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# The relation between given volume and heart rate during newborn resuscitation☆

J.E. Linde[a,*], J. Schulz[b,c], J.M. Perlman[d], K. Øymar[a,e], L. Blacy[f], H. Kidanto[g], H.L. Ersdal[h,i]

[a] Department of Pediatrics, Stavanger University Hospital, Norway
[b] Department of Research, Stavanger University Hospital, Stavanger, Norway
[c] Department of Electrical Engineering and Computer Science, University of Stavanger, Stavanger, Norway
[d] Department of Pediatrics, Division of Newborn Medicine, Weill Cornell Medical College, 525 East 68th Street, New York, NY, USA
[e] Department of Clinical Science, University of Bergen, Bergen, Norway
[f] Department of Clinical Research, Haydom Lutheran Hospital Mbulu, Tanzania
[g] Ministry of Health, Dar Es Salaam, Tanzania
[h] Department of Anesthesiology and Intensive Care, Stavanger University Hospital, POB 8100, 4068, Stavanger, Norway
[i] Department of Health Science, University of Stavanger, Stavanger Norway

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ABSTRACT

*Background:* During delivery room resuscitation of depressed newborns, provision of appropriate tidal volume (TV) with establishment of functional residual capacity (FRC) is essential for circulatory recovery. Effective positive pressure ventilation (PPV) is associated with a rapid increase in heart rate (HR). The relationship between delivery of TV and HR responses remains unclear.
*Objectives:* The study objectives were to determine (1) the relationship between a given TV during initial PPV and HR responses of depressed newborns, and (2) the optimal delivered TV associated with a rapid increase in HR.
*Methods:* In a Tanzanian rural hospital, ventilation and ECG signals were recorded during neonatal resuscitation and stored in Neonatal Resuscitation Monitors. Resuscitators without positive end-expiratory pressure were used for PPV. No oxygen was used. Perinatal events were observed and recorded by research assistants.
*Results:* 215 newborns of gestational age 37.3 ± 1.9 weeks and birth weight 3115 ± 579 g were included. There was a non-linear relationship between delivered TV and HR increase. TV of 9.3 ml/kg produced the largest increase in HR during PPV. Frequent interruptions of PPV sequences to provide stimulation/suctioning occurred in all cases and were associated with further HR increases, especially for newborns with initial HR < 100 beats/minute.
*Conclusions:* There was a consistent positive relationship between HR increase and delivered TV. The unanticipated finding of a further increase in HR with PPV pauses to provide stimulation/suctioning suggests that most newborns were in primary rather than secondary apnea.


## Background

An estimated 10 million newborns are born apneic every year [1]. Although advances in management of newborns requiring resuscitation have been made over the past decades, approximately 700,000 annual deaths result from a failure to restore cardio-respiratory function [2].

Establishment of functional residual capacity (FRC) and delivery of effective inflation volumes are essential for a good outcome in depressed newborns requiring positive pressure ventilation (PPV). Rapid increase in heart rate (HR) is considered indicative of effective ventilation, and provides positive feedback during resuscitation [3]. However, the ability to accurately assess HR is unreliable, particularly with bradycardia, whether determination is via auscultation or pulse oximetry [4]. We have recently reported on changes in HR in the immediate minutes after birth using dry ECG electrodes, in newborns initiating spontaneous breathing shortly after birth, and

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* Corresponding author at: Department of Pediatrics, Stavanger University Hospital and University of Stavanger, POB 8100, 4068 Stavanger, Norway.
*E-mail addresses:* joga@sus.no, joga@sus.no (J.E. Linde), hege.ersdal@safer.net (H.L. Ersdal).

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demonstrated a rapid increase in HR during the first 50 s following delivery [5]. These findings underscore the important relationship of establishing FRC and a prompt circulatory response. There is however limited data regarding the relationship between delivered tidal volume (TV), the establishment of FRC and HR responses, in the depressed newborn requiring PPV. Indeed, the recommended TV necessary to inflate the lungs during newborn resuscitation remains unclear [6–9].

The study objectives were to determine (1) the relationship between a given TV during initial PPV and HR responses of depressed newborns, and (2) the effective TV associated with the most rapid increase in HR.

