



# Management of Impending Periviable Delivery

Noor Niyar N. Ladhani<sup>1</sup>

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## Abstract

**Purpose of Review** To review the role of obstetric interventions, the evidence behind these interventions, and the importance of offering these interventions to women and their families as they make decisions on whether to provide active neonatal management.

**Recent Findings** Outcomes for infants born at periviability are improving with advancing neonatal care and management. Obstetric interventions play a role in helping to improve these outcomes. Administration of antenatal corticosteroids and magnesium sulfate should be considered if delivery is suspected. Cesarean delivery should be offered in cases of malpresentation or for other obstetric indications, with appropriate discussion around the associated maternal risks. Delayed cord clamping is considered beneficial and should be applied whenever possible. When active management is considered, or if further discussion is required, transfer to an advanced level NICU should be facilitated if possible.

**Summary** Obstetric management in the setting of an impending periviable delivery can have profound effects on neonatal outcomes. More research into what kind of impact these interventions have on outcomes is necessary. Until then, individualized counseling, shared decision-making, and interdisciplinary involvement are all needed to ensure women and families make as informed a decision as possible.

**Keywords** Periviability · Extreme prematurity · Antenatal corticosteroids · Antenatal counseling · Borderline viability

## Introduction

As technology advances, the lower limits of viability are shifting, and more women and families are offered full resuscitation of their infant when faced with possible extremely preterm birth. These clinical situations present challenges to the families and care providers involved. In these cases, it is important to present obstetric interventions that may optimize neonatal outcomes, all the while considering the health and values of the mother and her family.

These interventions include antenatal transfer to an advanced care center with an appropriate neonatal intensive care unit (NICU), administration of antenatal corticosteroids, magnesium sulfate, and considerations around mode of delivery. Here we describe the evidence and recommendations surrounding several interventions and considerations that may improve outcomes for the extremely preterm infant. These

cases ultimately require involved, interdisciplinary counseling and shared-decision making to allow for informed choices to be made by women and their families.

A periviable birth, or a birth at borderline viability, is any birth before 25 + 6 weeks, but the period of most question regarding intervention is usually less than 24 + 6 weeks. Deliveries may occur due to spontaneous onset of preterm labor, preterm premature rupture of membranes, or be medically indicated, in cases such as severe pre-eclampsia or antepartum hemorrhage. The Canadian Neonatal Network Report in 2017 [1] calculated survival rates among neonates who received active care to be 35%, 51%, and 69% among 22-, 23-, and 24-week neonates, respectively. These represent 2.5% of all tertiary level nursery admissions within the network.

When using these data to counsel families, however, several points should be considered. As an increased number of interventions are administered, both neonatal and obstetric, we expect survival, and intact survival, rates to increase as well. This has been shown in studies looking at between-hospital variation in administration of care and, consequently, in outcome measures [2•]. A recent population-based study in Sweden, where intervention rates were higher, showed

✉ Noor Niyar N. Ladhani  
noor.ladhani@sunnybrook.ca

<sup>1</sup> Sunnybrook Health Sciences Centre, M4-172 2075 Bayview Avenue, Toronto, Ontario M4N 3M5, Canada

significantly improved outcomes in infants born at 22 and 23 weeks gestation where active perinatal management was provided [3•]. When comparing rates of 1-year survival between the periods of 2004–2007 and 2014–2016, survival at 22-week GA increased from 29 to 58%. At 23 weeks, when comparing those who received care, survival increased from 29 to 44%.

In addition to the provision of active management, outcomes may be improved based on more than just gestational age. Birth weight, place of birth, administration of antenatal corticosteroids, and mode of delivery may have significant impact on outcomes. This was shown in Tyson's landmark study, where a large cohort of periviable gestations were assessed prospectively to determine antenatal risk factors that may help counsel families about their more specific likelihood of having an infant who survives and survives without morbidity [4]. Here they showed that singletons have different risk profiles compared with twins, and that factors such as birth weight, infant sex, and administration of antenatal corticosteroids (ACS) all play a role in the risk profile of the infant. Other interventions, such as delivery in a specialized center, administration of magnesium sulfate, and deferred cord clamping, also have a role to play in improving outcomes.

These studies help illustrate the need for personalized counseling, as well as the impact active obstetric and neonatal interventions may have on improving outcomes. A full picture, beyond the gestational age and including an estimated fetal weight, should be painted for a woman and her family as they decide whether or not to proceed with active management when they are potentially delivering in the periviable period.

