



2020 Korean Guidelines for Cardiopulmonary Resuscitation. Part 8. Neonatal resuscitation

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OUTLINE

The transition from the intrauterine to extrauterine environment occurring at birth requires several interdependent physiological processes to successfully adapt from placental gas exchange to pulmonary respiration.¹ As newborns breathe through the lungs, pulmonary vascular resistance rapidly decreases; consequently, the pulmonary blood flow increases. This increases the left ventricular filling and cardiac output, which maintains the coronary artery and cerebral blood flow.²

Unlike approximately 85% of term newborns who start breathing spontaneously within 10 to 30 seconds of birth,³ approximately 10% require tactile stimulation to breathe.⁴ Moreover, 5%, 2%, 0.1%, and 0.05% of term newborns require positive-pressure ventilation (PPV), endotracheal intubation, chest compression, and chest compression with epinephrine, respectively.⁵⁻⁸ Although most infants initiate successful respiration without intervention, appropriate resuscitation can prevent complications and save millions of newborns worldwide.

The 2020 Korean Neonatal Resuscitation guideline is a medical recommendation based on scientific evidence for neonatal resuscitation. This guideline is based on the Consensus on Science with Treatment Recommendations (CoSTR) suggested by the International Liaison Committee on Resuscitation (ILCOR) in 2020,⁹⁻¹¹ and studies on neonatal resuscitation have been further reviewed. For revised items of high clinical importance and requiring further review, evidence was reviewed through adaptation or hybridization, and a meta-analysis or scoping review was performed.



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Level of evidence and recommendation of class

The levels of evidence were divided into levels A–C, with A as the highest and C as the lowest level, using the American Heart Association's definition.¹² Level A refers to high-quality evidence from more than one randomized controlled trials (RCTs), meta-analyses of high-quality RCTs, or one or more RCTs collaborated through high-quality registry studies. Level B–R (randomized) refers to moderate-quality evidence from one or more RCTs, or meta-analyses of moderate-quality RCTs. Level B–NR (non-randomized) refers to moderate-quality evidence from one or more well-designed, well-executed, non-randomized studies, observational studies, or registry studies or meta-analyses of such studies. Level C–LD (limited data) refers to evidence based on randomized or non-randomized observational or registry studies with limitations of design or execution, meta-analyses of such studies, or physiological or mechanical studies in human subjects. Additionally, Level C–EO (expert opinion) refers to consensus of expert opinion based on clinical experiences.

The class of recommendation was evaluated based on the direction (benefit/harm) and strength (strong/weak recommendations) using the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) method and was classified into three categories used by the American Heart Association.^{12,13} Class I was assigned when the benefit of the treatment or intervention was significantly high relative to the risk (appropriate for most clinicians to provide the treatment or intervention to most patients). Class IIa and IIb were assigned when the treatment or intervention was generally useful (appropriate for most clinicians to provide the treatment or intervention, with some important exceptions), and when the treatment or intervention had positive effects without clear evidence, respectively. Class III (no benefit) was assigned when the treatment or intervention was ineffective (if high-quality studies did not demonstrate the effects), and Class III (harm) referred to treatment or intervention where the risk overrides the benefit.

Major changes in 2020 neonatal resuscitation guidelines and summary of the neonatal resuscitation algorithm

Major changes to the neonatal resuscitation guidelines in 2020

Intended subjects for neonatal resuscitation

Neonatal resuscitation is generally performed for 'newly born' infants. However, neonatal resuscitation can be performed in cases of cardiovascular failure caused by gas exchange disorders within several weeks of birth after the transition period.

Umbilical cord management

Based on the findings of a large-scale multicenter RCT, cord milking increases the frequency of intraventricular hemorrhage in extremely preterm newborns with a gestational age (GA) < 28 weeks; therefore, it is not recommended to milk the cord in such newborns (Class III: no benefit, Level B–R).

'Non-vigorous' newborns delivered through meconium-stained amniotic fluid

Studies conducted after the guidelines were changed in 2015 demonstrated that routine laryngoscopy with or without tracheal suctioning was not beneficial. More emphasis is placed on helping newborns quickly restore their breathing by applying PPV instead of direct laryngoscopy and endotracheal suctioning (Class IIb, Level C–LD).

Sustained inflation

In a study on a group of preterm newborns with a GA < 28 weeks, PPV with sustained inflation of ≥ 1 second increased the risk of mortality before discharge. Therefore, sustained inflation of initial breathing should not be performed in preterm newborns with PPV caused by bradycardia or inappropriate breathing at birth (Class III: harm, Level C–LD).

Oxygen administration

When initial respiratory support, such as continuous positive airway pressure (CPAP) or PPV, is provided in preterm newborns with a GA < 35 weeks, starting with low oxygen concentrations (21%–30%), may be considered instead of high concentrations (Class IIb, Level C–LD). An oxygen blender should be used to provide the correct oxygen concentration recommended for preterm newborns. When an oxygen blender is unavailable, adjusting oxygen flow using a self-inflating bag with a reservoir may be a useful method of titrating oxygen.

In term and late preterm newborns (a GA ≥ 35 weeks) receiving respiratory support at birth, initial use of 21% oxygen is recommended (Class IIb, Level C–LD); 100% oxygen should not be used (Class III: harm, Level C–LD).

