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Invited Commentary

# Invited Commentary on the Postpartum Preeclampsia ECMO Case Conference

*Key Words:* ECMO; extracorporeal membrane oxygenation; preeclampsia; eclampsia; mechanical circulatory support; bias

PREGNANCY, DESPITE its common nature and reputation as a "natural stage" of female existence, has profound physiologic effects. The cardiovascular system evolves as early as 6 weeks' gestation to establish appropriate uteroplacental circulation to support a growing fetus and supply the increased demands on maternal metabolism.[1] Cardiac output increases throughout pregnancy and can reach up to 150% of prepregnancy levels by the twenty-fourth week, and is largely achieved by an increase in stroke volume; cardiac magnetic resonance imaging demonstrates increases in left ventricular end-diastolic volume and left ventricular mass.[2] Cardiac output reaches a peak during labor and is still even greater in the moments after delivery, rising to 60%-to-80% above the onset of labor. This is largely due to the effect of catecholamines on stroke volume and heart rate, as well as the sudden increase in preload secondary to autotransfusion of 300-to-500 mL of blood from the uterus into the systemic circulation after each contraction.[3] After delivery of the fetus, this blood is transfused to the mother and remains in maternal circulation.

As pregnancy places maternal circulation at the brink of human physiology, pathology of the cardiovascular system can have wide-reaching effects. Preeclampsia can be thought of as a disease of small placental vessels that can result in multiorgan dysfunction. Although incompletely understood, the underlying mechanism is thought to be a disease of abnormal placentation by trophoblasts, which results in placental ischemia that leads to the proliferation of angiogenic markers that result in vasoconstriction, endothelial dysfunction, oxidative stress, and microemboli in maternal vasculature.[4] The outdated teachings of "hypertension and proteinuria after twenty weeks" hardly capture the system-wide and potentially profound effects of this disease. Preeclampsia can cause end-organ dysfunction of potentially every system of the body, which requires prompt diagnosis and treatment. In terms of the cardiovascular system, systemic vasoconstriction results in increased afterload to the heart. Cardiac output and intravascular volumes are also decreased, although preeclampsia is associated with increased total body volume and increased vascular permeability, resulting in interstitial edema. Although remodeling of the left ventricle is a normal physiologic response to pregnancy, the remodeling in women with preeclampsia is abnormal secondary to increased systemic vascular resistance; echographic findings demonstrate increased wall thickness, impaired left ventricular relaxation, and increased filling pressures of the left ventricle compared to normal pregnancy.[5] This is the cardiovascular context of the pre-eclamptic patient with diastolic dysfunction.

It is easy to envision how the physiologic and pathophysiologic circumstances described would contribute to profound hemodynamic compromise should the heart undergo an ischemic insult and be unable to keep up with the body's increased oxygen demand and consumption immediately after delivery. In the case described, the patient's left ventricular ejection fraction was reduced severely after her hypoxemic arrest secondary to myocardial stunning, which is ventricular dysfunction that persists after reperfusion of myocardium after an ischemic insult. It is distinct from myocardial infarction in that it occurs in the absence of evidence of cellular death; the tissue remains viable and is, thus, thought to be a completely reversible condition.[6] Proposed mechanisms for this injury include the generation of free radicals, sarcoplasmic reticulum dysfunction leading to excitation-contraction uncoupling, and calcium overload.[6] Despite that, myocardial stunning is thought to be reversible, and patients can be profoundly hemodynamically unstable secondary to acutely decreased cardiac function.

Mechanical circulatory support (MCS) has a growing role in the care of seriously ill gravid or postpartum patients. Fortunately, its need in this patient population is globally

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uncommon due to being a younger and healthier group, but the H1N1 and COVID-19 pandemics have put a spotlight on their use, as pregnant patients are more susceptible to life-threatening pulmonary disease from these viruses.[7] For peripartum women who required MCS for any cause, survival has been reported to be as high as 77%.[7,8] One review reported a survival rate of 88% for peripartum women requiring MCS for cardiac arrest; this survival is greater than the average adult requiring MCS for cardiac arrest (29%), possibly secondary to the fact that peripartum women are more likely to arrest from a reversible insult. It is also higher than maternal arrests that did not use MCS (59%), although the latter finding is likely confounded by multiple factors (arrest at a large medical center with MCS versus arrest at home or a smaller hospital with fewer resources).[8] There are no randomized clinical controlled trials evaluating MCS in this population, which limits the quality of the data available. However, it remains a viable option to improve morbidity and mortality in critically ill peripartum patients.

As the authors astutely asserted, the issue of this case was not the heroics (although certainly appreciated)—it was how this story happened at all. The authors described a 26-year-old multiparous woman who, after uneventful spontaneous vaginal delivery and tubal ligation, developed a missed diagnosis of preeclampsia with severe features, and went on to develop eclampsia with life-threatening consequences. This patient went to her local emergency department 3 times in as many days and was discharged each time after a modicum of diagnostics (computed tomography of the head for headache, a venous duplex for leg swelling) and symptomatic treatment. The case does not describe if she was prescribed medication for her blood pressure as an outpatient, but if it was, it was clearly inadequate. Her last blood pressure measurement in a healthcare setting before her seizure was 182/95 mmHg, leading to speculation about how seriously her hypertensive emergency was being taken by providers. Despite a relatively classic presentation of symptoms, the correct diagnosis was not determined until several days after her initial presentation in the neurocritical care unit, even after she had seized. It is notable that, upon her seizure, despite being only 8 days postpartum, she still was not empirically treated with magnesium but only with levetiracetam and lorazepam. This can lead to the assumption that pre-eclampsia was not on the radar of multiple providers who took care of her.

