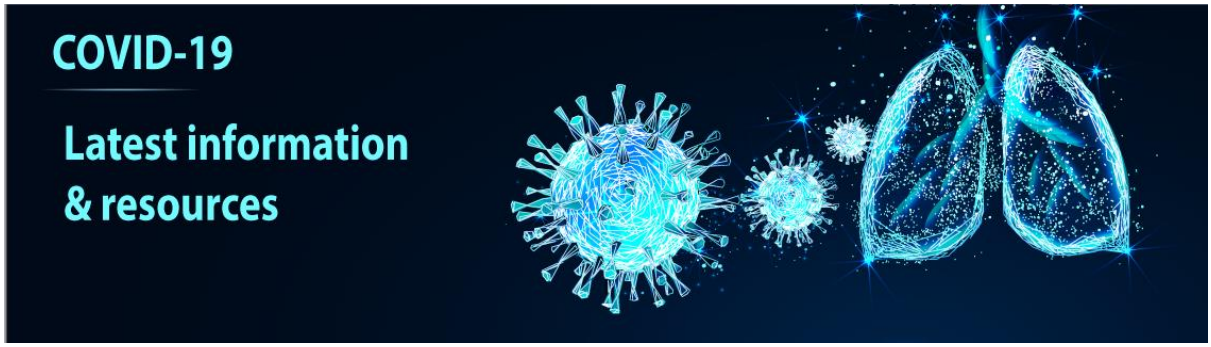

ESICM COVID-19 Marathon Webinar 28TH MARCH 2020 WORLDWIDE INTENSIVISTS CARE FOR LIVES!

#covidmarathon #ESICMtv

Introduction 4
World 4
China 4
Italy 5
Panamerica and Iberica 5
Spain 6
Norway 6
USA 7
Latin America 7
Low- and middle-income countries 7
Moderators 8
Clinical picture of COVID-19 10
Clinical presentation 10
Chinese Center for Disease Control and Prevention 10
COVID-19 Lombardy ICU network[2] 11
Reference 11
COVID-19: data on outcome 12
References 12
Previous experience with SARS and MERS 13
Outbreaks of coronavirus 13
Case-fatality rates 13
Presentation and management 14
Lessons learned from MERS 15

References 15
Containment 17
Containment and mitigation 17
A warning 17
Immunity – or the lack of 18
#Flattenthecurve – protect the individual and protect society 18
R0 18
Three rules 18
ICU contingency planning 19
Capacity 19
Equipment 19
Staff 19
A 'forgotten' issue 20
ICU nursing capacity and workload 21
Introduction 21
Nursing considerations: existing ICU staff 21
Expanding the critical care nursing workforce 22
New ways of working in the ICU 22
Challenges for staff 23
The future 24
ECMO Yes, no, when? 25
Rationale for VV-ECMO 25
What we know (based on the very limited information we have to date) 26
What we don't know 26
References 26
Basic non-invasive ventilation at the time of COVID-19 28
References 29
Challenges with family involvement during an outbreak 30
Challenges 30
5-S strategy 30
Improving communication 31
Long-term support for staff 31
References 31
Observations from JAMA 32
Journal response to COVID-19 32
Public health and scientific observations 32
Learning while doing in a pandemic 34
The problem 34
The solution 34
However 34
Drug testing 34
Conclusions 35

Reference 35
Guidelines on the management of critically ill adults with COVID-19 36

Introduction

On 28 March 2020, the European Society of Intensive Care Medicine (ESICM) brought together more than 130 000 intensivists from across the globe (160 countries) for an 8-hour marathon webinar on COVID-19. The sessions were moderated by Professors Jozef Kesecioglu, Maurizio Cecconi, John Laffey, and Massimo Antonelli.

World

Dr Janet Victoria Diaz (*World Health Organization [WHO]*) said that there were 465,915 COVID-19 cases and 21,031 deaths up to 26 March 2020. However, this figure is rising every day, so for the latest updates, please visit https://www.who.int/emergencies/diseases/novel-coronavirus-2019.

Public health interventions at present are focusing on 'flattening the curve'. However, countries need to put plans in place for screening, triage, patient information, patient transfer, isolation, and treatment. Also, planning is needed for surge actions, including increasing intensive care unit (ICU) capacity, ICU staff (including training in the use of personal protective equipment [PPE]), and equipment (ventilators, oxygen, PPE) as around 20% of cases will require ICU care (depending on the level of testing). We also need 'global solidarity', with the opening of 'humanitarian corridors' to help vulnerable countries obtain equipment, supplies, and human resources.

Mortality rates are widely known to vary considerably by age and comorbidities, but it is important to look for other predictors. Patients with moderate/severe acute respiratory distress syndrome (ARDS) will likely require lung-protective ventilation in the prone position and fluid conservative regimens. Ongoing trials (>300 have been registered) will hopefully provide some answers around which already-licensed drugs might be beneficial. The WHO is helping to prioritize research questions and share results.

Overall, the world needs to work together at this difficult time, to save lives and advance knowledge.

China

Professor Bin Du (*Peking Union Medical College Hospital, China*) said that the rate of new COVID-19 cases in China is now very low, with total cases plateauing at around 80,000. From their experience, he recommended:

- Hospitals need to prepare before an influx of COVID-19 patients: increase ICU capacity, obtain ventilators, monitors, etc., and recruit and train new ICU staff.
- Obtain supplies of PPE, e.g. N95 face masks, surgical masks, goggles, face shields, long-sleeved gowns, gloves.
- For patients with severe hypoxaemia, a lung-protective ventilation strategy should be used as non-invasive ventilation and high-flow nasal cannula have low success rates. Positive end-expiratory

pressure can be helpful, but can cause alveolar overdistention. Prone positioning is effective in almost all patients.

- The use of corticosteroids is highly controversial: short-term use may be beneficial, but long-term high-dose use could be harmful.

Italy

Professor Giacomo Grasselli (*CA' Granda Ospedale Maggiore Policlinico Foundation, Milan, Italy*) said that the numbers of cases and deaths are still increasing in Italy. Their case-fatality rate varies from <1% among those aged 0–49 years to 1.7%, 5.7%, 16.9%, and 24.6% among those aged 50–59, 60–69, 70–79, and 80–89 years, respectively. However, he pointed out that it is not possible to test all potential cases in Italy, so these are likely overestimations.

Support from an emergency task force allowed Italy to vastly increase its ICU bed capacity, and their network of COVID-19 ICUs is now coordinated centrally. They have also suspended elective surgical procedures and introduced strict containment measures.

Key messages from Italy are:

- Increase ICU capacity
- Setting up a network of 'COVID-19 ICUs' can help optimize patient allocation and isolation
- Healthcare professionals (HCPs) should be trained on the proper use of PPE
- Protocols for the triage and treatment of COVID-19 patients are needed
- Populations need to change their behaviour to stop the spread of disease.

Panamerica and Iberica

Prof. Maria Cruz Martín Delgado (*Hospital Universitario de Torrejón, Madrid, Spain*) said that the key issues in Panamerica and Iberica are the scarcity of mechanical ventilators and PPE, and that many professionals have been infected. Actions include collaboration with the Pan American Health Organization (PAHO), setting up a case register, and making action protocols.

Key requirements:

- Realistic contingency plans
- Centralized decision-making
- Dynamism and adaptability
- Leadership, teamwork, shared accountability, and good communication
- Information, training, sufficient PPE, and COVID-19 testing for staff
- Psychological support for staff
- Innovation and knowledge sharing.

Take-home messages:

- Prepare for the worst-case scenario

- Learn from experience
- Equitable distribution of resources
- Homogenize patient management criteria
- Accept change ('disaster medicine')
- Celebrate successes
- Ensure care is humanized (consider isolation, loneliness, fear, suffering, end-of-life care).

