balance calculated.
- Assessment of fluid and electrolyte requirement as part of every clinical review using a combination of clinical judgement, vital signs and chart records.
- Recent laboratory results with urea and electrolytes (at least once every 24 hours of fluid prescription).
- The use of cardiac output monitors to assess fluid responsiveness e.g. ultrasound (see below) and bioimpedance monitoring (**Figure 1**).

Resuscitation

- Use balanced crystalloids (e.g. plasmalyte).
- Do not use starch solutions or gelatins.
- Do not use albumin in the early stages.
- For patients in need of fluid resuscitation:

- Identify the cause of fluid deficit.
- Assess for presence of shock or hypoperfusion.
- Assess fluid responsiveness (see further).
- Give a bolus of 4 mL/kg of balanced crystalloids over 10-15 minutes.
- Fluid responsiveness is assessed before

fluid therapy, either too much or too little, can adversely affect patient outcome

- and after fluid administration with functional haemodynamics e.g. pulse pressure variation (PPV) or other tests e.g. passive leg raise test or end-expiratory occlusion test, or a combination.
- Mean arterial pressure and cardiac output are continuously monitored.
 - Early initiation of vasopressors: noradrenaline at low dose 0.05mcg/kg/min.
 - Consider the addition of vasopressin/argipressin when noradrenaline dose exceeds 0.5 mcg/kg/min
 - Assess for the presence of fluid overload (i.e. 10% increase in body weight or volume excess from baseline).
 - Start de-resuscitation whenever

possible.

- Replace serum albumin to approximately 30 g/L with albumin 20%.
- Use combination therapy of diuretics: loop + spironolactone + acetazolamide (when BE > 5) + indapamide (in cases of hypernatraemia).
- Consider ultrafiltration (even in the absence of acute kidney injury) when diuretics fail to achieve zero fluid balance.

Maintenance fluids

- Do not administer maintenance fluids in patients who are eating and drinking sufficiently.
- Use balanced solutions (e.g. Glucion 5% or Maintelyte).
- In patients requiring IV fluids for routine maintenance alone, the initial prescription should be restricted to:
 - 25–30 mL/kg/day (1 mL/kg/hr) of water
 - approximately 1 mmol/kg/day of potassium (K⁺)
 - approximately 1–1.5 mmol/kg/day of sodium (Na⁺)
 - approximately 1 mmol/kg/day of chloride (Cl⁻)
 - approximately 50–100 g/day (1–1.5 g/kg/day) of glucose to limit starvation ketosis
- The amount of fluid intake via other sources should be subtracted from the

basic maintenance need of 1ml/kg/hr e.g. nutrition and fluid creep (see below).

Fluid creep

- All sources of fluids administered need to be detailed: crystalloids, colloids, blood products, enteral and parenteral nutritional products, intravenous medication and oral intake (water, tea, soup, etc.)
- Precise data on the concentrated electrolytes added to these fluids or administered separately need to be documented.
- Fluid creep is defined as the sum of the volumes of these electrolytes, the small volumes to keep venous lines open (saline or glucose 5%) and the total volume used as a vehicle for medication.

The Role of Ultrasound

Although numerous monitoring devices are available to help the clinician formulate management plans, ultrasound ranks as one of the most versatile diagnostic and monitoring tools particularly when applied to fluid therapy. Its portability and therefore ease of use at the bedside is desirable in the presence of strict infection control measures. No other singular device is able to non-invasively evaluate and assess response to therapy for the cardiovascular, respiratory and renal systems. Indeed, critical care ultrasound has always enjoyed the benefit of providing a holistic, integrated approach to patient care, but it is during the COVID-19 pandemic that it has really come into its own.

A non-exhaustive summary of the potential ultrasonographic assessments that can be performed are listed below.

Fluid Stewardship - Knowing What we are Doing

As with antibiotic stewardship, fluid stewardship can improve the quality of

clinical care. Typically, this would involve a stepwise approach in assessing current practice and outcomes - a clear view of current practice will highlight the areas where we are performing well, and those that are lacking, so as to provide a basis for meaningful change (Malbrain 2018). Patients should have an IV fluid management plan, including a fluid and electrolyte prescription over the next 24 hours agreed by the intensive care team, taking into account clinical and laboratory findings, supplemented by the appropriate imaging e.g. ultrasound. These can be summarised by the 'Rules of Fours' in **Table 2**.

Of course, there will be colleagues who argue that trying to collect data on fluid prescription during an international pandemic is pointless or inconvenient. However, we maintain that there are several arguments against this.

Firstly, there has been, undoubtedly, significant change to our clinical practice due to changes in the logistics of critical care delivery. New clinical areas have been added or converted to care for critically ill patients. To staff these new critical care/high-dependency areas, healthcare professionals from outside of critical care are being redeployed, and require training and education. Whilst data collection requires the investment of time and energy, this time of upheaval is all the more reason for accurate documentation and data analysis so as to ensure that various aspects of patient care can be visualised on a larger scale.

Furthermore, we have seldom been more acutely aware of the limitations of medical resources - healthcare professionals, personal protective equipment, machines for mechanical ventilation and haemofiltration, right down to the drugs we consider to be basic essentials in critical care. The understanding of illness processes and patient outcomes, as well as how our interventions affect these, will enable us to streamline and rationalise

our utilisation of precious resources so as to maximise their benefits for our patients whilst avoiding undue harm. This principle is similarly applicable to the experimental use of existing medications in COVID-19 including anti-virals, anti-malarials etc, and is particularly relevant in the case of hydroxychloroquine where stock shortages will likely impact upon the patients requiring this drug for its prescribed usage.

Last but not least, given the extensive spread of COVID-19, there has been a dramatic shift in the patient population in many hospitals, with a preponderance of COVID-19 cases. There is the potential for a multitude of lessons we can learn in a very short space of time, from the management of these patients. These will help us refine our treatment plans for subsequent waves of infection, and could be extrapolated to other epidemics in future.

Ultimately when the pandemic is over, the collection of such data would allow for us to reflect, review and improve on clinical practice.

Conclusion

Fluid administration and management are one of the fundamental practices of intensive care. The principles of good fluid practice are built upon the foundations of a firm understanding of the underlying pathophysiological process. COVID-19 is a novel illness and presents unique challenges not just to clinical practice but the entire healthcare system.

We would argue that the principles of fluid stewardship have never been more important in clinical practice than now. The unique challenges present an opportunity to improve the quality of care delivered not just for the current pandemic but for future ones.

Just because it is difficult, doesn't mean it is not worth the effort. We are dealing with an unprecedented healthcare event in modern times, with mind-boggling

technology and the ability to swiftly disseminate information on our side. Whether we handle it 'the old way' or embrace all the tools and collaborative opportunities available to us may well decide how this pandemic goes down in history. We firmly believe in the latter approach. ■

Conflict of Interest

Manu Malbrain is the founder of the International Fluid Academy. Serene Ho and Adrian Wong are members.

