Delivery Room Resuscitation and Short-Term Outcomes in Moderately Preterm Infants

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Objectives To describe the frequency and extent of delivery room resuscitation and evaluate the association of delivery room resuscitation with neonatal outcomes in moderately preterm (MPT) infants.

Study design This was an observational cohort study of MPT infants delivered at $29^{0/7}$ to $33^{6/7}$ weeks' gestational age (GA) enrolled in the Neonatal Research Network MPT registry. Infants were categorized into 5 groups based on the highest level of delivery room intervention: routine care, oxygen and/or continuous positive airway pressure, bag and mask ventilation, endotracheal intubation, and cardiopulmonary resuscitation including chest compressions and/or epinephrine use. The association of antepartum and intrapartum risk factors and discharge outcomes with the intensity of resuscitation was evaluated.

Results Of 7014 included infants, 1684 (24.0%) received routine care and no additional resuscitation, 2279 (32.5%) received oxygen or continuous positive airway pressure, 1831 (26.1%) received bag and mask ventilation, 1034 (14.7%) underwent endotracheal intubation, and 186 (2.7%) received cardiopulmonary resuscitation. Among the antepartum and intrapartum factors, increasing GA, any exposure to antenatal steroids and prolonged rupture of membranes decreased the likelihood of receipt of all levels of resuscitation. Infants who were small for GA (SGA) had increased risk of delivery room resuscitation. Among the neonatal outcomes, respiratory support at 28 days, days to full oral feeds and length of stay were significantly associated with the intensity of delivery room resuscitation. Higher intensity of resuscitation was associated with increased risk of mortality.

Conclusions The majority of MPT infants receive some level of delivery room resuscitation. Increased intensity of delivery room interventions was associated with prolonged respiratory and nutritional support, increased mortality, and a longer length of stay. *(J Pediatr 2018;195:33-8).*

Approximately 85% of infants delivered at term gestational age (GA) require no assistance in transitioning from the intrauterine to extrauterine environment after birth; only 5% require positive pressure ventilation and 0.1% require chest compressions and/or epinephrine.[1] This transition is not as smooth for infants delivered prematurely. Finer et al reported that 6% of infants in the Vermont Oxford Network with birth weights between 501 and 1500 g received cardiopulmonary resuscitation (CPR) that included chest compressions and/or administration of epinephrine in the delivery room.[2] Compared with term infants, late and moderately preterm (MPT) infants delivered between 32 and 36 weeks of gestation are more likely to receive resuscitation at birth.[3] Besides prematurity, there are other antepartum and intrapartum risk factors that can be associated with receipt of delivery room resuscitation in late and MPT neonates.[4-6] Increasing intensity of delivery room resuscitation has been shown to predict risk of mortality and adverse neurodevelopmental outcome in extremely low birth weight and very low birth weight infants.[7-9]

ANS	Antenatal steroids	MPT	Moderately preterm
BPD	Bronchopulmonary dysplasia	NEC	Necrotizing enterocolitis
CPAP	Continuous positive airway pressure	NRN	Neonatal Research Network
cPVL	Cystic periventricular leukomalacia	NRP	Neonatal Resuscitation Program
CPR	Cardiopulmonary resuscitation	PPV	Positive pressure ventilation
GA	Gestational age		

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The Neonatal Resuscitation Program (NRP) guidelines published by the American Academy of Pediatrics recommend the presence of at least 1 qualified individual skilled in the initial steps of newborn care and positive pressure ventilation (PPV) at every birth; in the presence of risk factors, a qualified team with full resuscitation skills should be available.[10] However, the composition of the resuscitation team varies in different hospitals and comprises of personnel with varying expertise and experience. In small rural hospitals, it can be challenging to have a team prepared to provide neonatal resuscitation.[11] Although MPT infants delivered between $29^{0/7}$ and $33^{6/7}$ weeks of GA constitute about 2.8% of all births in the US,[12] data are limited on the frequency and extent of delivery room resuscitation in this population. The antepartum risk factors associated with receipt of resuscitation in MPT infants remain unexplored. Identification of these factors could help clinical staff prepare better for MPT delivery with attendance of skilled personnel in the delivery room to provide prompt stabilization.

