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.

ages and reported a similar result.[2] Finally, we noticed that ventilation conditions rarely are described in CT studies of airway dimension,[5-7] and we believe that this is a major confounding factor for the reliability and accuracy of the measurement. This is the reason why mechanically ventilated patients were excluded in our study and every airway measurement was made on awake and spontaneously ventilated patients to ensure accuracy.

However, we believe that the statement by Wani et al. that " . . . across all studies, the data revealed a progressive increase in the sizes of the RMB and LMB with age . . . "[1] might be misleading by suggesting a linear growth of the airway throughout the child's development. As we have shown in our work, the growth of the bronchial mainstems and the whole airway are closer to a cubic polynomial, similar to Sempé's growth curve (see Suppl Fig 3 of our work).[2]

Conflicts of Interest

None.

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https://doi.org/10.1053/j.jvca.2020.09.123

Anticoagulation Strategies and Determining the Rate of Fatal Intracerebral Hemorrhage Associated With Venovenous Extracorporeal Membrane Oxygenation in Patients With Coronavirus Disease 2019

To the Editor:

In their case series reporting experience from a single center of the first 10 patients with coronavirus disease 2019 (COVID-19) to receive venovenous extracorporeal membrane oxygenation (VV-ECMO), Usman et al.[1] described significant clinical challenges managing anticoagulation. Four (40%) suffered intracerebral hemorrhage (ICH), three (30%) of which led to death. They advised caution in the anticoagulation of COVID-19 patients undergoing VV-ECMO, and that heparin is monitored actively and frequently. Although we agree that COVID-19 presents new challenges for centers providing VV-ECMO, we wish to comment on some of the limitations of their study in the context of our own experiences. This will. hopefully, set out some of our own experiential learning, as well as aid in the interpretation of their case series and its applicability to future practice.

First, the number of patients included means our ability to draw any conclusions about the rate of ICH in similar, larger populations from these data is extremely limited. Although the authors acknowledge this, we wish to provide further mathematical rationale. It is possible to determine the 95% confidence interval of the proportion of those who died (30%) as 12% to 74%. This is a simple mathematical transformation of a nominator/denominator combination and is simply a way of incorporating sample size into any calculated proportion. A small sample size results in a wide confidence interval. It can be shown by simulating these calculations for different sample sizes that the confidence interval of any proportion is extremely sensitive to n when n is below 50, irrespective of the event rate.[2] As such, these data are useful, but the true rate of fatal ICH in patients with COVID-19 undergoing VV-ECMO may be much higher or even lower than that shown by Usman et al.

Second, the authors described the use of activated partial thromboplastin time (APTT) as the sole measure of effectiveness of anticoagulation with heparin but did not mention using any other laboratory measure. There is considerable evidence of discordance between anti-factor Xa levels (which arguably better reflects heparin effect) and APTT,[3] and the use of anti-factor Xa levels alongside APTT or as a lone measure may allow for more nuanced tailoring of anticoagulation strategies, especially in the context of COVID-19.[4] For patients with COVID-19, a prolonged APTT may indicate a specific or non-specific clotting factor deficiency, and the presence of lupus anticoagulant, which is an indirect deficiency and not associated with bleeding, may affect in vitro tests of anticoagulation. The presence of lupus anticoagulant and a discordance between APTT and anti-factor Xa levels for patients receiving intravenous unfractionated heparin was a common finding at our center for patients with COVID-19 on VV-ECMO. At the beginning of the pandemic and before we understood the limitations of APTT monitoring in COVID-19, we were more aggressive with anticoagulation due to concerns about severe thromboembolic disease, with a starting dose of 1,000 U/hr of unfractionated intravenous heparin titrated upward incrementally according to the APTT. A few early patients developed fatal ICHs, which led to a more conservative strategy of 250 U/hr titrated incrementally to a maximum of 1,000 U/hr with twice daily anti-factor Xa levels for titration. All heparin dosing prescriptions and changes were made on a case-by-case basis and according to the overall clinical picture, usually after

DOI of original article: http://dx.doi.org/10.1053/j.jvca.2020.07.063.

discussion among two or more consultants. We had one heparin-free run of 60 days due to airway bleeding and experienced no associated circuit problems with this case and other heparin-free/sparse runs.

