CLINICAL EVIDENCE GUIDE

DETECTING AND PREVENTING TISSUE HYPOPERFUSION DURING ECMO

INVOS™ cerebral or somatic oximetry guided management may assist clinicians in detecting and resolving regional tissue desaturation that may otherwise go unrecognized in these difficult-to-treat patients.[1,2]

Use this guide to review the evidence describing the utilization of INVOS™ cerebral or somatic oximetry monitoring in patients receiving ECMO.

Medtronic
Further, Together

TABLE OF CONTENTS

NEUROLOGICAL INJURY DURING ECMO

Neurological injury is a significant contributor to increased mortality and morbidity in critically ill ECMO patients.[3]

Incidence:

15.1%[3]

Risk Factors:[3]

- Older age
- Pre-ECMO cardiac arrest
- Post-ECMO hypoglycemia
- Intra-ECMO inotrope use

Hospital mortality:[3]

- Neurological injury: 89%
- No neurological injury: 57% (P<0.0001)

MONITORING HEMODYNAMICS IN ECMO PATIENTS VIA INVOS™ CEREBRAL MONITORING TECHNOLOGY

In patients requiring ECMO, guidelines recommend mixed venous oxygen saturation (SvO2) guided maintenance of tissue oxygenation.[4] However, insertion of a pulmonary artery catheter in critically ill patients is risky.[5,6] INVOS™ cerebral oximetry may provide a non-invasive, continuous alternative measure of tissue oxygen supply and consumption.[7] Paarman et al. evaluated the agreement of SvO2 and INVOS™ cerebral oximetry in 10 adult patients undergoing ECMO. The study found excellent agreement between INVOS™ cerebral oximetry and SvO2.[7]

Agreement of INVOS™ cerebral oximetry and SvO2 in ECMO patients[7]	
R	0.87-0.98 (P<0.01)
Mean difference (bias)	2.37%
Limits of agreement	13.72% to -8.99%

Additionally, INVOS™ cerebral oximetry has been demonstrated to be associated with outcome in ECMO patients.[8] Kim et al. retrospectively reviewed INVOS™ values in survivors and non-survivors among twenty-one VA-ECMO patients.[8] They found that cerebral oximetry values were predictive of 28-day mortality.

Areas under the ROC curves of INVOS™ cerebral oximetry values for 28-day mortality[8]		
	Area under the ROC curves	P Value
Right cerebral oximetry	0.87	p < 0.001
Left cerebral oximetry	0.86	p < 0.001

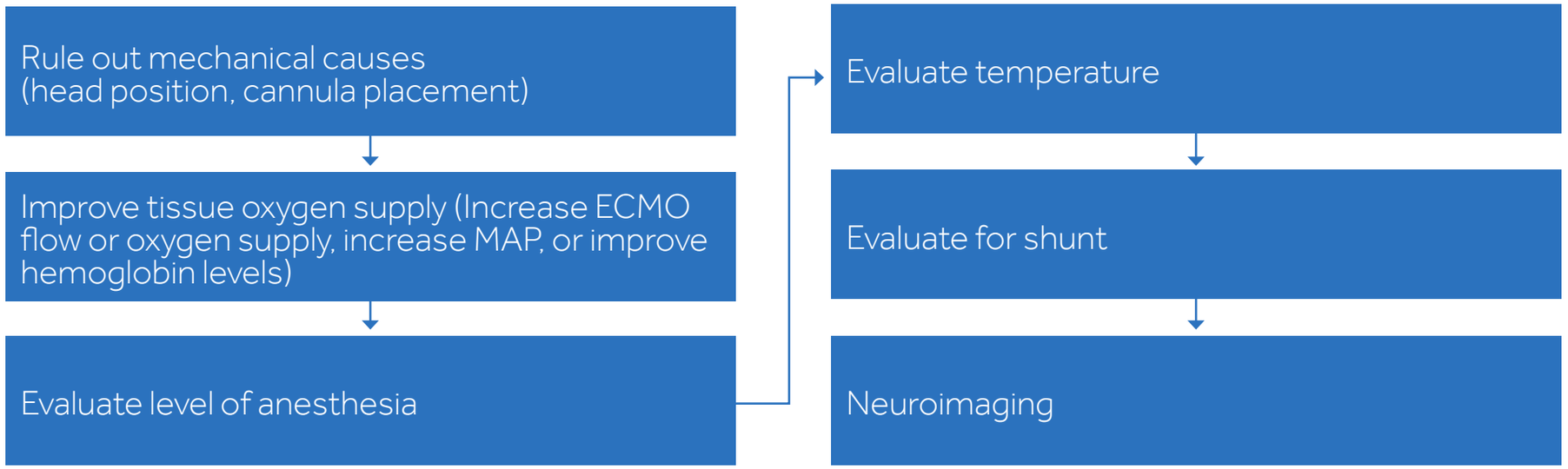
Sensitivity and specificity of INVOS™ cerebral oximetry value for predicting 28-day mortality[8]			
	Cutoff value	Sensitivity	Specificity
Right cerebral oximetry	58%	78.7%	83.3%
Left cerebral oximetry	57%	80.0%	70.8%