Data on neonatal outcomes following delivery room resuscitation are also scarce in the MPT population. Several investigators have reported increased risk of morbidity and mortality in extremely low birth weight and very low birth weight preterm infants who received CPR in the delivery room.[13,14] The association of varying intensity of delivery room resuscitation and neonatal morbidities in the MPT infants remains unstudied.

In the current study, we describe the frequency and extent of delivery room resuscitation in infants enrolled in the MPT registry of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Neonatal Research Network (NRN), and examine the association between antepartum and intrapartum factors and the extent of delivery room resuscitation. We also evaluate the association of delivery room resuscitation with occurrence of neonatal morbidities prior to initial hospital discharge.

Methods

The study population included infants delivered between February 2012 and November 2013 at $29^{0/7}$ to $33^{6/7}$ weeks GA who were enrolled in the NRN MPT registry.[15] Infants in whom a prenatal diagnosis caused a decision to withdraw or limit intensive care were excluded. Data were collected prospectively by trained research personnel using standard definitions. Maternal information included age and prenatal care, pregnancy complications including multiple births, insulin dependent diabetes, hypertension, prolonged rupture of membranes (>18 hours), clinical and histologic chorioamnionitis, receipt of antenatal steroids (ANS) and magnesium sulfate, and mode of delivery. Neonatal information included sex, GA, birth weight, and Apgar scores. Data on birth resuscitation included use of oxygen, continuous positive airway pressure (CPAP), bag and mask ventilation that included positive pressure ventilation with face mask and bag or T-piece resuscitator (Neopuff, Fisher and Paykel Healthcare, New Zealand), endotracheal intubation, chest compressions, and epinephrine.

Short-term outcomes were collected in the MPT registry at the time of discharge, transfer, death, or at 40 weeks of postmenstrual age, whichever occurred first. These included respiratory distress syndrome treated with surfactant therapy, respiratory support at 28 days of life including oxygen via nasal cannula, CPAP, noninvasive ventilation, or ventilatory support, presence and severity of intracranial hemorrhage based on Papile's classification,[16] and cystic periventricular leukomalacia (cPVL) diagnosed after 28 days of age (among those who had cranial sonography), early- and late-onset sepsis defined by positive blood cultures at or before and after 72 hours of age, days to full oral feeds, and proven necrotizing enterocolitis (NEC) defined by modified Bell Stage ≥IIA.[17] The study was approved by the institutional review board at each NRN center.

Delivery room resuscitation was defined as receipt of any assistance after birth besides routine care that included providing warmth, drying, and stimulation of the infant. Infants were divided into 5 groups according to the highest level of resuscitation they received: (1) routine care, (2) oxygen and/or CPAP, (3) bag and mask ventilation, (4) endotracheal intubation and (5) CPR including chest compressions and/or epinephrine use. This classification was based on the steps in the NRP algorithm and was similar to a previous study.[1,7] Oxygen and CPAP were combined in 1 group as the indications for PPV using bag and mask are distinct.

Statistical Analyses

Maternal and neonatal characteristics and neonatal outcomes of infants in the 5 groups were compared using ANOVA for continuous variables and χ^2 test for categorical variables. A generalized logistic regression model was used to explore neonatal and maternal characteristics significantly associated with the 5 intensity levels of delivery room resuscitation. The significant maternal and neonatal baseline characteristics were included and the best model was selected using the Akaike information criterion as a measure to balance model fit with model complexity.

Multivariable logistic regression analysis was performed to assess the association between levels of resuscitation with selected morbidities after adjusting for center, GA, SGA status, any ANS, and multiple births - variables selected a priori because of their known association with outcomes among extremely preterm infants. Statistical analyses were conducted using SAS/STAT software, v 9.4 (Cary, North Carolina). A 2-sided *P* value less of than .05 was considered to be statistically significant.

Results

A total of 7057 infants across 18 centers were enrolled in the MPT registry between February 2012 and November 2013. A prenatal decision to limit intensive care was made for 36 infants, and delivery room information was missing in 7 infants. Of 7014 infants included in the analysis, 1684 (24.0%) received routine care without additional resuscitation; 2279 (32.5%) received oxygen or CPAP but not ventilation, intubation or CPR; 1831 (26.1%) received bag and mask ventilation but not intubation or CPR; 1034 (14.7%) received endotracheal intubation but not CPR; and 186 (2.7%) underwent CPR.