Timing of discontinuing resuscitation

If all the resuscitation steps are completed and continuous cardiopulmonary resuscitation (CPR) is still required, as spontaneous circulation has not been restored after excluding reversible causes, discontinuation of CPR may be discussed with the team and the family at 10 to 20 minutes after birth (Class IIb; Level C–LD).

Summary of neonatal resuscitation algorithm (Fig. 1)

Umbilical cord management

Cord clamping can be performed with a delay of ≥ 30 seconds in term or preterm newborns who do not require resuscitation at birth. However, in newborns with unstable breathing and who do not cry, delayed cord clamping (DCC) may hinder respiratory support. Thus, DCC cannot be routinely applied to these newborns.

Three rapid evaluation questions

Responses to the following questions must be assessed to determine whether resuscitation is required. Preterm newborn? Weak muscle tone? Weak crying or breathing?

If none of these questions are answered, newborns can be

transferred to their mothers and can undergo the initial steps while maintaining skin-to-skin contact. However, if the newborn meets even one of these criteria, they need to be transferred to a radiant warmer for resuscitation.

Initial steps

These include warming, maintaining temperature, opening the airway, suctioning as needed, drying, and tactile stimulation.

Assessment of respiration and heart rates

- If the newborn has a heart rate > 100 beats/min and shows labored breathing or persistent cyanosis, oxygen saturation needs to be monitored using a pulse oximeter. Oxygen needs to be sup-

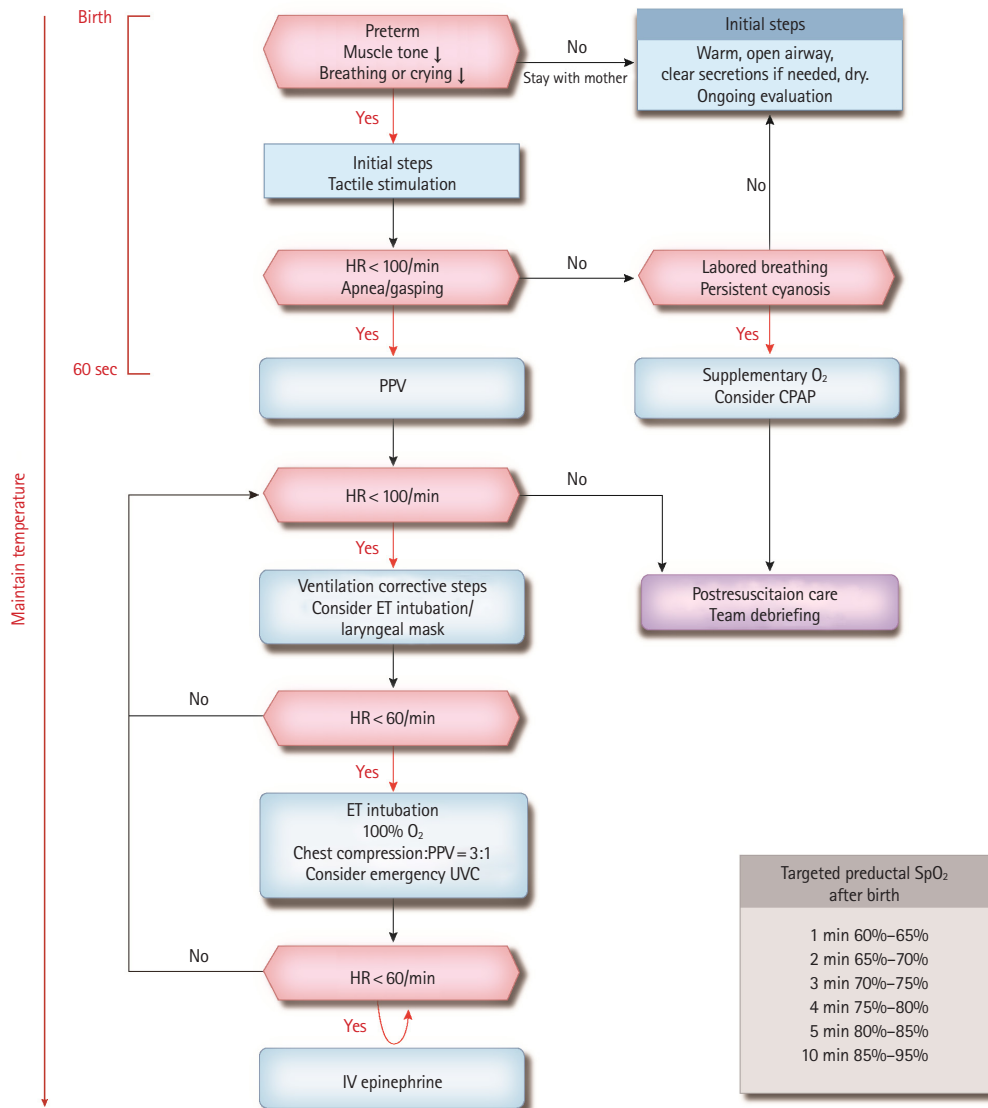


Fig. 1. Neonatal resuscitation algorithm. HR, heart rate; PPV, positive-pressure ventilation; CPAP, continuous positive airway pressure; ET, endotracheal; UVC, umbilical venous catheter; IV, intravenous; O₂, oxygen; SpO₂, saturation of percutaneous oxygen.

plied if necessary; CPAP can be considered.

