Cerebral microembolism upon intraoperative venoarterial extracorporeal membrane oxygenation initiation in postcardiotomy shock: A case series

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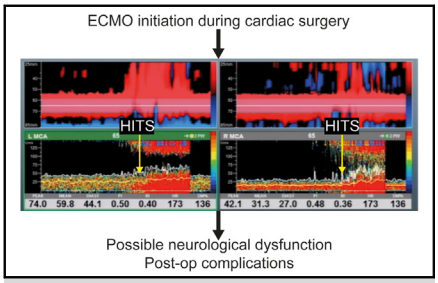


HITS diagnosed with TCD upon ECMO initiation can lead to postoperative complications.

CENTRAL MESSAGE

Three patients undergoing cardiac surgery required ECMO for inability to wean from CPB. Significant cerebral vascular microembolization was documented and associated with major postoperative complications.

Video clip is available online.

With the increasing use of transcranial Doppler (TCD) monitoring for patients undergoing cardiac surgery, the presence of cerebral vascular microembolic events related to cardiopulmonary bypass (CPB) has been documented in up to 76% of patients.[1,2] They have a deleterious influence on cerebral saturation and increase the risk of right ventricular dysfunction, difficult separation from CPB, postoperative organ dysfunction and mortality.[3] The presence of cerebral microemboli upon initiation of intraoperative venoarterial extracorporeal membranous oxygenation (VA-ECMO) has not been reported. We describe 3 cases of microembolic events upon VA-ECMO initiation during cardiac surgery. Institutional review board approval was not required. Informed written consent for the publication of the data was obtained by the patients.

CASE PRESENTATIONS

Case 1

A 28-year-old woman was admitted for an aortic valve replacement. Because of a failure to wean from CPB and absence of myocardial recovery, it was decided to initiate central VA-ECMO, following which numerous high intensity transient signals (HITS) occurred on TCD for a total of 3538 on the left at the end of surgery, associated with cerebral desaturation (Figure 1). Simultaneously, multiple gaseous bubbles, passing through the aortic valve, were observed using transesophageal echocardiography. The patient was subsequently transferred to the intensive care unit, and given the impossibility to wean from VA-ECMO, a heart transplant was performed. The patient presented also a prolonged delirium during the postoperative period.

Case 2

A 48-year-old man with end-stage heart failure was admitted for an elective bicaval heart transplant. A femoro-femoral VA-ECMO and an intra-aortic balloon pump were inserted for an inability to wean from CPB. Immediately after VA-ECMO initiation, we documented an increase in the number of microemboli from 23 to

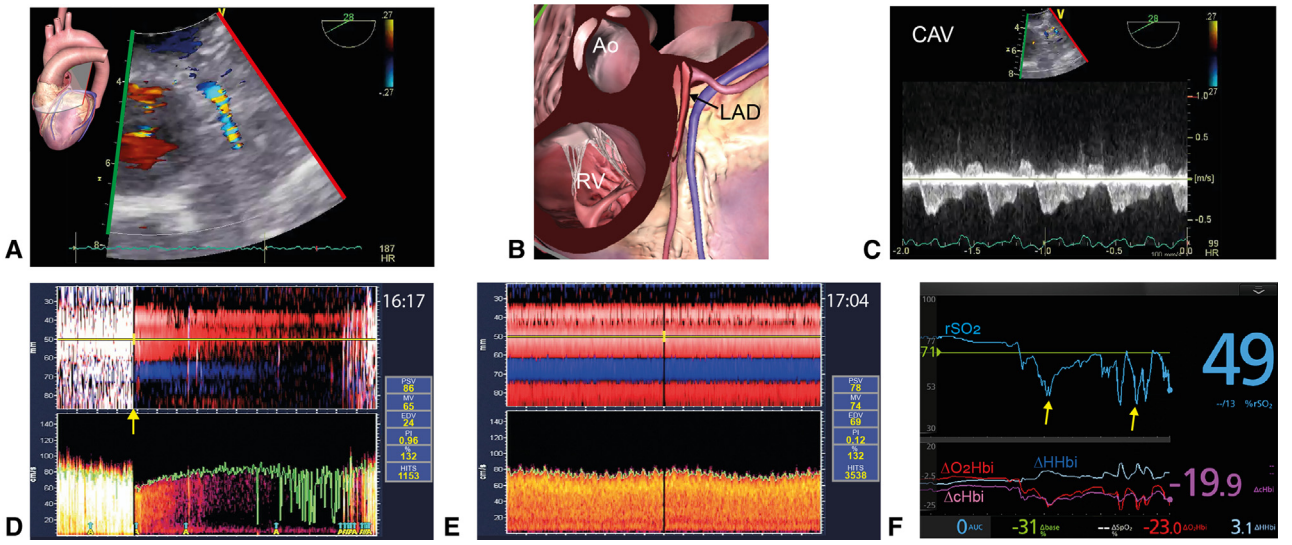
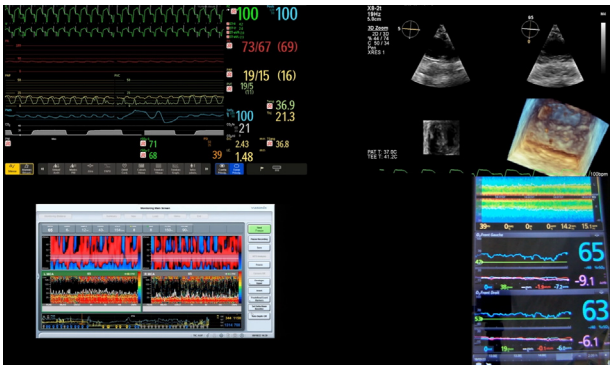


