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undergone serology tests as part of their COVID-19 status assessment. Close contacts who lived in migrant worker dormitories were excluded from this analysis because their living environments were contextually different from community close contacts and because there were separate challenges in identifying cases and their close contacts within the dormitories. Negative binomial regression was done using Python version 3.7.1 (Python Software Foundation, Wilmington, DE, USA) to calculate the incidence rate ratios of a quarantined person from the community testing positive for COVID-19, adjusting for the symptom and serology status of the index case; two-tailed statistical significance was set at 0.05.

628 people with COVID-19 were included in this analysis (appendix). 3790 people were close contacts of an index case and were quarantined. On average, 6.0 people from the community were quarantined per index case. Overall, 89 (2%) of 3790 close community contacts developed COVID-19 while in quarantine. Of these, 50 (56%) of 89 contacts were quarantined because of an asymptomatic index case, whereas 39 (44%) contacts were quarantined because of a symptomatic case. 43 (48%) contacts were quarantined because of a seronegative index case, whereas 46 (52%) were quarantined because of a seropositive index case.

Negative binomial regression revealed that when adjusted for age, gender, and serology of index case, the incidence of COVID-19 among close contacts of a symptomatic index case was 3.85 times higher than for close contacts of an asymptomatic index case (95% CI 2.06–7.19;  $p < 0.0001$ ; appendix).

Our findings suggest that people with asymptomatic COVID-19 are infectious but might be less infectious than symptomatic cases. We also identified that the proportion of close contacts who became infected

did not depend on the serology status of the index case. One reason for this observation could be that close contacts tend to live or work with the index case and are exposed because of their regular contact with a person who was infectious before turning seropositive.

The main limitation of this analysis is that cycle threshold values and viable shedding data were not available for all individuals included. Future studies should explore the relationship between viral loads, viable shedding, and transmission. Nevertheless, these findings suggest that where resources permit, contact tracing should proactively seek people with asymptomatic COVID-19 because they can transmit disease and will need to be contained if a national policy objective is to minimise cases and transmission. However, if resources are limited, then focusing contact tracing around symptomatic people who are easy to identify (by way of them seeking health care) might be more resource-effective in reducing transmission at the population level.

We declare no competing interests.

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- 1 Kronbichler A, Kresse D, Yoon S, Lee KH, Effenberger M, Shin JI. Asymptomatic patients as a source of COVID-19 infections: a systematic review and meta-analysis. *Int J of Inf Dis* 2020; **98**: 180–86.
- 2 Gao M, Yang L, Chen X, et al. A study on infectivity of asymptomatic SARS-CoV-2 carriers. *Respiratory Medicine* 2020; **169**: 1–5.
- 3 Yong SEF, Anderson DE, Wei WE, et al. Connecting clusters of COVID-19: an epidemiological and serological investigation. *Lancet* 2020; **20**: 809–15.
- 4 Peeling RW, Weddenburn CJ, Garcia PJ, et al. Serology testing in the COVID-19 pandemic response. *Lancet* 2020; **20**: e245–49.
- 5 Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis* **71**: 2027–34.

## ECMO support for COVID-19: a balancing act

We read with great interest the analysis of data from the Extracorporeal Life Support Organization (ELSO)<sup>1</sup> Registry. It provides valuable data that support the use of extracorporeal membrane oxygenation (ECMO) for patients with COVID-19. However, it is widely acknowledged that many critically ill patients with COVID-19 present with coagulation abnormalities that include thrombotic microangiopathy and venous and arterial thromboembolic complications.<sup>2,3</sup> Hence, anticoagulants have been used in these critically ill patients both therapeutically and prophylactically.<sup>4,5</sup>

During ECMO support, continuous contact of circulating blood cells with the surface of the extracorporeal circuit leads to the hypercoagulable state. As a result, anticoagulant therapy is necessary. Although heparin dosage, monitoring assays, and target values selected by most centres are specified in the 2014 ELSO anticoagulation guideline, balancing thrombosis and haemostasis under the double hit of COVID-19 and ECMO is a big challenge for clinicians.

For these reasons, it would have been valuable to record the types and dosages of anticoagulants, the anticoagulant monitoring methods, and the target values.

The big data survey and the authoritative statistical analysis of the ELSO Registry data would make it clear whether patients with COVID-19 who receive ECMO require higher doses of heparin to increase clinical benefits and which monitoring method is most suitable.

We declare no competing interests.

