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Cerebral and Lower Limb Near-Infrared Spectroscopy in Adults on Extracorporeal Membrane Oxygenation

Joshua K Wong
Thomas Jefferson University

Thomas N Smith
Thomas Jefferson University

Harrison T Pitcher
Thomas Jefferson University

Hitoshi Hirose
Thomas Jefferson University

Nicholas C. Cavarocchi
Thomas Jefferson University
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Joshua K Wong BS, Thomas N Smith BS, Harrison Pitcher MD, Hitoshi Hirose MD, Nicholas C Cavarocchi MD
Division of Cardiothoracic Surgery, Department of Surgery
Thomas Jefferson University, Philadelphia, PA

Correspondence:

Nicholas C Cavarocchi, MD
Associate Professor of Surgery
Division of Cardiothoracic Surgery and Critical Care
Director, Surgical Cardiac Care Unit
Department of Surgery, Thomas Jefferson University
1025 Walnut Street, College Bldg, Suite 605E, Philadelphia, PA 19107
Phone: (215) 955-6996, Fax: (215) 923-6010
Email: Nicholas.Cavarocchi@jefferson.edu

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ABSTRACT

Introduction: Percutaneous femoral Veno-arterial (VA) or jugular Veno-venous (VV) ECMO can result in delivery of hypoxic blood to the brain, coronaries and upper extremities.

Additionally, VA-ECMO by percutaneous femoral artery cannulation may compromise perfusion to the lower [limbs](#). Use of Near-Infrared Spectroscopy (NIRS) detects regional ischemia and warns of impending hypoxic damage. We report the first known series with standardized monitoring of this parameter in adults on ECMO.

Methods: This is an IRB approved single institution retrospective review of patients with NIRS monitoring on ECMO from July 2010 till June 2011. Patients were analyzed for drops in NIRS tracings below 40 or >25% from baseline. VA-ECMO and VV-ECMO were initiated by cannulation of the femoral vessels and the internal jugular vein respectively. Sensors were placed on the patients' foreheads and on the lower [limbs](#). NIRS tracings were recorded, analyzed and correlated with clinical events

Results: Twenty patients were analyzed (Median age: 47.5 years), 17 patients were placed on VA-ECMO, and 3 patients on VV-ECMO. The median duration on ECMO was 7 days (Range 2 – 26). 100% of patients had a significant drop in bilateral cerebral oximetry tracings resulting in hemodynamic interventions, which involved increasing pressure, oxygenation and/or ECMO flow. In 16 (80%) patients, interventions corrected the underlying ischemia. 4 (20%) patients required further diagnostic intervention for persistent decreased bilateral and/or unilateral cerebral oximetry tracings, and were found to have a cerebrovascular accident (CVA). Six (30%) patients had persistent unilateral [lower limb](#) oximetry events, which resolved upon placement or replacement of a distal perfusion cannula. No patient was found to have either lower limb ischemia or a CVA with normal NIRS tracings.

Conclusions: Use of NIRS with ECMO is important in detecting ischemic peripheral vascular and cerebral events. This allows for potential correction of the underlying process, thus preventing permanent ischemic damage.

Keywords: Extracorporeal Membrane Oxygenation, Adults, Near-Infrared Spectroscopy, Ischemia, Cerebral Oximetry, Extremity Oximetry

INTRODUCTION

Extracorporeal Membrane Oxygenation also commonly referred to as ECMO, is a form of extracorporeal life support by a modified heart-lung machine that is potentially life saving in patients with cardio-respiratory failure. Its use was first described by Hill et al. in 1972, in the treatment of a young man with acute respiratory distress syndrome (ARDS) after a motor vehicle accident,¹ and has since been increasingly used to temporarily support patients with cardiac, respiratory or combined cardio-respiratory failure for a period of days to weeks.

