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Pregnancy and Cardiovascular Disease (N Scott, Section Editor)

Management of Cardiac Arrest in the Pregnant Patient

Natalie Stokes, MD[1,*]
Jacqueline Kikucki, MD[2]

Address
[*,1]Department of Internal Medicine, Hospital of the University of Pennsylvania, 3400 Spruce St. 100 Centrex, Philadelphia, PA, 19104, USA
Email: Natalie.stokes@uphs.upenn.edu
[2]Department of Obstetrics and Gynecology, Uniformed Services University of the Health Sciences, Bethesda, USA

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Abstract

Purpose of review The goal of this review is to elucidate what is known about the science of maternal resuscitation and how treatment guidelines have developed to optimize management.
Recent findings There is limited data on maternal cardiac arrest. Case reports are providing some insight into safety and efficacy of certain mechanisms of treatment, including use of extracorporeal membranous oxygenation and thrombolysis, for example. Data increasingly supports the preventability of a significant portion of maternal cardiac arrest, which remains the most important target for intervention.
Summary maternal cardiac arrest has increased in incidence over the past several decades but remains a rare event. In recent years, guidelines have emerged in attempt to standardize treatment, although research on best practice is scarce. Ultimately, future progress in targeting the rise in rate of cardiac arrest will come from large scale collaboration in data sharing and development of mechanisms to identify at risk patients to prevent arrest.

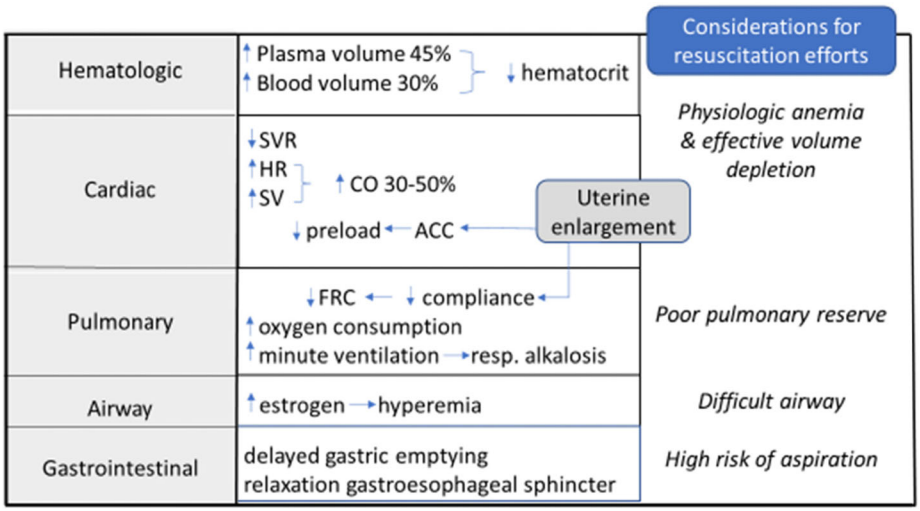
Introduction

The incidence of maternal mortality has increased in the USA over the past few decades despite worldwide efforts to optimize maternal and neonatal health [1, 2, 3••]. A notable contributor to this trend is an increase in the number of cardiac arrests [4]. Analysis of the *National Inpatient Sample* found that 1 in 12,000 women admitted for delivery between 1998 and 2011 in the US experienced cardiac arrest [4]. It is hypothesized that this is due to women getting pregnant at older ages and with more significant comorbidities and cardiac risk factors than in prior decades, although that does not fully explain this trend [2, 5–8]. Additionally, maternal cardiac arrest remains a relatively rare event, making analysis challenging.

There have been no randomized controlled studies to date that address ideal management of cardiac arrest during pregnancy. Management recommendations specific to the parturient are derived from expert opinion and case studies. In recent years, more efforts have been put forth to optimize and standardize treatment, as data have shown a relatively good prognosis for these patients with appropriate care. Moreover, analyses indicate a high proportion of cardiac arrest cases may be preventable [5, 7, 9]. The Society for Obstetric Anesthesia and Perinatology (SOAP) Consensus Statement on the Management of Cardiac Arrest in Pregnancy was released in 2014, and the American Heart Association (AHA) released a Scientific Statement of Maternal Cardiac Arrest in 2015 [3••, 10]. Both emphasize the importance of enhancing efforts to target preparedness of staff and facilities, as well as identification and management of high-risk patients pre-arrest.