- If the newborn has a heart rate < 100 beats/min or shows apnea or gasping, electrocardiogram (ECG) monitoring needs to be considered along with monitoring oxygen saturation, and PPV should be performed immediately. Remember that initial steps, re-assessment, and respiratory support must be initiated within 60 seconds after birth ("the Golden Minute").

PPV

If the chest movement is insufficient or heart rate is still < 100 beats/min during PPV, corrective ventilation steps must be performed. If bag-mask ventilation is unsuccessful, endotracheal intubation or insertion of a laryngeal mask airway should be considered.

Chest compressions

If the heart rate is < 60 beats/min even after adequate PPV is applied for > 30 seconds, endotracheal intubation should be performed. Chest compression and PPV are performed at a 3:1 ratio. If there is no response to low oxygen concentration, it can be increased to 100%. Inserting an emergency umbilical venous catheter may be considered to administer additional drugs and plasma volume expanders.

Medications and volume expansion

If the heart rate is consistently < 60 beats/min despite adequate PPV and chest compressions for > 60 seconds, intravenous epinephrine can be administered. If there is no response, other causes, such as hypovolemia and pneumothorax, must be considered. If there is no response to resuscitation and actual or suspected blood loss occurs, a plasma volume expander should be administered.

TARGETS OF NEONATAL RESUSCITATION

Neonatal resuscitation is applied to 'newly born' infants who are in the process of adapting from the intrauterine to extrauterine environment. However, neonatal resuscitation can still be performed after the transition period within a few weeks of birth if the primary cause of cardiovascular failure is gas exchange disorder. However, if the heart is the suspected primary cause, a higher ratio of chest compression to ventilation (e.g., 15:2) may be considered.¹⁴

PREDICTING THE NEED FOR RESUSCITATION

Adequate preparation for neonatal resuscitation requires assessing perinatal risk factors, a system wherein appropriate medical

personnel can be mobilized according to the risk level, ready-to-use medical equipment and supplies, effective teamwork, and clinicians with proficient medical techniques. Moreover, at least one medical staff member who can perform neonatal care, initial steps, and PPV is required. If a newborn has serious perinatal risk factors that may require resuscitation, additional personnel who can perform chest compression, endotracheal intubation, and emergency insertion of an umbilical venous catheter are required.^{15,16} Newborns without perinatal risk factors may also require unexpected resuscitation; therefore, each hospital must always have the necessary personnel available for neonatal resuscitation. Inadequate preparation and malfunctioning equipment prevent effective resuscitation; thus, a standardized checklist is recommended. In preterm newborns or those with perinatal risk factors, equipment to maintain body temperature and assist breathing is required.

When delivering newborns with perinatal risk factors, a team for resuscitation should be formed, and a team leader must be chosen. If there is time, a briefing should be conducted before resuscitation, and roles must be divided among the team members by predicting the procedure required for the newborn.^{17,18} Effective communication and cooperation among team members are critical for successful resuscitation and survival of the newborn.

UMBILICAL CORD MANAGEMENT

For term or late preterm newborns who do not require resuscitation, DCC may be considered until respiration and activity of the newborn are assessed when they are in contact with the mother (Class IIb, Level C-LD). Early cord clamping within 30 seconds of birth can disrupt the transition, as fetal blood may remain in the placenta without entering the newborn's circulatory system. A DCC of ≥ 30 seconds is reportedly associated with higher levels of hematocrit after birth and improved levels of iron during infancy.¹⁹⁻³¹ In preterm newborns who do not require resuscitation, DCC may be effective as it lowers the need for blood pressure management and blood transfusion and improves survival (Class IIa, Level B-R).³²⁻³⁹ However, there is little evidence supporting early or DCC in term or preterm newborns who require resuscitation at birth (Class IIb, Level C-EO).¹⁶

Early cord clamping must be considered in cases with a possibility of placental transfusion, such as maternal bleeding, hemodynamic instability, placental abruption, and placenta previa.

Cord milking is a possible alternative to DCC; however, a large-scale multicenter RCT reported that cord milking increased the frequency of intraventricular hemorrhage in extremely preterm newborns with a GA < 28 weeks.⁴⁰ Thus, cord milking should not be performed in such newborns (Class III: no benefit, Level B-R).

INITIAL STEPS

The initial steps of neonatal resuscitation include warming, maintaining body temperature, adopting the sniffing position to secure the airway, suctioning, wiping the amniotic fluid with a dry cloth (or wrapping in a plastic bag for preterm newborns with a GA < 32 weeks), and tactile stimulation for breathing.

Maintaining the appropriate body temperature

After birth, this is an initial step of neonatal stabilization; body temperature at admission in non-asphyxiated newborns is an important predictor of mortality.⁴¹ Hypothermia (temperature < 36°C) is associated with serious sequelae, including intraventricular hemorrhage, respiratory failure, hypoglycemia, and late-onset sepsis.⁴²⁻⁴⁴ Therefore, body temperature on admission must be measured and recorded as prognostic predictors and quality indicators (Class I, Level B-NR).¹ A body temperature of 36.5°C to 37.5°C is recommended on admission and at rest for non-asphyxiated newborns (Class I, Level C-EO).⁴⁵

Methods to maintain body temperature in the delivery room

Although a radiant warmer, hat, and plastic bag can help maintain body temperature, they do not completely prevent hypothermia in preterm newborns. Therefore, increased room temperature (23°C–25°C, or ≥ 25°C if the GA is < 28 weeks),¹⁴ heating mats, and warm humidified air are also required.