FIGURE 1. Case 1. Ross procedure and extracorporeal membrane oxygenation (*ECMO*). A through C, Biventricular failure in a 26-year-old woman after a Ross procedure. Mid-esophageal (*ME*) view of the left main coronary artery and pulsed-wave Doppler (*PWD*) showing adequate coronary artery diastolic velocities. (Left atrium removed on the sketch.) D and E, Transcranial Doppler (*TCD*) during ECMO initiation. A large number of high intensity transient signals (*HITS*) appeared upon venoarterial ECMO initiation for a total of 3538 on the left by the end of surgery. F, Left hemisphere brain oximetry showing several episodes of desaturation at the end of surgery. *HR*, Heart rate; *Ao*, aorta; *RV*, right ventricle; *LAD*, left anterior descending; *CAV*, coronary arterial velocity; *PSV*, peak systolic velocity; *MV*, mean velocity; *EDV*, end-diastolic velocity; *PI*, pulsatility index; %, percentage of mean velocity in relation to the baseline value; *A*, symbol of HITS detection; rSO_2, regional oxygen saturation; ΔO_2Hbi, change in oxygenated hemoglobin index; *ΔHHbi*, change in deoxygenated hemoglobin index; *ΔcHbi*, change in total hemoglobin index; *AUC*, area under the curve; *Δbase*, change in regional cerebral oxygen saturation compared with baseline; *ΔSpO2*, change in oxygen saturation.

1330 HITS in the left middle cerebral artery (MCA) and from 39 to 3483 in the right MCA (Figure 2 and Video 1). The patient presented a pathological awakening with a right ischemic stroke confirmed by computed tomography.

Case 3

Heart transplantation was undertaken in a 59-year-old man with ischemic cardiomyopathy and for whom a left ventricular assist device was installed. At the end of the transplantation, 732 and 680 HITS had been detected by TCD in the left and right MCA. The patient was placed on peripheral VA-ECMO and intra-aortic balloon pump after 2 failed attempts to wean from CPB. After 24 minutes of receiving ECMO, the TCD had detected more than 5364 and 1625 HITS in the left and right MCAs and 36,137 and 9190 HITS at the end of the case (Figure E1). The patient had significant postoperative delirium and died postoperatively of sepsis.



VIDEO 1. Recording of hemodynamic parameters from Figure 2. Note the simultaneous appearance of air in the aorta and high intensity transient signals on transcranial Doppler without any changes in regional cerebral oxygen saturation. Video available at: https://www.jtcvs.org/article/S2666-2507(24)00445-0/fulltext.

