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Chest Compressions in the Delivery Room

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Abbreviations

CC - Chest compression

DR - Delivery room

CPR - Cardiopulmonary resuscitation

C:V - Compression to ventilation ratio

ROSC - Return of spontaneous circulation

PPV - Positive pressure ventilation

CCaV - Continuous chest compressions with asynchronous ventilations

CPP - Coronary perfusion pressure

SI - Sustained inflation

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Abstract

Annually, an estimated 13-26 million newborns need respiratory support and 2-3 million newborns need extensive resuscitation, defined as chest compression and 100% oxygen with or without epinephrine in the delivery room. Despite such care, there is a high incidence of mortality and short-term neurologic morbidity. The poor prognosis associated with receiving chest compression alone or with medications in the delivery room raises questions as to whether improved cardiopulmonary resuscitation methods specifically tailored to the newborn could improve outcomes. This review discusses the current recommendations, mode of action, different compression to ventilation ratio, continuous chest compression with asynchronous ventilations, chest compression and sustained inflation optimal depth, and oxygen concentration during cardiopulmonary resuscitation.

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Background

Most newborn infants successfully make the transition from fetal to neonatal life without any help[1]. However, an estimated 10-20% of newborns (13-26 million worldwide) need respiratory support, which remains the most critical step of neonatal resuscitation[2-4]. Furthermore, 0.1% of term infants and up to 15% of preterm infants (2-3 million worldwide) need extensive resuscitation[5-8], defined as chest compression (CC) and 100% oxygen (O_2) with or without epinephrine in the delivery room (DR). Despite such care, there is a high incidence of mortality and short-term neurologic morbidity[7-12]. The poor prognosis associated with receiving CC alone or with medications in the DR raises questions as to whether improved cardiopulmonary resuscitation (CPR) methods specifically tailored to the newborn could improve outcomes[13,14]. The inability to predict which newborns need CPR, and the infrequent use of CPR in the DR have limited neonatologists' ability to perform rigorous clinical studies to determine the best method for delivering CC to newborn infants[13,14].

Current recommendations

The current neonatal resuscitation guidelines recommend a 3:1 compression to ventilation (C:V) ratio, which consists of 90 chest compression and 30 inflations[3,4,15]. This approach is composed of 90 CC and 30 inflations per minute, with a pause after every 3rd CC to deliver one effective inflation. Furthermore, inflations and CC should be synchronized to avoid inadequate oxygen delivery during CPR[3,4,15]. The current recommendation is based on expert opinions and consensus rather than strong scientific evidence[2-4]. Rationales for using 3:1 C:V include i) a higher physiological heart rate of 120-160/min, and ii) breathing rates of 40-60/min in newborn infants compared to adults[13,14]. Furthermore, profound bradycardia or cardiac arrest in newborn infants is usually caused by hypoxia/asphyxia rather than primary cardiac compromise[14,16]; therefore, providing ventilation is more likely to be beneficial in neonatal CPR compared to adult CPR. However, the optimal CC approach to optimize coronary and cerebral perfusion while providing adequate ventilation of an asphyxiated newborn remains unknown[17].

Mode of Action

During chest compression the blood is pumped mechanically through the body until the myocardium becomes sufficiently oxygenated to improve function[18-23]. Generation of blood flow and blood expulsion from the ventricles during CC is thought to occur by either direct compression of the heart between the sternum and vertebral column (cardiac pump theory), or phasic increases in intrathoracic pressure (thoracic pump theory). The "cardiac pump theory" postulates that CC directly eject blood from the heart into the circulation with each compression[19]. In comparison, the "thoracic pump theory" states that a phasic increase in intrathoracic pressure produced by compression of the chest creates a pressure gradient between the arterial and venous compartment[23-25]. This pressure gradient then serves as the driving force for antegrade blood flow. Optimized CC has been demonstrated to generate 30% of normal organ perfusion, with preferential (>50%) perfusion to the heart and brain[17].