Key Points

- The general principles of fluid management in critical care provides the foundation for fluid therapy in COVID-19.
- During the early stages of the COVID-19 pandemic, it was common advice to aim for a negative fluid balance but more recently there have been calls for a more liberal fluid strategy.
- It is important to take a concise history, clinically assess the patient and individualise therapy.
- Several guidelines have been published on the management of patients with COVID-19 including the Surviving Sepsis Campaign Group Guidelines, the WHO and the UK Joint Anaesthetic and Intensive Care Guidelines.
- Ultrasound ranks as one of the most versatile diagnostic and monitoring tools particularly when applied to fluid therapy.
- As we continue to learn, we can refine our treatment plans for subsequent waves of infection, which could be extrapolated to other epidemics in future.

About the IFA

The International Fluid Academy was founded in 2011 with the goals to foster education and promote research on fluid management and monitoring in critically ill patients, and thereby improve the survival of critically ill patients by bringing together physicians, nurses, and others from a variety of clinical disciplines. It aimed to improve and standardise care and outcome of critically ill patients with an emphasis on fluids, fluid management, monitoring and organ support by collaborative research projects, surveys, guideline development, joint data registration and international exchange of health care workers and researchers. We invite the reader to follow @Fluid_Academy and to check this website (www.fluidacademy.org) for more information on fluid management and haemodynamic monitoring (under FOAM resources).

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COVID-19: Overview of Nurse Assessment

Managing COVID-19 patients in south of Switzerland with lung ultrasound for the evaluation of SARS-CoV-2 infection.

Everything started at the beginning of March 2020. In one week, we went from eight to forty-five beds due to COVID-19 patients.

The pandemic virus in place has been scientifically called SARS-CoV-2:

- SARS stands for Severe Acute Respiratory Syndrome
- Co means Corona
- V means virus
- 2 because it is a variant of SARS-CoV (the virus responsible for SARS).

COVID-19 refers to the disease that can develop in patients infected with the SARS-CoV-2 virus, therefore it presents symptoms that can lead to acute interstitial pneumonia with severe respiratory failure, which is why we end up in intensive care. In the case of asymptomatic patients we can say they are SARS-CoV-2 infected, and in the case of sick patients, we can classify them as patients with COVID-19.

What We Know From First Autopsies in China

The macroscopic features of COVID-19 present in the thorax can include pleurisy, pericarditis, pulmonary consolidation and pulmonary oedema (Shi et al. 2020) (Figure 2). Lung weight may be higher than normal. It should be noted that a secondary infection can be superimposed on the viral infection which can lead to purulent inflammation more typical of bacterial infection generating oedema,

pneumocytic hyperplasia, focal inflammation and formation of giant multinucleated cells probably formed by groupings of histiocytes (Osborn 2020).

Our patients have severe hypoxaemia associated with compliance of the respiratory system higher than normally seen in cases of severe ARDS (Guidance-document-SARS-COVID19):

- Early intubation because they react poorly to non-invasive ventilation and intubation would be delayed.
- From these first experiences, the COVID-19 patient reacts well to 16-18 hour pronation cycles, and in some cases, 24 hours (Sud et al. 2010).
- Better if in controlled ventilation 4-8 ml/kg; at the moment VGRP seems the best solution with plateau under 30 cm/H₂O.
- FiO₂ high
- Low Driving Pressure (≤ 15) compared to high PEEP between 12 and 15 (Liu et al. 2020)
- Closed endotracheal suctioning for safety on contamination (Ling et al. 2020).
- HME seems to be enough but managing secretions is better with an active and heated humidifier (HH) (Cerpa et al. 2015). For invasive setting see schema in **Figure 1**.

In accordance with the AARC Clinical Practice Guideline Humidification During Invasive and Non-invasive Mechanical

Ventilation, I've made a clinical practice bedside assessment. We have the theoretical principles of HH in literature, but not how to set it in practice.

The first publications in this period of the pandemic suggest that patients with confirmed COVID-19 pneumonia demonstrate typical lung imaging (CT) characteristics with frosted glass lesions and consolidations that are located peripherally, bilaterally and primarily at the lung bases.

At this moment lung ultrasound gives similar results to chest CT for evaluation of pneumonia in adult respiratory distress syndrome (ARDS) with the added advantage of ease of use at point of care, repeatability, and low cost (Buonsenso et al. 2020; Blaivas 2012).

In this report, I would like to summarise my experience of how to manage COVID-19 patients in south of Switzerland, with lung ultrasound for the evaluation of SARS-CoV-2 infection. I performed lung ultrasound on 25 ventilated patients using a 12-zone method, 4 windows in supine and 2 windows in prone position on both lung (Doerschug and Schmidt 2013) (**Figure 4**).

In these patients I highlighted:

- B lines spread lower lobes, few in the middle and none in the apical (**Figure 3**).
- A discontinuous, jagged and thickening aspect of the pleural line.
- Focal consolidation and atelectasis found mainly in the posterior lung

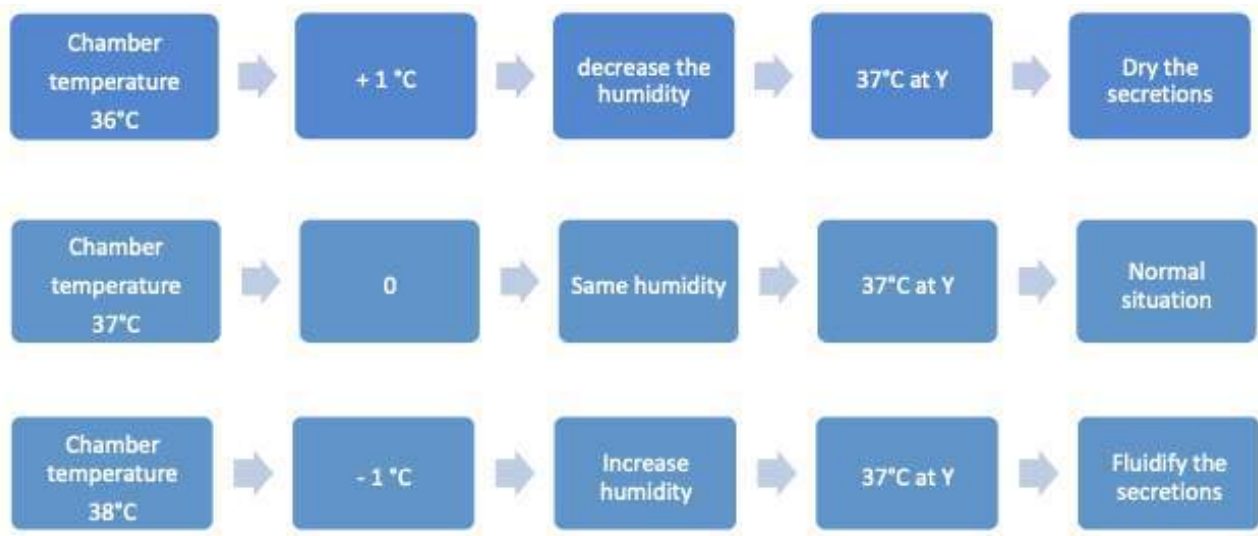


Figure 1. Invasive setting schema. Source Nicole 2020; Restrepo and Walsh 2012.

