SARS-CoV-2 does not spread through ECMO or Dialysis Membranes

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a major worldwide health threat in just a few weeks (1). Intensive care unit (ICU) admission and the recourse to extracorporeal organ support, such as continuous renal replacement therapy (CRRT) or veno-venous extracorporeal membrane oxygenation (VV-ECMO) may be needed in the most severe forms of the disease (2). Since SARS-CoV-2 viremia has been reported in some cases (3), it has been hypothesized that this small virus (average size of 125 nanometers (4) could pass through polymethylpentene ECMO membranes or acrylonitrile/sodium methallylsulfonate CRRT membranes. In this study, we investigated whether SARS-CoV-2 RNA was detected in the dialysis effluent fluid or in the condensate collected from the ECMO membrane exhalation port (gas outlet), when the virus was present in the lower respiratory tract and the plasma.

Methods | We evaluated consecutive patients admitted to 3 university ICUs in Paris, who had severe SARS-CoV-2 infection and required CRRT (hemodiafiltration or hemofiltration), VV-ECMO or both. Samples were obtained from respiratory tract, plasma, the dialysis effluent fluid and from 5-10 mL of condensate collected from the ECMO membrane gas outlet within 48 hours after ECMO initiation. Real-time reverse transcriptase (RT) polymerase chain reaction (PCR) targeting the E (envelope) gene gene of SARS-CoV-2 was performed as previously described (5). The cycle threshold (CT) values of RT-PCR were used as indicators of the RNA viral load in samples, the lower the CT, the higher the RNA viral load. The estimated probability (95% confidence interval [CI]) and the binomial probability of SARS COV-2 in the gas outlet and the dialysis fluid were reported, respectively. Ethical approval was applied to our local ethics committee (CER Sorbonne University, N°2020 – CER-2020-32).

Results | All 27 patients were on mechanical ventilation and 25/27 were supported by VV-ECMO (20 patients with Quadrox oxygenator (Getinge, Orléans, France) and 5 patients with

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Oxymedos oxygenator (Xenios, Fresenius, France). In addition, 8/27 patients received CRRT (Prismaflex, Baxter). CRRT was administrated using hemofiltration in four patients and hemodiafiltration in four patients. Main findings are presented in Figure 1. SARS-CoV-2 RNA was detected in all samples from patients' lower respiratory tract (median CT 28, 25-75% interquartile range, [22-31]), and in the plasma of 13/27 of them (median CT 29, IQR [29-30]). However, SARS-CoV-2 RNA was not detected in the membrane oxygenator gas outlet condensate, whether plasma RNA was positive (n=13/25) or negative (n=12/25). Similarly, SARS-CoV-2 RNA was not present in the dialysis effluent of the 8 patients on CRRT, whether plasma PCR was positive (n=4/8) or negative (n=4/8). Therefore, the estimated probability of a positive SARS-CoV-2 RNA in the membrane oxygenator gas outlet condensate and in the dialysis fluid were 0.0 (95%CI 0.00-0.14), and 0.0 (95%CI 0.00-0.37), respectively. Based on binomial probabilities of our results, the prevalence of a positive SARS-CoV-2 RNA in the ECMO gas outlet and in the dialysis fluid will likely be lower than 11% and 31 %. Individual data for SARS-CoV-2 RNA detection in lower respiratory tracts, plasma, dialysis fluid and ECMO membrane are given in Table 1 with the values of CT (cycle threshold) resulting from PCR for lower respiratory tracts (column 2) and plasma (column 3).

Discussion | To the best of our knowledge, this is the first study that investigated the risks of SARS-CoV-2 dissemination through membranes used for extra corporeal organ support in critically ill patients. While a recent report revealed that SARS-CoV-2 is almost always present in the lower respiratory tract, sometimes in the feces but never in urine samples (3), our findings are reassuring regarding the risk of ICU professionals contamination when treating patients on VV-ECMO or CRRT. Specifically, our findings do not support the routine use of a viral filter on the exhaust of the commonly used polymethylpentene based ECMO membrane lungs. Prevention and education of health care workers should therefore remain focused on

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limiting the risks of virus spreading during invasive respiratory procedures such as high flow oxygenation, mouth care, intubation, or microbiological sampling of nasopharyngeal, tracheal or bronchio-alveolar secretions. The number of patients with CRRT (n=8) is limited but the fact that SARS-Cov-2 PCR was negative in all dialysis effluent is somehow reassuring. Lastly, we cannot rule out that longer ECMO runs could progressively lead to membrane alteration, plasma leakage and ultimately SARS-CoV-2 aerosolization. However, we purposely chose to investigate the risk of virus spreading within 48 hours after ECMO and CRRT initiation as the viral load – if present in the plasma – is expected to progressively decline afterward. While our findings may not alter practices, they may contribute to address legitimate interrogations raised by the caregivers and reinforce adhesion and trust into infection control measures policies which is likely to play a major role against the outbreak spreading.