Table I. Maternal and Infant characteristics

Characteristics	Routine care n = 1684	Oxygen/CPAP n = 2279	Bag-mask ventilation n = 1831	Endotracheal intubation n = 1034	CPR n = 186	*P* value (trend)
Birth weight, g, mean (SD)	1855 (366)	1678 (433)	1636 (422)	1585 (449)	1679 (472)	<.0001
GA, wk mean (SD)	32.21 (1.1)	31.4 (1.3)	31.3 (1.3)	30.8 (1.4)	31.0 (1.4)	<.0001
Small for gestation, %	248/1682 (14.7)	387/2279 (17.0)	338/1830 (18.5)	157/1033 (15.2)	21/185 (11.4)	.0068
Maternal age, mean (SD)	28.5 (6.7)	28.7 (6.5)	28.2 (6.5)	28.1 (6.3)	27.5 (6.5)	.0566
Sex: % male	877/1682 (52.1)	1172/2279 (51.4)	936/1830 (51.1)	567/1033 (54.9)	106/186 (57.0)	.1945
Apgar score at 5 min <5, %	2/1668 (0.12)	4/2275 (0.18)	50/1824 (2.7)	178/1025 (17.4)	108/177 (61.0)	<.0001
Major congenital malformations, %	72/1683 (4.3)	127/2278 (5.6)	134/1831 (7.3)	223/1033 (21.6)	35/186 (18.8)	<.0001
Prenatal care, %	1617/1683 (96.1)	2216/2276 (97.4)	1794/1828 (98.1)	994/1033 (96.2)	171/184 (92.9)	<.0001
Maternal hypertension, %	487/1682 (29.0)	838/2274 (36.9)	694/1826 (38.0)	296/1030 (28.7)	49/181 (27.1)	<.0001
Maternal diabetes (insulin dependent), %	105/1682 (6.2)	188/2275 (8.3)	148/1828 (8.1)	73/1029 (7.1)	9/181 (5.0)	.0715
Chorioamnionitis, %	144/1673 (8.6)	143/2258 (6.3)	127/1820 (7.0)	70/1008 (6.9)	11/185 (6.0)	.0849
Chorioamnionitis, histologic, %	399/1422 (28.1)	420/1910 (22.0)	415/1534 (27.1)	204/806 (25.3)	32/110 (29.1)	.0005
Rupture of membranes >18 h, %	423/1581 (26.8)	400/2153 (18.6)	271/1712 (15.8)	146/953 (15.3)	19/170 (11.2)	<.0001
Cesarean delivery, %	735/1683 (43.7)	1489/2279 (65.3)	1273/1830 (69.6)	787/1034 (76.1)	154/186 (82.8)	<.0001
Antenatal steroids, %	1459/1668 (87.5)	1948/2261 (86.2)	1591/1819 (87.5)	833/1022 (81.5)	102/180 (56.7)	<.0001
Singleton, %	1205/1684 (71.6)	1512/2279 (66.3)	1311/1831 (71.6)	783/1034 (75.7)	156/186 (83.9)	<.0001
Antenatal magnesium sulfate, %	796/1659 (48.0)	1274/2239 (56.9)	1057/1796 (58.9)	506/993 (51.0)	58/176 (33.0)	<.0001

Denominator for each variable is based on the availability of data.

Maternal and neonatal characteristics are shown in **Table I**. Lower birth weight and GA, SGA, lack of prenatal care, lack of ANS, use of antenatal magnesium therapy, and Cesarean delivery were associated with a higher intensity of resuscitation. Maternal hypertension, prolonged rupture of membranes, and histologic chorioamnionitis were significantly associated with intensity of resuscitation. The proportion of singleton births was significantly higher (83.9% vs 71.6%) in the group that received CPR, compared with routine care. The final generalized logistic regression model exploring the relationship of maternal and neonatal characteristics with different levels of delivery room resuscitation included GA, SGA status, exposure to ANS and magnesium sulfate, multiple births, histologic chorioamnionitis, maternal hypertension, prolonged rupture of membranes (>18 hours), and prenatal care (**Table II**). All estimates of ORs in **Table II** have routine care in the delivery room as the reference group. Increasing GA, exposure to ANS, and prolonged rupture of membranes decreased the likelihood of all levels of resuscitation. Multiple births were associated with lower risk of endotracheal intubation and CPR. SGA status and presence of prenatal care were associated with more frequent need for oxygen/CPAP, bag and mask ventilation, and endotracheal intubation. Exposure to magnesium sulfate decreased the odds of endotracheal intubation and CPR. Maternal hypertension increased the need for oxygen/CPAP while histologic chorioamnionitis reduced the odds of oxygen/CPAP and intubation.