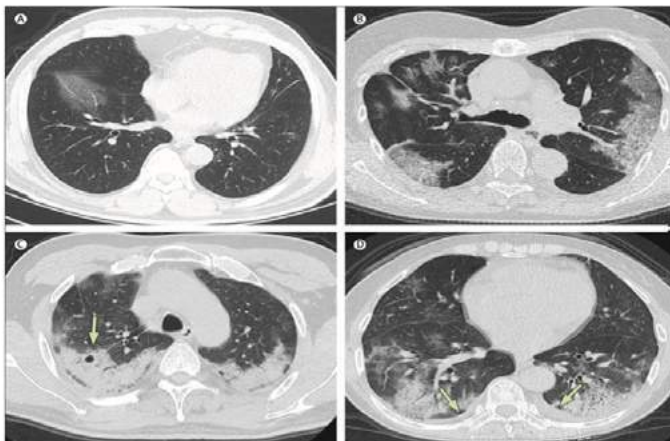


Figure 2: Transverse thin-section CT scans in patients with COVID-19 pneumonia. (A) 50-year-old man, day 3 after symptom onset: focal ground-glass opacity associated with smooth interlobular and intralobular septal thickening in the right lower lobes. (B) 24-year-old woman, day 10 after symptom onset: bilateral peripheral ground-glass opacity associated with smooth interlobular and intralobular septal thickening (creaky paving pattern). (C) 61-year-old woman, day 20 after symptom onset: bilateral and peripheral predominant consolidation pattern with a round cystic change internally (arrow). (D) 63-year-old woman, day 17 after symptom onset: bilateral, peripheral mixed pattern associated with air bronchograms in both lower and upper lobes, with a small amount of pleural effusion (arrows).

Figure 2. CT scans in patients with COVID-19 pneumonia. Source: Shie et al. 2020.

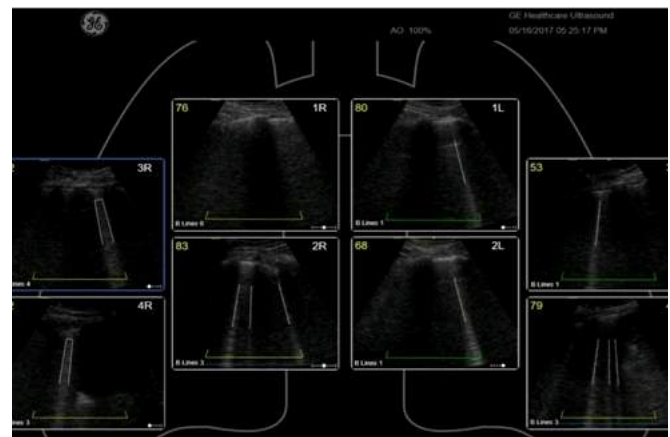


Figure 3. Pattern of distribution on B-Lines. Source: Noon 2020.

fields (paravertebral in prone position examination), in particular in the lower pulmonary fields and here we can deduce how much early pronation can help us. Speaking about PEEP, I would like to present my personal experience. I have come to understand that we have to keep a precarious balance between ventilation with high PEEP for oxygenation and a euvoemia in order not to compromise the heart pump and the kidneys.

To maintain best and protective ventilation, we have to perform PEEP based on

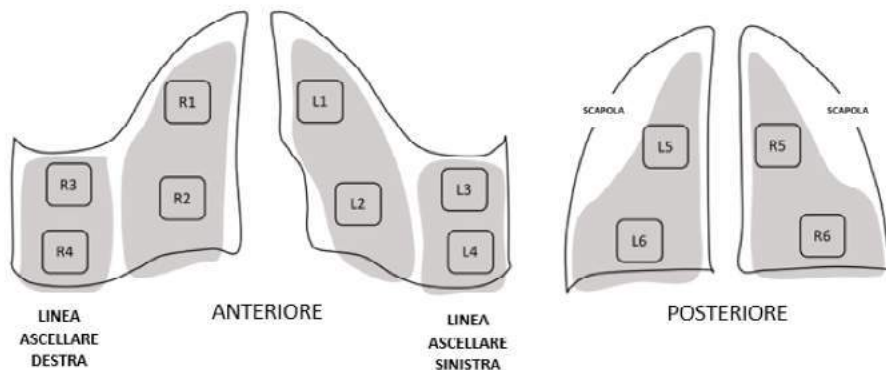
compliance. In these cases we assessed the driving pressure (the difference between plateau pressure and total PEEP keeping it below 16 cm/H₂O) maintaining a constant tidal volume (6 ml/kg) at different levels of PEEP: the level of PEEP that is associated with the lower driving pressure corresponds to the PEEP which determines the best compliance (obtained by dividing the current volume by the driving pressure) during the delivery of the current volume, is the best PEEP (Pintado et al. 2013).

In the first 7-10 pronation cycles, the

patients responded well to this assessment but gradually these measurers did not give the desired results. On an ultrasound level, I noticed that there was a substantial difference between the two lungs; the less affected one went into overdistention while the other tended to collab. At this point we proceeded positioning patients on the side or in semi-prone. This led to a substantial drop in plateau pressures and driving pressure. This was confirmed with the bedside use of the ultrasound.

Now that the lung has reopened (**Figure**

ECOGRAFIA POLMONARE – COVID-19



Effettua la scansione di ogni regione prendendo un'immagine da ogni area che rappresenta al meglio la patologia pertinente. Laddove un paziente non può essere pronato ed è supino, le immagini sulla linea ascellare posteriore possono sostituire le vere immagini posteriori.

DESTRA	DESCRIZIONE	SINISTRA	DESCRIZIONE
R1	Apice superiore destro	L1	Apice superiore sinistro
R2	Lobo medio destro	L2	Lobo medio sinistro
R3	Linea ascellare superiore destra	L3	Linea ascellare superiore sinistra
R4	Linea ascellare inferiore destra	L4	Linea ascellare inferiore sinistra
R5	Posteriore superiore destro	L5	Posteriore superiore sinistro
R6	Posteriore inferiore destro	L6	Posteriore inferiore sinistro

Legenda

Linee B	B0	<3 per immagine	/ normale
	B+	3-7 per spazio intercostale	/ blando
	B++	>7 per spazio intercostale	/ moderato
	B+++	Linee B confluenti	/ severo
Distribuzione Linee B	Descrivi come focale, multifocale o diffuso all'interno di quella regione		
Consolidamento	C0	Nessuno	
	C+	Linea pleurica irregolare, sottile consolidamento subpleurico	
	C++	Piccole aree di consolidamento (<1 cm di profondità)	
	C+++	Vaste aree di consolidamento	
Versamento	Descrivere includendo la profondità massima dalla parete toracica al polmone o dal diaframma al polmone		

COMMENTI

INFERMIERE: _____ DATA: _____

Figure 4. Lung Ultrasound in COVID-19. Source: Ripper 2020. Revised and translated by Nicole C.