REVERSING DESATURATION DETECTED BY INVOS™ CEREBRAL OXIMETRY

Cerebral desaturation has been demonstrated to be associated with worse outcome in ECMO patients.[8] Therefore, patients may benefit from interventions to reverse sudden drops in cerebral oximetry values.

Wong et al. implemented an interventional algorithm to reverse cerebral desaturation detected by INVOS™ cerebral oximetry in adult ECMO patients. The intervention allowed the investigators to reverse cerebral desaturation and potentially prevent permanent ischemic damage in 80% of cases. Neuroimaging confirmed cerebral injury in the remaining 20%.[1]

Algorithm for reversing bilateral cerebral desaturation in adult ECMO patients[1]



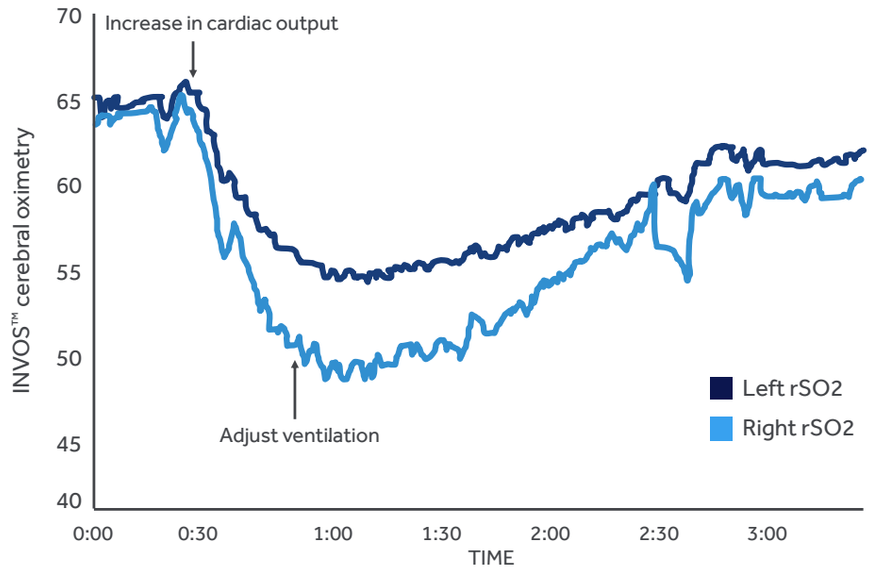
Desaturation events and resolution in adult ECMO patients treated via an interventional algorithm guided by INVOS™ cerebral oximetry (n=20)[1]	
Bilateral drop in cerebral tracings	100%
Resolved with interventions	80%
Persistent drop in cerebral tracings	20%
Confirmed neurological injury	20%