Newborns with a GA ≥ 32 weeks must be wiped with a cloth immediately and covered with pre-warmed clothes around the head and body except for the face. If CPR is required, resuscitation can be performed under a radiant warmer; if not, skin-to-skin contact with the mother is needed (Class IIa, Level B-R).⁴⁶

In newborns with a GA < 32 weeks, several methods like using a radiant warmer, plastic bag, and heating mat,⁴⁷⁻⁵¹ warm humidified air when a ventilator is needed,^{52,53} and increasing the room temperature/wearing a hat/heating mat⁵⁴⁻⁵⁷ are recommended (Class IIb, Level B-R, B-NR, C-LD).⁵⁸ Previous studies have reported concerns about hyperthermia.^{44,59} Therefore, hyperthermia above 38.0°C should be avoided due to the potential associated risks (Class IIa, Level C-LD).

There is a high risk of hypothermia if a newborn is delivered outside the hospital. Therefore, the newborn must be wiped with a cloth immediately after delivery and wrapped in plastic bags and cloth. Those born at a GA of ≥ 30 weeks need to maintain appropriate body temperature through skin-to-skin contact with the mother during transfer to the hospital (Class IIb, Level C-LD).^{60,61}

Warming hypothermic newborns

It is generally accepted that slowly raising the body temperature of hypothermic newborns after resuscitation may reduce complications such as apnea and arrhythmia. However, there is a lack of evidence to determine which is more effective: increasing the body temperature rapidly (> 0.5°C/hr) or slowly (< 0.5°C/hr). Thus, both methods can be used for hypothermic newborns (Class IIb, Level C-LD).^{3,16,17,62,63}

Effects of maternal hypothermia and hyperthermia on newborns

Maternal hyperthermia during labor is associated with poor prognosis, including increased mortality, convulsions, and encephalopathy in newborns⁶⁴⁻⁷⁴; this is in contrast to maternal hypothermia, which is not associated with a clinically significant poor prognosis in newborns.⁷⁵⁻⁷⁹ Although maternal hyperthermia is associated with poor prognosis in newborns, there is insufficient evidence for the effect of treatment of maternal hyperthermia on the prognosis of newborns.

Maintaining body temperature in resource-limited settings

The mortality rate increases in proportion to the severity of hypothermia at a body temperature ≤ 36.5°C. Therefore, it is important to maintain the body temperature in resource-limited settings.⁸⁰ Compared with term newborns, preterm newborns show a higher risk of hypothermia; preventing hypothermia after birth (within 1–2 hours) can help decrease mortality. In resource-limited settings, the newborn can be wrapped in a plastic bag up to the neck or wiped and wrapped with a cloth to maintain normal body temperature during the transition (1–2 hours after birth) (Class IIb, Level C-LD).^{61,81} Other alternatives include breastfeeding with skin-to-skin contact and kangaroo care (Class IIb, Level C-LD).⁸²⁻⁸⁹ However, few studies are available about the use of plastic bags or skin-to-skin contact during the stabilization period after resuscitation.

Clearing the airway

Non-meconium stained amniotic fluid

Suctioning of amniotic fluid using a bulb syringe or suction catheter does not help remove fluid from the lungs. Instead, it can cause side effects such as infection, bradycardia, apnea, hypoxia, decreased arterial oxygen tension, hypercapnia, failure to control cerebral blood flow, increased intracranial pressure, neonatal brain injury,⁹⁰⁻⁹⁹ and delayed ventilation in those without spontaneous breathing.^{3,100} Therefore, routine oropharyngeal or nasopharyngeal suctioning immediately after delivery is not recommended (Class

IIb, Level C-LD).^{9-11,101} Suctioning may be considered only if the airway appears obstructed or PPV is required (Class IIb, Level C-EO).³

Meconium stained amniotic fluid

Meconium stained amniotic fluid (MSAF) may indicate fetal distress; these newborns may require resuscitation, including endotracheal intubation after delivery. Therefore, trained personnel and equipment for endotracheal intubation must be prepared in advance.

If a newborn delivered with MSAF is 'vigorous' (heart rate \geq 100 beats/min, good respiratory effort, and good muscle tone), routine suctioning of meconium immediately after the head delivers but before the shoulders deliver is no longer recommended.¹⁰² The newborn may stay with the mother to receive the initial steps of newborn care. However, the meconium around the mouth and nose can be gently removed using a bulb syringe and suction catheter.

Since 2015, the guideline for the 'non-vigorous' (heart rate $<$ 100 beats/min, weak muscle tone, inadequate breathing effort) newborn delivered from MSAF has changed; routine intubation and tracheal suctioning are no longer required. Subsequently, four RCTs and three observational studies showed that direct laryngoscopy and tracheal suctioning did not have beneficial effects on survival at discharge, cognitive and motor development abnormalities, hypoxic ischemic encephalopathy, meconium aspiration syndrome, respiratory support, chest compression and use of epinephrine in the delivery room, and length of hospital stay.¹⁰³⁻¹⁰⁹ Thus, the effects of direct laryngoscopy and tracheal suctioning for 'non-vigorous' newborns with MSAF are unclear, and PPV is required to speed up the restoration of breathing (Class IIb, Level C-LD). However, endotracheal intubation and tracheal suctioning may be necessary if airway obstruction is suspected during PPV. (Class IIa, Level C-EO).