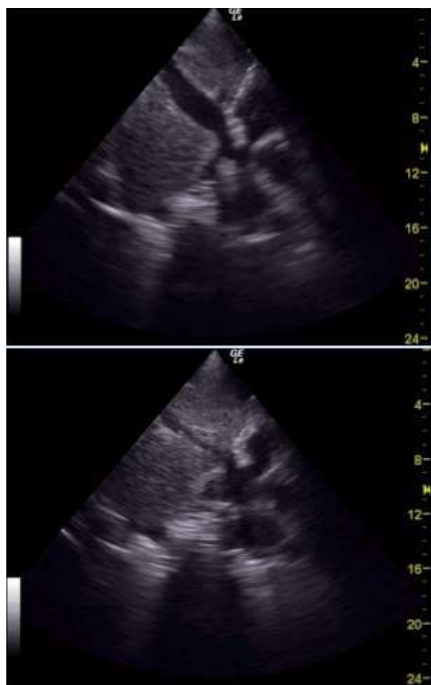


Figure 6. B-Mode: Subcostal Window/Inferior Vena Cava (IVC) before fluid filling



Figure 7. M-Mode: Subcostal Window/Inferior Vena Cava (IVC) after fluid filling

5a and 5b), I would like to go for a heart echography to evaluate contractility and filling. What can I expect to find in a 4-day hospitalised patient with high oxygen support admitted to the ICU? The patient doesn't have to eat and drink much, increased respiratory rate leads to a greater dispersion of water and if we add fever, the cardiac picture is still detected (Figure 6).

After a mild volume filling of 500 ml the picture has substantially changed (Figure 7).

When the patient is in prone position, can I still do the heart echography to assess contractility? The answer is

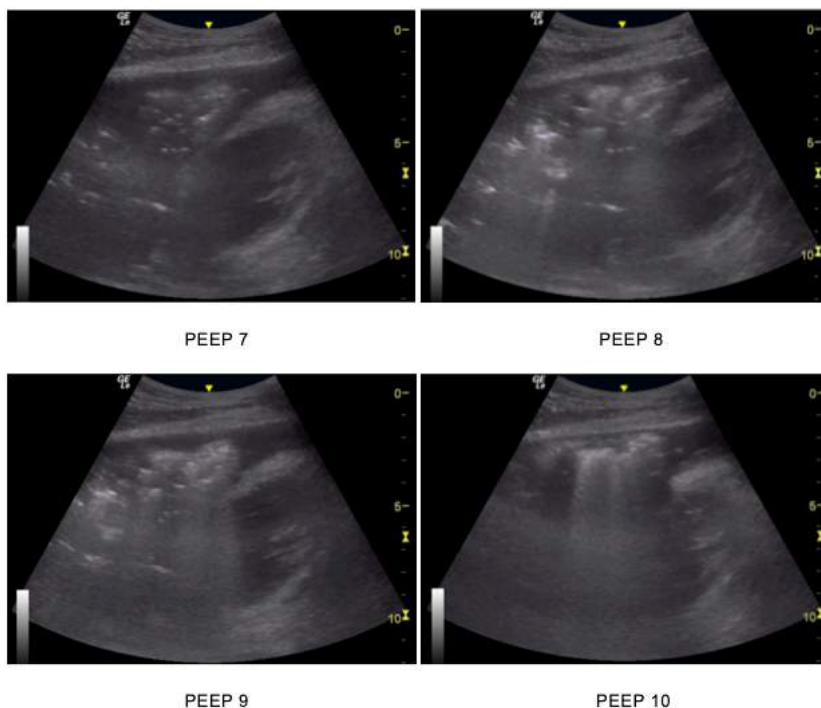


Figure 5a. Ultrasound PEEP assessment

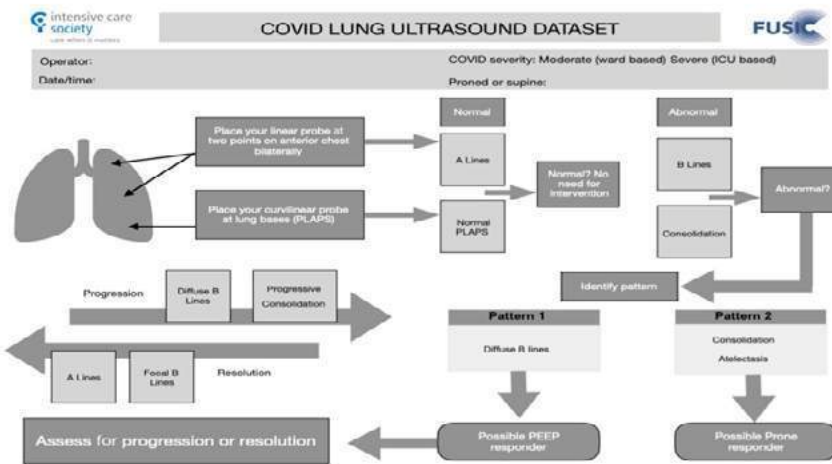


Figure 5b. COVID LUS dataset

yes! How? The patient must be in the swimmer's position with the left arm upwards. Operator positioned on the left of the patient, raise his left shoulder with a pillow forming a space to position the transducer. The ultrasound in a prone position offers all the apical views (2 and 4 rooms) and the relative measures, but no other acoustic window (Ugalde et al. 2018).

An American colleague sent me a

practical sheet to be used for the daily assessment which at the moment seems highly recommendable.

Conclusion

Most Clinical Nurses Specialist work directly with patients and develop effective health care techniques based on clinical evidence, solving complex problems, and educating nurses. Our professional figures work closely with doctor and nursing administrators,

and especially head nurses to improve the quality of care. Head nurses set goals, monitor important outcomes, and evaluate initiatives. This approach can improve new strategy and take nursing skills to a higher level. In this situation, nurses were able to put together different concepts, bringing an increased of quality care. For years, I have supported ultrasound as a complementary approach to constant patient evaluation and during this healthcare crisis more than ever it has helped to treat our ICU patients in the best possible way. ■

Ethics Approval

Images are entirely unidentifiable and there are no details on individuals reported within the manuscript. Consent for publication of images is not required and is Swissethics approved.

Conflict of Interest

The author declares no competing interests.

Funding/ Authorship Credit

The author is an active member of Winfocus, teacher of nursing ultrasound. No fee received for work.