Short-term outcomes among MPT infants with different levels of resuscitation are noted in **Table III**. Respiratory morbidities, including surfactant use and continued respiratory support at 28 days (ventilator, CPAP, or oxygen) increased with increasing level of delivery room resuscitation. Although cranial ultrasound was obtained in only 58% of infants in our cohort, any grade of intraventricular hemorrhage (IVH) and cPVL increased with increasing level of delivery room resuscitation. Similarly, rates of other neonatal morbidities including early-onset sepsis, late-onset sepsis, and NEC as well as days to full oral feeds, death before discharge, and length of stay among survivors progressively increased with level of resuscitation. Logistic regression analysis after adjusting for a priori selected covariates (center, GA, SGA, ANS, and multiple births) showed longer length of stay among survivors, older postnatal age at full oral feeds and increased need for respiratory support at 28 days among infants who received any level of delivery room

Table II. The aOR of risk factors for levels of resuscitation*

Variable	Oxygen/CPAP n = 2279	Bag-mask ventilation n = 1831	Endotracheal intubation n = 1034	CPR n = 186
GA (per increasing wk)	**0.55 (0.51-0.59)**	**0.52 (0.48-0.55)**	**0.37 (0.34-0.41)**	**0.41 (0.35-0.48)**
Small for gestation	**1.29 (1.05-1.59)**	**1.39 (1.12-1.73)**	**1.53 (1.17-2.00)**	0.99 (0.51-1.90)
Multiple births	1.18 (1.00-1.40)	0.95 (0.79-1.13)	**0.69 (0.55-0.86)**	**0.40 (0.22-0.73)**
Antenatal steroids	**0.69 (0.53-0.89)**	0.77 (0.58-1.01)	**0.56 (0.41-0.77)**	**0.20 (0.12-0.34)**
Magnesium sulfate	0.96 (0.81-1.14)	0.98 (0.82-1.18)	**0.65 (0.52-0.81)**	**0.40 (0.24-0.67)**
Histologic chorioamnionitis	**0.81 (0.67-0.99)**	0.99 (0.82-1.22)	**0.72 (0.56-0.92)**	1.18 (0.70-1.99)
Maternal hypertension	**1.26 (1.05-1.50)**	1.18 (0.99-1.43)	0.84 (0.66-1.06)	1.27 (0.77-2.09)
Rupture of membranes >18 h	**0.75 (0.61-0.91)**	**0.51 (0.41-0.63)**	**0.52 (0.40-0.68)**	**0.39 (0.20-0.75)**
Prenatal care	**1.72 (1.07-2.74)**	**3.23 (1.83-5.70)**	1.82 (1.00-3.28)	1.57 (0.52-4.75)

Values in bold are statistically significant.
Deviance goodness of fit test: *P* value = .99.
*Routine care in the delivery room is the reference level.