Traditionally the use of this form of support was reserved primarily for the pediatric population, especially in the treatment of neonatal respiratory failure,² but its initial application in adults was limited. Early trials in adults were disappointing, with poor outcomes and no survival benefit being reported over conventional treatment.^{3,4} However, with advancements in mechanical cardio-respiratory technology, such as the development and use of new and improved centrifugal pumps and oxygenators,⁵⁻⁷ and increasing center experience in the management of these patients, outcomes for adults that are placed on this form of support are improving, and the use of ECMO in this population is increasing.⁸⁻¹⁰

ECMO can be divided into 2 basic types. Veno-Arterial or VA-ECMO is used to support both the heart and lungs. Common indications for VA-ECMO are; failure to wean from cardiopulmonary bypass (CPB), cardiogenic shock secondary to multiple etiologies as a bridge to device or transplant for stabilization and/or recovery of end organs, etc. Veno-Venous or VV-ECMO is used for lung support alone and is used primarily in patients with potentially reversible respiratory failure, such as ARDS, that is refractory to conventional management.^{4, 10}

It is important to note that the successful use of ECMO is determined not only by technical factors related to circuit design or clinician experience, but also on the various monitoring systems that are employed by clinicians to evaluate the critically ill patient. Near-Infrared Spectroscopy (NIRS) is one such monitoring system. It employs the use of near-infrared wavelengths emitted by sensor pads to evaluate regional oxygenation of the organ or tissue being monitored. The difference in absorption of these wavelengths by oxygenated and deoxygenated hemoglobin is calculated, providing the clinician with information regarding the regional oxygen saturation (rSO₂) of the perfused tissue.

The use of NIRS is well described in the literature for use in patients undergoing cardiopulmonary bypass in cardiac surgery. The application of this technology in cardiac surgery patients has proven beneficial in many major studies,¹¹⁻¹² however there is yet to be a report in the English literature of its use in a series of adult patients on ECMO for the purpose of monitoring cerebral and femoral perfusion. In this report, we provide a single institution experience with the use of cerebral and lower limb NIRS in Adults on ECMO.

METHODS

We performed an Institutional Review Board (IRB) approved, review of all adult patients that were placed on ECMO with NIRS monitoring from July 2010 to June 2011 in the Surgical Cardiac Care Unit of Thomas Jefferson University Hospital. Patient data was reviewed retrospectively from a prospective data collecting system. Patient demographics, indications for ECMO, duration on ECMO, occurrence of cerebral or extremity events, and neurologic or lower limb complications were analyzed and reported.

Neurological injury was defined as the occurrence of a hemorrhagic and/or ischemic infarct and/or diffuse anoxic brain injury, that was confirmed by neuro-imaging (MRI, CT Scan, Nuclear brain perfusion scan, EEG) or in the case of brain death serial exams 24-hours apart by

two independent neurologists. Lower limb complications were classified into two categories; “need for fasciotomy” and “loss of limb”.

VA-ECMO/VV-ECMO Cannulation Method: All twenty patients were cannulated peripherally via percutaneous insertion of the ECMO cannula using the Seldinger technique. Femoral cannulation was the preferred placement in all patients on VA-ECMO. All patients on VV-ECMO were cannulated via the neck into the internal jugular vein using the AvalonTM bicaval dual-lumen cannula. Distal arterial perfusion ports were placed in all patients with peripheral femoral cannulation.

The heart and lung support (HLS) Maquet cannulae (bio-compatible polyurethane) from the patient’s blood vessels were connected to a closed crystalloid primed circuit (~300ml); both cannulae and tubing have heparin coating. The circuitry for ECMO consisted of the Quadrox-D (diffusion membrane hollow-fiber) oxygenator and a Rota flow centrifugal pump (Maquet Cardiovascular LLC, San Jose, California) with a heater or cooler exchange.

NIRS Device: The INVOSTM cerebral somatic oximeter sensor pads were placed bilaterally on the forehead (Figure 1a) in all patients, and medially on the left and right lower limbs midway between the knee and ankle (Figure 1b) in patients only on VA-ECMO. Sensor pads were replaced every 72 hours, or earlier if indicated. Values that represented the adequacy of tissue oxygenation were calculated by the device and assigned values called “rSO₂” (Regional Oxygen Saturation). A 4-channel monitor screen placed at the bedside of every patient, presented a 4-hour view of the cerebral and lower limb tracings (Figure 1c), which allowed the clinician to track the oxygenation of cerebral and distal limb tissues over time. Monitoring of this parameter was initiated within minutes upon placement on ECMO, and was discontinued only after a successful wean to recovery, bridge to a ventricular assist device or death.