Acknowledgements

The author is grateful to Michael Blaivas, MD for the availability and support. Thanks to the work and for strategy developing to all Winfocus members. I'm grateful to be a member of The Society of Critical Care Medicine (SCCM) and for their resources. I would like also to thank Barca Romina for language services.

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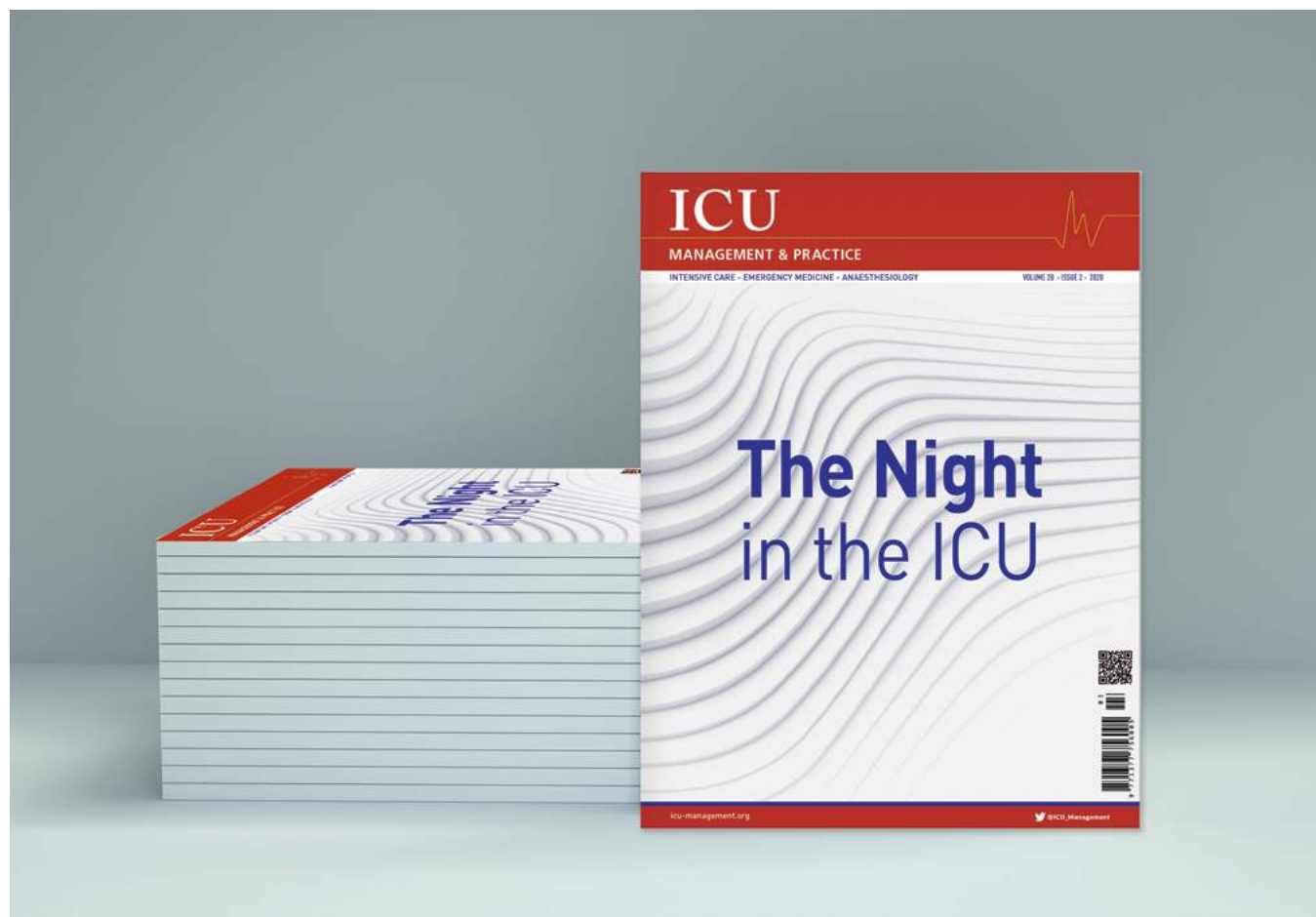
For full references please email editorial@icu-management.org or visit <https://jii.hm/1333>

COVER STORY: THE NIGHT IN THE ICU

What is it like during the night in the intensive care unit? In this issue, we discuss the role of the night-staff in the ICU, question whether intensivists should be present in the ICU around the clock, and talk about the overall ICU environment at night and how doctors, nurses, patients, and their families feel about it, consequences of noise in the ICU and strategies to reduce it, and how staff and patients deal with life-threatening emergencies.

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Feasibility and Potential Benefits of Immersive Virtual Reality in the Intensive Care Unit

Virtual reality (VR) is a developing technology with much current interest in its potential to improve patient outcome in a variety of clinical settings. Critically ill patients, their relatives and intensive care unit (ICU) staff are all at high risk of stress and anxiety and patients often experience pain. This study explores the potential benefits of virtual reality for stress, anxiety and pain management in the ICU.

Background

Patients in Intensive Care Units (ICU) often experience low mood, anxiety and fear (Choi et al. 2016). Stress factors include sensory overload and deprivation, isolation, temporal disorientation and a feeling of lack of control (Gerber et al. 2019). These symptoms are often a result of feeling vulnerable, lacking in stimulation and/or from an inability to relax and sleep (Ding et al. 2017). Anxiety also detrimentally affects perceived levels of pain and motivation for physical rehabilitation (Dubb et al. 2016).

Family members also experience depression, anxiety and fatigue during a relative's ICU admission (Day et al. 2013; Bolosi et al. 2018), and ICU staff report anxiety, stress and burnout (Colville et al. 2017).

Immersive virtual reality is well established in the gaming industry and is starting to be used more widely in education. There is now a lot of interest in its potential to improve patient outcomes in a variety of clinical settings. It is increasingly being used in rehabilitation (Llorens et al. 2015) and in the assessment, understanding and treatment of mental health disorders (Freeman et al. 2017).

Given that our critical care patients,

Inclusion criteria	Exclusion criteria
<p>Patient, relative or member of critical care staff</p> <p>Ability to provide informed consent</p>	<p>Inability to provide informed consent</p> <p>Major visual or hearing impairment rendering use of the VR equipment futile</p> <p>Head or facial injury or abnormality such that the VR goggles and earphones are unable to fit properly or safely</p> <p>Epilepsy</p> <p>History of motion sickness</p>

Table 1. Inclusion and exclusion criteria for virtual reality study.

their relatives and staff are all at high risk of stress, anxiety and depression and the patients often experience pain, we were particularly interested in exploring the potential benefits of virtual reality for stress, anxiety and pain management.

This pilot study aimed to assess the feasibility and potential effectiveness of virtual reality distraction therapy in the critical care environment for patients, staff and patient relatives.

