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Management of Massive Hemoptysis on Extracorporeal Membrane Oxygenation.

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Short running title: Massive hemoptysis on ECMO.

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Abstract

Background: Veno-arterial extracorporeal membrane oxygenation (VA ECMO) is a life-saving procedure in patients with both respiratory and cardiac failure. Bleeding complications are common since patients must be maintained on anticoagulation. Massive hemoptysis, while rare, can occur and unless managed thoughtfully and expeditiously will result in death.

Methods: A retrospective chart review was performed of consecutive ECMO patients from 7/2010-8/2014 to identify episodes of massive hemoptysis. The management of and the outcomes in these patients were studied. Massive hemoptysis was defined as an inability to control bleeding (> 300 mL/day) from the endotracheal tube with conventional maneuvers such as bronchoscopy with cold saline lavage, diluted epinephrine lavage and selective lung isolation. All of these episodes necessitated disconnecting the ventilator tubing and clamping the endotracheal tube causing full airway tamponade.

Results: During the period of review we identified 118 patients on ECMO and 3 (2.5%) patients had the complication of massive hemoptysis. One case was directly related to pulmonary catheter migration, and the other 2 were spontaneous bleeding events that were propagated by antiplatelet agents. All 3 patients underwent bronchial artery embolization in the interventional radiology suite. Anticoagulation was held during the period of massive hemoptysis without any embolic complications. There was no recurrent bleed after appropriate intervention. All 3 patients were successfully separated from ECMO.

Conclusions: Bleeding complications remain a major issue in patients on ECMO. Disconnection of the ventilator and clamping the endotracheal tube with full respiratory and cardiac support by VA ECMO is safe. Early involvement of interventional radiology to embolize any potential sources of the bleed can prevent re-hemoptysis and enable continued cardiac and respiratory recovery.

Introduction

Extracorporeal membrane oxygenation (ECMO) is an important tool in the management of severe respiratory and cardiac failure. According to the CESAR trial in 2009, implementation of ECMO in patients with severe respiratory failure significantly improves survival compared to patients who received continued mechanical ventilation [1]. However, the complications and associated risks of placing a patient on ECMO are myriad. Massive hemoptysis (> 300 ml/day) on ECMO is a rare complication [2], but represents a significant source of morbidity and mortality. This paper presents an organized approach to the management of this dreaded complication through a review of a series of patients who developed massive hemoptysis while on ECMO.

Methods

We performed an Institutional Review Board (IRB) approved review of all adult patients within our institution who were placed on ECMO from July 2010 to August 2014. During that period a total of 118 patients were placed on either venoarterial or venovenous ECMO and 3 patients experienced massive hemoptysis. Massive hemoptysis was defined as bleeding from the endotracheal tube (> 300 mL/day) and an inability to control the bleeding with conventional measures such as correcting a coagulopathy, bronchoscopy with cold saline or diluted epinephrine lavage, and placement of a bronchial blocker for lung isolation. All episodes necessitated disconnecting the patient from the ventilator and clamping the endotracheal tube to provide full airway tamponade. Patient data was reviewed retrospectively from an established ECMO database and medical records. Patient demographic information, cause of massive hemoptysis, anticoagulation protocols, sedation protocols, management and short-term outcomes were reviewed (Table 1).

Case reports

Case #1: A 49 year-old-female developed massive hemoptysis, secondary to manipulation of a Swan Ganz catheter 48 hours after being placed on veno-arterial ECMO (V-A ECMO) for decompensated biventricular heart failure [3]. Initial conservative measures including placement of a right-sided bronchial blocker were unsuccessful in controlling the bleeding. A bronchial arteriogram was performed

which demonstrated no extravasation of contrast. The endotracheal tube was clamped for 36 hours followed by repeat bronchoscopy that demonstrated no further evidence of bleeding. The patient was subsequently able to be weaned from ECMO and decannulated and underwent a successful implantation of a Heart Mate II LVAD.

