Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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CORRESPONDENCE

SARS-CoV-2 viral load in heat and humidity exchange filters during invasive mechanical ventilation of patients with COVID-19

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Editor—We read with interest the paper by Du and colleagues[1] concerning the importance of personal protection during the outbreak of COVID-19 for anaesthesiologists. This is of particular clinical relevance during invasive mechanical ventilation in the ICU when there can be spread of aerosols containing infectious agents with risks to healthcare workers. In this context, we report our experience with the use of heat and moisture exchange (HME) filters in mechanically ventilated patients with COVID-19 to assess whether these filters can reduce that risk.

A HME filter placed in the ventilatory circuit replaces normal heating, humidification, and filtering provided by the upper respiratory tract, preserving the mucociliary apparatus function and preventing thickening of secretions and drying of mucosal surfaces that can favour respiratory complications, such as atelectasis and infections.[2] Moreover, being positioned between the patient and the ventilator equipment, HME filters also have the ability to restrict environmental spread of aerosols containing infectious agents.[2,3] We evaluated the efficacy of HME filters as a barrier to SARS-CoV-2 shedding during invasive mechanical ventilation in the treatment of severe cases of COVID-19 pneumonia. The possible association between viral load in the lower respiratory tract and in filters was also evaluated.

The study was conducted in the ICU caring for patients with COVID-19 at Careggi University Hospital (Florence, Italy) from December 2020 to February 2022. Based on a pilot study, the project was authorised by the General Directorate of the Hospital and approved by the Departmental Internal Scientific Board (October 30, 2020), a database approved by the local Ethics Committee (number 17024; March 31, 2020). Written consent was waived because of the emergency circumstances and because patients were sedated. Next of kin was informed daily by telephone about patients' clinical condition and the investigation of HME filters. Of 18 patients who survived the ICU, follow-up retrospective verbal consent was obtained.

Inclusion criteria were age >18 yr, confirmed molecular diagnosis of SARS-CoV-2, and onset of symptoms <30 days. All enrolled patients (n=36) were on standard treatment with heparin and corticosteroids, with conventional approaches to treatment of acute respiratory distress syndrome.[4] Standard of care included analysis of a bronchoalveolar lavage (BAL) specimen within the first 24 h of invasive mechanical ventilation and possibly after 7 days (to detect and monitor possible co-infections).

The HME filters (BB50 and BB100; Pall Corporation) were positioned in the ventilatory circuit when invasive mechanical ventilation was started, and replaced every 24 h. The BB100 filter was placed in the expiratory line, whilst the BB50 filter was placed in the ventilator outlet port according to the manufacturer's instructions (Supplementary Fig. 1). After usage, HME filters were sealed in sterile bags and sent for quantitative SARS-CoV-2 RNA detection. Both the 'patient side' and the 'ventilator side' of each HME filter were rinsed for 60 s with sterile phosphate-buffered saline 10 ml (Sigma-Aldrich, St. Louis, MO, USA), pH 7.4 (0.2). The eluate was collected (corresponding to ~50% of the initial washing volume) and SARS-CoV-2 RNA extracted, retrotranscribed, and

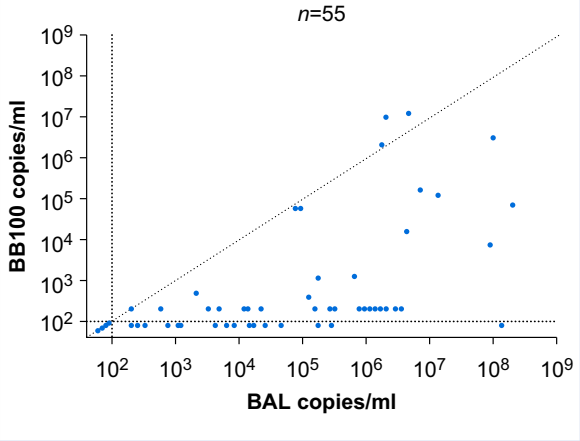

Fig 1. Comparison of bronchoalveolar lavage (BAL) and BB100 heat and moisture exchange filter patient side quantitative SARS-CoV-2 detection. Dotted lines represent the instrument limit of detection (100 copies/ml). Negative samples were plotted as <100 copies/ml. Sample size (*n*).

amplified with SARS-CoV-2 ELITe MGB® Kit on ELITe InGenius® automated system (ELITechGroup, Paris, France). Data, expressed in copies per millilitre calculated on the *rdrp* and *orf 8* genes, were normalised following the manufacturer's instructions, and 95% confidence intervals (CIs) were calculated using the 'Jeffreys' method. Data were plotted and analysed using GraphPad Prism 7.0 (GraphPad Software Inc., San Diego, CA, USA).

We analysed 55 HME filter sets (each comprising one BB100 and one BB50 filter from the same patient) collected from 36 patients (age 55.5 [12.5] yr), including the sets of filters removed after the first 24 h of invasive mechanical ventilation (T0) from all patients and 19 additional sets of filters removed after 1 week (T1) of invasive mechanical ventilation from a subgroup of 19 patients. None of the BB50 HME filters was positive for SARS-CoV-2 RNA in either side (0%; 95% CI: 0.0–4.4%). None of the BB100 filters was positive for SARS-CoV-2 RNA in the ventilator side (0%; 95% CI: 0.0–4.4%), whilst 33/55 (60.0%; 95% CI: 46.8–72.2%) were positive for SARS-CoV-2 RNA in the patient side, with a viral load ranging from 2.0×10^2 to 1.2×10^7 copies/ml. The SARS-CoV-2 viral load in BAL specimens ranged from 2.0×10^2 to 2.0×10^8 copies/ml. Overall, the viral load in the patient side of the BB100 HME filters showed a mean of 2.2 log reduction (range: −0.7 to 4.3) compared with BAL specimens (Fig. 1; Supplementary Table 1).

For 34 of the 36 enrolled patients, the SARS-CoV-2 lineage was determined as described,[5,6] showing the presence of the most important lineages in the study period: B.1.617.2 (delta; *n*=12), B.1.1.7 (alpha; *n*=11), wild type (*n*=6), P.1 (gamma; *n*=4), and B.1.1.529 (omicron; *n*=1) (Supplementary Table 1).

This is the first demonstration that BB100 HME filters are effective in preventing SARS-CoV-2 spread in mechanically ventilated patients with COVID-19. SARS-CoV-2 RNA was never detected in the external side of the filter, suggesting either the absence of viral RNA or its presence in amounts lower than the limit of detection. By contrast, viral RNA was detected in a number of cases (33/55; 60.0%) in the patient side of the BB100 device. Similarly, Heuer and collegues[7] documented that three filters retained H1N1 influenza virus input in an airstream model. Interestingly, when the BAL viral load was $>10^5$ copies/ml, most filters (23/25; 92.0%; 95% CI: 76.7–98.3%) were positive for SARS-CoV-2, whilst when the viral load was $\leq 10^5$ copies/ml only nine of 29 (31.0%; 95% CI: 16.6–49.0%) filters were positive ($P<0.001$).

Because SARS-CoV-2 shows a high transmission rate, implementation of increased infection control measures is important to reduce risk of transmission for both patients and healthcare professionals. HME filters have been investigated previously for SARS-CoV-2 detection from the patient side of the filter in a limited number of patients (*n*=4).[8] Our study showed the ability of HME filters to prevent SARS-CoV-2 permeation, independently of viral load and SARS-CoV-2 lineage, despite the relatively low number of filter sets analysed and the single-centre design.

Declarations of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2022.08.031.

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