Tactile stimulation

Additional stimulation is necessary when no spontaneous breathing effort is observed in the initial steps (Class IIa, Level B-NR).¹¹⁰ Stimulation methods include short and gentle rubbing of the back, trunk, and extremities using a pre-warmed cloth and light tapping of the feet two to three times.¹¹¹⁻¹¹³ Vigorous shaking of the newborn does not help restore breathing and may be harmful. If apnea continues after stimulation, PPV must be started immediately.¹¹¹

PHYSIOLOGICAL MONITORING AND FEEDBACK EQUIPMENT

Heart rate evaluation

Heart rate assessment of newborns immediately after birth is essential in determining the effectiveness of spontaneous breathing

and the need for resuscitation. An increased heart rate during resuscitation is the most sensitive indicator of the response to each step. Therefore, it is crucial to evaluate the heart rate rapidly and accurately.

Although auscultation is the preferred way to assess heart rate in the initial evaluation, it is inaccurate and less reliable.^{46,114} When comparing an ECG with pulse oximeter for continuous heart rate assessment, the pulse oximeter required more time to measure the heart rate, and the heart rate was underestimated during the initial 2 minutes.¹¹⁵⁻¹¹⁷ Comparatively, ECG is the fastest and most accurate way to measure the heart rate.¹¹⁸⁻¹²¹ A 3-lead ECG could be useful for assessing heart rate in preterm and term newborns who require resuscitation (Class IIb, Level C-LD). During chest compressions, an ECG is recommended to rapidly and accurately assess heart rate (Class IIa, Level C-EO). However, ECG cannot replace a pulse oximeter that evaluates the oxygenation level in newborns.

Respiratory function evaluation tool

Evaluation tools for respiratory function are useful in preventing excessive pressure and ventilation.¹²² An exhaled carbon dioxide (CO₂) monitor is useful for evaluating gas exchange during PPV with a face mask.¹²³ However, it is unclear whether it improves prognosis (Class IIb, Level C-LD).

VENTILATION AND OXYGENATION

Sustained inflation

In 2015, the ILCOR did not recommend using sustained inflation.^{1,124} In 2020, the ILCOR conducted a systematic review of 10 RCTs with 1,502 newborns.¹²⁵⁻¹³⁴ This review concluded that sustained inflation showed no significant reduction in mortality, the need for mechanical ventilation, bronchopulmonary dysplasia, and air leakage. Moreover, a study on preterm newborns with a GA $<$ 28 weeks showed that PPV with sustained inflation of \geq 1 second increased the potential risk of mortality before discharge.¹³³ Therefore, sustained inflation of initial breathing should not be performed in preterm newborns with PPV for bradycardia or inadequate breathing effort at birth (Class III: harm, Level C-LD). In term or late preterm newborns undergoing PPV, there is insufficient evidence to suggest an appropriate duration of sustained inflation.

Positive end-expiratory pressure

Although providing positive end-expiratory pressure (PEEP) to newborns requiring PPV likely helps prevent lung collapse at the end of expiration, human studies are limited. In 2015, ILCOR con-

ducted a review that showed that additional PEEP did not reduce the incidence of mortality, endotracheal intubation, chest compression, and drug use in preterm newborns. Moreover, the heart rate did not rapidly improve, and air leakage, bronchopulmonary dysplasia, and Apgar scores were also unaffected. However, PEEP reduced the maximum amount of oxygen; thus, PEEP was suggested for resuscitation in the delivery room.^{1,124,135} As there are no additional studies, we recommend that a PEEP of ≥ 5 cm H₂O be provided to preterm newborns who undergo PPV in the delivery room (Class IIb, Level C-LD). For term newborns, evidence suggesting PEEP is lacking.

Tools for PPV and advanced airway management *Comparison of the effects of a T-piece resuscitator and a self-inflating bag*

PPV can be effectively induced using a flow-inflating bag, self-inflating bag, and a T-piece resuscitator depending on the level of experience and preference (Class IIa, Level B-R).^{136,137} A self-inflating bag is a useful tool for delivering PPV when compressed gas is unavailable. However, it cannot provide CPAP as other tools, nor can it maintain PEEP during PPV.¹³⁸⁻¹⁴¹ In contrast, a flow-inflating bag requires training for effective use. A T-piece resuscitator is easier to use, and it can continuously provide the targeted inspiratory pressure for a longer period.¹⁴²⁻¹⁴⁴ However, there is no clear evidence that T-piece resuscitators can improve prognosis.^{136,137} Two additional studies published after guideline revision in 2015 demonstrated that the use of a T-piece resuscitator increased the survival rate and decreased bronchopulmonary dysplasia and the need for endotracheal intubation in the delivery room.^{145,146} However, there is insufficient evidence to recommend the use of a T-piece resuscitator or a self-inflating bag in newborns receiving PPV (Class indeterminate). Nevertheless, a T-piece resuscitator may be considered in facilities equipped with compressed gas (Class IIb, Level C-LD).

