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to determine whether to perform, defer, or cancel inpatient transthoracic echocardiography (TTE) requests on the basis of indication and clinical urgency. We compared clinical status between patients in whom TTE was deferred or canceled and those in whom it was performed, and we assessed in-hospital outcomes on the basis of triage decision (Figure 1).

A total of 145 TTE requests for patients ≥ 18 years of age hospitalized with possible or confirmed COVID-19 were triaged from March 19, 2020, through April 22, 2020. In-hospital outcomes, including subsequent TTE, length of stay, all-cause death, and adjudicated cardiovascular death, were assessed through May 6, 2020.

The median age of our cohort was 66 years (interquartile range, 53–76 years), and 43% were women. At triage, 94 (65%) had confirmed COVID-19, and 51 (35%) had COVID-19 test results pending. Forty-four patients (30%) underwent TTE, and TTE was deferred or canceled on triage in 101 (70%). Among those with confirmed COVID-19 at triage, TTE was performed in 32 (34%) and deferred or canceled in 62 (66%), seven of whom (11%) underwent TTE later. Among these seven patients, only one was found to have a left ventricular ejection fraction $< 50\%$; this patient initially underwent point-of-care ultrasound, and TTE was performed the day after triage. Among patients with deferred or canceled TTE who were eventually COVID-19 negative ($n = 37$), 35 (95%) underwent TTE within 24 hours of the order. No TTE requests were categorized as “rarely appropriate” by appropriate use criteria.⁵

Compared with patients with deferred or canceled TTE, more patients in the TTE-performed group were in the intensive care unit (68% vs 38%), were mechanically ventilated (55% vs 22%), or required intravenous vasopressors (46% vs 14%) at triage; patients in the TTE-performed group also had longer intensive care unit stays (median, 8 vs 1 days) and hospital stays (median, 16 vs 10.5 days; $P < .05$ for all variables). The TTE-performed group had a numerically higher incidence of inpatient death (14 of 44 [32%] vs 18 of 101 [18%], $P = .08$). The proportion of cardiovascular deaths was similar between groups (two of 14 deaths [14%] in the TTE-performed group vs three of 18 [17%] in the TTE-deferred/canceled group, $P > .99$). No sonographers who performed TTE on patients with COVID-19 over the study period were diagnosed with COVID-19.

We found that physician review on the basis of current guidelines selected TTE for more critically ill patients and reduced the number of transthoracic echocardiographic examinations for patients with confirmed COVID-19 by 60% (from 98 requests to 39 that were ultimately performed). This process did not significantly delay TTE for patients with pending COVID-19 test results and appeared to be safe in our initial experience, with no apparent adverse cardiovascular outcomes that could be attributed to deferring or canceling a request. Further outcomes studies on quality improvement initiatives implemented during the COVID-19 pandemic will be needed to ensure high-quality cardiovascular care.

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REFERENCES

1. Kirkpatrick JN, Mitchell C, Taub C, Kort S, Hung J, Swaminathan M. ASE statement on protection of patients and echocardiography service providers during the 2019 novel coronavirus outbreak: endorsed by the American College of Cardiology. *J Am Soc Echocardiogr* 2020;33:648-53.
2. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. *J Am Coll Cardiol* 2020;75:2352-71.
3. Skulstad H, Cosyns B, Popescu BA, Galderisi M, Salvo GD, Donal E, et al. COVID-19 pandemic and cardiac imaging: EACVI recommendations on precautions, indications, prioritization, and protection for patients and healthcare personnel. *Eur Heart J Cardiovasc Imaging* 2020;21:592-8.
4. Ward RP, Lee L, Ward TJ, Lang RM. Utilization and Appropriateness of transthoracic echocardiography in response to the COVID-19 pandemic. *J Am Soc Echocardiogr* 2020;33:690-1.
5. Douglas PS, Garcia MJ, Haines DE, Lai WW, Manning WJ, Patel AR, et al. Appropriate use criteria for echocardiography: a report of the American College of Cardiology Foundation appropriate use criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology. *J Am Coll Cardiol* 2011;57:1126-66.

