

## COVID-19: 10 things I wished I'd known some months ago

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The COVID-19 pandemic is ongoing and spreading, affecting individuals in over 200 countries now. While COVID-19-related articles are being published every day, including guidelines of optimal clinical management [1], there are several practical issues that we wished we had known earlier. This viewpoint addresses 10 points that may be of interest both the logistics, as well as actual clinical care of critically ill COVID-19 patients. We stay away from items that are self-evident and will not address aspects of treatment that are explicitly described elsewhere [1].

### 1. Crisis management in the ICU and planning to surge capacity

It cannot be stressed enough to prepare and anticipate [2-5]. Discuss logistics of upscaling the number of ICU beds and necessary resources (both equipment and personnel) required to treat these patients as early as possible, as both will become limited. There needs to be alignment with the hospital board of directors about allocation of resources, as shortage of ICU-nurses means that healthcare providers working in the operation room and anesthesiology department are needed in the ICU, implying that other (non-urgent, elective) tasks need to be down-scaled or stopped. (Risk of) shortage of personal protective equipment imposes a huge psychological pressure on medical staff and updates should be communicated transparently.

### 2. Personnel management

Start training residents, non-ICU nurses in advance [2]. Apart from ICU-related matters that non-ICU personal need to become familiar with, adherence to infection control precautions is paramount. Also, a clear policy to allow/not allow healthcare providers with a medical history that may increase their vulnerability to COVID-19 to work in the COVID-unit should be communicated. Personnel will be confronted with moral dilemmas and may experience fear and anxiety, that deserves attention. Peer-support and moral deliberation meetings help. Care-providers are extremely motivated and want to work hard, but, if feasible, try to facilitate days-off as well. Intensivists should act as leaders, and therefore delegate as much as possible: "Everything someone else can do as well should not be done by you". For example, ask competent colleagues to take care of patient transport, vascular access, intubations [2-5]. In some settings an 'airway team' or 'vascular access team' may tremendously facilitate intensivists.

### 3. The value of conventional biomarkers

Generally speaking, patients come in with a high CRP and low PCT. Over the days, typically CRP decreases while short-lived increases in PCT may be observed that appear not to relate to bacterial infection [6]. There is highly fluctuating fever. Typically, patients that can be extubated 'early' (after approximately 10 days) show decreasing CRP and temperature kinetics. Presentation with a bacterial or opportunistic co-infection appears to be uncommon. However, if a co-infection is suspected, e.g. because of progressive shock or multiple organ failure, empirical therapy using antibiotics with activity against both typical and atypical respiratory pathogens should be considered. Cytokine elevation profiles appear reminiscent of secondary hemophagocytic lymphohistiocytosis (HLH), or macrophage activation syndrome (MAS). However, while ferritin values are clearly elevated, in the vast majority of patients, this is less than one would observe during MAS.

D-dimer values may reach extremely high levels and hypercoagulation is discussed in the next paragraph.

#### 4. **The hidden problem: hypercoagulation and thrombosis**

There is a high incidence of thrombosis and pulmonary embolism [7-9]. In accordance, for patients on renal replacement therapy, the lifespan of filters appears to be much shorter compared to bacterial sepsis patients with AKI. There should be a low threshold to scan for pulmonary embolism, especially in patients that show a rapid and significant increase in their D-dimer level or a sudden increase in dead-space ventilation. Also a spontaneous prolongation of the prothrombin or activated partial thromboplastin time appears to be a predictor of thrombotic complications [8]. Massive pulmonary embolism with acute circulatory arrest may be the first presentation of COVID-19. Some have advocated to use therapeutic anticoagulation in all patients, but this is clearly not without risks. Physicians should be vigilant as cerebral bleeding following anti-coagulation may occur [10]. Doubling the thrombo-prophylactic dose in COVID-19 patients could be considered.

#### 5. **Cardiac involvement**

Most COVID-19 patients display only mild hemodynamic instability. However, especially patients with pre-existent cardiovascular disease are prone to hemodynamic decompensation. In addition to acute coronary syndrome, fulminant myocarditis may occur, with reduced systolic function, accounting for a large percentage of early deaths [11,12]. Overall mortality is significantly higher in individuals with high TnT compared to those with normal TnT levels. Although severe pulmonary hypertension is not frequently present in the early phase of acute respiratory failure,

#### 6. **Pharmacological treatment**

Antiviral, immunomodulating, and other compounds with possible therapeutic efficacy are discussed elsewhere [1]. So far, no specific treatment has shown clinical benefit. Use of unproven therapies requires informed consent and clearly also carry risks that should be discussed with the patient/family [13], while desperation may drive physicians to try therapies that are backed by little or no evidence. The difficult choice between this urge to treat ('just-do-it option') and the urgent need to generate knowledge on what actually works ('must-learn-option') is clear, but there are ways to blend these options [14]. The use of steroids during refractory shock is advocated [1], but this rarely occurs. Apart from this indication, later during the course some patients show a decrease in lung compliance in combination with high dead space ventilation, suspect for development of fibrosis. As in other cases of ARDS one may consider steroids in this subgroup of patients as well [15]