The unique physiology of pregnancy alters the approach to certain aspects of treatment. Cardiac, pulmonary, hematologic, and gastrointestinal changes in pregnancy can influence the etiology of and interventions for cardiac arrest (Table 1). Basic Life Support (BLS) and Advanced Cardiac Life Support (ACLS) guidelines for non-pregnant patients pertain in large part to maternal cardiac arrest, including basic cardiopulmonary resuscitation (CPR), pharmacology, and defibrillation. There are several additional recommended steps for management of the parturient, including lateral uterine displacement with CPR and peri-mortem cesarean delivery (PMCD). There is a larger differential for etiology of arrest in this population, which requires consideration of additional therapies outside the standard ACLS algorithm. In the present paper, we summarize current treatment guidelines, supporting data, and future avenues for investigation. We also highlight significant gaps in knowledge that remain given the rarity of maternal cardiac arrest, which may be better addressed by ongoing efforts to centralize information.

Table 1. Physiologic changes in pregnancy impacting resuscitation efforts



SVR, systemic vascular resistance; *HR*, heart rate; *SV*, stroke volume; *CO*, cardiac output; *ACC*, aortocaval compression

Treatment

Pharmacologic treatment

Physiologic changes in pregnancy alter the volume of distribution and clearance of medications; however, there is scant data available to guide changes to therapy. As a general rule, standard guidelines for medication administration during ACLS for the non-pregnant population should be applied to pregnant patients [3••]. Given the acuity and severity of the situation, concern for teratogenicity should not delay the administration of appropriate therapies [3••, 11]. There are considerations related to cause of arrest in pregnant patients that prompt discussion of additional pharmacologic therapies outside of the ACLS algorithm.

- *Epinephrine:* Epinephrine should be administered at standard dose 1 mg IV/IO push every 3 to 5 min during cardiac arrest, as per ACLS guidelines. In this setting, benefit of use outweighs potential side effects, and there are no hard contraindications. Meta-analysis concluded that there was no benefit to vasopressin over epinephrine, and its suggested use was removed from the AHA guidelines in 2015 [3••, 12]. For pregnant patients, vasopressin is particularly discouraged as it has not proven to have any additional benefit over epinephrine, and it creates risk of uterine contraction [13].
- *Amiodarone:* Amiodarone should be used for shock-refractory ventricular fibrillation or pulseless ventricular tachycardia. It is the preferred agent for use in suspected bupivacaine toxicity [14]. It has been shown superior to lidocaine for cardiac arrest, and thus lidocaine is not recommended [15]. Recommended dosing is 300 mg IV/IO for initial administration, followed by 150 mg doses. Amiodarone is pregnancy category D for risk of fetal hypothyroidism and goiter, as well as miscarriage; however, this pertains to chronic maternal use [16]. Use in the appropriate patient can be lifesaving and thus benefit far surpasses risk.
- *Thrombolytics:* Thrombolysis carries risk of both maternal and fetal complications; however, use should be considered if non-surgical pulmonary embolism or ischemic stroke is considered life-threatening and likely cause of arrest [3••]. If acute coronary syndrome is considered more likely, percutaneous intervention is preferable. Thrombolysis has been used successfully in several cases of massive pulmonary embolism and ischemic stroke in pregnancy [17–19]. A recent literature review of 141 cases of thrombolytic use in pregnancy found the complication rate to be similar to that in the non-pregnant population [20•]. In the cases cited, dosing of thrombolytic agents was the same as for non-pregnant patients, and cases of both tPa and streptokinase use were noted. There is high concomitant risk of transfusion-dependent bleeding, especially in patients undergoing PMCD, which should be anticipated and prepared for with any patient requiring thrombolytics [20•, 21].
- *Calcium:* Magnesium toxicity should be considered in the appropriate patient. Discontinuation of magnesium and administration of 10% calcium gluconate 10-30 mL IV/IO or 10% calcium chloride 10 mL IV/IO should be given early in patients with suspected toxicity [3••]. In the urgent setting, there are no contraindications that should limit use.