### Accurate Dating and Antenatal Care to Prevent Preterm Birth

The value of comprehensive antenatal care cannot be overstated. Routine confirmation of dates as early as possible in the pregnancy will prevent any confusion about gestational age if a question of periviable delivery becomes necessary. Antenatal care will also identify women at risk of preterm birth and allow for implementation of measures to prevent preterm birth such as smoking cessation, close follow up, and progesterone and cerclage where appropriate.

### Place of Birth

Neonatal survival at periviable gestations is largely dependent on the availability of advanced care immediately after birth. Generally, maternal transfer to a center with availability of an advanced level NICU has been shown to reduce neonatal morbidity and mortality [5, 6]. A retrospective study looking

at mortality and neurodevelopmental impairment in infants born within or outside a center with an advanced level NICU showed that outborn infants had higher odds of mortality or severe neurodevelopmental impairment (aOR 1.61, 95% CI 1.20–2.16) compared with inborn infants [7]. Beyond the neonatal survival benefits, maternal transfer has been shown to improve decision-making and to potentially prolong the pregnancy [8].

The decision to transfer a patient and her family away from her home community and local resources is not one that should be taken lightly. The general policy of transfer itself has important resource implications. If, when faced with a likely periviable delivery, a patient has been presented with all reasonable options and has made the decision not to provide active neonatal care, then it is appropriate to deliver locally, based on resources and expertise in the provision of appropriate obstetric care to the patient and comfort care of the newborn. If there is uncertainty in her decision, if more information is required, or if she has made a decision to provide active management, transfer to a center with an advanced level neonatal intensive care unit should be arranged.

### Antenatal Corticosteroids

The benefit of antenatal corticosteroids (ACS) for preterm births has been established, and a course of ACS is administered to women thought to be delivering between 24- and 34-week gestation [9]. The course of ACS is thought to reduce the risk of death, respiratory distress syndrome, intraventricular hemorrhage, and other neonatal complications.

The benefit of ACS in the periviable population has been studied through several observational studies. Carlo et al. showed, in a prospective observational study, that a risk of death or neurodevelopmental morbidity was significantly lower at 18–22 months when ACS were administered in periviable gestations (aOR 0.58 (95% CI, 0.42–0.80) at 23 weeks, AOR 0.62 (95% CI, .49–0.78) at 24 weeks) [10]. Similar findings were shown in a meta-analysis published in 2016, where findings from observational studies were analyzed and showed a significant reduction in mortality before discharge (aOR 0.48 (95%CI 0.38–0.61)) [11].

Judicious use of ACS at these early gestational ages is warranted. If given to a woman who does not deliver, but who then goes on to threaten delivery at a later, still preterm gestation, the question of repeat or rescue dose is difficult to answer. We know from the MACS trial that repeated courses of steroids, at 14-day intervals, does not confer a reduction in mortality and does raise questions of small head circumference [12]. In a randomized controlled trial, Garite et al. showed that a rescue course of ACS given before 33 weeks did reduce neonatal morbidity [13]. Larger trials assessing specifically those who were given ACS during the periviable

period are needed to assess for benefit and ensure safety in this population.

## Magnesium Sulfate

Magnesium sulfate administration for neuroprotection, specifically the prevention of cerebral palsy (CP), is recommended when an imminent preterm birth is expected in the periviable period [14–16]. The recommendations are largely based on data from five randomized controlled trials, two of which did not stipulate a lower limit of administration [17, 18]. The other studies included only pregnancies greater than 24 weeks. A recent individual patient data analysis, however, showed benefit regardless of gestational age, duration of treatment, timing with respect to delivery, or whether a maintenance dose was added to the initial bolus of 4 g administered intravenously over 30 min [19]. This review specifically showed clear benefit in a reduction of CP at gestational ages less than 28 weeks. Although a lower gestational age limit is not specifically stated, given the potential for benefit and increased risk of CP in the periviable period, it is prudent to administer magnesium sulfate when an imminent delivery is anticipated.

## Mode of Delivery

As women and families consider options for active management of the neonate, one of the most common questions that arise is whether they should undergo Cesarean delivery. Generally, a routine CD simply for periviability is not recommended, as it has not been shown to provide neonatal benefit [20, 21]. The question remains, however, about the benefit of Cesarean for malpresentation in this population.

A population-based cohort study conducted in the USA assessed the frequency of CD before and after published recommendations were made for management of periviable deliveries [22]. The rate difference found was 4.1% increase, with a 6.2% increase for malpresentation. The difference is mostly attributable to a change in management of the 23 + 0–23 + 6-week deliveries. This cohort also showed a slight reduction in neonatal mortality (2.7%); it is difficult to attribute this improvement to the CD itself or to the composite change in neonatal interventions administered.