#### 7. **Mechanical ventilation**

Endotracheal intubation is indicated for the usual thresholds. Both HFNO and NIV may be tried but patients that are unable to decrease their respiratory drive as measured by esophageal pressure have a very high risk for failure [16]. Considering mechanical ventilation, one size does not fit all. COVID-19 patients may present with divergent pathological features ranging from the so-called L-type (low elastance, low driving

pressure) to the H-type (high elastance, high driving pressure) [17]. Although the former appears to be more prevalent during the initial phase, this may change during the course of the disease [18]. Ultrasound could help at the bedside in identifying the different patterns [19]. The potential for recruitment for the L-type appears to be limited. Mechanical ventilation should be tailored to the mechanical lung properties. Lower PEEP and prolonged proning in case of severe hypoxia should be considered for L-type. The H-type may benefit from higher PEEP levels. Following the acute phase, pressure support mode is feasible in prone position. In our opinion this is safe, if an excessive respiratory drive is monitored by using  $P_{O.1}$ ,  $P_{mus}$  or transpulmonary pressure. Excessive respiratory drive may result in “patient-self-inflicted lung injury” (P-SILI) and explain the transition from the L- to the H-type [17].

### 8. **The thing nobody wants to think about**

It is extremely important that a triage decision system is agreed upon before an overwhelming number of critically ill patients flood ICU capacity and additional resources [20]. Deciding between two patients that under normal circumstances would both receive critical care treatment will pose an immense burden on those involved in decision making. We think that a triage decision team including intensivists, geriatricians, ethicists, nurses and lawyers should operationalize guidelines issued by a national Critical Care Society, achieve consensus with different medical specialists, nursing organizations and patient representatives and prepare the hospital for this worst-case scenario. Full immunity from prosecution and moral support for those involved are essential components of this process.

### 9. **Management of the tsunami of research ideas, email spamming and info-overload**

Clearly, intensive care physicians should be sure to keep informed of the evolving knowledge related to new insights into the new disease and its treatment [21], while at the same time huge logistic challenges (that are extremely time-consuming) present themselves. National societies could play a role in providing cyclic updates in guidelines, or establish a committee that selects clinically relevant papers and distribute these among their members. For research in this specific patient population, the risk of a situation like this is that too many sub-optimally designed, small (and therefore statistically underpowered) interventional studies are initiated and we may end with no clinically relevant answers. From the start of the outbreak, dozens of emails with suggestions for treatments were/will be sent to all of us. Central coordination and prioritizing is useful and will increase the chances of performing meaningful studies [22].

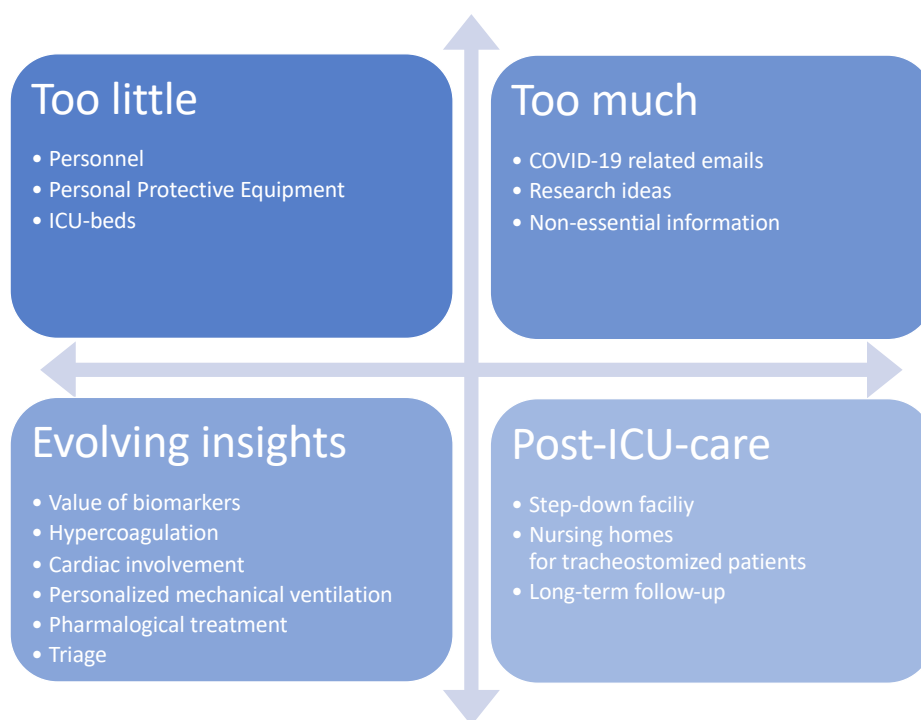
### 10. **Post-intensive care follow-up**

Post-intensive care follow-up should be organized early. A large step-down facility is needed as the number of tracheostomized patients with severe muscular weakness will likely be immense. If ignored, discharge from the ICU will not be possible. We also need to organize nursing homes and rehabilitation centers that can facilitate e.g. care for patients with a tracheal canula. Psychological support should be offered early on because the lack of human contact caused by personal protection clothing and visitor limitations

will likely result in a higher incidence of post-traumatic stress disorder, anxiety and depression in COVID-19 patients, as well as their families. Longer-term consequences are for now largely unknown but will present themselves in the near future.

### Concluding general remarks

Current times in the ICU are unprecedented. During this pandemic we are learning about a new disease and its treatment and optimal support, and knowledge is evolving by the day. Logistic challenges are immense and time-consuming and information overload is a threat. We wished to provide a summary of our first experience with critically ill COVID-19 patients, 10 things that in our view were relatively underexposed in previous publications.



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