- *Lipid emulsion therapy:* Peripartum patients frequently undergo combined spinal-epidural anesthesia, a complication of which is local anesthetic systemic toxicity (LAST), prompting central nervous system and cardiovascular collapse. LAST has been reported to occur at traditionally subthreshold dosing, so suspicion should be high in any patient who has received anesthesia. Lipid emulsion therapy is indicated for these patients. Notably, successful use of lipid emulsion therapy has also been documented for arrest secondary to amniotic fluid embolism [22]. Recommended dosing of 20% lipid emulsion therapy is initial bolus 1.5 mL/kg over 1 min, followed by 0.25 mL/kg/min infusion [23]. Infusion should be continued until the patient is hemodynamically stable, or a cumulative dose of 8-10 mL/kg is reached. Relative contraindications are severe hyperlipidemia and acute pancreatitis, which are outweighed by mortality of arrest.
- *Sodium bicarbonate:* ACLS guidelines no longer recommend routine use of sodium bicarbonate in cardiac arrest. Use is indicated for hyperkalemia and tricyclic antidepressant overdose [24], but not for all acidosis. 50 mEq IV/IO over 5 min should be administered [25]. There is risk of CO2 accumulation and resultant acidemia of the fetus with excessive sodium bicarbonate [26]; however, in patients for whom it is indicated, this should not dissuade from use.

Interventional procedures

- *Basic Life Support and Advanced Cardiac Life Support:* The basic tenets of treatment for maternal cardiac arrest follow the guidelines of BLS and ACLS as taught to all medical professionals. There are important unique characteristics of pregnancy that need to be considered and addressed in the resuscitation phase.

- *Chest compressions:* CPR is most successful with early initiation, and minimal interruption, of high-quality chest compressions. Compressions should be performed at a rate of 100–120 per minute with 5–6 cm depression, in a ratio of 30 compressions to 2 breaths prior to intubation, and continuous thereafter [24]. Use of a firm backboard improves effectiveness of compressions [27]. Imaging data revealed no difference in vertical placement of the heart within the thoracic cavity for women in the third trimester of pregnancy from the non-pregnant patient and thus past recommendations to perform compressions higher on the sternum are now moot [28]. Breaks greater than 10 s decrease chance of return of spontaneous circulation (ROSC) and should be avoided [29]. Use of capnography to evaluate compression quality is recommended when possible; levels of end tidal CO2 > 10 mmHg are considered adequate.
- *Uterine displacement:* Aortocaval compression (ACC) can significantly compromise CPR, limiting venous return to the heart. Previous teaching encouraged left lateral tilt to relieve ACC; however, recent guidelines recommend lateral uterine displacement for several reasons. The degree of tilt necessary to ensure decompression was demonstrated to be greater than 15 degrees—in some situations greater than 30 degrees—and was

shown to compromise the efficacy of chest compressions [30, 31]. Comparing methods found that patients with manual displacement had significantly less hypotension during cesarean delivery [32]. Guidelines encourage the first provider to arrive at site of arrest to start chest compressions, and the second provider to manually displace the uterus for all women at 20 weeks gestation or later [3••]. ACC can develop as early as 12 weeks and thus uterine displacement should be used in any situation in which the team considers this a possibility irrespective of gestational age [33]. Relieving pressure requires pushing the uterus upwards in addition to lateral, since direct lateral displacement can worsen venous compression. Ideally, this is performed from the left side by cupping and lifting the uterus, but it is also acceptable to push upward and to the left if the provider must be on the right [3••] [Fig. 1].

- *Airway management and ventilation*: Physiologic changes in pregnancy pose several unique concerns for providers performing cardiopulmonary resuscitation [Table 1]. Initial airway management with bag mask with 100% oxygen should be started immediately. Oral airways are preferable to nasal given high risk of epistaxis [10]. A recent trial in the general population questioned the importance of early intubation in cardiac arrest; however, given reduced reserve and high risk for difficult airway and aspiration, guidelines strongly encourage early intubation for pregnant patients [3••, 34]. The most experienced provider should perform intubation to minimize attempts. A smaller endotracheal tube (6–7 mm) should be used on first attempt, and no more than two attempts at endotracheal intubation should be made before progressing to emergent invasive airway [3••, 35]. Following intubation, ventilations should be set at a rate of 10 to 12 per minute, taking care to avoid hyperinflation. Pregnant patients are at risk for hyperinflation due to decreased lung compliance. Application of cricoid pressure is no longer advised, as there is no evidence to support its benefit in reducing aspiration [36, 37].

Fig. 1. Manual left uterine displacement during CPR Credit: Kikuchi et al. (2018).