It is easy to reflect on a case for which that readers were not present and ask questions about how the correct diagnosis was missed, but given the facts of the case, the diagnosis is glaring. Many questions arise from the case presented; despite a lack of history of hypertension, gestational or otherwise, why was it not considered strange that a young, immediately postpartum woman would present with a blood pressure that was so elevated? Was her abdominal pain chalked up to posttubal ligation pains, or was her headache related to taking care of a newborn at home in addition to 2 other children? If this patient's pre-eclampsia had been diagnosed appropriately, she would have been admitted for a magnesium infusion, blood pressure management, and surveillance for other end-organ dysfunction. Instead, she was sent home with a blood pressure that was so high that her home blood pressure cuff struggled to read it.

In 2013, the American College of Gynecologists removed proteinuria as a requirement for preeclampsia; proteinuria is instead considered one of the surrogates for end-organ damage via glomerular dysfunction.[9,10] It is curious that she lacked proteinuria on her initial presentations, but once proteinuria was evident in the intensive care unit, the correct diagnosis was achieved. This leads to the concern that providers are not up to date, by several years, on the diagnostic criteria of common postpartum complications.

The authors argue that this patient's missed diagnosis could be at least partially secondary to implicit (unconscious) bias against her. Racial bias is well-described in healthcare; differences in care based on race have been observed even after controlling for socioeconomic and educational differences.[11] Physicians may be blind to their own implicit bias; a study featuring Implicit Association Tests, which are computer programs that measure implicit bias by measuring the time it takes for subjects to pair a social group with a descriptor or attribute, demonstrated that even physicians who do not report explicit (conscious bias) and express an equal preference for Black and White patients will demonstrate negative implicit bias toward Black patients.[12] When these same physicians were asked to decide which theoretical patients would receive thrombolysis for acute coronary artery syndrome, their implicit bias predicted their decisions; as the level of anti-Black bias increased, decisions to administer thrombolysis to Black patients decreased. Interestingly, explicit bias was not significant for predicting decision-making.[12] Despite these associations, there have not been a wealth of studies that have evaluated this decision-making in real time. The singular study that evaluated the implicit bias and real medical decision-making found no difference in prescribers' hypertension medicine prescribing practices based on their implicit biases.[13]

In addition to being a victim of bias as a Black person, it is conceivable that this patient was a victim of bias in 2 other ways—as both an obese person and as a woman. Bias against obese people is pervasive in medicine, even in those medical professionals who are involved in the treatment of obesity itself.[14] Obese people are much more likely to feel marginalized at healthcare appointments regardless of chief complaint, and are more likely to have their medical conditions ascribed to personal decision-making than nonobese individuals. In one very large study of physicians, there was strong implicit and explicit weight bias regardless of ethnicity or sex of the physician, indicating that antifat bias among physicians is widespread.[15] Evidence suggests that providers spend less time with obese patients and may view obese patients as being less adherent.[16] One can speculate that this patient's hypertension (classically associated with obesity, whether appropriately or not, is beyond the scope of this argument) was attributed to her body size, despite not having a history of hypertension previously.

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Finally, there was possible bias against this patient as a woman. Bias against women in healthcare is well-documented; women are more likely to be considered histrionic or emotional, which can make their concerns seem less valid to healthcare providers. Compared to men, women's pain reports are more likely to be taken less seriously and are more likely to be considered psychic in nature.[17] In a computer-based study in which videotaped patients of varying sex, race, and socioeconomic status described coronary artery disease symptoms to physicians, younger female patients were diagnosed with the least confidence, and physicians often diagnosed them with mental health disorders, showing that psychological symptoms can predominate in the differential diagnosis of younger women.[18] It can be imagined that an immediately postpartum woman who has had a recent tubal ligation and simultaneously is experiencing a notoriously challenging time physically and emotionally as a parent of a newborn could have her abdominal pain and malaise attributed to female emotionality and postoperative pain instead of having it considered part of an alternative diagnosis.

When all of these potential sources of bias and lack of contemporary understanding of postpartum disease states are considered in concert, a bleak picture of this patient's fractured care is cobbled together. A Black, obese woman repeatedly presents (*women are emotional*) with high blood pressure (*as fat people are prone to have*), headache (*surely common for all new sleep-deprived parents*), abdominal pain (*she just delivered a newborn and had a tubal ligation, after all*), and leg swelling (*all pregnant women seem to have swollen legs, do they not?*). Add this to *this certainly is not preeclampsia because there is no protein in the urine*, and it is easy to see how this severely ill patient was dismissed. Because each of her complaints could be attributed to either a characteristic or circumstance of hers, it was much easier to miss the overarching diagnosis, which nearly cost the patient her life. That is the ultimate harm of bias; it is quiet in nature, yet it can alter providers' cognitive ability to deliver the effective care that patients deserve.

This case brings to the forefront the life-saving use and generally positive outcomes of MCS in pregnant and postpartum women. However, the lingering concern is how physicians can better serve their patients on a systemic level and improve recognition and early intervention on postpartum patients suffering from complications so that such interventions are not needed. It can be challenging to recognize personal biases, but ultimately it is necessary to recognize them and address them.

## Conflict of Interest

None.

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