Spain

Prof. Ricard Ferrer (*Vall d'Hebron University hospital, Barcelona, Spain*) said that they have increased their ICU bed capacity threefold in response to the COVID-19 pandemic, by using other areas of the hospital and expanding into other buildings. However, there is a lack of medical equipment, medication, PPE, and guidelines. Even more problematic is finding sufficient staff for new units. Those they do have need support (rest times and areas, psychological support) and proper training on: (1) how to perform high-risk procedures (e.g. intubation) safely; and (2) the effective use of PPE. New staff are being recruited from more junior HCPs, but they need strong leadership from more senior staff. An international effort to move HCPs to the worst-affected countries at any one time was suggested.

Spain likely has a high number of cases due to the late introduction of containment and a lack of rapid testing. Given the high numbers, they are having to prioritize patients who are most likely to benefit (e.g. age <70 years). Ideally, treatments that could be given in the community to prevent patients needing ICU care would be incredibly useful, possibly hydroxychloroquine, azithromycin, or anti-inflammatories.

Key messages from Spain are:

- Prepare national contingency plans
- Allocate resources and professionals centrally
- Expand ICU capacity before it is required
- Test any patients with pneumonia for COVID-19
- Establish uniform triage criteria for ICU, mechanical ventilation, and extracorporeal membrane oxygenation (ECMO)
- Work in multidisciplinary teams.

Norway

Prof. Hans Flatten (*Haukeland University Hospital, Bergen, Norway*) said that the numbers of COVID-19 cases and deaths are currently relatively low in Norway, but are increasing steadily. There are only around 5 ICU beds per 100,000 population, which is being increased three- to fourfold, but will likely need further increases. They are using the Norwegian Intensive Care Registry (established in 1998) to track ICU COVID-19 patients. In Norway, the proportion of patients requiring ICU care has increased from around 10% to 25–30% over the past 2 weeks. However, they have a lack of beds,

equipment (particularly ventilators), and skilled nurses and physicians. They are therefore discharging hospitalized patients where possible, have introduced 'crash courses', and are involving medical students. There may be fewer cases in Norway than in Southern Europe as fewer older people live with their families in Northern Europe. He also suggested that, if there is a lack of ventilators, manual ventilation (by medical students) might be an option… However, he cautioned against using one ventilator for two patients at the same time.

USA

Prof. Lewis J Kaplan (*Perelman School of Medicine, Pennsylvania, USA*) said that the US has learnt valuable lessons from China and Europe. Different US states are currently very differently affected, so it is important to redistribute resources appropriately. However, the differences in social isolation rules need to be harmonized across all US states. The different US government agencies are working together to implement crisis standards, allowing emergency use authorization pathway, relaxation of bed designation criteria, opening of secure stockpile, device manufacture augmentation, and professional society collaboration. They are drawing on PPE supplies from industry, retail, and private citizens. He said that it would have been very helpful to have created a 'national dashboard' of resources and requirements that could have been integrated across the US.

Pr Kaplan advised against the use of hydroxychloroquine but mentioned the possibilities of monoclonal antibodies and plasma from recovered patients. He also thought that the option of one ventilator for two patients, while far from ideal, might be better than doing nothing…

Latin America

Prof. Luciano Azevedo (*ICU Hospital das Clinicas, São Paulo, Brazil*) said that while the situation in Europe and the USA is bad, it is catastrophic in Latin America, due to poverty, overcrowding, poor sanitation, underlying chronic diseases, and endemic diseases (e.g. dengue fever, malaria, yellow fever). There is also a lack of COVID-19 testing, ICU beds, ventilators, HCPs, and PPE, and great inequality for patients in the public and private healthcare systems. A major concern is what will happen to the economy if months of lockdown are required. Also, many people do not have 'formal' jobs so will need government support.

Low- and middle-income countries

Prof. Mervyn Mer (*CMJAH. Johannesburg, South Africa*) said that 87% of the world's population live in low- and middle-income countries (LMICs). These populations tend to be younger than in high-income countries but have high levels of disease, including hypertension, heart disease, hepatitis B, HIV/AIDS, and tuberculosis. The health systems are poorly-funded, with few HCPs per population. There is also a lack of transportation to move patients to appropriate hospitals.

Fortunately, in South Africa, they have received good warning of the COVID-19 pandemic, allowing them time to prepare. However, owing to a lack of resources, the focus there has to be on simplicity (of guidelines and interventions) and basic principles (sanitation, social distancing, infection prevention, education), although the latter is hampered by poverty, overcrowding, and illiteracy. Unfortunately, South Africa has a very limited ICU capacity, so patients will have to be carefully-selected, which poses many ethical questions.

What LMICs can do:

- Use impeccable clinical acumen, support and encourage HCPs, and take steps to prevent infection
- Benefit from their experience treating HIV/AIDS patients with pneumocystis, who are treated in 'polymask wards' (using rebreather masks). In the absence of sufficient ventilators, it is hoped that this technique will also benefit patients with COVID-19
- Use novel PPE, e.g. construction helmets with visors (these can be cleaned and reused) and Perspex boxes around patients to protect staff during risky procedures (e.g. intubations)
- In the absence of negative-pressure rooms and extraction systems, simply opening windows can be very beneficial
- Overall, offer the best care they can using simple, basic interventions.

Moderators

Jozef Kesecioglu, Professor of Intensive Care Medicine at the Department of Intensive Care Medicine, University Medical Center, Utrecht, the Netherlands and President of the European Society of Intensive Care Medicine (ESICM).

Maurizio Cecconi: Head of the Anaesthesia and Intensive Care Department at Humanitas Research Hospital; President-elect of the European Society of Intensive Care Medicine (ESICM) for 2020-2021;; Director of the Master in Patient Blood Management at Humanitas University

John Laffey, Professor of Anaesthesia Intensive Care Medicine at the School of Medicine of the National University of Ireland, Galway and a Consultant in Anaesthesia and Intensive Care Medicine at Galway University Hospitals.

Massimo Antonelli, Professor of Intensive Care and Anesthesiology at the “Università Cattolica del Sacro Cuore”, Rome, Italy and past President of the European Society of Intensive Care Medicine (ESICM).

Clinical picture of COVID-19

Prof. Giacomo Grasselli

Associate Professor of Anaesthesiology and Intensive Care Medicine in the Department of Pathophysiology and Transplantation, University of Milan

Medical Director, Intensive Care Unit « E. vecla » at the CA' Granda Ospedale Maggiore Policlinico Foundation, Milan

Regional Coordination Center of the LOMBARDY COVID-19 ICU NETWORK

Moderators: Massimo Antonelli, Jozef Kesecioglu, Maurizio Cecconi

Clinical presentation

Knowledge of the baseline characteristics and outcomes of critically ill patients with COVID-19, while currently limited, is crucial for health and governmental officials engaged in planning for local outbreaks.

- **February 20, 2020:** first patient diagnosed with COVID-19 diagnosed in Lombardy
- **March 11, 2020:** WHO declares the SARS-CoV-2 outbreak as a pandemic
- **March 20, 2020:** Italy is the second most affected country in the world, after China

COVID-19 is more complex than initially thought, being more than a 'violent' pneumonia. It can become very severe, affecting multiple organs. In China, the proportion of hospitalized patients requiring ICU care varies widely, ranging from 5% to 32%. Nevertheless, these figures help to plan for local outbreaks.

COVID-19 typically presents with systemic and/or respiratory manifestations. The most common presentations are fever (85−90%), cough (65−70%), fatigue (35−40%), sputum production (30−35%), and shortness of breath (15−20%). Less common features are myalgia/arthralgia (10−15%), headaches (10−15%), sore throat (10−15%), chills (10−12%), and pleuritic pain. Rarely, patients report nausea (<10%), vomiting (<10%), nasal congestion (<10%), diarrhoea (<5%), palpitations (<5%), and chest tightness (<5%). Some individuals are asymptomatic and can act as carriers. Viral shedding is highest 2 days before the infected person becomes symptomatic.