- *Defibrillation:* In patients with a shockable rhythm, defibrillation is an essential part of the treatment algorithm. Transthoracic impedance is not changed with pregnancy [38]. Guidelines currently support the same standard for use in pregnant patients as with non-pregnant patients. AED use is acceptable in settings where staff are less familiar with rhythm analysis to accommodate defibrillation within 3 min of arrest onset [3••, 10, 39•]. It is crucial that there be the option for provider override with use of AED [10]. Notably, defibrillation should not be delayed for removal of fetal monitoring; electrocution of fetus or mother is a theoretical concern and delay of standard of care would be detrimental [36].
- *Intravenous access:* Early intravenous or intraosseous access should be obtained. It is advised to avoid placement of intravenous and intraosseous lines below the diaphragm given concern for venous compression [3••].

– *Fetal monitoring*: Management decisions in the setting of maternal cardiac arrest are based on the status of the parturient; thus, fetal monitoring is not necessary, and in fact discouraged [3••, 10]. Fetal monitors should be removed if possible; however, standard of care, including defibrillation and PMCD, should not be delayed to accommodate removal.

– *Determining the etiology of arrest*: Pharmacologic treatment and further interventions will largely be determined by what is felt to be the etiology of arrest. The AHA proposed a mnemonic to encompass a general differential for cardiac arrest in the pregnant patient: *ABCDEFGH*; representing anesthesia, accidents, bleeding, cardiovascular, drugs, embolism, fever, general and hypertension [3••]. This information should be kept accessible to staff during the code with other emergency materials.

Surgery

– *Peri-mortem cesarean delivery* (*PMCD)*: PMCD definitively resolves ACC for the mother and limits time of fetal hypoxia. PMCD is currently recommended for all pregnant women greater than 20 weeks gestation or for whom the uterus extends to the level of the umbilicus who have not obtained ROSC 4 min after initiation of resuscitation efforts, with goal of delivery within 5 min [3••, 10, 40]. If considered possible in this time frame, it is reasonable to deliver via operative vaginal delivery [3••]. These guidelines are based on analyses of past outcomes. An early review of 38 cases of PMCD found 12 of 20 women had ROSC after the procedure, and the delivered infants had greater likelihood of survival [41]. A subsequent review of 94 cases of PMCD found approximately one third of women had benefit from the procedure [42]. No cases in either review demonstrated detrimental impact from PMCD [41, 42]. Notably, of the 94 patients examined by Einav et al. (2012), only 4 were delivered within the suggested time frame. Delivery within 10 min of resuscitation efforts was associated with improved maternal survival [42]. Successful maternal and fetal outcome has been documented with PMCD after 30 min of resuscitation efforts [41]. To expedite delivery, the procedure should be

performed at the site of the arrest, as timing of delivery is paramount and thus supersedes location. Simulation trials reveal delay to delivery and decreased efficacy of CPR with attempted transport to the operating room [43]. CPR and lateral uterine displacement should continue throughout PMCD. One provider should pour antiseptic over the abdomen early in resuscitation efforts to prepare the abdomen [39•]. Discretion is left to the provider to use the surgical approach s/he is most comfortable and experienced with. A vertical incision is typically faster and will allow for better visualization of the abdomen if there is concern for trauma [44••]. Closure of uterus and abdomen should be performed either in situ or upon transport to an OR, depending on the clinical status of the patient. If the patient does not quickly obtain ROSC post-delivery, Zelop et al. (2018) recommend closure of the uterus with "absorbable suture in running interlocking fashion…with the idea of tissue re-approximation" as goal [44••]. With ROSC after PMCD, providers should anticipate significant bleeding and be prepared to manage this.

Assistive devices

- *Extracorporeal membranous oxygenation* (*ECMO*): The population of patients with maternal cardiac arrest is unique in that it is comprised of a young group with largely reversible etiologies of arrest. Use of ECMO or cardiopulmonary bypass should be considered in all patients with refractory arrest in the setting of likely reversible cause. The AHA 2015 statement specifically references patients with concern for local anesthetic toxicity, amniotic fluid embolism, and cardiogenic shock as appropriate candidates for consideration [3••]. Data from ECMO use in parturients—notably, only one of whom experienced cardiac arrest—showed approximately 80% maternal survival, and 65–70% fetal survival [45–47]. Case studies of ECMO use for patients with cardiac arrest secondary to amniotic fluid embolism [48], and pulmonary hemorrhage [47] have demonstrated good outcomes with use. Limitations of use are typically secondary to preparation time to implementation.