Table III. Neonatal outcomes

Characteristics	Routine care n = 1684	Oxygen/CPAP n = 2279	Bag-mask ventilation n = 1831	Endotracheal intubation n = 1034	CPR n = 186	*P* value (trend)
Surfactant use, %	82/1684 (4.9)	461/2279 (20.2)	447/1830 (24.4)	706/1034 (68.3)	129/185 (69.7)	<.0001
Respiratory support at 28 d, %	66/1611 (4.1)	261/2116 (12.3)	245/1753 (14.0)	332/944 (35.2)	54/145 (37.2)	<.0001
Ventilator, CPAP, O_2						
Ventilator at 28 d, %	8/1611 (0.5)	15/2116 (0.7)	28/1753 (1.6)	69/944 (7.3)	13/145 (9.0)	<.0001
CPAP at 28 d,	3/1611 (0.2)	16/2116 (0.8)	24/1753 (1.4)	40/944 (4.2)	2/145 (1.4)	<.0001
Oxygen at 28 d,	55/1611 (3.4)	230/2116 (10.9)	193/1753 (11.0)	223/944 (23.6)	39/145 (26.9)	<.0001
Any IVH, %	93/657 (14.2)	135/1296 (10.4)	134/1124 (11.9)	137/800 (17.1)	37/144 (25.7)	<.0001
Grades 1,2,3,4						
cPVL after 28 d, %	2/213 (0.9)	15/639 (2.4)	16/614 (2.6)	19/484 (3.9)	9/69 (13.0)	<.0001
Early-onset sepsis, %	10/1683 (0.59)	13/2279 (0.57)	13/1831 (0.71)	10/1031 (1.0)	5/185 (2.7)	.0171
Late-onset sepsis, %	33/1677 (2.0)	56/2272 (2.5)	64/1829 (3.5)	63/1030 (6.1)	5/183 (2.7)	<.0001
Days to full oral feeds (120 mL/kg/d) mean (SD)	17.8 (11.7)	26.8 (20.7)	27.6 (15.0)	35.8 (17.4)	35.4 (17.3)	<.0001
Proven NEC, %	25/1684 (1.5)	47/2274 (2.1)	50/1829 (2.7)	40/1034 (3.9)	7/185 (3.8)	.0008
Death before discharge, %	11/1684 (0.6)	22/2279 (1.0)	29/1831 (1.6)	74/1034 (7.2)	39/186 (21.0)	<.0001
Death among infants with major congenital malformations, %	5/72 (6.9)	9/127 (7.1)	13/134 (9.7)	51/223 (22.9)	23/35 (65.7)	<.0001
Length of stay (d), mean (SD)	24.9 (14.6)	34.0 (21.6)	35.8 (18.3)	43.7 (26.3)	37.2 (23.4)	<.0001
Min, median, max	1, 22, 213	1, 31, 395	2, 33, 214	1, 44, 434	1, 38, 83	

Denominator for each variable is based on the availability of data.

resuscitation (Table IV). Mortality was unchanged in the group that received oxygen/CPAP, but increased significantly with higher levels of resuscitation. The adjusted risk of early-onset sepsis, late-onset sepsis, and NEC did not increase with delivery room resuscitation. The odds of IVH and cPVL increased in the group who received CPR.

Discussion

In a large multicenter cohort of MPT infants born at $29^{0/7}$ to $33^{6/7}$ weeks of GA, the majority (76%) received some level of resuscitation in the delivery room; with nearly 15% undergoing endotracheal intubation and 2.7% full CPR. The intensity of resuscitation decreased significantly for each advancing week of gestation. Prolonged rupture of membranes, and exposure to any ANS were associated with a reduced likelihood whereas SGA status and prenatal care were associated with increased likelihood of resuscitation levels other than CPR. Receipt of higher intensity of resuscitation after birth was associated with increased mortality, prolonged hospitalization and time to attain full feedings, and higher likelihood of receipt of respiratory support at 28 days of age. CPR was associated with increased risk of intraventricular hemorrhage and cPVL among the MPT infants who had screening cranial sonograms.

MPT infants are a high-risk group that accounts for utilization of a large proportion of neonatal intensive care unit resources. Rates of delivery room resuscitation among late preterm infants, which range between 14% and 46% in different studies, are significantly lower than the rate in MPT infants, likely because of lower GA and antepartum factors predisposing to preterm delivery.[3,4,18-20] In a study from Korea, almost 93% of infants between 29 to 32 weeks of GA received supplemental oxygen and 3% received CPR in the delivery room.[21] These findings may reflect a difference in delivery room resuscitation practices in Korea compared with NRN centers. Boyle et al reported that 36.9% of infants delivered at 32-33 weeks received active resuscitation in the delivery room.[3] However, their study did not include infants of 29-31 weeks of GA. Our study confirmed that infants delivered at higher GA within the 29-33

Table IV. The aORs (and 95% CIs) of neonatal outcomes for levels of resuscitation*