Chinese Center for Disease Control and Prevention

According to data from the Chinese Center for Disease Control and Prevention (44,672 confirmed cases of COVID-19 from 72,314 case records), 81% of patients had mild disease (non-pneumonia or mild pneumonia), 14% had severe disease (dyspnoea, respiratory frequency ≥ 30/min, blood oxygen saturation [SpO_2] ≤93%, PaO_2/FiO2 ratio or P/F <300, and/or lung infiltrates >50% within 24−48 h), and 5% had critical disease (respiratory failure, septic shock, and/or multiple organ dysfunction [MOD] or failure [MOF]). The overall case-fatality rate was 2.3% (1023 deaths), and 49.0% among critical cases.[1] Median duration of hospitalization was 16 days.

COVID-19 Lombardy ICU network[2]

Retrospective Italian data are available from the 'COVID-19 Lombardy ICU network' (72 ICUs), coordinated by Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan. Among 1591 critically ill patients hospitalized in the ICU with confirmed COVID-19 (20 February to 18 March 2020), 82% were men, median age was 63 (interquartile range 56, 70) years, and 68% had at least one coexisting medical condition. The most common conditions were hypertension (49%), cardiovascular disease (21%), and hypercholesterolaemia (18%). A minority (4%) had a history of chronic obstructive pulmonary disease.

Respiratory support

99% required circulatory support (88% mechanical and 11% non-invasive ventilation) and 5 patients (1%) required ECMO. At admission, 27% of patients (based on available data) were treated with prone ventilation. Most patients had relatively high compliance of the respiratory system.

Outcome

At the time of this presentation, 58% of the patients were still admitted to the ICU, 16% had been discharged alive, and 26% had died in the ICU. The majority of deaths (71%) were among those aged ≥64 years. The median length of ICU stay was 9 (6, 13) days. These figures will change in due course.

Reference

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA.* 2020.

2. Grasselli G, Pesenti A, Cecconi M. Critical Care Utilization for the COVID-19 Outbreak in Lombardy, Italy: Early Experience and Forecast During an Emergency Response. *JAMA.* 2020;doi: 10.1001/jama.2020.4031. [Epub ahead of print].

COVID-19: data on outcome

Prof. V. Marco Ranieri

Policlinico di Sant'Orsola

Servizio Sanitario Regionale, Emilia-Romagna, Azienda Ospedaliero, Universitaria di Bologna

Alma Mater Studiorum, Università di Bologna

Moderators: Massimo Antonelli, Jozef Kesecioglu, Maurizio Cecconi

In a study of 191 hospitalized patients from Wuhan,[1] non-survivors had similar clinical courses to survivors in terms of fever, cough, and dyspnoea. The major difference was that non-survivors were significantly more likely to have sepsis, respiratory failure, acute respiratory distress syndrome (ARDS), heart failure, septic shock, acute cardiac injury, acute kidney injury, and secondary infection.[1] Non-survivors also had dramatic increases in various biomarkers, including interleukin-6, indicating cytokine storm.[1] Clinical trials of drugs designed to interact with interleukin-6 are currently underway.

Another study from Wuhan reported that intensive care unit (ICU) patients who were critically ill with COVID-19 pneumonia (n=52) had a 28-day Kaplan-Meier mortality rate of 62%.[2] This was much higher than the 4% mortality reported in another Wuhan study of 138 patients hospitalized with COVID-19 pneumonia.[3] However, the latter study only reported a point estimate of survival, and only 26% of patients had been transferred to the ICU.[3]

A study from the US has reported a point mortality rate of 52% among 21 ICU patients critically ill with COVID-19.[4] As yet unpublished data from Italy indicate mortality rates of 13% among hospitalized patients and 4–17% among patients in various ICUs. In Italy, around 5–10% of hospitalized patients require ICU care for around 2 weeks.

References

1. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-62.

2. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020.

3. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020.

4. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. JAMA 2020.

Previous experience with SARS and MERS

Prof. Yaseen Arabi, MD, FCCP, FCCM, ATSF

Chairman, Intensive Care Department, Medical Director, Respiratory Services, Professor, College of Medicine, King Saud Bin Abdulaziz University for Health Sciences (KSAU-HS), King Abdullah International Medical Research Center (KAIMRC), King Abdulaziz Medical City Riyadh (KAMC-R), Kingdom of Saudi Arabia.

Moderators: Maurizio Cecconi, Jozef Kesecioglu, Massimo Antonelli

Outbreaks of coronavirus

Of the seven coronaviruses known to cause upper respiratory tract infections in humans, SARS-CoV, MERS-CoV and SARS-CoV-2 (causing COVID-19) are responsible for three major outbreaks in the past two decades. SARS-CoV-2 shows 75−80% genomic similarity to SARS-CoV, 50% similarity to MERS-CoV, and 96% similarity to a bat coronavirus. Both SARS-CoV and SARS-CoV-2 attach to the ACE2 receptor and MERS-CoV to the DPP4 receptor.[1-3]

All three viruses are zoonotic, with SARS linked to civet cats and bats, MERS to dromedary camels, and COVID-19 to bats. They are also transmitted from human to human, can cause nosocomial (hospital) transmission, and pose a risk to healthcare workers. The number of countries and territories with reported cases is low for MERS (27 countries/territories; 2494 cases) and SARS (26 countries/territories; 8437 cases), but has almost global coverage for COVID-19 (193 countries/territories; >550,000 cases as of 27 March 2020). COVID-19 represents a novel coronavirus and a new challenge for critical care.

Case-fatality rates

The case-fatality rate for COVID-19 (4%) is much lower than MERS (34%) or SARS (10%). However, with the huge number of cases of COVID-19, the overall number of deaths is already much higher than for the other two infections combined.

In China, 80% of COVID-19 infections are not severe, 15% are severe but not critical, and 5% are critical. The overall case-fatality rate is 2−3%. When broken down by disease severity, the rate is 8% in critically-ill hospitalized patients and 42−62% in those admitted to the ICU.[4]

In Italy, 70% of infections are not severe, 25% are severe, and 5% are critical. The overall case-fatality rate – regardless of severity – is much higher than that for China, at 7%, and may reflect the older population and higher prevalence of comorbid conditions.[5]

Presentation and management

Acute respiratory distress syndrome (ARDS) or pneumonia are the main presenting features of patients hospitalized with COVID-19, SARS or MERS, along with shock and multi-organ failure. A high percentage of hospitalized patients require invasive mechanical ventilation, vasopressors and renal-replacement therapy.

Use of non-invasive ventilation (i.e. with a face mask) in critically ill patients with MERS had a very high failure rate (92.4% required intubation and invasive mechanical ventilation).[6] Patients treated with a face mask were more likely to become hypoxic than those intubated at the start. High rates of failure of non-invasive ventilation have also been reported for SARS and influenza.[7, 8]

In severe MERS, extracorporeal membrane oxygen (ECMO) had a lower rate of hospital mortality than conventional therapy, supporting the use of ECMO as a rescue therapy in hypoxemic respiratory failure.[9]

The role of corticosteroids is the subject of debate. A recent review in *The Lancet* reported that the clinical evidence does not support corticosteroid treatment for COVID-19 lung injury.[10]

The HIV antivirals lopinavir/ritonavir and ribavirin have been used to treat SARS, and showed a lower rate of ARDS or death (2.4% vs 28.8%, $P<0.001$), but this small study (41 patients with SARS versus 111 historical controls on ribavirin alone) was subject to several confounders and the results require further investigation in a randomized trial.[11]

A randomized, controlled, open-label trial in which 199 hospitalized adults with COVID-19 were randomized to receive lopinavir/ritonavir (400 mg and 100 mg, respectively) twice a day for 14 days, in addition to standard care, or standard care alone, failed to demonstrate any difference in time to clinical improvement, or in death or viral shedding between treatment groups.[12] However, the time between symptom onset and starting treatment was very long (median 13 days) and may have affected the outcome.