Using different Compression to Ventilation ratio

The current recommendation of using a 3:1 C:V ratio is based on expert opinions and consensus rather than strong scientific evidence[2-4]. Animal studies using cardiac arrest induced by asphyxia in newborn piglets demonstrated that combining CC with ventilations improves ROSC and neurological outcome at 24 hours compared to ventilations or CC alone[26]. Solevåg *et al* performed a study investigating alternating 9 CC and 3 ventilations in asphyxiated piglets with cardiac arrest, with the hypothesis that 9 CC would generate higher diastolic blood pressure during CPR than only 3 CC in a series[27]. However, increasing the number of CC in a row should not be at the expense of

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ventilation, hence the ratio of CC and ventilation was maintained at 3:1. The time to ROSC was similar between the two approaches (150 and 148 sec for 3:1 and 9:3, respectively). In addition, there were no differences in diastolic blood pressure during CC[27]. Similarly, C:V ratios of 3:1 and 15:2 were compared using the same model[28]. Although the 15:2 C:V ratio provided a higher mean CC rate per minute (75 vs. 58 CC/min for 15:2 and 3:1, respectively), time to ROSC was similar between groups (median time of 195 and 150 sec for 15:2 and 3:1, respectively)[28]. Most recently, Pasquin *et al* compared 2:1, 3:1, and 4:1 C:V ratios during asphyxia induced CPR in newborn piglets and reported no difference in the median (IQR) time to ROSC with 127 (82-210), 96 (88-126), and 119 (83-256) sec, respectively (p=0.67 between groups), similar oxygen requirement, and epinephrine administration between the groups[29]. These studies suggest that different C:V ratios might not be the optimal approach for neonatal CPR.

Continuous chest compression with asynchronous ventilations

In both adult and pediatric advanced life support, continuous CC with asynchronous ventilations (CCaV) are recommended after a secure airway has been established[18,19]. In contrast, current neonatal resuscitation guidelines recommend using a coordinated 3:1 C:V ratio if CC are needed. Manikin studies reported higher ventilation rates in 3:1 C:V during simulated CPR compared to higher C:V ratios[30-32]. In addition, a 3:1 C:V ratio delivered significantly a minute ventilation of 191 mL/kg compared to the minute ventilation at 9:3 and 15:2 C:V ratios (140 and 77 mL/kg/min, respectively)[33]. A further manikin study compared 3:1 C:V with CCaV using 90 CC and 30 non-synchronized inflations and reported similar V_T of 6.4 and 5.6 mL/kg, respectively. However, minute ventilation was significantly higher in the CCaV group compared to the 3:1 group (221 versus 191 mL/kg/min, respectively)[28]. *Schmölzer et al* compared 3:1 C:V CPR with CCaV in a piglet model of neonatal asphyxia and reported similar median V_T (14.7 versus 11.0 mL/kg) and minute ventilation

(387 versus 275 mL/kg). However, there was a trend to reduced median time to ROSC (143 and 114 sec for 3:1 and CCaV, respectively), and survival (3/8 and 6/8, respectively)[34]. Most recently, Solevåg *et al* compared 3:1 C:V and CCaV with either 21% or 100% oxygen and reported similar times to ROSC (heart rate ≥100min^{-1}) ranging from 75 to 592sec and mortality of 50-75% between groups[34]. An argument of synchronized CPR is the potential interference of non-synchronized CC with V_T delivery, hence impairment of oxygen delivery. However, the study by Schmölzer *et al* observed 29% and 25% of manual inflations were similarly affected by CC during CCaV and 3:1 C:V CPR, respectively[34]. These studies suggest that a similar oxygen delivery can be achieved with coordinated CC and ventilation at a ratio of 3:1 or CCaV.

Optimal depth

In infants and neonates, current guidelines recommend external compression to a depth of approximately 33% of the anterior-posterior (AP) diameter of the chest, which is relatively greater than that recommended for adults (20% of AP diameter)[35]. Studies in adult animals and humans show positive correlation between receiving adequate CC and improved outcomes[18]. Adequate CC are important to achieve adequate cardiac output, however over-compressing the chest, and therefore leaving inadequate residual chest depth during CPR, has its own potential risks. Some of these risks may include rib fractures, cardiac contusion, and other thoracic injuries[14]. Despite the importance of delivering appropriate CC, adequate CC AP depth has not been rigorously evaluated in neonates.