Outcomes	Oxygen/CPAP n = 2279	Bag-mask ventilation n = 1831	Endotracheal intubation n = 1034	CPR n = 186
Death	1.43 (0.68-2.99)	**2.63 (1.29-5.34)**	**12.73 (6.53-24.80)**	**48.02 (23.10-99.83)**
Respiratory support at 28 d	**1.91 (1.41-2.57)**	**2.31 (1.71-3.13)**	**5.40 (3.97-7.35)**	**4.89 (3.02-7.89)**
Intraventricular hemorrhage	0.74 (0.55-1.0)	0.81 (0.60-1.10)	1.20 (0.89-1.64)	**1.75 (1.09-2.81)**
cPVL after 28 d	2.45 (0.54-11.08)	3.19 (0.71-14.34)	4.06 (0.90-18.25)	**9.71 (1.89-49.82)**
Proven NEC	1.06 (0.63-1.77)	1.43 (0.86-2.38)	1.41(0.81-2.44)	1.64 (0.67-4.00)
Early sepsis	0.79 (0.32-1.91)	0.86 (0.35-2.14)	0.86 (0.32-2.30)	2.70 (0.82-8.92)
Late-onset sepsis	0.77 (0.49-1.22)	1.00 (0.64-1.58)	1.29 (0.81-2.07)	0.76 (0.28-2.03)
Age at full oral feed (d)†	**2.98 (2.02-3.93)**	**2.99 (1.97-4.00)**	**6.72 (5.43-8.02)**	**6.28 (3.52-9.04)**
Length of stay (d)†,‡	**2.81 (1.71-3.91)**	**3.91 (2.75-5.08)**	**9.30 (7.88-10.73)**	**8.75 (5.81-11.68)**

Values in bold are statistically significant.
*Routine care in the delivery room is the reference level. The covariates included in the regression are center, GA, small for GA, ANS, and multiple births.
†For continuous outcomes, an estimate of the difference between means and the 95% CI of the estimate is reported.
‡Average length of stay among survivors.

week range had lower adjusted odds for resuscitation in the delivery room. Each increasing week of gestation decreased the risk of receiving resuscitation in the delivery room.

Prenatal care, defined in the data base as at least one prenatal visit prior to the delivery, was associated with increased receipt of oxygen, CPAP, or bag and mask ventilation in our study. The reason for this association is unclear though we speculate that better prenatal care helped to identify higher risk women who subsequently delivered prematurely at tertiary centers.

There is limited literature evaluating the risk of delivery room resuscitation with maternal hypertension and SGA status in MPT infants. Aziz et al reported a 2-fold increase in respiratory support (positive pressure ventilation-endotracheal intubation) among moderate-high risk infants born to mothers with hypertension during pregnancy across all GAs.[5] Similar associations have been reported between pregnancy-induced hypertension and advanced resuscitation (endotracheal intubation and CPR) in infants greater than 34 weeks of GA,[6] and maternal hypertension and bag and mask ventilation in late preterm infants.[4] Maternal hypertension was a significant risk factor among extremely low birth weight infants receiving CPR in the delivery room.[8] In contrast, in the current study, maternal hypertension was independently associated with increased need for oxygen/CPAP alone. Magnesium sulfate was associated with reduced receipt of endotracheal intubation and CPR. We did not have available data on duration, dose, or indications for its use. Magnesium may cause adverse events including diminished deep tendon reflexes and respiratory depression when used in the pregnant women.[22] However, published reports do not show any association between magnesium sulfate exposure and level of delivery room resuscitation in the neonates.[23,24] The association between SGA status and all levels of resuscitation except CPR in MPT infants in our study is consistent with previously reported data in late preterm infants.[4,6,20] Maternal hypertension is an important risk factor for preterm delivery and SGA status, which could lead to emergency Cesarean delivery and use of antepartum magnesium sulfate.[25] Because of the complex interaction between maternal hypertension, use of magnesium sulfate, and SGA status, it is hard to dissociate the individual effects of each risk factor in this population.