Baseline values were established early in the course of ECMO therapy and rSO₂ numbers were compared to the previously established baseline daily. Clinically significant events warranting interventions were defined as below;

- 1) Drop in rSO₂ values below 40.
- 2) Drop in rSO₂ values more than 25% from baseline.

A bilateral drop in cerebral tracings that responded to interventions was termed a “Systemic Event”, a bilateral or unilateral drop in cerebral tracings that was secondary to neurological injury was termed a “Cerebral Event” and a unilateral drop in extremity tracings that required an intervention was termed a “Lower Limb Event”. Tracings were recorded, analyzed and correlated with clinical events.

ECMO Cerebral Oximetry Management: Management protocols for intervention were established at the beginning of the study period for patients who had clinically significant drops in cerebral rSO₂ values. All patients who had drops in either bilateral or unilateral cerebral rSO₂ values were managed first by ruling out mechanical causes (head position, proper placement of ECMO cannulae, and sensor pad placement). Should mechanical causes be ruled out, our next step in management involved increasing the oxygen and/or blood supply to tissues by increasing ECMO flow, ECMO oxygen supply, mean arterial pressure and ensuring normal hemoglobin levels. If the interventions delineated above did not resolve the low values, patients with persistent low bilateral rSO₂ readings were placed on the “Persistent Bilateral Decreased Cerebral Tracing Protocol” (Figure 2a), whereas patients with persistently low unilateral rSO₂ readings went directly to neuro-imaging (Figure 2b).

ECMO Lower Limb Oximetry Management: Similar management protocols were established for patients on VA-ECMO with clinically significant drops in lower limb oximetry

values. Patients with significant drops in rSO_2 values on the side of arterial cannulation were started on the “[Decreased Lower Limb](#) Tracing Protocol” (Figure 2c). Interventions invariably led to a restoration of previously established baseline readings or prophylactic fasciotomy to prevent the development of compartment syndrome and subsequent limb loss.

VV-ECMO Oximetry Management: The application of NIRS in patients on VV-ECMO is similar to its use in patients on VA-ECMO. It is used to [primarily](#) monitor for neurological injury. [However, our unit also relied on NIRS in conjunction with Chest X-Ray's, Arterial Blood Gas values and Pulse oximetry in guiding our weaning protocol. Patients were weaned off VV-ECMO if all the following criteria were met; NIRS tracings were similar to or > baseline readings, Pulse oximeter readings >85%, Minimal ventilator settings, ECMO \$FiO_2\$ at 50% or less, and a clear or markedly improved chest x-ray.](#)

RESULTS

During the study period, twenty-three patients were placed on extracorporeal life support via ECMO. [A total of](#) twenty patients had cerebral and/or [lower limb](#) oximetry monitoring using NIRS technology. Of these twenty, eleven (55%) were male. [The median age of our patient population was 47.5 years \(Range 17 – 74\) and the median duration on ECMO was 7 days \(Range 2 – 26\).](#) Seventeen (85%) patients were supported by VA-ECMO and the remaining three (15%) by VV-ECMO. The main and only indication for placement on VV-ECMO was ARDS (3/3, 100%). The two most common indications for initiation of VA-ECMO were; Failure to wean from CPB (4/20, 20%) and Cardiogenic shock secondary to Acute Myocardial Infarction (4/20, 20%). The remaining indications for placement on VA-ECMO are as described in Table 1.

Upon analysis of tracings and correlation with clinical events, it was noted that all twenty (100%) patients on ECMO had a bilateral drop in cerebral tracings. Interventions as outlined above were undertaken to resolve these low readings, which succeeded in sixteen patients (16/20, 80%) (Systemic Event, Table 2). An example of [this](#) is shown in Figure 3a and Figure 3b. Of the four that did not respond to interventions (Cerebral Event), two patients had persistent bilateral low rSO_2 readings, and were eventually sent for neuro-imaging as outlined in the “Persistent Bilateral [Decreased](#) Cerebral Tracing Management Protocol”, which confirmed diffuse anoxic brain injury in both patients. Following serial neurological exams 24-hours apart by neurologists, they were declared brain dead. The remaining two patients had persistent [unilaterally](#) low rSO_2 readings, and were sent directly for neuro-imaging that revealed large unilateral infarcts. These events are summarized in Table 2 and [the](#) cerebral tracing graph demonstrating this event is shown in Figure 4.