Method

Ethical approval for the study was given by the West of Scotland Research Ethics Service (19/WS/0102) on 2nd August 2019 and by HRA and Health and Care

Research Wales on 14th August 2019 (IRAS ID 264717). Critical care patients, their relatives and staff members were approached by a member of the research team and invited to participate in the study. They were shown the equipment, given a detailed information sheet explaining the study, time to think about it and the opportunity to ask questions. See **Table 1** for list of inclusion and exclusion criteria.

After informed consent, participants were asked to complete a brief questionnaire about their mood, anxiety levels and pain score using visual analogue scales (VAS) (**Figure 1**). They then chose their virtual reality experience from a selection of documentary-style or guided relaxation-

VR experiences offered
Wildlife
Around the World
Cities
Underwater
Relaxation
Space
Guided breathing exercises in a variety of different peaceful surroundings.

Table 2. List of virtual reality experiences offered.


	Whole Cohort			
	Pre-VR	Post-VR	Mean change	P value
Mood	6.3	8.68	2.38	<0.0001
Anxiety	4.27	2.2	-2.07	<0.0001
Pain	2.84	1.99	-0.85	<0.0001

Table 3.1 Summary of VAS results pre- and post-VR intervention.

BEFORE THE VIRTUAL REALITY EXPERIENCE


Question 1
 Draw a circle around the face and number that best describes how you feel at the moment. 1 means very bad and 10 means fantastic.

1 2 3 4 5 6 7 8 9 10



Question 2
 Draw a circle around the face and number that best describes how worried/anxious you feel at the moment. 1 means not worried/anxious at all and 10 means extremely worried/anxious.

1 2 3 4 5 6 7 8 9 10



Question 3
 Draw a circle around the face and number that best describes how much pain you have at the moment? 1 means you have no pain at all and 10 means you have the worse pain ever.

1 2 3 4 5 6 7 8 9 10




Figure 1. Pre-VR experience Questionnaire



Figure 2. Examples of virtual reality scenes

experiences. See **Table 2** for list of experiences offered and **Figure 2** for examples of patient view during experiences.

We used the DR.VR™ system; a PICO VR headset and noise cancelling headphones. This is operated using DR.VR™ closed system which allows a Samsung tablet to control the VR. The system was designed and provided by Rescape Innovation (**Figure 3**).

The headset is made of hard plastic, which can be wiped clean with sporicidal wipes used to clean equipment in intensive care, and a soft cushioned part in contact with the user's face. Disposable sanitary masks were worn to prevent skin contact with this soft material during each use. The programmed experiences were created to appeal to a wide demographic and were

produced in 4K with a static 3600 camera to reduce the risk of motion sickness. All experiences were between 7 and 10 minutes in duration. If the participant enjoyed the experience and requested further uses, this was permitted.

After the VR experience(s), the participant was asked to complete a further brief questionnaire to assess their mood, anxiety

	Staff				Patients				Relatives			
	Pre-VR	Post-VR	Mean change	P value	Pre-VR	Post-VR	Mean change	P value	Pre-VR	Post-VR	Mean change	P value
Mood	7.19	9.16	1.97	<0.0001	5.97	8.46	2.09	<0.0001	5.07	8.14	3.86	<0.0001
Anxiety	3	1.5	-1.5	<0.0001	4.91	2.83	-1.87	<0.0001	5.57	2.21	-3.43	<0.0001
Pain	1.4	1.19	-0.22	0.02	4.23	2.91	-1.48	0.001	2.64	1.5	-0.71	0.27

Table 3.2. More detailed summary of VAS results pre- and post-VR intervention.

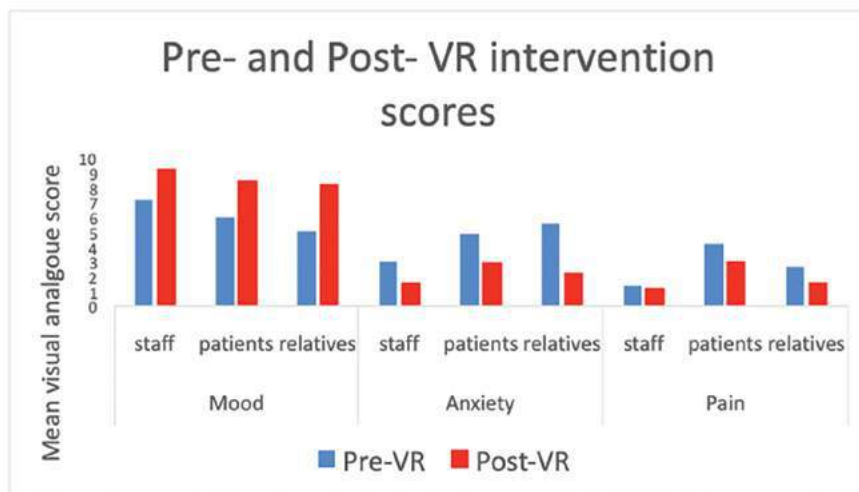


Figure 4. Graphical representation of VAS results pre- and post-VR intervention.



Figure 3. Virtual reality equipment used.

and pain scores again. On this questionnaire there was the opportunity to write free-text feedback if desired.

Mood, anxiety and pain scores were put into Microsoft Excel and SPSS and free-text feedback was transcribed into a Microsoft Word document and then analysed by both authors for emerging themes.

Results

In total we had 80 separate uses of VR from 72 participants. Usage by cohort: 32 staff members; 34 patient uses and 14 patient relatives. More than one VR experience on the same occasion was counted as one use. VR experiences on different occasions were regarded as separate uses. Seven patients chose to use the VR on more than one

occasion. One patient felt nauseated before starting his VR experience, felt worse on application of the headset (within the first few seconds of use) so abandoned the experience and did not complete the post-experience questionnaire. Therefore we analysed data from 79 VR uses. There were two further reports of mild motion sickness, not sufficient to want to stop the VR experience. No other negative effects were reported and all other users completed one or more VR experience. There were no issues with fitting the headset on patients receiving oxygen via facemask, nasal cannulae, or with an endotracheal tube or tracheostomy tube. There was no interference between the VR kit and any other electrical equipment surrounding

the patient. The compact case containing the VR equipment was placed on a chair or table at the bedside. See **Table 3** and **Figure 4** for summary of VAS results pre- and post-VR intervention.