The protective effect of ANS exposure has been shown in extremely low birth infants.[7,8] We found that exposure to ANS confers an advantage in MPT infants as well. Prolonged rupture of membranes decreased the odds of resuscitation in our cohort whereas histologic chorioamnionitis was associated with reduced frequency of oxygen/CPAP and endotracheal intubation; the association did not retain significance for bag and mask ventilation or CPR. Histologic chorioamnionitis has been associated with reduced incidence of respiratory distress syndrome in preterm neonates,[26,27] which could lower the need for resuscitation. On the other hand, stress and an increased risk of sepsis may render these infants less vigorous at birth, accounting for the inconsistent associations noted. Multiple births, in our study, were associated with decreased risk for endotracheal intubation and CPR in the delivery room. There have been conflicting reports in the literature about the association of multiple births with delivery room resuscitation. Aziz et al reported that in infants less than 35 weeks of GA, multiple births doubled the risk of receiving positive-pressure ventilation and/or endotracheal intubation in the delivery room; the association was not seen in infants >35 weeks of gestation.[5] Berazategui et al did not find an association between multiple births and advanced resuscitation in infants delivered at >34 weeks of GA.[6] The reason for this discrepancy is not clear. We speculate that increased surveillance in the antenatal and intrapartum period for multiple births might have contributed to our results.

There is a paucity of literature on the effects of neonatal resuscitation in MPT infants. We demonstrate that delivery room resuscitation in MPT infants was associated with adverse short-term outcomes, including increased receipt of respiratory support at 28 days of age, delayed attainment of oral feedings, and prolonged length of hospitalization after adjusting for GA, center, SGA, ANS, and multiple births. It is intriguing that even with low rates of mortality overall, the need for bag and mask ventilation or higher levels of resuscitation in the delivery room was a predictor for mortality. CPR in the delivery room was associated with an increased risk of IVH and cPVL. Although we acknowledge that cranial ultrasound was only obtained in 58% of MPT infants enrolled in the registry, the increased risk of IVH and cPVL following delivery room CPR suggests the need for neurodevelopmental monitoring for sequelae, at least in this select group of MPT infants. Delivery room resuscitation has been shown to be associated with adverse neonatal outcomes in other neonatal cohorts. In late preterm infants, higher intensity of resuscitation was associated with mortality, respiratory distress, pneumothorax, late-onset sepsis, and length of stay.[20] In a large cohort of extremely low birth infants from NRN centers, CPR in the delivery room was associated with increased risk of pneumothorax, bronchopulmonary dysplasia (BPD), grade 3-4 IVH, death by 12 hours, and death or neurodevelopmental impairment among survivors at 18 months of corrected age.[8] DeMauro et al reported higher rates of BPD and severe retinopathy of prematurity in very low birth weight infants who received higher levels of resuscitation in the delivery room.[7] Increased risks of death, neurologic morbidity, retinopathy of prematurity, and BPD were observed with the use of chest compressions and/or epinephrine in infants less than 32 weeks by Shah et al.[9] Finer et al described increased frequency of IVH in very low birth weight infants from Vermont Oxford Network database who received CPR in the delivery room.[2]

Our study used prospectively collected data from large level 3-4 neonatal intensive care units across the US. Although there may be variation in the personnel and organization of delivery room practices, all the centers follow NRP guidelines published by the American Academy of Pediatrics, and standardized definitions were used for data collection. Although extremely preterm infants are electively intubated in the delivery room in some centers, MPT infants would be expected to be intubated only if they required PPV. Hence, we believe that endotracheal intubation and CPR in the delivery room can be

reliable predictors of common neonatal intensive care unit morbidities in MPT infants. The knowledge that a large proportion of MPT neonates receive resuscitation at birth and that the need for resuscitation can be predicted by antepartum factors is important information for planning appropriate resources and staffing in the delivery room.

We had limited information about the indications for Cesarean delivery as well as indications for and duration of resuscitation. The information about the dose and indication for use of magnesium sulfate was not collected, and we acknowledge that higher doses of magnesium sulfate could increase the intensity of resuscitation required in the delivery room. Whether resuscitation guidelines were consistently followed could not be determined. Some of the noted associations were inconsistent across intervention groups, which could be related to the different sample sizes of the groups. Another limitation of our study is the difference in certain practices, such as obtaining cranial ultrasounds in MPT infants across the centers, which reduced the denominators in some of our analyses.

In conclusion, our study suggests that a significant proportion of MPT infants receive some level of resuscitation in the delivery room. Increased awareness of need for delivery room intervention, with appropriate staffing and resources should be available in the centers delivering these infants. A higher intensity of resuscitation appears to be a harbinger of adverse neonatal outcomes in this population. ■

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Appendix

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