A retrospective single-center study comparing outcomes with CD versus vaginal delivery for breech presentation, in cases where active management was planned, found a significantly lower rate of neonatal death with CD (44.4% vs 23.6%,  $p = 0.0127$ ) [23]. Similarly, a meta-analysis of observational studies showed a reduction in death before discharge (OR 0.59, 95% CI 0.36–0.95), 122 fewer deaths per 1000 with CD) and in rates of severe intraventricular hemorrhage (OR 0.51, 95% CI (0.29–0.91), 80 fewer cases per 1000 with CD). [24]

While randomized-controlled trials are lacking, observational data does support the likely benefit of CD of nonvertex presentations in the periviable period, when active neonatal management is planned.

Delivery in the periviable period, regardless of mode of delivery, has been shown to have higher maternal risks compared with deliveries in later gestations, although Cesarean delivery may confer an even higher risk. A large, retrospective study showed higher composite risks in the group delivering at 23–27 weeks compared with those delivering at 28–31 weeks and 32–33 weeks (11.5%, 9.5%, and 6.3%, respectively). [25] The increase was mostly driven by a statistically significant increase in maternal hemorrhage in the earlier GA group. Hemorrhage, infection, and ICU admission were all shown to be more frequent in the CD group, regardless of the type of uterine incision. Similarly, Niles et al. showed an increased risk of estimated blood loss in the CD group of periviable breech deliveries, from an average of 327 mL in the vaginal delivery group to an average of 706 mL in the CD group [23]. Beyond the affected pregnancy, a periviable CD may have implications for future pregnancies. These deliveries are often performed through a vertical uterine incision, necessitating CD in subsequent pregnancies, and thought to potentially confer an increased risk of uterine rupture in future pregnancies [26].

The question of mode of delivery comes with some uncertainty, and ultimately, it is the role of the care provider to relay this uncertainty to the patient and her family, so that an informed choice can be made.

## Delayed Cord Clamping

The role of delayed or deferred cord clamping the preterm population (< 37 weeks) has been studied widely and has been shown to confer benefit in a recent, large meta-analysis [27]. The authors show a reduction in neonatal mortality with a delay in cord clamping, potentially due to an increased cell mass that in turn increases total oxygen carrying capacity. The deferral in cord clamping until the infant has started breathing on their own may also contribute to the observed reduction in the need for endotracheal intubation, and is hypothesized to generally reduce the need for postnatal interventions. Similar efficacy was shown in the subgroup analysis of 3 trials that assessed those born at less than 28 weeks gestation. Among these trials, a reduction in hospital mortality was found (996 infants, RR 0.70; 95% CI 0.51–0.95) and a reduction in those who needed blood transfusion. There was no significant difference in other neonatal outcomes. The largest study included in the analysis used 60 s of delay and avoided cord milking [28]. There was no consistency with respect to the height of the infant relative to the introitus or abdominal incision, or regarding the timing of oxytocics relative to the timing of clamping of the cord. This review also found no increase in the maternal risk of postpartum hemorrhage or blood

transfusion. The findings suggest this easy intervention may provide benefit under the right circumstances. We usually defer clamping for 60s while stimulating the infant, keeping them warm, and ensuring the placental bleeding is within normal limits.

## Conclusion

General guidelines and consensus statements may help drive local policies on the best interventions for improving outcomes, and such guidelines exist in many jurisdictions [14, 16, 29]. These guidelines stress the importance of shared, individualized decision making is paramount in the counseling of families deciding how to proceed when faced with a possible and imminent periviable birth. Interdisciplinary counseling, with Maternal-Fetal Medicine or Obstetrics and Neonatology or Pediatrics will allow for a balanced approach and will allow for families to make decisions with considerations for the infant and mother.

In situations where active neonatal management is planned, the benefits of the interventions discussed, such as transfer to a hospital with an advanced care nursery, antenatal corticosteroids, magnesium sulfate, Cesarean delivery for obstetrical indications, and delayed cord clamping should all be offered and decisions about each individual intervention should be made. The uncertainty in the evidence, especially around such questions as mode of delivery, should be stated explicitly. The data show outcomes of infants born during periviable gestations continue to improve as more interventions are offered, and the provision of obstetric management is an important contributor. Ultimately, the choice to provide active management and the corresponding interventions is the patient's to make; health care providers have the duty to provide all the options available to ensure the patient makes the best decision for her and her family.

## Compliance with Ethical Standards

**Human and Animal Rights** All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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