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We thank Imamura (1) for their interest in our recently published study (2) in *Critical Care Medicine*.

Patient-related outcome measures are crucial in clinical studies. We looked at all thrombotic events that would require therapeutic anticoagulation as a standard outcome metric. As for severe or fatal thrombosis as the primary endpoint and causation, this was a retrospective study with its recognized limitations. Those with thrombosis did not have a causal relationship with admission D-dimer, WBC, lactate dehydrogenase, or ferritin. We did not look at severe thrombosis, a clinico-physiologic determination subject to definitions. We did not look at physiologic parameters, but echocardiographic evidence of right ventricular dysfunction (RVD) in our coronavirus disease 2019 (COVID-19) acute respiratory distress syndrome (ARDS) cohort has been reported separately (3). Of our cohort, 31 patients had moderate or severe RVD at admission by echocardiography, of whom 24/31 had macrothrombosis on CT angiography. Of the 24 with thrombosis and RVD, 13 were on vasoactive agents for hemodynamic support; one patient died. Vasopressor use was not necessarily for RVD. One patient with RVD without thrombosis on noradrenaline died. Thus, in the study by Mirsadraee et al (2), analysis of outcomes by degree of severity did not differentiate survivors from nonsurvivors. Inhaled nitric oxide was used in a few patients, for rescue oxygenation, rather than RVD (4). Moderate or severe RVD was too infrequent for valid subgroup analysis.

Cause of death is an important determinant. Of 72 patients, 14 with and three without thrombosis died. Indeed, we did report that the presence of thrombosis portended a higher chance of death than absence. However, it is difficult to prove direct causality. A meta-analysis of studies demonstrated increased thrombotic events in those on ICU with high admission D-dimer levels. However, a cutoff has not been suggested due to uncertainty of its validity (5).

In regard to enhanced treatment interventions, a prospective propensity matched cohort study found a priori therapeutic heparin versus thromboprophylaxis to reduce the prevalence of thromboses without an increase in bleeding complications. However, this is not reproduced or recommended by international guidelines. Thus, data from several clinical trials show benefit of thromboprophylaxis in moderate or severe COVID-19 disease, but uncertainty about treatment versus enhanced or extended thromboprophylaxis without confirmed thrombosis (6). In our cohort, only a few patients had a repeat scan within a few days, indicated by a clinical deterioration. Therapeutic anticoagulation was maintained on confirmation. Systemic thrombolysis was used occasionally in selected cases of arteriovenous pulmonary thromboses, and if thrombotic burden, or its impact were life threatening.

The burden of thromboses in patients with COVID-19 ARDS requiring ICU was higher than pre-COVID-19 ARDS (2). Furthermore, the prevalence of thrombosis in our cohort was higher than other published reports. Either due to the severity of disease of these patients, many of whom were on extracorporeal membrane

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oxygenation, or the fact that all patients systematically underwent contrast-enhanced CT at admission to ICU. The ideal investigational algorithm for screening patients admitted to ICU with COVID-19 ARDS remains elusive, as do unified anticoagulation treatment recommendations in the absence of confirmed thrombosis (6).

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Should We Really Use Respiratory Stroke Volume Variation to Assess Fluid Responsiveness in Cardiac Surgical Patients?

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To the Editor:

We read with a great interest the study published by Parke et al (1), published in a recent issue of *Critical Care Medicine*. They performed a well-designed prospective, multicenter, randomized clinical trial including 715 patients and comparing a predefined hemodynamic strategy with a standard of care in the first postoperative hours following cardiac surgery. The primary outcome was the length of stay in ICU. Patients in the intervention group received less fluid (1,000 mL [250–2,000 mL] vs 1,500 mL [500–2,500 mL]; $p < 0.001$). No significant difference between the groups was however observed neither for ICU length of stay nor for any secondary outcome, excepting mortality in ICU (but not in hospital).

The predefined hemodynamic strategy guided fluid administration on respiratory stroke volume variation (SVV). To receive fluids, patients should have a known or suspected inadequate cardiac output associated with SVV greater than 13 %. They were excluded if they had atrial fibrillation, open-chest condition, or mechanical circulatory support. Furthermore, the strategy was applied when patients were under invasive mechanical ventilation and sedation. However, it remains very unlikely that all criteria validating the use of SVV were satisfied.

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