Case #2: A 57-year-old male required V-A ECMO due to cardiogenic shock secondary to a myocardial infarction. Cardiac catheterization was performed with placement of a drug-eluting stent which required the use of Integrellin. Subsequent to this intervention the patient developed massive hemoptysis. Conservative measures failed to control bleeding originating from the left lower lobe. The endotracheal tube was clamped for 13 hours but bleeding reoccurred when a heparin drip was restarted. The patient underwent bronchial arteriogram that demonstrated no extravasation, but a subsequent embolization of bilateral bronchial arteries was empirically carried out. No subsequent bleeding occurred and anticoagulation was resumed 48 hours later without complication.

Case #3: A 56-year-old female underwent the placement of a drug eluting stent for a totally occluded left descending coronary artery, which was complicated by subsequent malignant ventricular tachycardia requiring V-A ECMO for stabilization. Integrellin was started at half dose for stent protection after which the patient developed hemoptysis from the left main bronchus. Attempts at conservative measures (including lung isolation with bronchial blocker) failed to control the bleeding and the endotracheal tube was clamped for 48 hours. Arteriography demonstrated active bleeding from the left bronchial artery that was successfully embolized. The heparin drip was initiated 24 hours later, with no evidence of bleeding. Three days post embolization there was recurrent hemoptysis. Repeat arteriography demonstrated no extravasation of contrast. Right bronchial artery embolization was empirically performed and hemostasis was achieved. The patient underwent ECMO decannulation 72 hours later and subsequent successful LVAD implantation.

Discussion

ECMO in the adult population is quickly gaining popularity as a tool for rescue, bridge to transplantation or LVAD and bridge to recovery. While there have been tremendous advances in ECMO

technology and management the mortality rate remains high with survival rates of 53% for adult respiratory failure and 32% for patients with cardiogenic shock. The occurrence of massive hemoptysis in the heparinized ECMO patient, although rare, is a serious and potentially lethal complication. We have developed an algorithm for the management of massive hemoptysis while on ECMO (Figure 1). The foundations of this algorithm require a staged, timely and fluid interaction between the Intensivist, thoracic surgeon and interventional radiologist in order to achieve an optimal outcome. We discuss our algorithm as a series of questions posed to the clinical team, reflecting a step by step management of this group of patients.

To the Intensivist: “What are your initial steps in management of an ECMO patient who develops massive hemoptysis?”

Intensivist: Our initial management includes the cessation of anticoagulation, transfusion of blood products as needed to resuscitate and correct any ongoing coagulopathy, and appropriate adjustments of the ECMO and the ventilator to ensure adequate oxygenation followed by immediate bronchoscopy.

To the Intensivist: “What do you do if you cannot see anything but blood in your endotracheal tube?”

Intensivist: This would require an immediate consult to thoracic surgery and start the process for lavage and bronchial blocker.

To The Thoracic Surgeon: “What can you do to stop the bleeding at this point?”

Thoracic surgeon: Under bronchoscopic guidance I would attempt conservative control of the bleeding using iced saline irrigation and lavage with epinephrine (1 /10,000) diluted with saline in a 1/10 mix.

Note: While this was unsuccessful in all three cases above, this is maintained in our algorithm since it is an easy step that has the potential to arrest a focal site of bleeding. Following iced saline lavage, insertion of a bronchial blocker is performed in an attempt to cause tamponade. Patient #3 above was hemodynamically maintained with a bronchial blocker for 24 hours. If these steps do not stop the bleeding, a clamp can be placed on the endotracheal tube to provide full airway tamponade, since the patient is fully supported with V-A ECMO.

To the Intensivist: “What do you do now that the endotracheal tube is clamped?”