The randomized MIRACLE (MERS-CoV Infection tReated with A Combination of Lopinavir/ritonavir and intErferon-β1b) trial of lopinavir/ritonavir and recombinant interferon-β1b provided with standard supportive care, compared to placebo provided with standard supportive care, in hospitalized patients with laboratory-confirmed MERS is ongoing, with 95 patients currently recruited (ClinicalTrials.gov, NCT02845843).[13]

Ribavirin and recombinant interferon were used for critically ill patients with MERS. A cohort study showed no difference in rates of death or viral clearance.[14] The type of interferon used may, however, make a difference to inhibition of MERS-CoV.[15]

Preliminary data from China suggest rates of coinfection in patients with COVID-19 of 20% (Wuhan) and 80% (Qingdao); 6% of patients with COVID-19 had other infections. Coinfections are common in critically ill patients with MERS (18% bacterial coinfections and 5% viral coinfections).[16]

The Infectious Diseases Society of America clinical practice guidelines recommend standard antibacterial therapy to be prescribed for adults with community-acquired pneumonia who test positive for influenza.[17]

There are many similarities and differences between SARS, MERS, and COVID-19. Several aspects of management and antivirals are of considerable interest for the treatment of COVID-19.

Lessons learned from MERS

A major outbreak of MERS occurred in 2014 in Saudi Arabia. MERS was not initially suspected, and the outbreak continued unrecognised for several days, leading to widespread infection and huge peaks in infected patients, including healthcare workers, half of whom died. With COVID-19, Saudi Arabia initiated major infection controls and preventive measures early on and expects a decline in cases very soon.

If a highly infectious disease is suspected, put infection control precautions into place early. Have a low threshold for suspecting COVID-19. Triage patients at the point of entry into the hospital according to their symptoms, isolating those with respiratory infections in a separate and dedicated respiratory infection unit. Essentially, divide the hospital into two parts: COVID-19 and non-COVID-19, and consider dividing hospitals in this way for the foreseeable future.

The management strategy of MERS and COVID-19 is essentially similar, with provision of supportive care of ARDS and multi-organ failure. Acute kidney injury is common with MERS, but this may reflect the high prevalence of diabetes in Saudi Arabia.

In MERS, one-third of cases was diagnosed from samples taken from the upper respiratory tract, with the remaining cases diagnosed from the lower respiratory tract. In Italy, the false-negative rate was high at the start and may reflect limited sensitivity or the quality of the sample. Do not rule out a negative test result. Be prepared to repeat a negative test result. One-tenth of patients with COVID-19 may not have any respiratory tract infections. We need a screening tool that includes other symptoms (e.g. gastrointestinal).

References

1. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med.* 2020;382:727-733.

2. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet.* 2020;395:565-574.

3. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature.* 2020;579:270-273.

4. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med.* 2020.

5. Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA.* 2020.

6. Alraddadi BM, Qushmaq I, Al-Hameed FM, et al. Noninvasive ventilation in critically ill patients with the Middle East respiratory syndrome. *Influenza Other Respir Viruses.* 2019;13:382-390.

7. Kumar A, Zarychanski R, Pinto R, et al. Critically ill patients with 2009 influenza A(H1N1) infection in Canada. *JAMA.* 2009;302:1872-1879.

8. Cheung TM, Yam LY, So LK, et al. Effectiveness of noninvasive positive pressure ventilation in the treatment of acute respiratory failure in severe acute respiratory syndrome. *Chest.* 2004;126:845-850.

9. Alshahrani MS, Sindi A, Alshamsi F, et al. Extracorporeal membrane oxygenation for severe Middle East respiratory syndrome coronavirus. *Ann Intensive Care.* 2018;8:3.

10. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet.* 2020;395:473-475.

11. Chu CM, Cheng VC, Hung IF, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax.* 2004;59:252-256.

12. Cao B, Wang Y, Wen D, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. *N Engl J Med.* 2020.

13. Arabi YM, Asiri AY, Assiri AM, et al. Treatment of Middle East respiratory syndrome with a combination of lopinavir/ritonavir and interferon-beta1b (MIRACLE trial): statistical analysis plan for a recursive two-stage group sequential randomized controlled trial. *Trials.* 2020;21:8.

14. Arabi YM, Shalhoub S, Mandourah Y, et al. Ribavirin and Interferon Therapy for Critically Ill Patients With Middle East Respiratory Syndrome: A Multicenter Observational Study. *Clin Infect Dis.* 2019.

15. Hart BJ, Dyall J, Postnikova E, et al. Interferon-beta and mycophenolic acid are potent inhibitors of Middle East respiratory syndrome coronavirus in cell-based assays. *J Gen Virol.* 2014;95:571-577.

16. Arabi YM, Al-Omari A, Mandourah Y, et al. Critically Ill Patients With the Middle East Respiratory Syndrome: A Multicenter Retrospective Cohort Study. *Crit Care Med.* 2017;45:1683-1695.

17. Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenzaa. *Clin Infect Dis.* 2019;68:895-902.

Containment

Dr Lennie Derde

Consultant in ICU and ID, University Medical Center Utrecht, The Netherlands

EU lead and ITSC member for REMAP-CAP, a global adaptive platform trial created for a respiratory pandemic since 2014, recruiting in almost 60 ICUs globally (and increasing)

Chair Dutch ICU Taskforce Infectious Threats, member ESICM/SCCM/SSC COVID-19 guideline group, ESICM COVID-19 task force, chair ESICM CTC, member ESICM sCAP group

Moderators: John Laffey, Jozef Kesecioglu, Maurizio Cecconi

Containment and mitigation

Containment is the action of keeping something harmful under control or within limits. *Mitigation* is the action of reducing the severity, seriousness, or painfulness of something. Containment and mitigation are interrelated. By containing a virus, you mitigate its harmful effects, at least for the time being. To mitigate harmful effects, you have to try and contain it, at least partly.

Infectious diseases are essentially different from all other diseases in that they are contagious: they spread. ProMed-mail (http://www.promedmail.org), a mail service from the International Society for Infectious Diseases, published a report on undiagnosed pneumonia in China (Hubei) on 30 December 2019. The following day the cluster was reported to the WHO as being a potential new disease and a potential threat.

A warning

Dr Li Wenliang, who worked as a physician at Wuhan Central Hospital, told his colleagues in December 2019 about a possible outbreak of an illness that resembled SARS, warning them to wear protective clothing to avoid infection. Li subsequently contracted the virus and died, in February 2020. Dr Li is widely regarded as a hero for trying to warn his fellow doctors, and the world, about this disease. To identify a new disease, you have to recognize something is different, to be open to the possibility of a new disease, to see it. We owe Dr Li and his colleagues a great deal for recognizing this new clinical syndrome.

In COVID-19, the most probable source was the Huanan Seafood Market, a live animal market. Of the initial 41 people hospitalized with pneumonia who were officially identified as having COVID-19 by 2 January 2020, two-thirds had links to the market. Identifying the source represents classic public health, classic epidemiology, and classic doctoring. By asking questions, and taking a history, you can identify a common theme. The market was closed on 1 January 2020, cutting off the source of the virus, but human-to-human transmission had already started, via droplets, and the process of containment began.

Immunity – or the lack of

No one in the world has immunity from a new disease. If the virus is left unchecked, everyone will become infected and many people could die. With the rapid spread of disease, there is no time to find a treatment or to develop a vaccine. By containing the virus, we buy ourselves time and save lives. From a societal perspective, by stopping people from dying, we ensure that normal processes can continue, whether it is growing food or delivering food, paying salaries or bills, running IT systems, driving trains, conducting research, or running our hospitals… Indeed, without preventing the spread, the complete healthcare system will collapse. For this issue, we need to #flattenthecurve.

#Flattenthecurve – protect the individual and protect society

'Flatten the curve' means slowing the spread of the virus, by containment and/or mitigation measures, so that even if the number of cases remains the same ('the same area under the curve'), they are spread over a longer time, to prevent the hospital systems from collapsing.