CASE STUDY: RECOGNIZING CHANGES IN NATIVE CARDIAC OUTPUT VIA INVOS™ CEREBRAL OXIMETRY

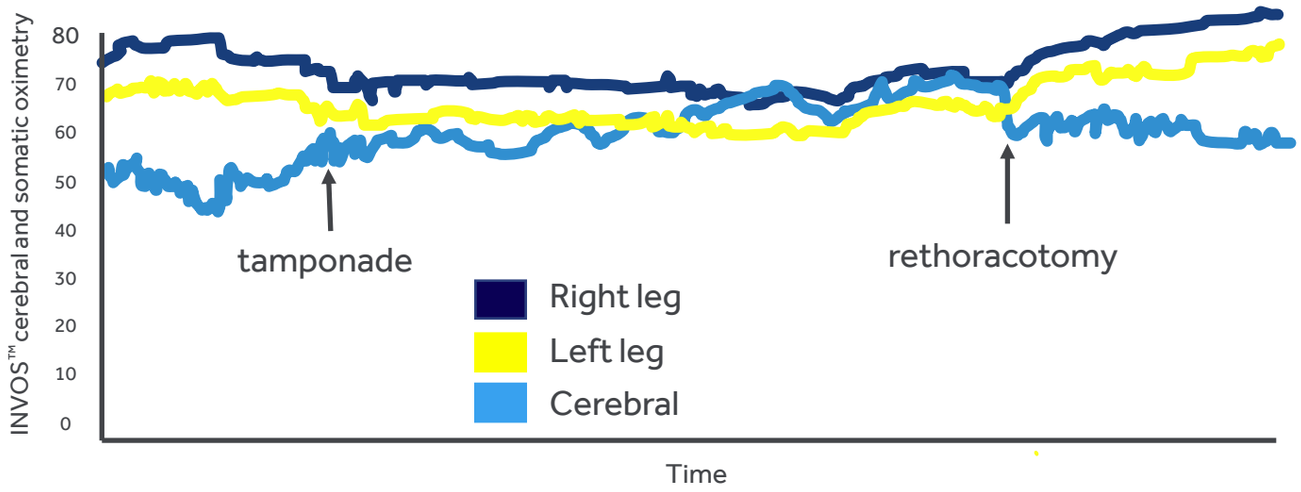
In patients receiving femoral veno-arterial ECMO with limited native heart function, the right heart is unloaded, resulting in minimal lung circulation and reduced ventilatory settings. In this circumstance, an increase in cardiac output due to myocardial recovery will result in deoxygenated blood being ejected from the left ventricle, which will converge with oxygenated blood from the ECMO circuit flowing retrograde up the aorta. If that convergence occurs prior to the aortic arch, deoxygenated blood will be provided to the upper body and brain, resulting in bilateral cerebral desaturation.[1] Vraken et al. documented this phenomenon in one-third of ECMO patients via INVOS monitoring technology and the subsequently corrected cerebral desaturation via the alteration of ventilation settings.[9]

Conversely, complications that reduce cardiac output in patients with intact native heart function may result in increases in INVOS™ values.[10] For example, Hofer et al. documented a case of pericardial tamponade, a common complication in post cardiotomy ECMO,[10] resulting in an increase in cerebral oximetry and decrease in lower limb oxygenation that was resolved by rethoracotomy.[10]

Cerebral desaturation resulting from increases in CO resulting in increased output of deoxygenated blood from the left ventricle[9]



Changes in cerebral and lower limb regional oximetry resulting onset and resolution of pericardial tamponade[10]



LIMB ISCHEMIA DURING ECMO

Cannulation of the femoral artery in veno-arterial ECMO may result in occlusion of the artery and subsequent limb ischemia.[2] Without timely recognition, limb ischemia will progress to compartment syndrome requiring fasciotomy or limb amputation.[2] Current monitoring options may be inadequate to detect emerging limb ischemia in ECMO patients.[2] Changes in temperature occur after a delay.[9] Likewise, conditions common in ECMO (shock, nonpulsatile flow, and vasopressors) patients make doppler pulse evaluation difficult.[12] Finally, intermittent monitoring can allow ischemia to go undetected for several hours. Tissue necrosis occurs in as little as three hours.[13]

ECMO- related limb ischemia:

Incidence*:[11]

- Limb Ischemia: 16.9%
- Compartment syndrome and fasciotomy: 10.3%
- Lower extremity amputation: 4.7%

Risk Factors:[14]

- Absence of distal pulsation pre-cannulation or immediately after post-cannulation
- Smaller common femoral artery diameter
- Known peripheral arterial occlusive disease
- Higher vasoactive-inotropic score

*In patients receiving ECMO treatment for treatment of cardiogenic shock or cardiac arrest