Of the seventeen patients that were placed on VA-ECMO, six (6/17, 35%) had a clinically significant drop in unilateral [lower limb](#) tracings ([Lower Limb](#) Event). Interventions as outlined above in the “[Decreased Lower Limb](#) Tracing Protocol” were undertaken, which resolved the low rSO_2 readings in all six patients (6/6, 100%). However, four patients (4/6, 67%) required [prophylactic](#) distal limb two-compartment fasciotomies against compartment syndrome. There was no loss of limbs in patients peripherally cannulated via [the](#) femoral vessels in our study (Table 3). Figure 5 depicts the development of a “[Lower Limb](#) Event” in a patient monitored by [NIRS technology](#). Lastly, no patient with *normal* cerebral or [lower limb](#) tracings was found to have neurological injury or [lower](#) limb ischemia.

[In the three patients that were placed on VV-ECMO in our study, two were successfully weaned off ECMO using the criteria as mentioned above. NIRS along with other factors guided the weaning of these patients from ECMO and contributed to their successful discharge and](#)

overall survival. However, one patient had a large stroke that was detected by cerebral oximetry and due to her poor prognosis care was withdrawn.

DISCUSSION

The potential application of NIRS technology in patients was observed as early as 1977 by Jobsis et al. in a report that described the possibility of real time noninvasive monitoring of tissue oxygen saturation using trans-illumination spectroscopy which was possible due to the high degree of transparency of myocardial and brain tissue in the near-infrared (NIR) range.¹³ However, it was not until 1985 that Ferrari et al. studied the application of this technology (NIRS) in human patients, and was among the first to report its use and application in a clinical setting.¹⁴

As stated above, the use and application of NIRS in patients is well studied, particularly in the cardiac surgical population. In a retrospective study by Goldman et al. in 2004, 1034 patients (study group) who underwent cerebral oximetry monitoring using NIRS technology during cardiac surgery were compared to 1245 patients (control group) who were not monitored by this oxygenation parameter. It was found that patients in the study group had fewer permanent strokes, and shorter hospital stays.¹¹ Murkin et al. published further evidence to its utility in 2007 in an important prospective randomized trial. In his report, 100 patients that were stratified to intra-operative cerebral regional oxygen saturation (rSO₂) monitoring with active treatment of declining values demonstrated shorter intensive care unit duration stays, and lower major organ morbidity or mortality, when compared to a group of patients that underwent blinded rSO₂ monitoring.¹² The reliability of this device in detecting neurological events has also been well reported in the literature. Samra et al reported a sensitivity of 80% and a specificity of 82.2% in detecting strokes at a NIRS tracing threshold of >20% change from baseline,¹⁵ whereas Ali et al reported a sensitivity of 75% and a specificity of 97.5% at a similar threshold in patients undergoing carotid endarterectomies.¹⁶

To the best of our knowledge, there are only two mentioned reports of NIRS use in patients on ECMO, and all of them in neonates or children.^{17, 18} Papademetriou et al. described the monitoring of cerebral and tissue oxygenation of 4 children on ECMO as they underwent manipulations in circuit flow. The aim of his study was to compare variation in rSO₂ values at different near-infrared light frequencies¹⁷ whereas Rais-Bahrami et al. in another study attempted to validate NIRS value accuracy by periodically obtaining cephalic blood samples and comparing it to rSO₂ numbers in 17 neonates.¹⁸ No study to date has described its use, application and utility in a clinical setting in a series of adult ECMO patients.

A question could then be posed as to why NIRS monitoring is beneficial in patients on ECMO? The authors believe that it is so for the following reasons. Firstly, in a peripherally cannulated ECMO patient, oxygenated blood flows in a retrograde fashion, travelling proximally towards the heart. This flow is opposed by potentially poorly oxygenated or deoxygenated blood (dependent on respiratory status) pumped by a still beating, although weakened heart. With high ECMO flow and a low pulse pressure, the mixing oxygenated and poorly oxygenated (or deoxygenated) blood occurs at a level proximal to the bifurcation of the great vessels allowing for the provision of oxygenated blood to the brain and upper extremities (Figure 6 a). However, with increasing pulse pressures or increased resistance to ECMO flow, this level of mixing can potentially occur distal to the bifurcation of these vessels rendering these organs susceptible to ischemic damage⁵ (Figure 6 b). The level at which this mixing occurs can be hard to define with no good technique reported to date. However, the side effects of mixing distal to the great vessels

can be evaluated by cerebral oximetry, which potentially prevents the development of permanent ischemic damage to an already vulnerable brain.