Intensivist: With the patient disconnected from the ventilator, the endotracheal tube cuff is maximally inflated to allow for tamponade of the entire airway and the ECMO settings are adjusted to insure adequate oxygenation. It is imperative to monitor the ECMO circuit by inspecting the oxygenator at least every twelve hours to ensure there is no significant clot formation while off anticoagulants. If there is concern that the oxygenator is not properly functioning obtain a pre and post oxygenator blood gas. A oxygenator gradient of less than 100 mm Hg of oxygen at 100% ECMO FiO₂ setting is an indication for exchange of the oxygenator. We have successfully managed patients with bleeding complications while on ECMO by diligent monitoring while off anticoagulation. In addition to monitoring the circuit, we utilize cerebral oximetry to assess the cerebral perfusion to ensure cerebral oxygenation [4]. Patients should have a complete blood count checked every six hours to follow hemoglobin and platelets. Packed red blood cells should be transfused to maintain a hemoglobin > 10 mg/dL and platelets should be transfused to maintain a level >100,000 B/L. The patient should be sedated and paralyzed to minimize airway pressures and provide hemodynamic stability.

To the Thoracic Surgeon and Intensivist: “How long would you leave the endotracheal tube clamped?”

Thoracic surgeon and Intensivist: We recommend a trial of unclamping after 36 hours. Once unclamped a repeat bronchoscopy should be performed and obstructive clot removed. If the bleeding continues, the endotracheal tube can re-clamped for an additional 24 hours.

To the Intensivist: “What if the bleeding persists despite these maneuvers?”

Intensivist: If bleeding continues after 72 hours, consultation with an interventional radiologist is carried out in order to obtain a pulmonary arteriogram and attempt embolization.

To the Interventional Radiologist: “How effective is embolization and what are the pertinent issues in a patient on ECMO with acute unremitting hemoptysis?”

Interventional Radiologist: After discussing the case with the Intensivist and thoracic surgeon, and reviewing any available cross-sectional imaging, the patient be brought to the interventional radiology

suite and bronchial arteriography should be performed. The bronchial arteries are the offending vessels in the majority of cases of acute hemoptysis. While the aorta and pulmonary artery may contribute to hemoptysis, they only account for about 5% of instances of massive hemoptysis. Non-bronchial arterial involvement should be considered in patients who have hemoptysis that recurs despite previous percutaneous embolic therapy.

Vascular access is usually acquired via the right common femoral artery. The presence of cannulas in one or both groins can render access challenging and may be facilitated with ultrasound guidance. While access can be acquired from the brachial artery, complication rates could be higher. If the bleeding source is successfully embolized, patients are usually placed back on anticoagulation immediately after the intervention. Manual arterial compression after arteriotomy may be challenging alongside the ECMO cannula. If necessary, an arteriotomy closure device can be placed at the end of the procedure. The presence of the cannulas may also necessitate working in oblique projections so that the field of view is maintained.

In the absence of chronic inflammatory lung disease, the bronchial arteries in patients on ECMO are usually very small (normal vascular diameter averages 1.5mm) [5]. The interventionalist needs to be familiar with the variability that occurs with bronchial artery anatomy. Approximately 70% of bronchial arteries arise from the descending thoracic aorta between T5 and T6, 10% arise as a first order branch from the thoracic aorta at levels of T5 and T6, and the remaining 20% arise from other thoracic or abdominal branch vessels. For bronchial arteries that arise directly from the aorta, a number of different branch patterns have been described [6]. Using CT scan of the thorax in conjunction with conventional angiography findings may enhance localization of the bronchial arteries. Active extravasation of contrast is appreciated in only 10.7% of cases [7].

Digital subtraction bronchial arteriograms are acquired at high frame rates to optimize visualization of the anatomy. Transverse myelitis due to spinal cord ischemia is the most serious complication associated with the embolization of the bronchial circulation. This complication is reported to occur at a rate of 1.4-6.5% [7, 8, 9]. The use of super selective micro catheter techniques with

positioning of the catheter tip distal to the anterior medullary artery has reportedly reduced the incidence of this complication. High quality angiography is critical if such structures are to be appreciated. This is often hampered by ECMO cannula movement artifact.