DETECTING AND PREVENTING LIMB ISCHEMIA WITH INVOS™ SOMATIC OXIMETRY

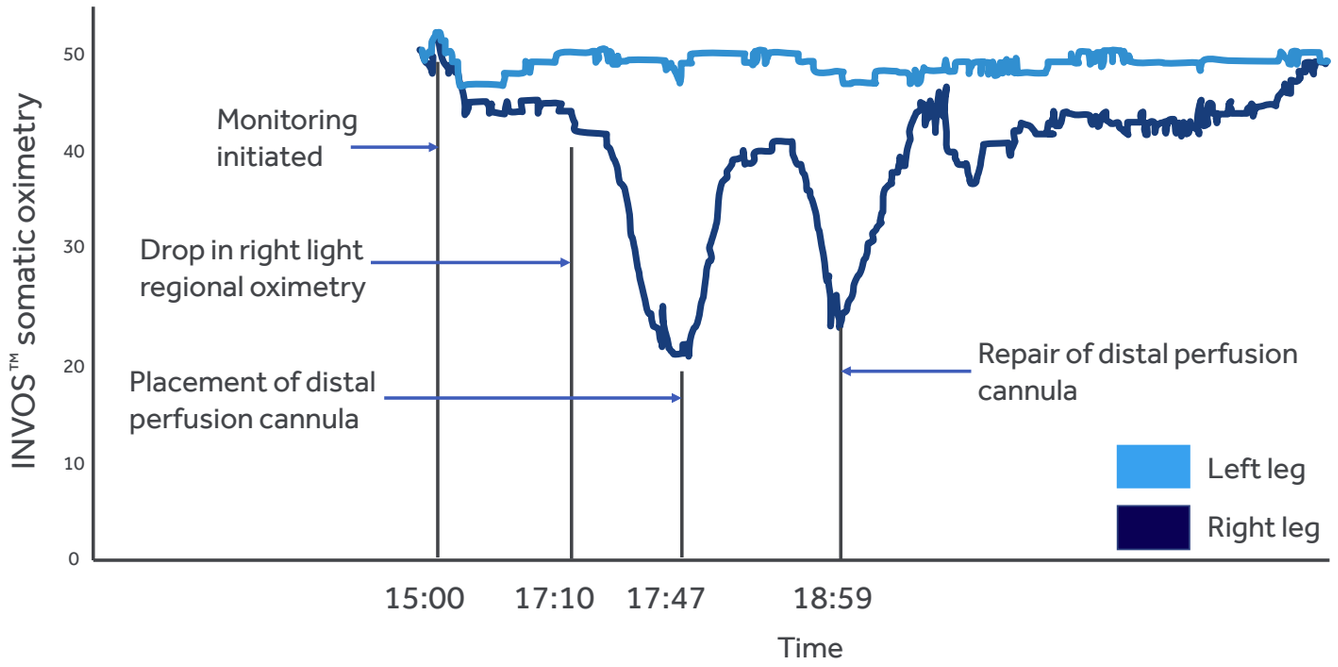
INVOS™ somatic monitoring detects onset of limb ischemia and provides clinicians with feedback on the effectiveness of treatment.

- Kim et al.[2] implemented a simple algorithm for detecting and resolving limb ischemia with INVOS™ somatic monitoring. Upon detection of desaturation, the investigators attempted to improve tissue oxygenation via increasing ECMO flow, mean arterial pressure, or level of hemoglobin. If this intervention failed, placement of distal cannula was performed. INVOS™ somatic monitoring was then utilized to confirm successful placement and recovery.
- 11 of 28 (39.3%) demonstrated a significant drop in INVOS™ values.[2]
- INVOS™ values recovered due to interventions to increase oxygen supply in two patients. The remaining nine required distal perfusion, followed by a recovery of INVOS™ values.[2]

Other studies have noted that once a distal cannula is placed, INVOS™ monitoring technology will alert clinicians to potential cannula issues.

- Wong et al. noted a case where a misplaced distal cannula was detected via INVOS™ monitoring technology. The cannula was subsequently repaired and INVOS™ value recovered.[1]
- In another study of INVOS™ regional oximetry-guided monitoring of limb perfusion, Vraken et al. discovered and resolved cannula clotting in four of six patients requiring a distal cannula.[9]