DISCUSSION

We describe 3 cases of postcardiotomy cardiogenic shock and failure to wean from CPB in whom multiple cerebral microemboli upon VA-ECMO initiation were detected by TCD. In cases 2 and 3, this was also confirmed by the CPB air detection monitor. To our knowledge, this is the first documentation of intraoperative microembolization on initiation of VA-ECMO. The third case represented the largest number of HITS observed in cardiac surgery since our implementation of TCD in 2015. Cerebral arterial microemboli could possibly be associated with clinically significant brain injury, even in cases of small bubbles. However, there is no high-quality human data to confidently determine the cerebral circulation microembolic load safety threshold.

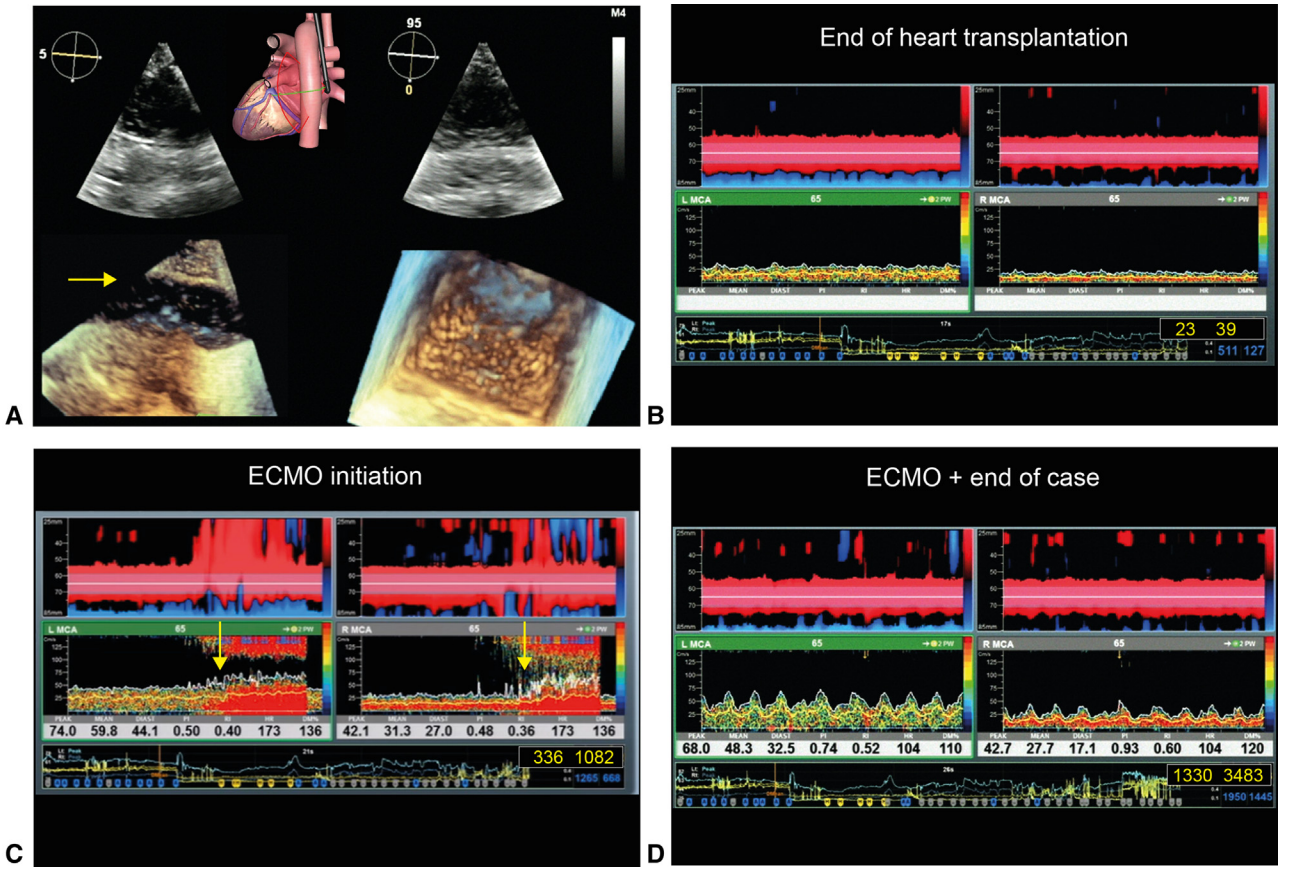


FIGURE 2. Case 2. Heart transplantation and extracorporeal membrane oxygenation (*ECMO*). A, Descending aorta biplane and 3-dimensional views showing air (*arrows*) in the aortic lumen. B through D, This was associated with the appearance of high intensity transient signals (*HITS*) in both the left and right cerebral territory (*yellow arrows*). The total number of HITS increased significantly from 23 and 39 on the right and the left to 1330 and 3483, after heart transplantation with ECMO initiation. *MCA*, Middle cerebral artery; *PI*, pulsatility index; *RI*, resistance index; *HR*, heart rate; *DM%*, delta mean percentage of mean velocity change or delta in relation to the baseline value.

The improvement of TCD technology and the standardization of signal interpretation have enabled CPB microemboli detection and quantification in the arterial cerebral circulation. Recently, an observational study of 354 patients suggested a dose-response correlation between microembolic load and difficulty separating from CPB after cardiac surgery, intensive care unit length of stay, duration of organ dysfunction, duration of vasopressor use, bleeding, and mortality.[3] The technology used in those patients did not allow us to distinguish a gaseous nature or not of the microemboli.

Several techniques and devices have been developed and implemented to reduce microemboli and its consequences. The VA-ECMO circuit differs from the CPB circuit and does not have a device or filter to limit air microemboli. The air and debris present in the ECMO drainage cannula are at least partially filtered by the membrane, the rest being directly injected into the arterial circulation. On most ECMO devices, there is a bubble detector on the venous and on the arterial cannulas, allowing operators to stop the pump only in the event of massive embolus but the detection threshold is $\geq$5 mm. Bubble diameters >35 to 40 μm have been causally linked with morbidity in cardiac surgery.[4] Surgery involving CPB results in a general inflammatory response of varying intensity.[5] Neutrophils, which are well known as the principal cells involved in host defense, play a key role in the inflammatory response to injury.