The choice of embolic agents depends on the size of the vessel to be embolized and micro catheter lumen size. Gel foam is difficult to deliver via a micro catheter and is only a temporary agent. Since the bronchial arteries supply mediastinal structures such as the esophagus, non-target embolization with associated necrosis is a risk if distal occlusion with small particulate matter occurs. Proximal vessel occlusion has a higher rate of recurrence. It is preferred that the mid vessel be targeted with a 500-700 micron particle “embosphere” to accomplish the embolization. Overall, the technical success rate is greater than 90% for bronchial artery embolization with an immediate clinical success rate of 73-99% [10, 11, 12]. Failure to stop the bleeding is usually due to inadequate identification and occlusion of the vessel responsible for the hemorrhage. In the cases presented only one patient had a clear feeding vessel that was embolized successfully. In the other patients bronchial artery embolization was empirically performed on the side clinically identified as actively bleeding.

To the Intensivist: “Why is embolization not always initially successful?”

Intensivist: Our trigger for interventional radiology is becoming earlier with each patient that develops massive hemoptysis. The patients presented went for angiography at different times in the course of the bleed. Erring on the side of early embolization will prevent the patient from decompensating due to continued bleeding and worsening hemodynamics. Early embolization is preferred over multiple repeat bronchoscopies post hemoptysis, since bronchoscopy carries a small, but significant risk of worsening the bleed. If the hemoptysis cannot be stopped with cold saline, diluted epinephrine and a bronchial blocker it is unlikely the hemoptysis will stop without further intervention. Clamping the ET tube provides tamponade, but the arteriogram and subsequent embolization may prevent recurrence. One thought that may explain the initial failure may be related to the time required for dilation of the bronchial vessels to allow identification by the interventional radiologist. The dynamics of flow on an ECMO circuit may require time for the dilation of the bronchial vessel to occur over a few days.

“Now that the hemoptysis has been controlled, what is the next step?”

Once the patient demonstrates that they are no longer bleeding, anticoagulation should be restarted as soon as possible with close monitoring. Post-embolization bronchoscopy was performed in all of our patients for removal of bronchial casts and assurance that the bleeding had stopped. The debridement should be done with caution and utilizes generous irrigation during its course. The bronchial lining following clamping becomes friable and recurrent bleeding can be initiated if cast removal is done aggressively. Once the ET tube has been unclamped, the patient should be connected to the ventilator and ARDS net protocol should be initiated to prevent further barotrauma to the lungs.

Conclusions:

Although our series is small, we have established an effective protocol for the successful management of patients with massive hemoptysis on ECMO. Massive hemoptysis itself often carries a high mortality and morbidity and has not been described in the ECMO patient population. Early identification and rapid intervention are of primary importance for an optimal outcome in such a precarious population. This necessitates a fluid and timely interaction between the Intensivist, thoracic surgeon and interventional radiologist.

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Table 1: Patient characteristics.

	Patient #1	Patient #2	Patient #3
Age	49 yo	57 yo	56 yo
Sex	Female	Male	Female
Days on ECMO	14 days	20 days	17 days
Day on ECMO prior to hemoptysis	2 days	1 day	3 days
Hours off anticoagulation	60 hours	72 hours	72 hours
Total number of red packed cell transfusion	7	21 *	9
Immediate blood gas post-hemoptysis	7.27/54/354, Sat 94%	7.44/40/62, Sat 92%	7.40/45/49, Sat 84%
Blood gas after episode	7.54/27/474, Sat 99%	7.55/28/418, Sat 99%	7.45/42/189, Sat 99%
Succeeful arteriogram?	No	Yes with 2 procedures	Yes with 2 procedures
Outcome	Survived	Survived	Survived
Anticoagulation before hemoptysis	Heparin	Integrin for stent protection	Integrin for stent protection
Change of oxygenator	No	Yes, secondary to suspension of heparin for GI bleed	Yes

* Transfusion requirement may be modified by concurrent gastrointestinal bleed.

Blood gas analyses are showed in the format of pH/PaCO₂/PaO₂, saturation.

Legends of Figure

Figure 1: Algorithm of management of massive hemoptysis of patient on ECMO.