This 'flattening' is achieved by preventing a person with the virus from transmitting it to another person, by stopping contact, or 'social distancing'. In practice, the term 'physical distancing' is more appropriate, given the need to stay socially connected, even if physically apart. The advice about social distancing remains essentially unchanged from that introduced for the 1918 influenza pandemic. The most effective strategy involves closing schools and shops, working from home, stopping social gatherings, etc., to keep physically distant.

R0

In an epidemic, the average number of people who are infected by one person is three, giving an R0 = 3, leading to exponential growth of the epidemic. In reality, the situation is not so simple, and the R0 is affected by super-spreading events (e.g. a religious gathering at a church in South Korea), but also by containment and mitigation measures. In theory, if every person on average infects less than two other people, the epidemic eventually dies out.

Three rules

There is a huge task ahead, and many critically ill people will be admitted to the ICU. According to Mike Ryan of the WHO, the three most important rules in containment and mitigation are to:

1. Move fast (otherwise the virus will get you).
2. Accept unknowns (not everything will be clear at the start).
3. Accept mistakes (base decisions on the best available evidence).

This is the best you can do.

ICU contingency planning

Prof. Armand RJ Girbes

Intensivist-clinical pharmacologist; Chair and Professor, Department of Intensive Care, Amsterdam University Medical Centres; Chair Division Scientific Affairs ESICM

Moderators: John Laffey, Jozef Kesecioglu, Maurizio Cecconi

Capacity

Before the COVID-19 pandemic, the number of critical care beds per 100,000 population varied widely (e.g. 3.6 in China, 12.5 in Italy, 29.2 in Germany, and 34.7 in the USA). Hospitals around the world are now having to vastly increase their intensive care unit (ICU) capacity. They are achieving this by taking over operating rooms, critical care units, post-anaesthesia care units, etc. In some places, new ICU hospitals are being built or other premises are being repurposed. Elective surgery is being suspended in many hospitals to increase capacity to care for patients with COVID-19.

Equipment

There is a huge increased demand for equipment such as ventilators, monitors, infusion pumps, continuous renal-replacement therapies, and even extracorporeal membrane oxygenation. Hospitals are, therefore, having to take ventilators, etc., from other areas (e.g. research, training, animal studies, and other departments). They are also having to obtain large amounts of disposables for this equipment, along with huge amounts of personal protective equipment (PPE) for their staff.

Staff

Problems

Most ICUs in western hospitals have a dedicated specialist staff of intensivists and ICU nurses. Hospitals are now having to recruit and train new staff, at a time when they are already incredibly busy and their usual staff members may be becoming infected and having to self-isolate. These new teams have a number of difficulties to face, beyond caring for patients with COVID-19: (1) having to care for more patients per staff member than usual; (2) risk of becoming infected despite using PPE; (3) having to communicate effectively with new team members; and (4) inexperienced staff may feel ‘out of their depth’. Staff also need to find time to schedule remote contact between patients and their families.

Actions

It is vitally important to look after the ICU teams (e.g. by providing psychological care due to the risk of post-traumatic stress disorder, and measures to try to avoid exhaustion). Simple things are also important, such as providing parking, childcare, shopping, sustenance, and even compliments. We also need to accept that, at this difficult time, standards of care cannot be as high as normal. Staff members also need to be flexible and willing to do tasks that may be below their level of expertise and training. It may also be helpful to make task-directed teams (e.g. for intubating, turning/proning, and

checking for bed sores). Overall, these vitally important healthcare teams need to take care of themselves and their co-workers.

A ‘forgotten’ issue

At this time when the main focus is on COVID-19, we must not forget that there are other patients who also need ICU care, many of whom will likely have a higher chance of survival.

ICU nursing capacity and workload

Carole Boulanger FFICM

Consultant Nurse / Advanced Critical Care Practitioner

ESICM N&AHP Immediate past chair & committee member

Royal Devon & Exeter NHS Foundation Trust, UK

Moderators: John Laffey, Jozef Kesecioglu, Maurizio Cecconi

Introduction

Even before the COVID-19 pandemic, critical care in England had a nursing vacancy approaching 10%. Staff were leaving the workforce due to the ethical climate in the ICU, having to face morally distressing situations related to end-of-life decision-making, combined with irregular and long shift patterns, low staffing levels, and increased patient ratios. ICU staff, who were already at risk of burnout, are at much greater risk today. Staff at the bedside are major assets, who need to be cared for as much as the patients themselves.

The information from China, Italy and Spain is vital, as it allows the NHS to prepare, to be proactive, to build resilience in its staff, and to identify issues early. The Italian data show that healthcare practitioners (HPCs) are at risk, with 15% being infected with the virus, 10% of whom are admitted to the ICU. The risk of infection from patients, necessitating the use of personal protective equipment (PPE), raises anxiety levels for all, is physically demanding, and presents a barrier between the nurse and their patient, and their colleagues.

New teams and new working practices need to be established, setting out a foundation for staff to look after one another and thereby look after patients. It is clear that critical care networks are vital to generate and manage effective pandemic plans, and that extensive and ongoing PPE training is essential.

Nursing considerations: existing ICU staff

Critical care nurses need to prepare for a new way of working: they will become supervisors of care for *multiple* patients, rather than managing complete episodes of care for the *individual* patient. They will be supporting and directing the redeployed workforce, providing supervision and expertise in the delivery of critical care. They will be under increased pressure to teach and train redeployed staff in the ‘pre-surge’ period. They need to cease all unnecessary work-related activity, and up- or side-skill to supervise and support others in delivering care.

Whereas the pandemic will increase pressure and introduce challenges to providing safe, effective, quality care to critically ill patients, the primary objective is to act in the best interests of the patient and the public according to professional guidance. Nurses need to be made aware that care may not be perfect in terms of the pre-pandemic ICU, and that this is acceptable.

The relationship between ICU staff and patients has also changed dramatically: patients have become a significant health risk to staff, and maintaining a therapeutic relationship between the nurse, the patient and their families, is challenging. ICU staff have had to change the way in which they interact with the patient's relatives and loved ones, communicating by phone/Skype instead of face-to-face. The three-way relationship of nurses supporting the family to support the patient has been lost, and new ways of communicating need to be established.

Expanding the critical care nursing workforce

Increasing the ICU workforce should be phased, avoiding high numbers of staff in the ICU early on, escalating in line with increasing bed capacity. The workforce can be supplemented by individuals with a range of experience: nurses with recent or previous critical care experience or some transferable skills; registered nurses with no critical care skills (who may prefer task-related activities and clear direction); non-critical care staff in critical care; assistants or helpers; and turning teams, personal care teams, and proning teams.

Non-ICU staff will not have the same skills and cannot be trained to the same level as ICU staff. They are equally valued members of these new teams, and will be trained with the skills essential for their allocated tasks while also keeping patients safe.

Training can involve simulation (turning, positioning patients and orientation to area); video snapshots of key aspects of care and management; and clinical guidelines and educational packages, including flashcards.

New ways of working in the ICU

The new ICU teams will comprise members with a wide range of competencies, skills and confidence. A team culture ('we're all in this together') should be rapidly established. The new teams and members should be easily identifiable. Psychologists recommend establishing a check-in, check-out system. The use of checklists can help standardize daily 'routine'. Buddy systems are essential ('clean buddy', 'dirty buddy'), as is strict adherence to PPE protocols, including breaks, to prevent pressure sores and exhaustion. The staff room should be a 'safe space', but should be closely monitored. Each designated CCU should provide a designated critical care trained supernumerary nurse-in-charge of each shift for supervision, advice, support and coordination including the new or established cohorted critical care areas.

Logistics

The logistics of providing ICU care in a non-ICU environment encompass strict safety checks, standardizing equipment, marking floors and sealing doors, and strict entry and exit routes. Processes need to be set up to enable nurses to call for help (e.g. walkie-talkies are effective, and mobiles

should be avoided), especially those isolated in side-rooms with no eye contact. Non-CCU nurses may need to work in pairs to provide one another with support and avoid isolation.