Third, regarding the wider disease process, the authors described issues with extracorporeal thrombosis and specifically, oxygenator failure. Since the start of the COVID-19 pandemic and with 37 patients treated, we have not seen an oxygenator or pump failure due to thrombosis, and certainly not to the extent described by Usman et al. However, we have found venovenous hemofiltration to be an issue, with the circuits clotting off at a higher rate than we would normally expect. This runs alongside another issue not addressed by the authors—what to do in patients presenting with thromboembolic disease, such as pulmonary embolism (present in up to 30% of patients), more so when there is radiologic evidence of ICH.[5] If pulmonary embolic disease is a contributor to respiratory failure before ECMO, decisions about anticoagulation strategies have no easy answers. Such pathology might be seen on a whole-body computed tomography (CT) scan and we decided, early in the pandemic, to undertake interval CT scans after admission and throughout the ECMO run. Although not without risk, this was an extremely beneficial strategy to enable individual decisions to be made about anticoagulation, and we saw our ICH rate reduce as a result.

Finally, in our own experience as a regional ECMO center for the North West of the United Kingdom, we had 37 patients (again, with $n < 50$ it is difficult to generalize our experiences) with COVID-19 undergo VV-ECMO. Of these, 14 (37.8%) were discharged home and 23 (62.2%) have died. Eight (21.7%) had ICHs, of which five (13.5%) were fatal. We did not see any cases of heparin-induced thrombocytopenia in patients with COVID-19, which is usually a common occurrence (~5%) during non-COVID-19 VV-ECMO. The reasons for this are not yet known, but when heparin-induced thrombocytopenia was suspected clinically due to, for example, a relative or absolute decrease in platelet count, we retained a high degree of suspicion and tested for it. We did not experience problems with circuitry and/or oxygenators, in contrast to the authors who described 10 circuit changes in their 10 patients, nine of which were due to oxygenator clots. Perhaps the type of equipment is important, and the magnetic levitating centrifugal pump systems we use may be associated with less thrombogenesis.[6] We also have accumulated much clinical experience with the dynamic nature of cerebral compromise associated with VV-ECMO in patients with COVID-19. We have seen subarachnoid hemorrhage, isolated intracranial hemorrhages and posterior reversible encephalopathy syndrome, sometimes in the same patient. There always should be hope for patients who develop ICH, as one case of a large ICH almost completely resolved by the end of the run, after which hospital discharge ensued.

Overall, Usman et al. should be congratulated for their detailed analysis during a difficult time at the start of the pandemic, but there is now an urgent need for the analysis and publication of larger registry datasets to reveal the true incidence of problems associated with anticoagulation, together with a consensus approach on how best to tailor anticoagulation strategies for individual patients. Our understanding of the neurologic and hematologic sequalae of VV-ECMO in patients with COVID-19 is at a very early stage and we hope we can continue to add to this understanding by learning from each other through collaboration and data sharing among centers.

Conflict of Interest

No funding or conflicts of interest to declare.

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https://doi.org/10.1053/j.jvca.2020.10.039

Liposomal Bupivacaine–Based Erector Spinae Block for Cardiac Surgery

To the Editor:

Inadequate pain relief after cardiac surgery increases morbidity and persistent post-sternotomy pain syndrome significantly, and regional analgesia could improve pain control and outcomes in cardiac surgery.[1-4] Opioid-based analgesia has many adverse effects such as nausea, vomiting, sedation, urinary retention, respiratory depression, and delayed tracheal extubation. Neuraxial analgesia and deep regional anesthesia techniques, such as thoracic epidural and thoracic paravertebral block, are concerning because of the administration of heparin and antiplatelet agents in the perioperative period.[5]

Erector spinae plane (ESP) block recently has been studied as an effective and safe modality of pain control after sternotomy or thoracotomy. Bilateral ESP block performed at the T5 spinous process provides analgesia from the T2-to-T9 sensory level and results in both somatic and visceral analgesia by