Manikin studies compared the CC depth using C:V ratios of 3:1, 5:1 and 15:2 during two-minute simulated CPR[30]. Participants had higher and more consistent CC depth during 3:1 C:V CPR, however the CC rate was lower in CPR with C:V ratio of 3:1 compared to 15:2. In addition, the depth decay during CC was significantly higher during 5:1 C:V and 15:2 C:V ratios compared to 3:1 C:V[30]. A recent analysis of CT images of neonates predicted better ejection fraction (EF) using 1/3 AP CC depth compared to 1/4 AP CC depth[36]. Furthermore, no subjects receiving the 1/3 AP CC depth were under-compressed (i.e. had a predicted EF <50%), whereas 54% were predicted to be under-compressed at the 1/4 AP CC depth. The 1/3 AP compression depth was much less likely to meet criteria for predicted over-compression than 1/2 compression depth. Our own observations also suggest that even experienced resuscitation do not achieve the required CC depth during neonatal CPR[37]. This is concerning as a decrease in CC depth due to rescuer fatigue can potentially lead to reduced cardiac output and increase mortality.

Oxygen Concentration During CPR

Oxygen (O_2) has been used in neonatal resuscitation for over 200 years[38]. Its use spread rapidly in response to reports of brain damage in infants who survived birth asphyxia. The inclusion of skin color in the Apgar score in 1965 further contributed to an increased O_2 use in the delivery room[38]. However, over the past decades 100% O_2 during delivery room resuscitation has been questioned as even a brief exposure of asphyxiated infants to 100% O_2 are associated with adverse effects[39-42]. Current neonatal resuscitation guidelines recommend 100% oxygen (O_2) during cardiopulmonary resuscitation (CPR)[3,4,15], however the most effective O_2 concentration in severely bradycardic or asystolic newborns remains controversial.

High concentrations of O_2 delivery during CPR generates O_2-free radicals, which play major role in reperfusion/reoxygenation injury after asphyxia, especially to oxyregulatory tissues (e.g., myocardium). In addition, 100% O_2 exposure at birth has been associated with increased risk of neonatal mortality and childhood cancer[39,43]. 100% O_2 during mask ventilation resulted in higher rates of time to first breath >3 min (28/284 vs. 60/321 [relative risk (RR) (95% Confidence Interval (CI)) 0.53 (0.35–0.8)], Apgar scores <7 at 5min (71/288 vs. 102/321 [RR (95%CI) 0.78 (0.6–1.0)], and death (70/616 vs. 107/659 [RR (95%CI) 0.71 (0.54–0.94)] compared with 21% O_2[41,42]. The neonatal resuscitation guidelines have recognized this and recommend air instead of 100% O_2 during mask ventilation[3,4,15]. However, during CPR the guidelines continue to recommend an increase to 100% O_2[3,4,15].

Studies in asphyxiated term infants reported that 100% O_2 during respiratory support in the delivery room resulted in hyperoxemia (PaO_2, 126±22mmHg), and increased oxidative stress, but not higher cerebral oxygenation, which does not occur with 21% (PaO_2, 72±7mmHg)[44]. Therefore, oxygen delivery during CPR must balance the prevention of tissue damage from O_2 deprivation, while limiting adverse effects of oxidative stress damage from O_2-free radicals[44,45]. Solevag *et al* resuscitated asphyxiated piglets with 21% vs. 100% O_2 and reported similar time to ROSC ranging from 75 to 592 sec with a very high mortality rates (50–75%) in both groups[34]. Resuscitation with 21% O_2 was also associated with improved left ventricular stroke volume after ROSC and lower myocardial oxidative stress (median (IQR) GSSG/GSH ratio 0.1 (0.09-0.12) vs. 0.13 (0.11-0.2) p=0.04) compared to 100% O_2[34]. Thus, air might be a more appropriate gas than 100% O_2 and could reduce morbidity and mortality in asphyxiated infants. However clinical trials are urgently needed before this can be translated into the delivery room.