[E1] The release of neutrophil extracellular traps (NETs) by activated neutrophils may contribute to organ damage by acting as scaffolds that trap blood cells and fibrin clots that can occlude the vasculature, promoting thrombosis and tissue hypoperfusion. In recent studies, we observed an increase in circulating NETs in patients undergoing on-pump cardiac surgery. The level of circulating NETs post-CPB increased proportionally with the duration of CPB[E2] and the longer CPB the higher the amount of microembolism.[3] More recently, we observed in patients undergoing lung transplant, that those who are developing

grade 3 primary graft dysfunction undergoing ECMO present a significantly higher level of circulating NETs, which was maintained for at least the first 48 hours after transplantation. These data demonstrate that ECMO procedures contribute to NETosis and postoperative complications in patients that could be secondary to microembolism.[E3]

There are limited data on the consequence of microemboli caused by ECMO. In a prospective study of 6 patients receiving VA-ECMO in whom MCA flow was measured by TCD for 15 minutes after ECMO initiation, numerous HITS were noted. Two patients died and 1 experienced minimal conscious state; there was no cognitive performance evaluation on survivors.[E4] Another prospective study of 53 patients, including 42 receiving venovenous (VV) ECMO and 11 receiving VA-ECMO, recorded 60 minutes of TCD signals per day during the first 72 hours after ECMO initiation.[E5] The number of thromboembolic events was higher with VA-than VV-ECMO. In patients receiving VA-ECMO, there was an inverse correlation between left ventricular ejection fraction and the amount of microemboli. After a 6-month follow-up, the survival rate was 50%. In the survivors, neurological impairment did not correlate with HITS detection.[E5] In 2019, Cho and colleagues[E6] performed TCD examination postoperatively in patients receiving ECMO. The authors demonstrated an association between arterial-sided oxygenator clot and showers of microemboli because the microemboli were eliminated upon change-out of the oxygenator. Another more recent study attempted to describe the quantity and nature of microemboli recorded by TCD in 20 patients receiving VA- and VV- ECMO.[E7] There was a greater presence of microemboli in patients receiving circulatory support and in these patients, a high microembolic rate (>100/30 minute) seemed to be associated with neurologic complications like ischemic stroke or delirium.[E7] Finally, in 2022, Caturegli and colleagues[E8] included 145 patients with at least 1 TCD examination. Similar microembolic signals were more common in VA-than VV-ECMO as in the study by Marinoni and colleagues.[E5] The conclusion is that the clinical associations and significance of TCD microembolic signals remain unresolved. Controversy remains between neurologic complications and the amount of HITS.[E9-E11]