Laryngeal mask airway

A laryngeal mask can help induce effective ventilation in term and preterm newborns with a GA ≥ 34 weeks. However, evidence for preterm newborns with a GA < 34 weeks or weight < 2 kg is lacking. When facial mask ventilation is inefficient, a laryngeal mask can be used instead of endotracheal intubation (Class IIb, Level B-R).¹⁴⁷ The use of a laryngeal mask is recommended when endotracheal intubation fails or is impossible in term newborns and preterm newborns with a GA > 34 weeks (Class I, Level C-EO). The use of a laryngeal mask during chest compression and drug administration has not been assessed.

Positioning the endotracheal tube in the airway

During resuscitation, endotracheal intubation is required when inefficient PPV is continued, continuous PPV is required, chest compression is necessary, or in special circumstances such as the presence of a congenital diaphragmatic hernia. Successful ventilation induced by endotracheal intubation is indicated by an increased heart rate. An exhaled CO₂ detector is the most useful device to determine the position of the endotracheal tube in the airway. When no exhaled CO₂ is detected, insertion of the tube into the esophagus is suspected. However, when the pulmonary blood flow is reduced in cardiac arrest, the exhaled CO₂ detector shows false negatives despite correct tube position, which can lead to unnecessary reintubation in critical newborns. Signs such as chest movement, breathing sounds symmetrically audible in both lung fields on auscultation, and condensation of water vapor in the tube can be used to correct the tube's position in the airway.

CPAP

In three RCTs with 2,358 preterm newborns with a GA < 30 weeks, initial CPAP use was more beneficial than PPV after endotracheal intubation.¹⁴⁸⁻¹⁵⁰ Initial CPAP lowers the rate of endotracheal intubation in the delivery room and reduces the period of mechanical ventilation while lowering the mortality rate and frequency of bronchopulmonary dysplasia. Additionally, the incidence of side effects such as air leakage and intraventricular hemorrhage does not increase following initial CPAP. For spontaneously breathing preterm newborns who require respiratory support immediately after delivery, it is recommended to use CPAP, not intubation (Class IIb, Level B-R).

Assessment of oxygen need and oxygen administration

Use of a pulse oximeter

The use of a pulse oximeter is recommended when resuscitation is expected, PPV is required, central cyanosis persists for 5 to 10 minutes after birth, or oxygen administration is required.

Oxygen administration

Term and late preterm newborns (a GA ≥ 35 weeks)
The debate on the risk of hypoxia and the risk of exposure to excessive oxygen in term and late preterm newborns who require respiratory support at birth continues. In 2019, the ILCOR conducted a systematic review and meta-analysis of five RCTs and five quasi-RCTs comprising 2,164 newborns.¹⁵¹ The results demonstrated that starting resuscitation with 21% oxygen was more beneficial in reducing short-term mortality than with 100% oxy-

gen in term and preterm newborns with a GA \geq 35 weeks. However, there was no difference in the rates of hypoxic ischemic encephalopathy and moderate-to-severe neurodevelopmental impairment. No previous study has investigated starting resuscitation with intermediate oxygen concentrations.

In term and late preterm newborns (a GA \geq 35 weeks) receiving respiratory support at birth, the initial use of 21% oxygen is recommended (Class IIb, Level C-LD); 100% oxygen should not be used (Class III: harm, Level C-LD). Subsequent oxygen administration can be adjusted depending on whether the pre-ductal oxygen saturation target is achieved according to the standard set for healthy term newborns.¹⁵²

Preterm newborns with a GA < 35 weeks

In 2019, a systematic review and meta-analysis of RCTs¹⁵³⁻¹⁶⁴ and four cohort studies¹⁶⁵⁻¹⁶⁸ published until August 2018 was conducted by the ILCOR.¹⁶⁹ Subsequently, a meta-analysis including one more RCTs published in 2019¹⁷⁰ was conducted for the Korean CoSTR. No difference was observed in short- or long-term mortality when respiratory support was started with low (21%–30%) compared with high (60%–100%) oxygen concentrations in preterm newborns with a GA < 35 weeks. Additionally, high oxygen concentrations were not beneficial in preventing neurodevelopmental impairment, retinopathy of prematurity, bronchopulmonary dysplasia, and necrotizing enterocolitis.

When initial respiratory support, such as CPAP or PPV, is provided in preterm newborns with a GA < 35 weeks, starting with low oxygen concentrations (21%–30%) may be considered instead of high oxygen concentrations (60%–100%) (Class IIb, Level C-LD). An oxygen blender should be used to provide the correct oxygen concentration recommended for preterm newborns. When an oxygen blender is unavailable, adjusting the oxygen flow using a self-inflating bag with a reservoir may be a useful method of titrating oxygen.¹⁷¹

CHEST COMPRESSIONS

Initiating chest compression is reasonable if the heart rate is < 60 beats/min despite adequate PPV for at least 30 seconds (Class IIa, Level C-EO).^{1,16,135} Chest compression must be performed on the lower 1/3 of the sternum,^{172,173} and the depth of compression should be at least 1/3 of the anteroposterior diameter of the chest (Class IIb, Level C-LD).¹⁷⁴ There are two techniques to perform chest compression. The first is to use the thumbs of both hands and surround the rib cage with the remaining fingers supporting the back (two-thumb encircling hands technique). The second is to use two fingers of one hand and support the back with the

other hand (two-finger technique). The two-thumb encircling hands technique may generate higher blood pressure, higher coronary perfusion pressure, and lower fatigue for the performers.¹⁷⁵⁻¹⁷⁸ The two-thumb encircling hands technique may be a better technique for cardiac compression in newborns (Class IIb, Level C-LD), and can be continued from the head of the newborns while accessing the umbilical venous catheter.