Most of the differences in VAS scores pre- and post-VR intervention were normally distributed and were analysed using paired t-tests. Only change in pain scores for staff and relatives were non-normally distributed and were analysed using Wilcoxon signed-rank test. For the whole cohort of users mean improvement in mood score was 2.38 points; anxiety score 2.07 and pain score 0.85. All three parameters had p values <0.0001. The change in VAS scores pre- and post-VR intervention was statistically significant ($p < 0.05$) for all

Theme	Example Statements	User
Positivity	"The virtual reality made me feel as if I didn't have a care in the world."	Member of staff
	"Wow I have never in my life seen anything like this. I was bored and down a little but when I went on this I have never in my life seen anything like it. Fantastic is too small a word."	Patient
	"I'd like to get one for myself! Fun and educational."	Patient
	"That was fab, Took me away from my stress for 10 minutes. Want to do it again please."	Patient
	"I really enjoyed finding out about the animals and getting up close and personal with the elephant, lion and polar bear. It definitely distracted me from the world outside for the duration of the experience."	Patient
Relaxation	"I have thoroughly enjoyed my virtual reality experience. After using it I now feel calm, peaceful and grounded."	Staff member
	"I felt relaxation flowing all around me. Any problems I currently face did not surface."	Patient
	"I feel that it helps take away the tension and stress."	Relative
	"It was very relaxing. The pictures were lovely and made you feel as though you were there."	Staff member
	"A wonderful experience, very calming."	Patient
Escape	"Just for 5 minutes it took me away from the ward environment and made me smile and forget my problems."	Patient
	"I think it takes you out from what is going on around you. It gives you that break from hospital and the ward."	Relative
	"Helped me to forget distressing memories."	Staff member
	"I felt transported away from the hospital environment for 8 minutes and re-energised to start work."	Staff member
Would recommend for others	"I can see how this would improve the patient experience in critical care by transporting them out of a distressing reality."	Staff member
	"An essential piece of kit for ICU."	Patient
	"Very beneficial considering how intense the ICU can be. This tool would most definitely benefit both patients and the family/friends."	Relative
	"Would highly recommend."	Patient
	"I believe it will help a patient a lot, for a few minutes it can take them away from reality being on the ward. It can take their mind away on holiday exploring for a few minutes some different worlds."	Patient

Table 4. Examples of user feedback themes after VR experience

Negative Statements	User
"Felt like the mask pressed down on my nose. Good experience, Relaxing."	Member of staff.
"Cities experience, needed to be stood to gain full experience. Gave the impression of being there." Smiley face drawn on feedback form.	Member of staff.
"Very enjoyable experience however nausea after a while (usually suffer with motion sickness)."	Member of staff.
"Thoroughly enjoyed. Pain increased when looking directly down but if lying or standing, I think this would be fine – stomach surgery. Great tool."	Patient

Table 5. Negative feedback after VR experience.

parameters except pain scores in patient relatives (p 0.27).

Perhaps unsurprisingly, patients had higher pain scores than staff or relatives, and also had the biggest improvement in pain scores (mean change of 1.48 points on a 10-point scale versus 0.22 and 0.71 points respectively for staff and relatives). Interestingly, of the 12 patients with higher pain scores (6 out of 10 or greater), all but one (92%) reported an improvement in pain score after VR, and the mean change was 3.41 points. Patient relatives had the lowest mood scores and the highest anxiety, higher than the critically ill patients themselves. This group also reported the biggest improvements in mood and anxiety scores after VR.

Qualitative Feedback

The majority of users (86%) took the opportunity to give extra feedback and this was overwhelmingly positive. 28/32 staff, 31/33 patients and 9/14 relatives chose to give additional feedback. Feedback was transcribed verbatim and analysed for common themes by highlighting frequently used words and sentences and classifying them into groups. Four main themes emerged:

1. Positive experience (48 statements).

Assigned when there was a sentence stating that the user enjoyed the experience, or words such as "great" "fantastic" or fabulous" were used.

2. Relaxation (30 statements). When words such as "calm" "relaxed" were used, or sentences mentioning reduction of stress or tension.

3. Escape (18 statements). When users reported feeling like they had left the room and gone elsewhere or forgotten their worries.

4. Recommendation (13 statements). When comments were made suggesting the VR would be useful for others. Some feedback fitted into two themes, for example:

- **Positivity/relaxation:** "I really enjoy the VR. It put me at ease and made me feel relaxed." (Patient)
- **Recommendation/escape:** "I would recommend the VR experience as it can transport you from your surroundings and distract patients from their situations allowing medical staff opportunities to carry out procedures." (Patient)
- **Relaxation/recommendation:** "I feel completely relaxed and wish I was still 'there.' As a member of staff I can defi-

nately see the advantage of using this technology to calm patients and distract them. It's amazing!" (Staff member). Of 113 total statements, 4 (3.5%) were coded as negative. These comments were usually written along with positive comments (**Table 5**).

Discussion

There is increasing interest in using virtual reality for a variety of medical conditions, but so far, very limited experience with hospital inpatients and even less in the intensive care setting. We wanted to explore the safety, feasibility and acceptability of using this technology in the intensive care unit, and whether it may have any benefits for three groups of users: critical care staff; patients and relatives.

We found that VR is safe, feasible and acceptable to all of these three groups, and visual analogue scales demonstrated mean improvements in all three parameters measured.

Mosadeghi et al. (2016) explored the feasibility of immersive virtual reality in 28 hospitalised patients and found that 86% reported a positive experience, 7% neutral and 7% negative. Only 50% found the device comfortable to use, with complaints including that it was too heavy, hard to fit, uncomfortable and difficult to focus. The headset used in this study was a Samsung Gear VR which is an older version. Pain and anxiety were not measured but on questioning, 75% of patients believed VR could improve pain by means of distraction and 43% thought it could change anxiety level. This is in contrast to our study where only one person (a staff member) found the facemask uncomfortable. However, we had similarly positive feedback rates (96.5%).

Gerber et al. (2019) performed a feasibility study to investigate the acceptability, comfort and recollection of immersive nature-related VR stimulation for 33 cardiac surgery patients prior their ICU admission, during their stay and 3 months after discharge. They found that VR stimulation

was considered pleasant, immersive and easy to use. They noted a reduction in respiratory rate during the VR session which was interpreted as a sign of relaxation, which again fits with our self-reported effect of relaxation and reduced anxiety in our ITU patients.

Mood and Anxiety

Our findings showed a measurable improvement in self-reported mood scores in all three groups. The biggest change in score of 3.86 out of 10 was seen in patient relatives, who reported the lowest pre-intervention mood rating, although all changes in mood with VR were statistically significant.

Patient relatives were also the most anxious of the three groups, followed by patients, then staff. This was interesting, as we all assume critically ill patients to be highly anxious about their condition, ongoing treatment and prognosis. However, their families are going through the experience as well, with the fear and frustration of not being able to do much to help. This group reported the greatest change in anxiety level (mean score of 5.57 to 2.21 out of 10) with VR. This is important, as post traumatic stress disorder, complicated grief, anxiety and depression are well recognised in family members of critically ill patients with reported rates of between 14 and 82% depending on the diagnostic tool used and the timing of assessment (Petinec et al. 2016).

If there is a simple intervention such as VR, that could potentially ameliorate these feelings of anxiety, low mood and helplessness, it could make a significant difference to the quality of life of these families. It would be easy to have a couple of VR headsets, along with instructions for their use, available in the relatives' waiting room for use at their own discretion.