CONCLUSIONS

Microembolic events in the cerebral arterial circulation are frequent during ECMO initiation during cardiac surgery. Prospective studies are required to characterize the neurologic impact of ECMO microembolic events and prevent them.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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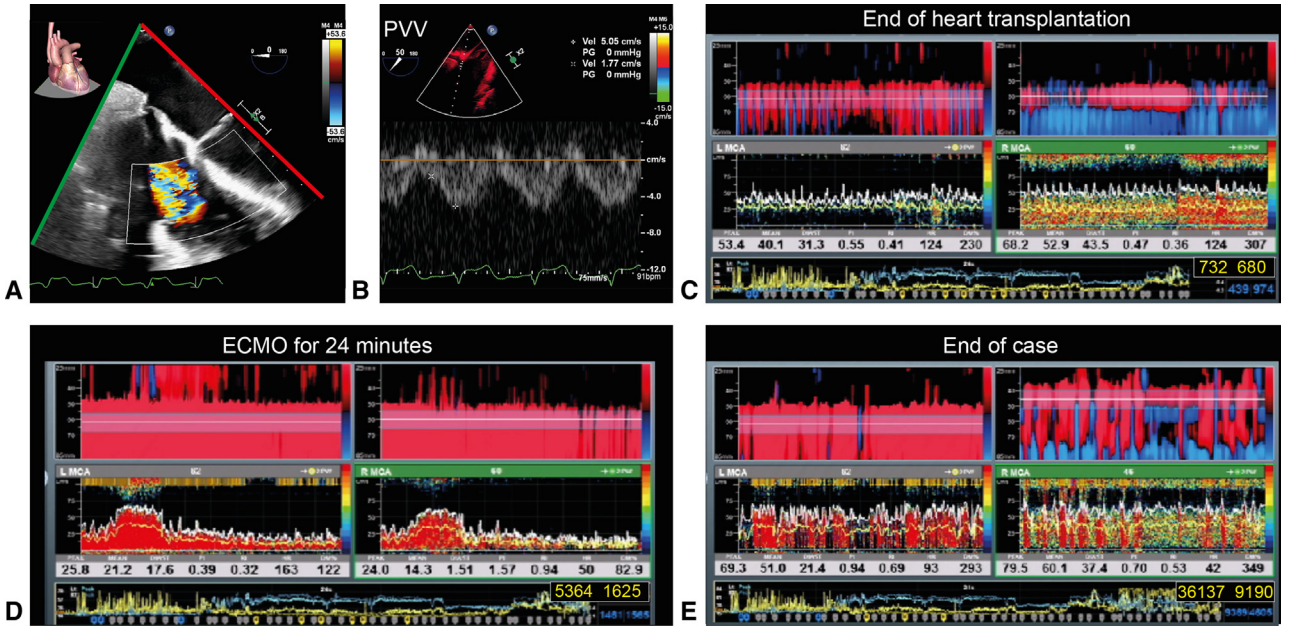

FIGURE E1. Case 3. Heart transplantation and extracorporeal membrane oxygenation (*ECMO*). A and B, Midesophageal (*ME*) right ventricle (*RV*)-focused view following heart transplantation. Biventricular failure with severe tricuspid regurgitation was present with reduced and pulsatile portal vein velocities (*PVV*). C through E, transcranial Doppler (*TCD*) values before venoarterial ECMO initiation, 24 minutes after initiation, and 2 hours later. Note the large amount of left and right middle cerebral artery (*MCA*) HITS for a total of 36,137 on the left and 9190 on the right. *Vel*, Velocity; *PG*, pressure gradient; *PI*, pulsatility index; *RI*, resistance index; *HR*, heart rate; *DM%*, percentage of mean velocity change or delta in relation to the baseline value.