It is recommended to perform synchronized chest compressions and PPV at a ratio of 3:1 (three compressions and one PPV) (Class IIb, Level C-LD).^{1,124,135,179-183} Approximately 120 compressions and ventilations need to occur within 1 minute, and each action should last 0.5 seconds. If cardiopulmonary failure is of cardiac origin, a higher ratio of 15:2 may be used (Class IIb, Level C-EO).¹⁴

No previous clinical study has assessed the adequate level of inhaled oxygen during chest compressions. In a meta-analysis of eight animal studies, administration of 100% oxygen did not result in significantly better effects than administration of 21% oxygen.¹⁸⁴ Nonetheless, when there is no response at low oxygen concentrations during chest compressions, the oxygen concentration may be increased up to 100% (Class IIb, Level C-EO). After the heart rate is restored, the oxygen concentration must be lowered immediately to reduce the risk of complications caused by hyperoxia.^{1,16,135}

Heart rate is the best indicator to assess the progression of neonatal resuscitation. The exhaled CO₂ detector and pulse oximeter may also help evaluate the recovery of spontaneous circulation.¹⁸⁵ However, their effects have not been demonstrated in newborns with asystole or bradycardia. Therefore, the routine use of exhaled CO₂ detector and pulse oximeter is not recommended to determine the recovery of spontaneous circulation (Class IIb, Level C-LD).

MEDICATIONS AND VOLUME EXPANSION

Drugs are not commonly used in neonatal resuscitation. Bradycardia in newborns is mostly caused by insufficient lung expansion and severe hypoxia; both are often corrected by adequate ventilation. However, if the heart rate is < 60 beats/min despite adequate ventilation with 100% oxygen and chest compressions for \geq 60 seconds, epinephrine or volume expanders may be considered.

Epinephrine

If the heart rate is < 60 beats/min despite optimizing ventilation and chest compressions, 0.01 to 0.03 mg/kg of epinephrine (diluted 1:10,000) must be administered intravenously (Class IIa, Level C-LD). If intravascular access is not yet available, higher

doses of epinephrine (0.05–0.1 mg/kg) can be administered via an endotracheal tube (Class IIa, Level C-LD). However, administration of endotracheal epinephrine should not delay attempts to establish vascular access. If the response to endotracheal epinephrine is inadequate, intravenous administration should be performed as soon as vascular access is obtained, regardless of the interval after any initial endotracheal dose (Class IIa, Level C-LD). If the heart rate is consistently below 60 beats/min, additional intravenous administration of epinephrine is recommended every 3 to 5 minutes (Class IIa, Level C-LD).

Volume expander therapy

Volume expander therapy was reviewed in the 2010 guideline^{17,18,186}; there are no subsequent human studies. Early volume expansion with isotonic crystalloid or red blood cells is indicated for newborns with blood loss or suspected blood loss (pale skin, poor perfusion, and weak pulse) who do not respond to resuscitation (Class IIb, Level C-EO). The recommended dose is 10 mL/kg, and repeated administration is possible if necessary. For preterm newborns, the administration should be as slow as possible to reduce the risk of complications such as intraventricular hemorrhage.¹⁸⁷ There is little evidence on the administration of a volume expander when there is no response to resuscitation in newborns without blood loss.

Intraosseous versus intravenous access

Although few studies have shown successful administration of drugs and volume expanders through intraosseous injection in neonatal resuscitation,^{188,189} there are also reports of complications related to the use of intraosseous catheters.^{188,190-194} Therefore, it is reasonable to use the umbilical venous route as the primary method of vascular access during neonatal resuscitation in the delivery room (Class IIa, Level C-LD). If umbilical venous access is not feasible, the intraosseous route can be accessed as an alternative (Class IIa, Level C-LD).

Outside the delivery room setting, we suggest that the umbilical venous or intraosseous route be used depending on the equipment, training, and experience (Class IIb, Level C-LD).

POST-RESUSCITATION CARE

Post-resuscitation glucose management

In newborns, both hypoglycemia and hyperglycemia increase the risk of brain injury and poor neurological prognosis.¹⁹⁵⁻²⁰¹ Therefore, blood glucose levels should be monitored immediately after resuscitation, and both hypoglycemia and hyperglycemia must be controlled through appropriate treatment (Class I, Level C-LD). The use of protocols to control blood glucose levels may avoid

both hypoglycemia and hyperglycemia as well as prevent large swings in blood glucose levels.