Documentation and charting

Critical care nursing needs to follow key principles, ensuring that anyone can safely take over the patient's care, without a detailed handover. Only the key elements of patient care should be documented, in a consistent manner across patients. Decisions must be made on who collects what information and the role of administrative support. Key concerns and the plan should be immediately evident to all, with clear goals set at ward round and escalation points established (who and how) in advance.

End of life

Managing end of life will present key challenges in this new world. Often it is the first 'face-to-face' contact between ICU staff with families, and PPE is seen as an intrusion. Families may also have to be informed of the death of their loved one by telephone. HCWs who are less familiar with end-of-life need to be supported, and the need to debrief must be recognized. End-of-life matters should ideally be managed by the most senior ICU nurse available.

Challenges for staff

Both the staff supervising and those working a shift face significant challenges. These range from managing a roster and team that is likely to change daily, to concerns about accountability in these changing times. Risk can be minimized by setting clear goals and parameters for the day, with pre-established escalation points.

ICUs will face high rates of staff sickness and self-isolation across all staffing levels, and will need to provide support for junior ICU nurses who take on supervisory roles. Staff will experience feelings of guilt about not working. They may also feel anxious about coming to work and infecting their families with a potentially life-threatening disease.

Staff will also be faced with having to deliver care at a level not normally considered acceptable and to cope with high death rates.

Expectations should be managed at the start, explaining that care will be delivered differently to current standards, and that the time each member needs to adjust and become comfortable with their roles and responsibilities will vary. The aim now is to minimise risk (to patients and staff) and complications.

Early provision of psychological support is vital to help nurses cope with the new ways of working and caring for increased volumes of sick patients, many of whom will die. Checking in and checking out of shifts and welfare calls provide a window for checking how staff are coping.

Resilience ('adapting or bouncing back after being exposed to stressful situations or adversity') is not innate. Staff should be encouraged to develop personal strategies, such as creating a balance [of eating, exercise, rest and recreation], yoga, mindfulness, social support, reach out, and supportive social media, but avoiding overload. ICU leaders and nursing colleagues also have a role to play in developing resilience in other staff members.

Several ICU-related strategies can help encourage resilience, including communicating with nurses (especially during isolation in side-rooms), managing patient and family distress, monitoring workload, providing telephone support both on and off duty, and effective leadership. Nursing staff should be allowed to express themselves, whether to vent their frustrations, or through humour. This support will be needed in the short and the long term.

Small, achievable things also help build resilience, such as providing food and hydration, hand and face care, and somewhere to shower and change clothes before going home. Telephone calls to check in when staff are off sick, as well as insisting that staff take days off are important. Acknowledging that it's tough, and will continue to be so, for a protracted period, and saying thank you are also valuable.

The future

The current focus is on the pandemic, but preparations must be made for the future. The new and more diverse team of nurses will require immediate and ongoing psychological support to deal with the long-term consequences. We can and should focus on the successes, but also allow time to reflect and grieve. Nurses may also need to accept a 'new normal' in ICU care.

For now, prepare, prepare, prepare, but be flexible and expect frequent changes to plans. Ultimately, caring for the staff will translate into caring for the patients. Do not underestimate the physical, psychological and emotional effects of the pandemic on the team, which are likely to be long lasting. This is a marathon, not a sprint.

ECMO Yes, no, when?

Prof. Alain Combes

Professor of Intensive Care Medicine at Sorbonne University, Paris and head of Department of Intensive Care Medicine at the Hôpital Pitié-Salpêtrière, Paris, France

Moderators: Jozef Kesecioglu, Massimo Antonelli, Maurizio Cecconi

Rationale for VV-ECMO

The rationale of high-flow venovenous extracorporeal membrane oxygenation (VV-ECMO) in severe acute respiratory distress syndrome (ARDS) is to completely replace pulmonary function in patients with very severe hypoxemia who are at risk of dying of refractory hypoxemia or for whom mechanical ventilation becomes dangerous. Starting ECMO early ('the earlier the better') is important in severe ARDS supported by ECMO, to reduce the risk of acute lung injury with mechanical ventilation.

The overall results of the international EOLIA trial, in which patients with very severe ARDS were assigned to receive immediate VV-ECMO or continued conventional treatment, were negative.[1] For the key secondary endpoint (composite of death or death or crossover to ECMO in control patients) there was a significant benefit for those in the early ECMO group. A post-hoc analysis, using a Bayesian statistical model, showed that probability of ECMO saving lives was over 90%.[2]

In subgroup analyses, patients with the less-severe forms of ARDS (taking into account the P/F ratio) on ECMO had the better prognosis. These data suggest that it may be better to start ECMO early, before the P/F decreases. There was a signal towards benefit of early ECMO for the least severe forms of organ failure (lactate <2 mmol/L and SOFA score <11).

The duration of ECMO is usually very long (mean±SD 15±13 days in EOLIA[1]). In our experience in less-selected patients, the duration may be 3−4 weeks.

ECMO has been shown to be beneficial in patients with H1N1-associated severe ARDS.[3-5] H1N1 is, however, a very different type of disease to COVID-19.

ECMO was also used in two patients with MERS-CoV associated ARDS, one of whom died and the other survived after spending 2 months in hospital.[6] In a small study in patients with severe MERS, ECMO had a lower rate of hospital mortality than conventional therapy (65% vs 100%), supporting the use of ECMO as a rescue therapy in hypoxemic respiratory failure.[7]

Very early data from Wuhan, in 52 critically ill adults with COVID-19, reported that six patients received ECMO, one of whom survived.[8] In another series of 191 patients from Wuhan, three patients received ECMO, all of whom died.[9]

Consequently, it is too early to know whether ECMO is beneficial for patients with COVID-19. Indeed, a note of caution has been raised in relation to lymphopenia, but there are no data to support this comment.[10]

In Europe, as of 27 March 2020, 154 cases of ECMO have been recorded by the European/Euro-ELSO Survey for Adult ECMO-COVID-19 patients.

Interim guidelines from WHO recommend considering ECMO for eligible patients with COVID-19-associated ARDS. As ECMO is used relatively infrequently, it is largely restricted to specialized centres. Therefore, the use of ECMO in the context of COVID-19 will present issues, and requires careful planning, resource allocation, and training of personnel.[11]

Indications for ECMO are based on the entry criteria for the EOLIA trial.[1] Contraindications (to be discussed case by case) are: age >65−70; severe comorbidities (advanced chronic obstructive pulmonary disease, cardiac failure, cirrhosis (child B / C), home O_2…); severe immunocompromised status (haematological cancer, advanced metastatic cancer…); cardiac arrest (except witnessed, with bystander CPR, low-flow <15 min); MV duration > 10 days; and multiple organ failure (maybe except isolated AKI…).

ECMO is resource heavy, requiring a lot of involvement of healthcare workers. It should only be performed if there are sufficient beds for all patients needing ICU.

What we know (based on the very limited information we have to date)

- Most patients with COVID-19 who were put on ECMO were stabilized in the following days.
- They all have very severe lung disease, frequently associated with kidney injury.
- Not all patients die on ECMO; some patients have been weaned after <10 days of support, whereas others may require weeks of support.

What we don't know

It is too early to draw any conclusions. We need time to evaluate our results

References

1. Combes A, Hajage D, Capellier G, et al. Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome. *N Engl J Med.* 2018;378:1965-1975.

2. Goligher EC, Tomlinson G, Hajage D, et al. Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome and Posterior Probability of Mortality Benefit in a Post Hoc Bayesian Analysis of a Randomized Clinical Trial. *JAMA.* 2018;320:2251-2259.

3. Australia, New Zealand Extracorporeal Membrane Oxygenation Influenza Investigators, Davies A, et al. Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome. *JAMA.* 2009;302:1888-1895.

4. Pham T, Combes A, Roze H, et al. Extracorporeal membrane oxygenation for pandemic influenza A(H1N1)-induced acute respiratory distress syndrome: a cohort study and propensity-matched analysis. *Am J Respir Crit Care Med.* 2013;187:276-285.