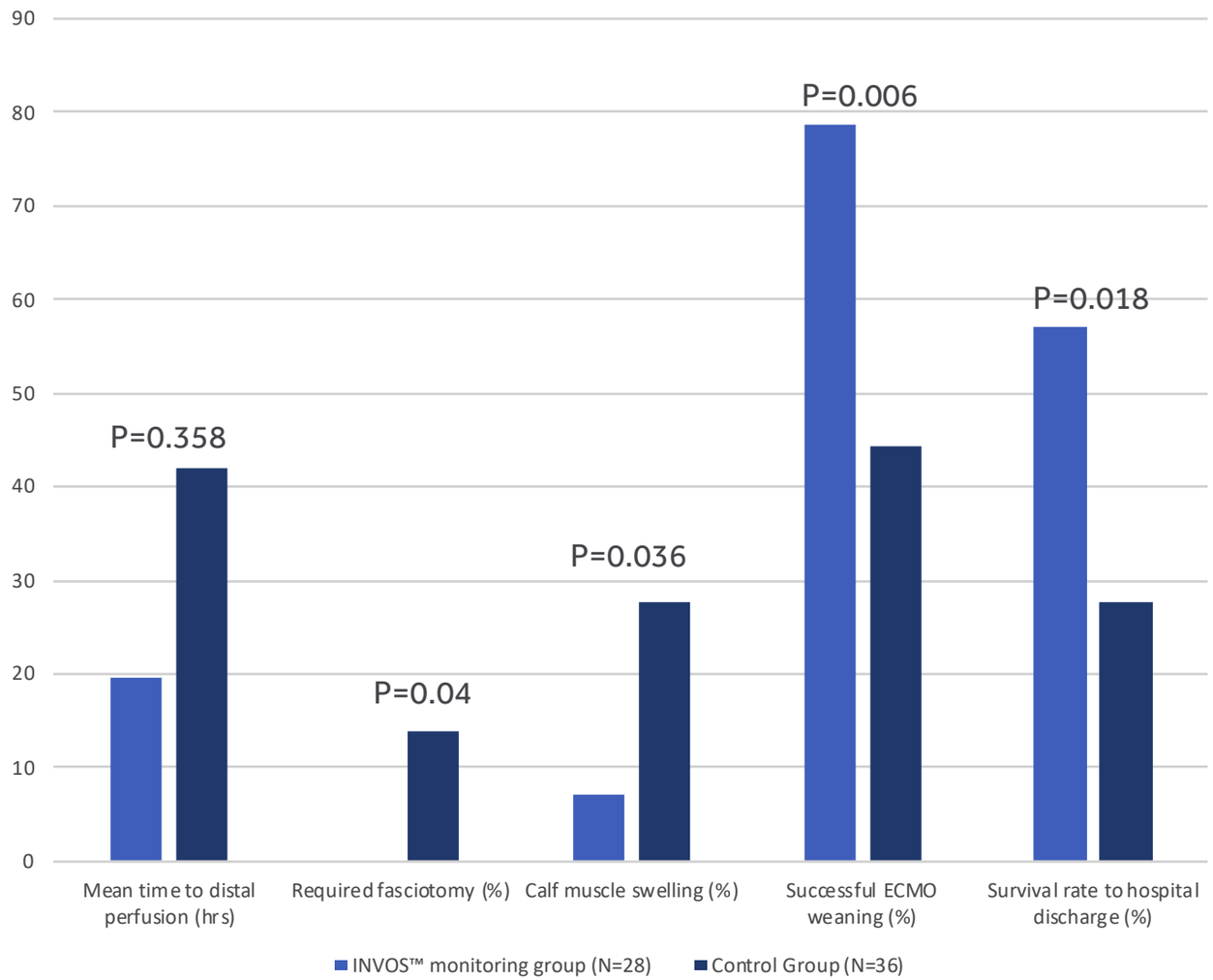
Left and right lower limb INVOS™ values for patient who suffered limb ischemia followed by distal cannula placement, followed by misplacement and repair



MINIMIZING LIMB ISCHEMIA WITH INVOS™ SOMATIC MONITORING

Kim et al.[1] compared ECMO patients treated with an INVOS™ somatic oximetry guided limb ischemia prevention protocol with a historical control group receiving ECMO prior to implementation of monitoring. Patients with limb ischemia in the INVOS™ oximetry guided group received distal perfusion sooner, required fasciotomy less frequently, and suffered fewer incidents of calf muscle swelling. Furthermore, the INVOS™ oximetry guided group successfully weaned from ECMO and survived to discharge more frequently.