Secondly, a major complication that can occur in patients supported by ECMO is the development of neurological injury. Studies have shown that neurological complications are greatly underappreciated and occur with relative frequency in ECMO patients. A recent retrospective review by Mateen et al. noted that of 84 patients that underwent ECMO at the Mayo Clinic, 42 (50%) patients developed some form of neurological injury.¹⁹ This rate may seem relatively high compared to other similar studies, but it is noteworthy that the authors definition of neurological injury was broader and included categories such as “encephalopathy, myoclonus, and comatose without further explanation”. Most other studies report only the rates of ischemic or hemorrhagic strokes, and that ranges from 7% - 21%.^{20, 21} This however represents a still high number and warrants concern in any ECMO center. In our experience, neurological complications occurred in 20% of our patients, which is in accordance with the rates reported in the literature. It emphasizes the importance of having a clinically validated neuro-monitoring system that can detect developing ischemic damage with the hope of potentially reversing it. Furthermore, the ability of the clinician to know objectively that the brain is well perfused is an essential piece of information as it can be difficult to determine the true neurological status of an intubated, often paralyzed and heavily sedated patient.

Lastly, in VA-ECMO patients with peripheral femoral artery cannulation, distal limb ischemia represents a potentially hazardous complication. This is due to the large cannula size relative to the diameter of the femoral artery that near occludes the vessel with resultant downstream ischemia. In our experience, placement of a distal perfusion cannula into a vessel distal to the site of ECMO cannulation ensures that there is downstream flow and lower limb oximetry (NIRS) monitors the adequacy of that flow. A report of distal limb ischemic complications in ECMO patients observed a complication rate of 21% in patients who did not receive a distal perfusion cannula, and no distal limb complications in patients who had one placed.²² In our group of 17 patients, distal perfusion cannulae were placed prophylactically but femoral events still occurred that warranted intervention, highlighting the still likely possibility of developing distal limb ischemic damage with a distal perfusion cannula. Clinical assessment of compartment syndrome has always been subjective and unreliable especially in critically ill patients that are incapable of communicating pain or sensation. The only reliable method to diagnose and prevent the development of this syndrome in such situations (manual measurement of compartment pressure) is invasive, which requires the use of hollow bore needles attached to pressure transducers that are inserted into muscle compartments. However, recent literature suggests that ischemia and decreased blood flow may increase muscle damage at lower compartment pressures making the diagnosis of this syndrome inherently more difficult and the use of pressure transducers less effective.²³ In 1999, Arbabi et al studied the ability of NIRS to detect compartment syndrome in conditions of severe shock by firstly reducing mean arterial pressure and oxygen delivery (induce shock), and subsequently infusing colloidal albumin into the muscle compartments of pigs (induce compartment syndrome). They found that there was a significant difference in NIRS values in pigs prior to infusion of albumin compared to values after the development of compartment syndrome. Additionally, they noted that there was a significant difference in NIRS values in pigs that developed compartment syndrome compared to a control group of pigs in which compartment syndrome was not induced.²³ Recently the same group then directly compared the utility of NIRS against compartment pressure in diagnosing compartment syndrome in human volunteer subjects. They found that NIRS had a higher

sensitivity when compared with compartment pressure at the same specificity.²⁴ In summary, NIRS is a better modality to monitor for compartment tissue ischemia due to its non-invasive nature and may even prove to be better at diagnosing this syndrome because it is a direct measure of tissue ischemia and also due to its ability to integrate the multiple factors that contribute to the development of compartment syndrome.

LIMITATIONS

Despite its obvious benefits, NIRS technology is not without any limitations. Its absolute values can be quite inaccurate and there exists significant variation in readings between patients. This potentially makes it difficult for the clinician to interpret the actual numbered readings but we emphasize the importance of establishing a baseline, in order to better understand any subsequent reading.