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Table 1. Detection of SARS-CoV-2 RNA in the condensate collected from the ECMO membrane gas outlet and in the dialysis effluent fluid

	Lower respiratory tracts RT-PCR (CT)	Plasma RT-PCR (CT)	Dialysis RT-PCR (CT)	ECMO membrane gas outlet RT-PCR (CT)
Patient 1	32	Undetectable	No CRRT	Undetectable
Patient 2	13	29	Undetectable	Undetectable
Patient 3	Positive*	33	Undetectable	Undetectable
Patient 4	28	Undetectable	Undetectable	No ECMO
Patient 5	Positive*	Undetectable	Undetectable	No ECMO
Patient 6	29	30	No CRRT	Undetectable
Patient 7	35	Undetectable	No CRRT	Undetectable
Patient 8	21	Undetectable	No CRRT	Undetectable
Patient 9	24	28	No CRRT	Undetectable
Patient 10	24	Undetectable	Undetectable	Undetectable
Patient 11	19	30	Undetectable	Undetectable
Patient 12	26	30	Undetectable	Undetectable
Patient 13	29	Undetectable	No CRRT	Undetectable
Patient 14	36	Undetectable	No CRRT	Undetectable
Patient 15	33	Undetectable	No CRRT	Undetectable
Patient 16	Positive*	50	No CRRT	Undetectable
Patient 17	Positive*	Undetectable	No CRRT	Undetectable
Patient 18	18	29	No CRRT	Undetectable
Patient 19	18	30	No CRRT	Undetectable
Patient 20	27	Undetectable	No CRRT	Undetectable
Patient 21	15	28	No CRRT	Undetectable
Patient 22	30	Undetectable	No CRRT	Undetectable
Patient 23	30	29	Undetectable	Undetectable
Patient 24	29	Undetectable	No CRRT	Undetectable
Patient 25	23	29	No CRRT	Undetectable
Patient 26	33	Undetectable	No CRRT	Undetectable
Patient 27	32	28	No CRRT	Undetectable

*Patient was tested positive before being transferred in our centre, no CT was provided. CRRT: continuous renal replacement therapy; ECMO: extracorporeal membrane oxygenation

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Figure 1. Detection of SARS-CoV-2 RNA in dialysis effluent fluid or in the exhalation port of the ECMO membrane according to plasma detection of the viral RNA.

ECMO: extracorporeal membrane oxygenation; CRRT: continuous renal replacement therapy

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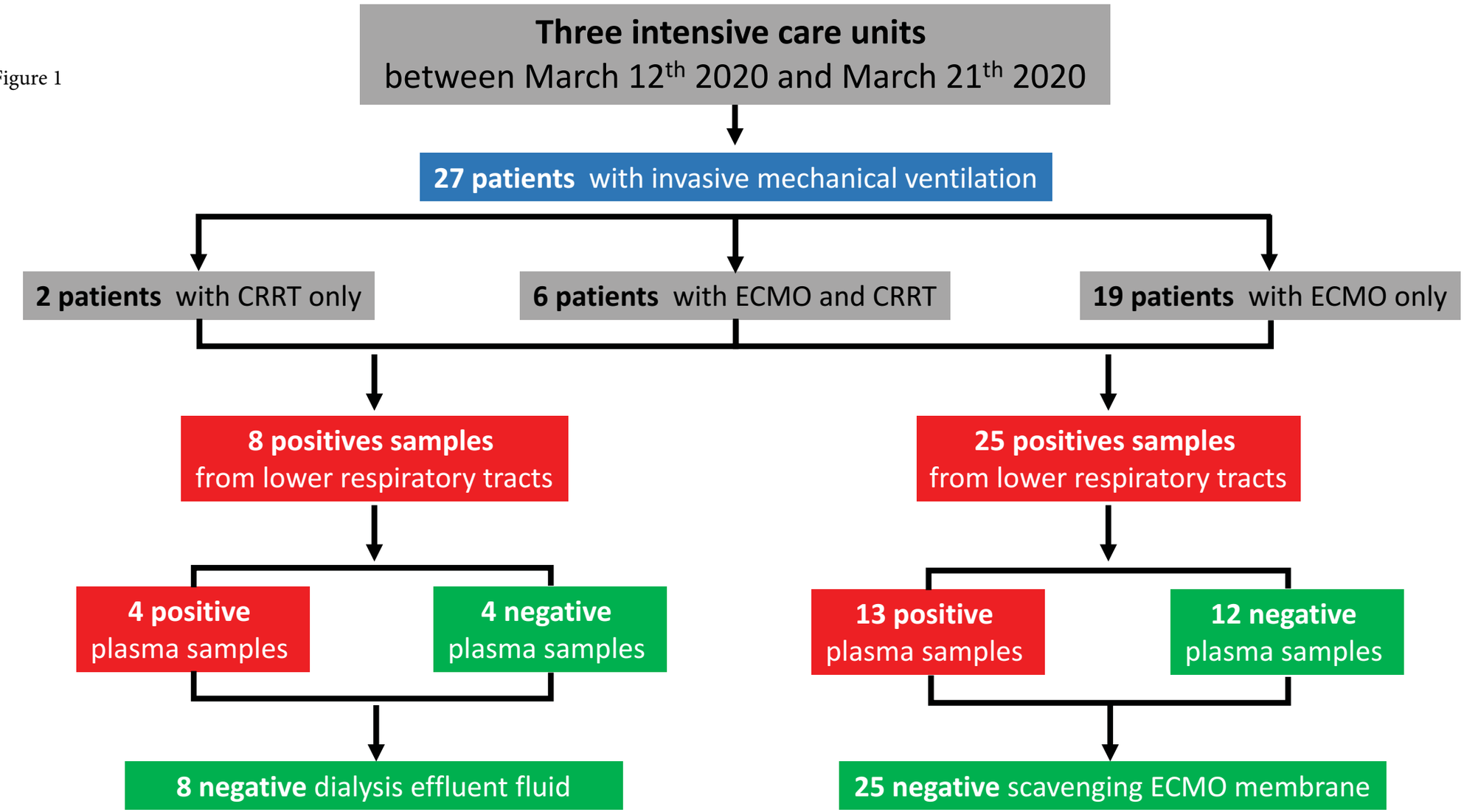
Figure 1



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