Mean time in placement of distal cannula, fasciotomy rate, calf muscle swelling rate, successful ECMO weaning rate, and survival to hospital discharge in the INVOS™ oximetry monitoring and control groups[1]

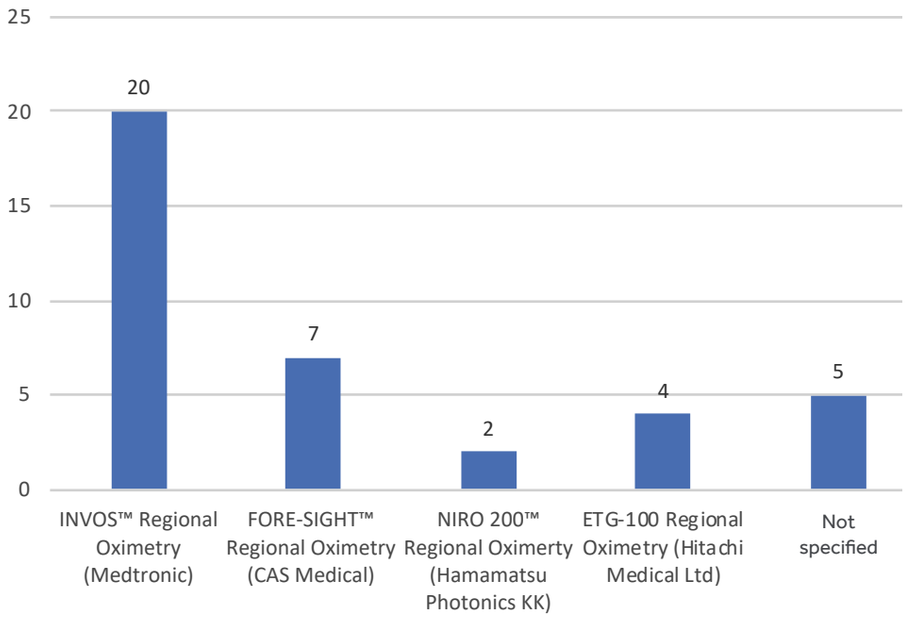


THE INVOS™ REGIONAL OXIMETRY EVIDENCE ADVANTAGE

When it comes to clinical evidence, the INVOS™ cerebral/somatic oximeter stands alone.[15] This body of evidence provides clinicians with the necessary information to implement cerebral or somatic monitoring with confidence.

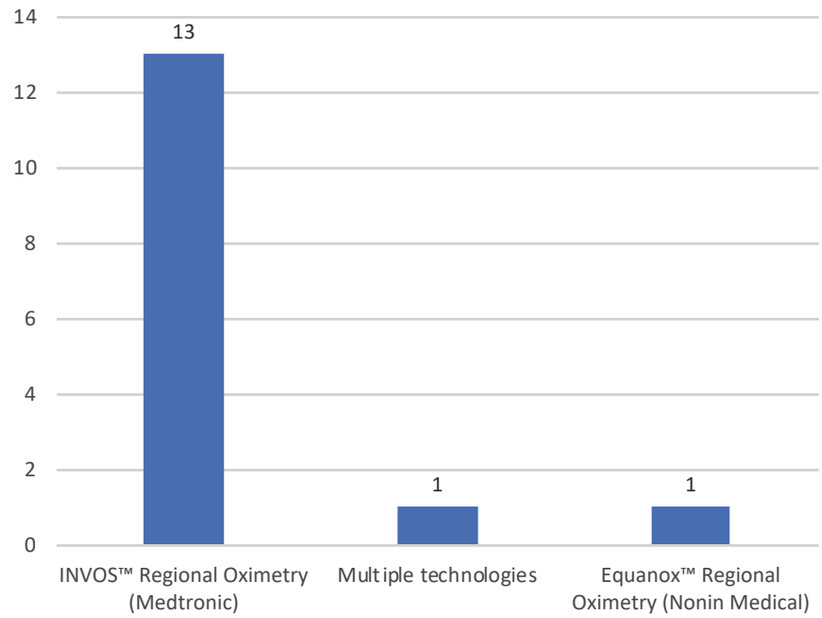
Cerebral or somatic monitoring publications in ECMO patients.