Chest Compression and sustained inflation

An alternative approach of neonatal CPR has been recently described by Schmölzer *et al*[46]. The group performed CC during sustained inflation (SI) (= constant high airway pressure while providing CC) (CC+SI) in asphyxiated piglets and reported significantly improved systemic and regional hemodynamics, tidal volume delivery and minute ventilation, and time to ROSC compared to 3:1 C:V[46]. CPR with CC+SI had an improved recovery with mean arterial pressure: 51 vs. 31 mmHg; pulmonary arterial pressure: 41 vs. 31 mmHg; mean minute ventilation: 936 vs. 623 mL/kg; and median time to ROSC: 38 vs. 143 sec, respectively compared to 3:1 C:V[46]. In addition, during CC+SI a constant lung recruitment and establishment of functional residual capacity was observed (a gain of 2.3mL/kg/CC+SI cycle)[47]. This improvement in tidal volume lead to better alveolar oxygen delivery and lung aeration. During 3:1 C:V a cumulated loss of tidal volume of 4.5 mL/kg occurred for each 3:1 C:V cycle[47]. This is concerning as a loss in tidal volume could cause lung derecruitment, which could hamper oxygenation and therefore ROSC.

Furthermore, the paper by Schmölzer et al was the first description of passive tidal volume delivery and passive ventilation during neonatal CPR[46,47]. During compression of the chest, volume is exhaled and during chest recoil, gas passively flows back into the lungs. The required distending pressure to achieve passive lung ventilation and adequate tidal volume delivery is ~25cmH_2O, which correlated in cadaver piglets ($r=0.83$, $p<0.001$), manikins ($r=0.98$, $p<0.001$), and when combined (piglets + manikins) ($r=0.49$, $p<0.001$)[48]. A similar observation was reported during chest recoil after a downward force was applied to the chest of infants undergoing surgery requiring general anesthesia[49]. Overall, median (IQR) tidal volume generated was 2.4 (0.8-4.0)mL/kg[49], which suggests that chest recoil generates a distending pressure-dependent tidal volume to allow passive ventilation during CC. However, in the original study by Schmölzer *et al* CC was performed at a rate of 120/min in the CC+SI group, which is higher than the currently recommended CC rate of 90/min, and this could have contributed to the improved outcomes[46]. Subsequently, we reported that CC+SI 90/min compared to 3:1 C:V ratio resulted in a reduction in median (IQR) time to ROSC 34 (28-156) vs. 210 (72-300) sec ($p=0.05$), less oxygen (3/8 vs. 8/8 required 100% O_2 during CPR, $p=0.03$), and 3/8 vs. 6/8 piglets received epinephrine ($p=0.32$)[50]. Two further randomized piglet trials compared CC rates of 90/min vs. 120/min during CC+SI and CC+SI with either 20sec or 60sec SI and reported similar time to ROSC, survival rates, and respiratory parameters[51,52]. More importantly during CC, carotid blood flow, mean arterial pressure, percent change in ejection fraction, and cardiac output were higher in the CC+SI 90/min group compared to CC+SI 120/min[51]. Similarly, Vali *et al* reported that CC+SI is feasible in a transitional model of near-term lambs[53]. Most recently, a small pilot trial compared CC+SI and 3:1 C:V CPR in 9 preterm infants <32 weeks' gestation (CC+SI group (n=5; GA 24.6±1.3); 3:1 C:V group (n=4; 25.6±2.3) group)[54]. Infants in the CC+SI group had significant shorter mean±SD time to ROSC compared to 3:1 C:V (31±9 vs. 138±72sec, p=0.011)[54]. While CC+SI is mentioned in the knowledge gap section of the resuscitation guidelines[2-4], more evidence is needed before CC+SI could translated into clinical care. A large multicenter cluster randomized trial comparing CC+SI with 3:1 C:V during neonatal CPR in the delivery room (SURV1VE-trial) is currently recruiting (https://clinicaltrials.gov/ct2/show/NCT02858583).

Future Directions

Studies reviewing current guidelines for chest compressions are primarily in animals. Results from these studies suggest changes to CC methodologies to increase the efficacy and decrease morbidity of CPR. There is a need for randomized control trials in the humans. Before changes are made to guidelines more studies are needed in how CC protocols vary among, and effect rescuers. Additionally, long term studies are needed on infants receiving CC to determine possible long-term effects of neonatal CPR.

Conclusion

Successful cardiopulmonary resuscitation from cardiac arrest requires the delivery of high-quality chest compression encompassing several factors including optimal Compression:Ventilation ratio, depth of chest compression, and oxygen concentration during cardiopulmonary resuscitation. Although, there is an agreement that these factors are all important for a successful resuscitation neither has been extensively studies to optimize coronary and cerebral perfusion while providing adequate ventilation of an asphyxiated newborn.

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