5. Noah MA, Peek GJ, Finney SJ, et al. Referral to an extracorporeal membrane oxygenation center and mortality among patients with severe 2009 influenza A(H1N1). *JAMA.* 2011;306:1659-1668.

6. Guery B, Poissy J, el Mansouf L, et al. Clinical features and viral diagnosis of two cases of infection with Middle East Respiratory Syndrome coronavirus: a report of nosocomial transmission. *Lancet.* 2013;381:2265-2272.

7. Alshahrani MS, Sindi A, Alshamsi F, et al. Extracorporeal membrane oxygenation for severe Middle East respiratory syndrome coronavirus. *Ann Intensive Care.* 2018;8:3.

8. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med.* 2020.

9. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020;395:1054-1062.

10. Henry BM. COVID-19, ECMO, and lymphopenia: a word of caution. *Lancet Respir Med.* 2020.

11. Ramanathan K, Antognini D, Combes A, et al. Planning and provision of ECMO services for severe ARDS during the COVID-19 pandemic and other outbreaks of emerging infectious diseases. *Lancet Respir Med.* 2020.

Basic non-invasive ventilation at the time of COVID-19

Prof. Massimo Antonelli

Professor of Intensive Care and Anaesthesiology at the Università Cattolica del Sacro Cuore, Rome

Director of the Department of Anaesthesiology and Intensive Care at the Fondazione Policlinico Universitario A Gemelli IRCCS

Past President of the ESICM and former Editor-in-Chief of Intensive Care Medicine

Moderators: Jozef Kesecioglu, Massimo Antonelli, Maurizio Cecconi

Owing to a lack of evidence, European/American guidelines do not give a recommendation on the use of non-invasive ventilation (NIV) for patients with de novo acute respiratory failure.[1] COVID-19 American guidelines suggest that patients on NIV require close monitoring for the need to intubate.[2] Lastly, the acute respiratory distress syndrome (ARDS) task force indicate that NIV is only potentially suitable for patients with mild ARDS.[3]

However, owing to a lack of intensive care unit (ICU) beds, ventilators, and staff, some patients may only be able to have NIV. For these patients, non-invasive pressure support ventilation (NPSV) by helmet (see picture) may be beneficial.

In a pilot study of patients with hypoxemic acute respiratory failure, helmet NPSV treatment was successful and was better tolerated and caused fewer complications than face-mask NPSV.[4] Such helmets can also be used to deliver non-invasive continuous positive airway pressure (CPAP).[5] They have the added benefit of containing coughs and sneezes, and use of a high-efficiency particulate air (HEPA) filter on the exit should contain any virus particles. However, helmets are less effective at decreasing inspiratory effort and patient-ventilator synchrony is worse.[6] Carbon dioxide rebreathing also has to be minimized.

A study in patients with non-COVID-19 ARDS reported that patients randomized to a helmet versus face mask had significantly less chance of needing intubation (18% vs 62%) and significantly higher 90-day survival (56% vs 34%).[7] It was also possible to achieve higher positive end-expiratory pressure (PEEP) in the helmet group, due to improved patient tolerance and less air leakage.[7] Helmet NIV also has advantages over high-flow nasal cannula (HFNC) in patients with hypoxemic respiratory failure in terms of improved oxygenation and reduced dyspnoea and inspiratory effort.[8]

Among patients with acute hypoxemic respiratory failure, predictors of NIV failure include: higher expired tidal volume, higher Simplified Acute Physiology Score (SAPS) II score, lower PaO2/FiO2, older age, presence of ARDS or pneumonia, and higher HACOR score (which incorporates heart rate, acidosis, consciousness, oxygenation, and respiratory rate).[9-11]

Suggestions for successful helmet use:

- Pressurize the helmet before placement
- Do NOT use pressure support without PEEP
- Do NOT use pressure support <10 cm water
- Use the fastest pressurization ramp (if present)
- It is ok if patient-ventilator dyssynchrony or delayed inspiratory triggering occur.

References

1. Rochwerg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J 2017;50.

2. Poston JT, Patel BK, Davis AM. Management of Critically Ill Adults With COVID-19. JAMA 2020.

3. Ferguson ND, Fan E, Camporota L, et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. Intensive Care Med 2012;38:1573-82.

4. Antonelli M, Conti G, Pelosi P, et al. New treatment of acute hypoxemic respiratory failure: noninvasive pressure support ventilation delivered by helmet–a pilot controlled trial. Crit Care Med 2002;30:602-8.

5. Patroniti N, Foti G, Manfio A, Coppo A, Bellani G, Pesenti A. Head helmet versus face mask for non-invasive continuous positive airway pressure: a physiological study. Intensive Care Med 2003;29:1680-7.

6. Navalesi P, Costa R, Ceriana P, et al. Non-invasive ventilation in chronic obstructive pulmonary disease patients: helmet versus facial mask. Intensive Care Med 2007;33:74-81.

7. Patel BK, Wolfe KS, Pohlman AS, Hall JB, Kress JP. Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. JAMA 2016;315:2435-41.

8. Grieco DL, Menga LS, Raggi V, et al. Physiological Comparison of High-Flow Nasal Cannula and Helmet Noninvasive Ventilation in Acute Hypoxemic Respiratory Failure. Am J Respir Crit Care Med 2020;201:303-12.

9. Carteaux G, Millan-Guilarte T, De Prost N, et al. Failure of Noninvasive Ventilation for De Novo Acute Hypoxemic Respiratory Failure: Role of Tidal Volume. Crit Care Med 2016;44:282-90.

10. Antonelli M, Conti G, Moro ML, et al. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. Intensive Care Med 2001;27:1718-28.

11. Duan J, Han X, Bai L, Zhou L, Huang S. Assessment of heart rate, acidosis, consciousness, oxygenation, and respiratory rate to predict noninvasive ventilation failure in hypoxemic patients. Intensive Care Med 2017;43:192-9.

Challenges with family involvement during an outbreak

Professors Elie Azoulay, Jozef Kesecioglu, Nancy Kentish-Barnes

Moderators: Maurizio Cecconi, Massimo Antonelli, Jozef Kesecioglu

Challenges

One of the greatest challenges during the COVID-19 outbreak is interacting with families whose loved ones are isolated in the ICU. Containment is mandatory, limiting family visits to the ICU and the ability to provide empathy, optimal communication, and decision-making. The psychological effects of quarantine are also felt by the patient's family, who can feel a broad range of symptoms including stress, confusion, fear, stigma, and anger.[1] Patients isolated in the ICU are also at higher risk of suffering delirium.[2]

Family members of patients hospitalized with ARDS are as 'sick' as the patients themselves, and can be burdened with symptoms including post-traumatic stress disorder (PTSD), post-ICU syndrome, etc., long after the patient has been discharged (or died).[3] Seeing a family member suffering with dyspnoea, who is not breathing peacefully, leads to a complicated form of grief and increased risk of PTSD and depression relative to the survivors themselves.[4]

Media coverage is overwhelming and is shaping the fears of the family members who are unable to visit their relatives in the ICU, adding to panic, stress, and the potential for hysteria. Reducing exposure to media content and relying on trusted forms of communication are essential to achieving the delicate balance of staying informed while not feeling overwhelmed by the news.

5-S strategy

Acute respiratory failure and ARDS are putting family members at high risk of emotional burden; isolation and containment worsen these symptoms. Rather than preventing all family visits, the approach adopted in the Medical ICU at Hôpital St Louis, Paris, is to follow the 5-S strategy:

1. Stimulate family visits (with limits, effective PPE for family, limited to one member per day).
2. Standardized written information for the family.
3. Set up routine telephone calls with the relatives (done by medical students, but with doctors and nurses also responding to direct contacts).
4. Solicit family members' creativity / use video / diaries / text messages / media groups.
5. Start up a different model close to the end of life.