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See Online for appendix

For the 2014 ELSO anticoagulation guideline see <https://www.else.org/portals/0/files/elsoanticoagulationguideline8-2014-table-contents.pdf>

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- 1 Barbado RP, MacLaren G, Boonstra PS, et al. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization Registry. *Lancet* 2020; **396**: 1071–78.
- 2 Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. *Lancet Haematol* 2020; **7**: 438–40.
- 3 Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. *Blood* 2020; **135**: 2033–40.
- 4 Susen S, Tacquard CA, Godon A, et al. Prevention of thrombotic risk in hospitalized patients with COVID-19 and risk in hospitalized patients with COVID-19 and hemostasis monitoring. *Crit Care* 2020; **24**: 364.
- 5 Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost* 2020; **18**: 1094–99.

### Authors' reply

We thank Yang Zhang and colleagues for their thoughtful letter in response to our study of extracorporeal membrane oxygenation (ECMO) support for COVID-19 from the Extracorporeal Life Support Organization (ELSO) Registry.<sup>1</sup> They raise difficult questions concerning bleeding, thrombosis, and the use of anticoagulation in patients with COVID-19 receiving ECMO support.

Before the COVID-19 pandemic, considerable international practice variation and uncertainty existed regarding the optimal anticoagulation strategy during ECMO.<sup>2</sup> In part, consensus is lacking because the key outcomes of bleeding and clotting are multifactorial in origin and might also be disease-specific. Consequently, determining the role of ECMO and anticoagulation in bleeding and clotting events is difficult outside of randomised clinical trials. For example, in the ECMO to Rescue Lung Injury in Severe ARDS Trial,<sup>3</sup> bleeding that led to transfusion was more common in patients receiving ECMO support, but massive bleeding and haemorrhagic stroke occurred at comparable rates between the treatment and control groups.

COVID-19 has compounded this uncertainty. Compared with patients in the ELSO Registry who received ECMO support in 2019, we found no evidence of increased rates of mechanical failure or patient-related bleeding complications in patients with COVID-19.<sup>1</sup> However, in another report,<sup>4</sup> 19% of patients with COVID-19 receiving ECMO support had pulmonary embolism during ECMO; in response, the investigators increased the anti-Xa target. It is unknown to what extent higher doses of anticoagulation reduce thrombotic complications in patients with COVID-19 receiving ECMO support and whether these higher doses of anticoagulation increase the risk of major haemorrhagic events.

We acknowledge that the pathophysiology of COVID-19 might put patients at greater risk of haematological complications. However, the observational nature of our study and the absence of comparison groups prevent us from addressing whether ECMO in general, or whether specific anticoagulation strategies, were differentially associated with bleeding or thrombotic complications.

To address the relationship between anticoagulation, bleeding, and thrombosis in patients receiving ECMO support, investigators need to identify core data elements that rigorously characterise anticoagulation practice, address plausible confounders, and measure validated indices of bleeding, thrombosis, and related outcomes. Without this foundational work, observational studies of anticoagulation, bleeding, and thrombosis during ECMO might yield misleading results. Once completed, ECMO databases such as the ELSO Registry should incorporate that work. Both mechanistic and randomised clinical trials will be required to discern the relationship between ECMO anticoagulation strategies and haematologic outcomes.

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- 1 Barbaro RP, MacLaren G, Boonstra PS, et al. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization Registry. *Lancet* 2020; **396**: 1071–78.
- 2 Protti A, Iapichino GE, Di Nardo M, Panigada M, Gattinoni L. Anticoagulation management and antithrombin supplementation practice during veno-venous extracorporeal membrane oxygenation: a worldwide survey. *Anesthesiology* 2020; **132**: 562–70.
- 3 Combes A, Hajage D, Capellier G, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *N Engl J Med* 2018; **378**: 1965–75.
- 4 Schmidt M, Hajage D, Lebreton G, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study. *Lancet Respir Med* 2020; **8**: 1121–31.

### Adhesions after open and laparoscopic abdominal surgery

In the SCAR update, Pepijn Krielen and colleagues<sup>1</sup> suggested that laparoscopic abdominal surgery reduces the incidence of adhesion-related readmissions. In a linked Comment, Liane S Feldman and Raul J Rosenthal argued for more widespread use of laparoscopic surgery.<sup>2</sup> Laparoscopic surgery is increasingly used<sup>3</sup> and has advantages, such as reduced hospital stay, but it has limitations too.<sup>4</sup> We have concerns about the generalisability of the SCAR data and



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