Equally, the patients themselves reported improvements in mood and anxiety after using VR. As we already know patients are at high risk of anxiety, depression and PTSD after critical illness (Burki 2019), this

simple, non-pharmacological intervention is worth offering if there is a chance it may improve psychological outcomes.

Staff members had the highest mean mood scores and lowest anxiety scores. However, some staff members reported high anxiety and low mood. In the nine staff members reporting anxiety scores of 5 out of 10 or higher, the mean improvement in

virtual reality has the potential to reduce the risk of long term psychological sequelae of critical illness in patients and their relatives and reduce the risk of stress and burnout in ICU staff

anxiety score was 3.3 points out of 10. Staff members also frequently commented on feelings of escape, relaxation and forgetting their worries. Intensive care is well known to be a specialty with a high risk of burnout (Brindley 2017) and anything that could help reduce this risk is worth exploring, for the benefit of staff and patients.

The effect of VR on mood and anxiety may partly be explained by the feeling of being removed from an unpleasant and overwhelming reality and immersed in a "soothing, comforting environment" (Beaucote et al. 2019). All the VR experiences in our study were set outside and it has been suggested that being outside in nature has a restorative effect (Berto 2014). It may be that this effect also holds true for exploring nature in VR.

Pain

The improvement in patients' reported pain after VR, particularly for those patients with higher pain scores (3.41 points of out 10) was remarkable and is comparable with

opioid analgesics. This has been noted in other studies in different patient cohorts including hospitalised patients with pain scores >3/10 from any cause (Tashjian 2017), during repeated burns dressing changes (Faber et al. 2010; Hoffman et al. 2019) and during dental procedures (Wiederhold et al. 2014).

It is well-recognised that psychological factors, including fear, anxiety or depression can amplify the subjective experience of pain (Hoffman et al. 2019). Hoffman et al. (1998) proposed that VR is "attention grabbing," reducing the amount of attentional resources the brain has available for pain perception. Hoffman et al. (2007) used functional magnetic resonance imaging to demonstrate that VR reduced pain-related brain activity. The degree of pain reduction from VR was comparable to that from a moderate dose of hydromorphone, and when VR was combined with opioids, larger reductions in pain were seen.

This study has some important limitations. As it was a pilot feasibility trial we were unable to perform an initial power calculation to ensure an appropriate sample size and there was no randomisation and no control group for comparison. Our study findings can now be used as a basis for future randomised controlled studies exploring the use of VR for specific purposes such as pain relief and anxiety management. All outcomes were user-reported and therefore subjective and there were no objective measurements. However, several nursing staff anecdotally reported observing reductions in patients' heart rates and respiratory rates whilst using the VR. Additionally, mood, anxiety and pain measurements are usually subjective ("pain is what the patient says it is") and the pain visual analogue scale is widely used throughout hospitals to assess pain and the effect of analgesics.

Another limitation is that because this was a clinical trial requiring informed consent to participate, it excluded patients with delirium. It would be interesting to

explore the use of virtual reality in this population who have significantly increased mortality with no treatment yet shown to be truly effective.

Conclusion

We have shown that immersive virtual reality is safe, acceptable and feasible to use in the critical care unit with significant benefits to patients, their relatives and staff members in terms of mood, anxiety and pain management. Feedback was overwhelmingly positive with 100% of users reporting an improvement in at least one of the modalities measured and every free-text feedback containing at least one positive statement. Future randomised trials should focus on timing and frequency of virtual reality sessions for specific purposes. For example, physical rehabilitation, weaning from ventilatory support, during procedures such as line insertion and dressing

changes and prevention and management of anxiety, PTSD and burnout. Objective measurements such as heart rate variability and skin conductance could be incorporated into some of these studies to observe whether there is correlation with the self-reported data. ■

Acknowledgements

The authors wish to thank Rescape Innovation for lending us the DR.VR™ kit and their technical support free of charge for the duration of the trial; Professor John Geen, Mrs Rebecca Brooks, Miss Keri Turner and Mrs Leanne Jones from Cwm Taf Morgannwg Research and Development team for acting as study sponsor, help with protocol development and ethical approval and data collection respectively; and Dr Tim Gibbs and Dr Peter Dorrington for statistical advice.

Conflicts of Interest

None to declare.

Key Points

- A study explored the potential benefits of virtual reality for stress, anxiety and pain management in the ICU.
- Critical care unit patients, staff and relatives were asked to complete a visual analogue scale (VAS) questionnaire on mood, anxiety and pain before and after a virtual reality experience.
- 100% of users reported an improvement in at least one of the modalities measured and every free-text feedback contained at least one positive statement.
- 92% of patients with higher pain scores reported improvement in pain after VR.
- Changes in mood, anxiety and pain with VR were statistically significant for all groups except pain scores in patient relatives.
- Four main themes emerged in qualitative assessment: positive experience; relaxation; escape and recommendation for others.

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AGENDA

For a full listing of events visit <https://iii.hm/133l>

SEPTEMBER

- 3-5** 16th Emirates Critical Care Conference
Dubai, UAE
<https://iii.hm/133m>
- 5-9** European Respiratory Society (ERS) International Congress 2020
Virtual conference
<https://iii.hm/133n>
- 14-15** British Association of Critical Care Nurses (BACCN) Conference 2020
Virtual conference
<https://iii.hm/133o>
- 15-18** ISICEM
Virtual conference
- 16-19** European Society of Regional Anaesthesia (ESRA) Congress 2020
Thessaloniki, Greece
<https://iii.hm/133p>

OCTOBER

- 2-7** ANESTHESIOLOGY 2020
Washington, D.C., USA
<https://iii.hm/133r>

NOVEMBER

- 3-5** 38th Vicenza Course on AKI & CRRT
Vicenza, Italy
<https://iii.hm/133t>
- 19-21** World Congress on Infectious Diseases - WCID 2020
Rome, Italy
<https://iii.hm/133u>
- 28-30** Euroanaesthesia 2020
Barcelona, Spain
<https://iii.hm/133v>

DECEMBER

- 1-3** 10th World Congress of the World Federation of Pediatric Intensive & Critical Care Societies
Mexico City
<https://iii.hm/133w>
- 5-9** 33rd Annual Congress - ESICM LIVES 2020
Madrid, Spain
<https://iii.hm/133x>
- 9-11** 31st SMART 2020 - Anaesthesia, Resuscitation & Intensive Care 2020
Milan, Italy
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ICU MANAGEMENT AND PRACTICE IS PUBLISHED BY

MindByte Communications Ltd
9, Vassili Michailidi CY-3026 Limassol, Cyprus
Email office@icu-management.org
Website icu-management.org

SUBSCRIPTION RATES

One year 55 Euros + 5% VAT if applicable
Two years 90 Euros + 5% VAT if applicable
Note: For a free digital subscription please contact Samna Ghani, editorial@icu-management.org

PRODUCTION, PRINTING AND DISTRIBUTION

Total distribution: 21,500
ISSN = 1377-7564

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