Number of clinical trials or case studies evaluating cerebral or somatic monitoring in critically ill ECMO patients indexed on PubMed*



Randomized controlled trials evaluating perioperative cerebral oximetry monitoring[15]

Number of randomized controlled trials included in an independent systematic review of the evidence[15]



*Queried for ("near infrared spectroscopy" or "Oximetry"[Mesh] or "Spectroscopy, Near-Infrared"[Mesh] or "cerebral saturation" or "cerebral oxygenation" or "cerebral oxygen saturation" or "tissue oximetry") AND ("Extracorporeal Membrane Oxygenation"[Mesh] or ECMO or "extracorporeal life support") on 1/14/2019

REFERENCES

1. Wong JK, Smith TN, Pitcher HT, Hirose H, Cavarocchi NC. Cerebral and lower limb near-infrared spectroscopy in adults on extracorporeal membrane oxygenation. *Artif Organs.* 2012;36(8):659-667.
2. Kim DJ, Cho YJ, Park SH, et al. Near-Infrared Spectroscopy Monitoring for Early Detection of Limb Ischemia in Patients on Veno-Arterial Extracorporeal Membrane Oxygenation. *ASAIO journal (American Society for Artificial Internal Organs : 1992).* 2017;63(5):613-617.
3. Lorusso R, Barili F, Mauro MD, et al. In-Hospital Neurologic Complications in Adult Patients Undergoing Venoarterial Extracorporeal Membrane Oxygenation: Results From the Extracorporeal Life Support Organization Registry. *Critical care medicine.* 2016;44(10):e964-972.
4. Extracorporeal Life Support Organization. ELSO Guidelines for Cardiopulmonary Extracorporeal Life Support, Version 1.4 August 2017. *www.elso.org.* 2017.
5. Harvey S, Harrison DA, Singer M, et al. Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial. *Lancet* (London, England). 2005;366(9484):472-477.
6. Binanay C, Califf RM, Hasselblad V, et al. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *Jama*. 2005;294(13):1625-1633.
7. Paarmann H, Schön J, Schmidt W, et al. Agreement of noninvasive cerebral oxygenation with mixed venous oxygen saturation in patients undergoing ECMO-therapy. *Applied Cardiopulmonary Pathophysiology.* 2011;15:55-61.
8. Kim HS, Ha SO, Yu KH, et al. Cerebral Oxygenation as a Monitoring Parameter for Mortality During Venoarterial Extracorporeal Membrane Oxygenation. *ASAIO journal (American Society for Artificial Internal Organs : 1992).* 2018. May 15. doi: 10.1097/MAT.0000000000000827.
9. Vranken NPA, Lindelauf A, Simons AP, Aries MJH, Maessen JG, Weerwind PW. Cerebral and Limb Tissue Oxygenation During Peripheral Venoarterial Extracorporeal Life Support. *Journal of intensive care medicine.* 2017:885066617735270.
10. Hofer A, Leitner S, Kreuzer M, Meier J. Differential diagnosis of alterations in arterial flow and tissue oxygenation on venoarterial extracorporeal membrane oxygenation. *The International journal of artificial organs.* 2017;40(11):651-655.
11. Cheng R, Hachamovitch R, Kittleson M, et al. Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: a meta-analysis of 1,866 adult patients. *Ann Thorac Surg*. 2014;97(2):610-616.
12. Steffen RJ, Sale S, Anandamurthy B, et al. Using near-infrared spectroscopy to monitor lower extremities in patients on venoarterial extracorporeal membrane oxygenation. *Ann Thorac Surg*. 2014;98(5):1853-1854.
13. Vaillancourt C, Shrier I, Vandal A, et al. Acute compartment syndrome: how long before muscle necrosis occurs? *Cjem.* 2004;6(3):147-154.
14. Yen CC, Kao CH, Tsai CS, Tsai SH. Identifying the Risk Factor and Prevention of Limb Ischemia in Extracorporeal Membrane Oxygenation with Femoral Artery Cannulation. *The heart surgery forum.* 2018;21(1):E018-e022.
15. Yu Y, Zhang K, Zhang L, Zong H, Meng L, Han R. Cerebral near-infrared spectroscopy (NIRS) for perioperative monitoring of brain oxygenation in children and adults. *The Cochrane database of systematic reviews.* 2018;1:Cd010947.

6135 Gunbarrel Avenue
Boulder, CO 80301 800.635.5267 medtronic.com/covidien

Medtronic