- *Post arrest care—therapeutic hypothermia:* Patients should be transferred to an ICU setting as soon as possible after PMCD. All patients who achieve ROSC, including those who were delivered, should be placed in left lateral decubitus position at 90 degrees to minimize ACC. Therapeutic hypothermia is strongly recommended for comatose non-pregnant patients after ROSC. There are cases of successful maternal and fetal outcomes with use of targeted temperature management (TTM) for post-arrest care in pregnant patients [49, 50]. For women who delivered or hemorrhaged during resuscitation, the risk of coagulopathy with TTM should be considered. For non-delivered patients, close fetal monitoring should be used to assess for bradycardia and decreased variability, as risk to fetus is not fully understood. The SOAP and AHA both recommend consideration of TTM on a case-by-case basis. Importantly, all patients should avoid hyperthermia post-arrest [51].

Other treatments

Maternal cardiac arrest is a relatively rare event and thus a great part of optimizing treatment and outcomes is with appropriate training and preparation, as well as prevention. Research supports the following interventions for improving outcomes.

- *Organization of OB Code team:* More teams are required to be present at a maternal cardiac arrest than in a code for a non-pregnant patient, which presents logistical challenges. In simulation studies, there was delay in contacting neonatal team members in greater than 80% of cases [52]. The AHA and SOAP proposed that facilities enact a "bundled" notification system that would alert all appropriate teams, suggesting "maternal code blue" or "Code OB" [3••, 10]. The adult resuscitation team, anesthesia, obstetrics, adult intensive care, and neonatal intensive care teams should be included. Code carts in areas of high-risk patients should carry critical equipment, including scalpel, umbilical cord clamps, and both general and neonatal resuscitation supplies. To ensure all parties are familiarized with this specific code system, periodic simulation drills are suggested.
- *Simulation and provider education:* Lack of education on proper management has been identified as a prominent factor limiting care [53]. In one analysis, approximately one third of women who died from cardiac arrest in pregnancy were not delivered at the time of death despite guidelines [7, 54]. Studies have shown significant improvement in resuscitation skills and timeliness of patient care after simulation training [55, 56]. Facility-specific factors were implicated in 75% of preventable maternal deaths [5]. Hospitals are encouraged to institute mock maternal codes to identify and address facility barriers to management and enhance knowledge base and familiarity of practitioners. Confidential Enquiries into Maternal and Child Health of the UK, SOAP and AHA recommend periodic emergency drills involving all teams for maternal cardiac arrest [3••, 10, 57]. Studies have shown improved outcomes with use of point of care checklists during acute events; however, this tool is most efficacious in settings where staff are familiarized with the checklist and tasks via simulation training [58, 59].

Emerging therapies and areas for future research

- *Prevention, risk stratification, and pre-arrest care:* Ultimately, patients are best served by avoiding cardiac arrest, and the literature suggests that a large portion of arrests in parturients are preventable [5, 7, 9]. Experts acknowledge the complexity of identifying appropriate at-risk patients, and review of past cases of maternal mortality reveal frequent lack of recognition of potential early signs of injury [4, 9, 60•]. Efforts are underway to establish a validated "early warning" scoring system for parturients. The *National Partnership for Maternal Safety* developed "The Early Warning Maternal Criteria"—a composite of blood pressure, heart rate, respiratory rate, oxygen saturation, and markers of end organ change via mental status and urine output. A degree of change in any of the parameters triggers bedside evaluation by a physician [61]. Hospital systems will need to

address barriers to enacting appropriate response to criteria, and randomized controlled trials are needed to help ensure efficacy. For patients identified as critically ill, it is appropriate to place in left lateral decubitus position and provide 100% oxygenation while performing further work-up, as well as transitioning the patient to an appropriate level of care. Better outcomes did result when the arrest occurred in highly monitored clinical settings [42]. The breadth of risk factors for maternal cardiac arrest is not fully understood, and further research is urgently needed in this space. Markedly, cardiovascular conditions are the top cause of maternal cardiac arrest in the United States [4]. As such, appropriate at-risk patients should be counseled and monitored closely throughout pregnancy.

– *Database development:* Progress in caring for maternal cardiac arrest will require collaboration and data collection across international borders. The International Liaison Committee on Resuscitation recommended development of thorough international prospective database to facilitate research [44••]. Additional calls for a mandatory national database are being made by experts to improve understanding of etiology, maternal resuscitation science and outcomes [44••].

Compliance with Ethical Standards

Conflict of Interest
The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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The most recent American Heart Association statement on maternal cardiac arrest is the most thorough review of supporting evidence for current guidelines for management. It is essential reading for this subject

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A detailed synopsis of maternal physiology and maternal resuscitation science by top experts in the field

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A recently published piece by leaders in the field chronicling the current state of knowledge and identifying specific needs for improvement at a systems level.

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