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Contrast Echocardiography in VV-ECMO-Dependent Patients with COVID-19



To the Editor:

The use of contrast echocardiography in patients receiving venovenous extracorporeal membrane oxygenation (VV-ECMO) for severe acute respiratory failure is not widely published, and there is understandable caution surrounding its use in this population. The coronavirus disease 2019 pandemic resulted in an unprecedented burden on critical care facilities¹ due to severe acute respiratory failure. Our center is one of five nationally commissioned VV-ECMO services in the United Kingdom and has seen VV-ECMO activity quadruple during the first pandemic surge. Consequently, there has been growing emphasis on transthoracic echocardiography (TTE) to diagnose cardiac complications of coronavirus disease 2019 supported with VV-ECMO.^{2,3}

Mechanically ventilated patients receiving VV-ECMO are among the most challenging in whom to obtain diagnostic images on TTE. Predictably, we found that as the volume of VV-ECMO patients increased, so too did the requirement for TTE using ultrasound-enhancing agents (UEAs). Contrast echocardiography is routinely

used at our institution, and this work was approved through the local governance board as a service evaluation. We carried out bedside TTE in 37 consecutive VV-ECMO patients, among whom SonoVue (Bracco International, Milan, Italy) TTE was performed in 10 (27%). SonoVue boluses (0.5–0.7 mL), reconstituted in the standard format, were administered via the postoxygenator limb of the ECMO circuit. Repeated boluses of the UEA were required in all cases, with a maximum total dose in any one patient of 2.5 mL. All patients met criteria for the use of UEAs as outlined in the recently published guidance.⁴ Very low mechanical index imaging was performed with standard commercially available tissue cancellation sequences (Philips Medical Systems, Andover, MA). Very low mechanical index imaging allows excellent tissue delineation and results in less microbubble destruction than the higher mechanical index left ventricular opacification settings. Diagnostic images were obtained in all cases.

In line with our institutional protocols for critical care echocardiography in extracorporeal support (developed in collaboration with our specialist perfusion team), during each contrast study, the VV-ECMO circuit was managed by experienced perfusionists. This included disabling the appropriate interventions on the ECMO console before UEA administration to ensure safe administration. UEAs are known to activate the protective integrated air bubble alarms, which trigger interventions to disable flow, a safety feature of the Cardiohelp ECLS system (MAQUET Medical Systems USA, Wayne, NJ),⁵ and in all cases, the integrated detector for air bubbles was indeed triggered by the UEA. This would usually lead to a pump shutdown because of activation of additional safety interventions, and unless this alarm is cleared, a further “zero-flow mode” is engaged. This mode provides sufficient revolutions per minute to prevent backflow from the return cannula without providing forward flow, so equilibrium is maintained in the circuit. However, the resultant cessation of flow, and consequently oxygenation, can result in rapid desaturation and potentially hypoxic arrest. It is therefore of pressing importance that centers offering VV-ECMO adopt protocols and staff training to allow the safe administration of UEAs, facilitating diagnostic echocardiography in the most critical patients.

To our knowledge, this is the largest published series affirming the applicability of a UEA in VV-ECMO. Appropriate protocols should be instituted at centers offering VV-ECMO, ensuring safe management of the circuit by the perfusion team. Enhanced echocardiography may therefore be an appropriate bedside technique during the current viral surge in critical VV-ECMO supported severe acute respiratory failure, helping address diagnostic uncertainty in cases with challenging echocardiographic visualization.

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REFERENCES

1. World Health Organization. Coronavirus disease (COVID-19) pandemic. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. Accessed July 16, 2020.
2. European Society of Cardiology. ESC guidance for the diagnosis and management of CV disease during the COVID-19 pandemic. Available at: <https://www.escardio.org/Education/COVID-19-and-Cardiology/ESC--COVID-19-Guidance>. Accessed July 16, 2020.
3. Kirkpatrick JN, Mitchell C, Taub C, Kort S, Hung J, Swaminathan M. ASE statement on protection of patients and echocardiography service providers during the 2019 novel coronavirus outbreak. *J Am Soc Echocardiogr* 2020; 33:648-53.
4. Porter TR, Mulvagh SL, Abdelmoneim SS, Becher H, Belcik JT, Bierig M, et al. Clinical applications of ultrasonic enhancing agents in echocardiography: 2018 American Society of echocardiography guidelines update. *J Am Soc Echocardiogr* 2018;31:241-74.
5. Grecu L, Fishman MA. Beware of life-threatening activation of air bubble detector during contrast echocardiography in patients on venoarterial extracorporeal membrane oxygenator support. *J Am Soc Echocardiogr* 2014;27:1130-1.