Small actions by HCPs can translate into large benefits for family members. By reducing the pain and sickness experienced by the family members − thereby reducing the risk of PTSD and other conditions − the family will be better placed to care for the patient after their discharge from hospital and over the long term.

Improving communication

Restricting visits has been very painful for HCPs, patients and their families, with patients dying alone, without their families. Ways to improve communication with patients and families include:

- HCPs using iPads and telephones to communicate between rooms.
- Taking photos of the patient and sending them to the family.
- Providing the patient with electronic devices to contact their family.
- Establishing times when the HCP will contact the family to provide an update (don't call us, we'll call you).
- When wearing PPE, using your eyes to express emotion (as your mouth is covered).
- Setting up dedicated teams (e.g. colleagues in other wards with less work) to communicate with families, releasing doctors to carry on treating patients.
- Changing the mindset: expectations should be different (care may not be as high), and warn the family.

Long-term support for staff

- Provide psychological help for HCPs, not all of whom are familiar with end-of-life issues, who are at risk of infection themselves and are having to look after their sick colleagues.
- Give credit to teams and understand how important their actions were.
- Allow time now (twice a day), and in the future, to debrief.
- Prioritize training and PPE, with the support of senior management.

References

1. Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet.* 2020;395:912-920.

2. Van Rompaey B, Elseviers MM, Schuurmans MJ, Shortridge-Baggett LM, Truijen S, Bossaert L. Risk factors for delirium in intensive care patients: a prospective cohort study. *Crit Care.* 2009;13:R77.

3. Dinglas VD, Chessare CM, Davis WE, et al. Perspectives of survivors, families and researchers on key outcomes for research in acute respiratory failure. *Thorax.* 2018;73:7-12.

4. Sanfilippo F, Ippolito M, Santonocito C, et al. Long-term functional and psychological recovery in a population of acute respiratory distress syndrome patients treated with VV-ECMO and in their caregivers. *Minerva Anestesiol.* 2019;85:971-980.

Observations from JAMA

Dr Howard Bauchner, MD

Editor in Chief, JAMA and the JAMA Network

Moderators: Jozef Kesecioglu, Maurizio Cecconi, Massimo Antonelli

Journal response to COVID-19

JAMA has received >500 submissions in the last 2 months. They are publishing papers on research, opinions, and reviews. To date, there have been nearly 10 million views / listens to their content. Along with most other major journals, JAMA is taking steps to help disseminate information about COVID-19, including:

- **Free** content
- **Fast** manuscript processing
- Translating manuscripts into Chinese
- Dedicated landing site / home page (www.ja.ma/covid)
- Links to the World Health Organization (WHO) website
- Use of **social media** and electronic tables of content
- **Live streaming** of events, podcasts, infographics, crowdsourcing.

Public health and scientific observations

- It is likely that China's quarantine worked
- China gave the world 3–4 weeks' notice, but most countries squandered that time
- Taiwan, Hong Kong, Singapore, and Korea have had tremendous success, but most have small populations and sophisticated health information technology
- The lack of rapid testing (within hours, not days) has resulted in organizational and logistical nightmares, with additional misuse of personal protective equipment
- Protecting healthcare workers is essential
- The US is currently coping, but the next week will be critical, until they reach the end of the incubation period after social distancing began
- There is tension over unapproved therapies in intensive care units (ICUs)
- There is speculation that angiotensin converting enzyme inhibitors and angiotensin receptor blockers could worsen COVID-19 infection
- It is unclear why so few children are impacted
- There are uncertainties around the route of spread, vertical transmission (i.e. mother to baby), and passive protection
- What happens in September will be critical, i.e. will COVID-19 act more like influenza or other pandemics
- The hospitalization rate is 20–30%, of whom around 1/3 need ICU beds

- The case fatality rate ranges from <1% in some countries to >5% in others (possibly related to population age, comorbidities, coding differences, number of ICU beds, preparedness)
- Predictive model results vary substantially (up to 1000-fold differences). Some models are too simplistic (e.g. dynamic models are better than static models) and they need constant updating (e.g. social distancing changes the number of people each case infects)
- The potential roles of antivirals, steroids, and chloroquine need to be tested and reported.

Learning while doing in a pandemic

Prof. Derek C. Angus, MD, MPH

Section Editor, Caring for the Critically Ill, JAMA

Moderators: Jozef Kesecioglu, Maurizio Cecconi, Massimo Antonelli

The problem

During the COVID-19 pandemic, there are two compelling (and competing) priorities: **treating** patients and **testing** treatments (drugs). Exploiting existing knowledge or beliefs is helpful in the short-term, but not in the long-term. However, learning something new is risky in the short-term, but essential for the long-term. In this uncertain situation, we need to try and do both **simultaneously**.

The solution

We need to find the right **balance** between treating and testing to ensure the best possible outcomes for patients, while also managing to gain knowledge about new treatments. This then needs to be **disseminated** as quickly as possible. In artificial intelligence, exploitation and exploration are combined in a single integrated mathematical problem: there is a central tenet of reinforcement learning.

However

Doing (clinical practice) and learning (clinical research) are separate in medicine for various reasons, including ethical ones. There are also many separate organizations, cultures, people, funding, procedures, and goals. Nobody has the goal of searching for the most efficient way to simultaneously 'do' and 'learn', especially during a pandemic.

Drug testing

Clearly, the best test for a drug is a randomized controlled trial (RCT), but there are ethical issues, RCTs are very cumbersome, and there is a lack of worldwide coordination. Some potential solutions include:

- Design more **ethical** RCTs
  - Multiple active arms, only one control arm
  - Use adaptive randomization[1] to preferentially assign patients to best therapy over time
- Use master protocols with standard entry criteria, outcomes, etc.
- Accept that trials will not be perfect, e.g. do not insist on a placebo arm
- Minimize the burden on clinicians as they are already swamped
- Make use of electronic health records, etc.
- Physicians to reflect on uncertainty and equipoise
- Physicians could engage in enrolment and informed consent.

Conclusions

This pandemic makes us **do and learn simultaneously**. An **integrated effort** is required to learn while doing, by combining practice with research. To put this into context, the question as to whether quinine could be beneficial among patients with viral pneumonia was asked back in 1919, and we still do not know the answer…

Reference

1. Adaptive Platform Trials Coalition. Adaptive platform trials: definition, design, conduct and reporting considerations. Nat Rev Drug Discov 2019;18:797-807.

Guidelines on the management of critically ill adults with COVID-19

Drs. Waleed Alhazzani[a,b] and Laura Evans[c]

[a]*Department of Medicine, McMaster University, Hamilton, Canada*

[b]*Department of Health Research Methods, Evidence, and Impact, McMaster University, Canada*

[c]*Department of Pulmonary and Critical Care Medicine, University of Washington, USA*

Moderators: Jozef Kesecioglu, Maurizio Cecconi, Massimo Antonelli

Guidelines for the management of critically ill patients with COVID-19 have been compiled based on literature searches (of studies of patients with COVID-19, other coronaviruses, ARDS, and shock) and an expert panel. They include 50 recommendations relating to infection control and testing, haemodynamic support, ventilatory support, and therapy.

These guidelines are based on the information available at the time they were written. They are subject to uncertainty and lack a strong evidence base. They will change, but they are the best we can do right now.

Best practice statements are:

1. Use of fitted respirator masks by HCPs performing aerosol-generating procedures on patients with COVID-19 in the ICU
2. Performing aerosol-generating procedures in a negative pressure room
3. Endotracheal intubation should be performed by the most experienced available HCP to minimize the number of attempts and risk of transmission
4. Patients receiving NIPPV or HFNC should be closely monitored for worsening respiratory status, and early intubation in a controlled setting should be done if their condition worsens

For details of the remainder of the recommendations (which are either strong or weak, depending on the level of evidence), please access the full guideline, which is available at https://www.esicm.org/wp-content/uploads/2020/03/SSC-COVID19-GUIDELINES.pdf. This guideline will be updated as new evidence becomes available.