NIRS values can also be affected by extraneous factors such as ambient light and skin color (correlates with the amount of melanin in the skin), however our experience with use of this technology has posed no difficulty in minimizing or compensating for these factors.

CONCLUSION

We conclude this report with a reiteration on the importance of monitoring tissue oxygenation in patients on ECMO, particularly in the brain and distal limb. We have found that NIRS technology is a useful and highly applicable monitoring parameter that not only provides us with important bedside “point of care” information, but also serves as a new “*vital sign*” that has improved the quality of care and outcomes of critically ill ECMO patients in the surgical cardiac care unit at our institution.

Table 1. Indications for extracorporeal membrane oxygenation (ECMO)

<i>Indications</i>	<i>Number (n = 20)</i>
Cardiac arrest or cardiogenic shock	7 (35%)
Post-cardiotomy shock or failure to wean off cardiopulmonary bypass	4 (20%)
Acute respiratory distress syndrome	5 (25%)
Myocarditis	2 (10%)
Decompensated heart failure	1 (5%)
Rejection of heart transplant	1 (5%)

Table 2. Summary of systemic and cerebral events

<i>Patients on ECMO (VA- and VV-)</i>	<i>Number (n = 20)</i>
Bilateral drop in cerebral tracings (<i>Systemic event</i>)	20 (100%)
Resolved with interventions	16 (80%)
Persistent bilateral/unilateral drop in cerebral tracings (<i>Cerebral event</i>)	4 (20%)
Confirmed neurological injury	4 (20%)

Table 3. Summary of lower limb events

<i>Patients on VA-ECMO</i>	<i>Number (n = 17)</i>
Unilateral drop in extremity tracings (<u><i>Lower limb event</i></u>)	6 (35%)
Resolved with interventions	6 (35%)
Need for fasciotomy	4 (24%)
Loss of limb	0 (0%)

Legends of figures

- Figure 1:** 1a (top). Left and right INVOS™ cerebral somatic oximeter sensor pads placed on the forehead of the patient
 1b (middle). INVOS™ cerebral somatic oximeter sensor pad placed on lower limb (mid calf).
 1c (bottom). INVOS™ cerebral somatic oximeter 4-channel monitor screen showing ing left cerebral regional oxygen saturation, $rSO_2 = 48$, right cerebral $rSO_2 = 58$, left leg = $rSO_2 69$, and right leg = $rSO_2 47$ (bottom).

Figure 2: 2a (Left). Treatment protocol for persistent unilateral decreased cerebral tracings.
 2b (Middle). Treatment protocol for persistent bilateral decreased cerebral tracings.
 2c (Right). Treatment protocol for persistent decreased lower limb tracings.

Figure 3. 3a (Top). Baseline tracing of a patient on ECMO (top). Blue line indicates trend of the right cerebral regional oxygen saturation (rSO₂), gray line indicates trend of the left cerebral rSO₂, orange line indicates trend of the right lower limb rSO₂, and green line indicates trend of the left lower limb rSO₂.

3b (Bottom). Development of a systemic event noted by INVOSTM. Decreased bilateral cerebral and lower limb rSO₂ tracings was observed and returned to baseline by blood transfusion.

Figure 4. A cerebral event noted by NIRS. Day 1: Normal bilateral cerebral rSO₂ tracings. Day 2: Left cerebral rSO₂ tracing drop indicating early perfusion decompensation. Day 4: Further investigation (neuro-imaging) of persistently low cerebral rSO₂ diagnosed a left middle cerebral artery infarct. Day 5: Subsequent drop in right cerebral rSO₂ secondary to severe cerebral edema and loss of bilateral cerebral blood flow.

Figure 5. A lower limb event noted by NIRS in a patient initially without a distal perfusion cannula; 1700: Lower limb NIRS monitoring initiated. 1710: Right lower limb rSO₂ tracing drop with normal left rSO₂ tracings. 1747: Placement of a distal perfusion cannula in the right femoral artery improved right rSO₂ to baseline. 1850: Distal perfusion cannula displacement with subsequent right rSO₂ tracing drop. Replacement of cannula returns the tracings to baseline.

Figure 6. 6a (Left). Mixing of oxygenated and deoxygenated blood proximal to bifurcation of great vessels.
6b (Right). Mixing of oxygenated and deoxygenated blood distal to bifurcation of great vessels.

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