

Standard treatment procedure

All COVID-19 patients were treated according to the COVID-protocol of the JESSA hospital, based on the latest insights on COVID-19 at that timepoint³. According to this protocol, all patients admitted to our ICU received an IV-infusion with glucose 5% at 60 ml/h as maintenance fluid and stress ulcer prophylaxis with Pantoprazole 40 mg intravenously daily. Prophylactic antibiotic therapy was initiated for 5 days, using Amoxicillin-clavulanic acid 1 g intravenously 4 times a day or Moxifloxacin 400 mg intravenously once daily in case of known allergy to penicillin. Initially, corticosteroids were administered with caution and minimally after 1 week of ICU admission, based on the clinical judgement of the attending intensivist. After publication of the first results of the RECOVERY-trial, published in February 2021, all patients received intravenous dexamethasone at a dose of 6 mg once daily for ten days after admission. Ventilatory support was initiated with a high-flow nasal cannula or non-invasive mechanical ventilation as long as the patient was cooperative with this treatment. Awake prone positioning was also applied in cooperative patients who required support with a high-flow nasal cannula to prevent intubation. In case of respiratory fatigue, patients were sedated and intubated and invasive mechanical ventilation was started according to the ARDS-network guidelines. This was based on the first reports that viral pneumonia caused by SARS-CoV-2 mimicked an ARDS-like pattern³. Sedation was performed by a combination of propofol, midazolam, and piritramide aiming for the lowest level of sedation required to tolerate mechanical ventilation. Adjustments were made guided by pulse oxymetry-levels, which were continuously monitored, and arterial blood gasses taken every 4 hours. In case of hypotension due to vasoplegia, norepinephrine was used as the first choice vasopressor.

Anticoagulation

Between March 13th, 2020 and March 30th, 2020, all patients received routine low dose pharmacological VTE prophylaxis, i.e. once-daily subcutaneous injection of nadroparin calcium 2850 IU. On March 30th, 2020, a high incidence of deep venous thrombosis was discovered¹⁹, for which we

changed our prophylactic anticoagulation protocol from prophylactic to intermediate dosages of low molecular weight heparin (LMWH) with plasma anti-Xa activity monitoring²⁰. Anti Xa activity was measured daily and targeted at 0,3 to 0,5 IU/ml in patients without echographic findings of deep venous thrombosis (DVT) and 0,4 to 1 IU/ml in patients with screening duplex positive for DVT. Patients were systematically screened with Doppler ultrasonography for DVT twice per week. Other hemostasis parameters were also measured daily and included the activated partial thromboplastin time (aPTT), international normalized ratio (INR), platelete count and fibrinogen. At initiation of ECMO therapy, LMWH therapy was stopped and unfractionated heparin (UFH) was started for anticoagulation management of ECMO patients. In these patients, aPTT was measured six times per day and targeted at 60-80 seconds in patients without echographic findings of DVT and 80-100 seconds in patients with screening duplex positive for DVT.