Therapeutic hypothermia

Settings with sufficient resources

In a meta-analysis of 8 RCTs involving 1,344 term and late preterm newborns with moderate-to-severe encephalopathy, therapeutic hypothermia significantly reduced the combined outcome of mortality or major neurodevelopmental disability to 18 months of age (odds ratio, 0.75; 95% confidence interval, 0.68–0.83).²⁰² In newborns born at ≥ 36 weeks of gestation with evolving moderate-to-severe hypoxic ischemic encephalopathy, therapeutic hypothermia, which must be executed in accordance with clearly defined protocols, i.e., cooling to commence within 6 hours, strict temperature control at 33°C to 34°C for 72 hours and rewarming over at least 4 hours, should be performed in neonatal care facilities with multidisciplinary approaches to treatment and long-term follow-up (Class I, Level A).^{203,204}

Settings with limited resources

In settings with limited personnel and equipments, therapeutic hypothermia may be considered for term and late preterm newborns with evolving moderate-to-severe encephalopathy (Class IIb, Level B-R).^{205,206} Cooling should only be conducted under clearly defined protocols with treatment in neonatal care facilities with the multidisciplinary care.

WITHHOLDING AND DISCONTINUING RESUSCITATION

Non-initiation of resuscitation and withdrawal of cardiorespiratory support during or after resuscitation are ethically equivalent (Class I, Level C-EO).^{207,208} Treatment decisions for newborns who are on the lower limit of viability or who are expected to have high mortality and morbidities may depend on the treatment environment and available resources. Parents of severely ill newborns often want to play a large role in determining the initiation and maintenance of resuscitation. In the 2010 guideline, it was stated that the parents' views on resuscitation should be supported in conditions associated with uncertain prognosis, when there is borderline survival and a relatively high rate of morbidity and when the burden to the child is high.^{17,18} There have been no follow-up studies that could change the 2010 guidelines.

Prenatal judgments about the survival prognosis or disability of extremely preterm newborns are based on the GA. Several scoring systems involving variables such as sex, prenatal steroid use,

and multiple gestations were developed to predict prognosis and can also be used to predict mortality and morbidity.⁴¹

Withholding resuscitation

When determining the prognosis of newborns with a GA <25 weeks immediately after birth, there was no other prediction method better than GA; additionally, no other prediction method to help estimate the likelihood of survival during the first 18 to 22 months after birth. If the newborn is extremely preterm based on the GA and birth weight or the likelihood of survival is low due to congenital anomalies (e.g., predicted survival <50%, GA <23 weeks, birth weight <400 g, trisomy 13 or 18, anencephaly), then resuscitation can be withheld. However, when advising families on the prognosis of newborns with a GA <25 weeks, the estimation of GA, presence of chorioamnionitis, and the level of medical service need to be considered on a case-by-case basis. Regional guidelines may affect whether resuscitation is appropriate for those with a GA <25 weeks (Class IIb, Level C-LD). It is reasonable to obtain an expert opinion and discuss with the parents to determine withholding resuscitation for newborns who are at the lower limit of viability (Class IIa, Level C-EO).^{207,208}

Discontinuation of resuscitation

In previous studies about the prognosis of newborns who underwent CPR for ≥ 10 minutes after delivery, the proportion of those admitted to the neonatal intensive care unit and the proportion of surviving newborns were significantly different depending on the studies.²⁰⁹⁻²²² Newborns who underwent CPR for ≥ 10 –20 minutes immediately after birth and did not show recovery of spontaneous circulation had a high risk of mortality and moderate-to-severe neurological impairment even if they survived. However, there is currently no evidence that a specific CPR duration is associated with death or neurological sequelae. The decision to discontinue resuscitation should be made on a case-by-case basis, and factors such as cause, GA, neonatal intensive care, and the application of neuroprotective strategies such as therapeutic hypothermia after resuscitation must also be considered. If all steps of CPR have been performed and continuous CPR is required, as spontaneous circulation is not restored after excluding reversible causes, discontinuation of CPR may be discussed with the team and family. Communication with the newborn's family is essential when deciding whether to discontinue resuscitation. The discussion can be considered at 10 to 20 minutes after birth (Class IIb, Level C-LD).⁹⁻¹¹

RESUSCITATION TRAINING PROGRAM

Training for the medical staff

Simulation must be a standard component in the training of neonatal resuscitation.¹⁸⁷ The training frequency provided to the medical staff or medical school students did not affect the patients' prognostic outcomes (Level C-EO). However, training at intervals of ≤ 6 months is particularly effective in improving psychomotor performance (Level B-R), knowledge, and confidence (Level C-LD) (Class IIb, Level B-R).^{223,224} Therefore, neonatal resuscitation training, which is currently provided every 2 years, may need to be provided more often (Class IIb, Level C-LD).^{223,225-228}

Training for instructors

There was no association between the provision of training to instructors involved in resuscitation and their performance.^{229,230} Until further studies on the optimal training method for instructors are reported, objectified, structured, and individualized training based on oral/written feedback may be considered (Class IIb, Level C-EO).

EFFECTS OF BRIEFING AND DEBRIEFING

A scoping review involving one RCT²³¹ and three observational studies²³²⁻²³⁴ that assessed the effects of briefing and debriefing showed improvement in the knowledge and performance skills of the medical staff members as well as the short-term clinical outcomes of newborns. Therefore, briefing and debriefing for neonatal resuscitation are suggested (Class IIb, Level C-LD). The long-term effects have not yet been established, and there is a lack of evidence from systematic reviews. Therefore, further studies on the effects of briefing and debriefing are needed.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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