## Methods

This cross-sectional observational study was performed June 2013- October 2014 at Haydom Hospital in Tanzania, a rural hospital with ~4500 births annually, providing emergency obstetric and basic emergency newborn care. Deliveries are conducted by midwives. Doctors on call are trained to perform cesarean section. Eighteen research assistants have been trained to observe and document time of birth events, clinical characteristics of the newborns, and outcome [10]. Newborn Resuscitation Monitors (NRM) (Laerdal Global Health, Stavanger, Norway) was developed as research tool with the purpose of monitoring newborn resuscitations (Fig. 1A). A NRM with a ready-to-use bag-and-mask resuscitator and a dry-electrode HR sensor was placed in each delivery room and in the operating theatre. The NRM has sensors that synchronously records ECG, applied pressure, flow, volume, and exhaled $CO_2$ ($ECO_2$). The HR was displayed on a wall-mounted cabinet. A self-inflating neonatal resuscitator (Neonatalie, Laerdal, Stavanger, Norway) without a positive end-expiratory pressure (PEEP) valve or oxygen supply was used. The sensor is similar to a respiration monitor used previously in clinical studies (Acutronic AG, Switzerland) [11,12]. All midwifes were trained as to the operational capabilities of the monitor. During the study period resuscitation trainings were conducted weekly.

All midwives were trained in Helping Babies Breathe (HBB), emphasizing initiation of PPV within one minute after birth in non-breathing newborns not responding to stimulation, chest compressions are not performed. Newborns in need of resuscitation were brought to the resuscitation table. The HR sensor was applied over the abdomen, and the HR appeared on the monitor in front of the provider. Resuscitations followed the HBB guidelines, which was not clear on how to apply PPV (continuous versus interrupted). At Haydom, it has been a longstanding practice to apply interrupted PPV sequences of 5–20 s. During pauses the newborn is assessed for spontaneous respirations and if apneic, stimulation/suctioning are applied. All newborns delivered vaginally or by cesarean section were included if both respiratory and HR parameters were detected. Signal data and observational data for each newborn was paired and used for analysis.

Ethical approval was granted by the National Institute for Medical Research in Tanzania and the Regional Committee for Medical and Health Research Ethics in Western Norway.

### *Response and dependent variables*

The response variable HR was calculated as the mean HR during each of the first five sequences of PPV. A sequence was defined as the period of continuous PPV without an interruption for more than five seconds. An interruption was defined as more than five seconds duration, generally consistent with the mask being completely removed from the newborns face (Fig. 1B). A ventilation episode was defined as summation of all PPV and pause sequences from the first to last inflation, until discontinuation of PPV due to start of spontaneous respiration or death. The TV was calculated as the mean exhaled volume in each sequence. The first five sequences of PPV were examined, during the period when FRC was likely to be established.

Using a Directed Acyclic Graph [13], the following covariates (written in *Italic*) were included in the statistical model: The first detected HR (*Initial HR*) after birth was categorized in HR intervals <60, 60–100, 100–140, 140–180 and >180 beats per minute (bpm) with the *Initial HR <60* bpm as the reference category. Further covariates were *Gender* (female as reference category); *Birth weight* (grams); *Gestational age* (weeks); *Time from birth to start of PPV* (seconds); *Time providing PPV* (seconds) that is the total time of PPV in each episode; *Pause time between PPV* (seconds) with no ongoing PPV longer than five seconds; *PPV rate* (inflations per minute); and *Inflation Pressure* ($cmH_2O$), the mean peak inflation pressure during a sequence.

### *Statistical analyses*

The descriptive changes in HR over each PPV sequence (Table 1 and Fig. 2) were calculated as delta HR (last HR – first HR in the sequence), and similarly for changes in HR during pauses. The association between delivered *mean tidal volume* (ml/kg) and mean HR of each sequence was analyzed by a general additive model (GAM) (Fig. 3 and Table 2). The model was adjusted for the set of above described covariates in addition to the number of PPV sequences, and the interaction between the first measured HR and the number of the given sequence (*Initial HR (<60)*Sequence*). This interaction variable interprets the expected change in HR for each added sequence of PPV for newborns with different initial HRs (*Initial HR*). The association between TV and HR was modeled by a non-linear relationship, whereas the remaining covariates were modeled by a linear relationship in the GAM. To support the interpretability of the model intercept, all continuous covariates were centered.

A separate GAM analysis was performed for the first two PPV sequences in newborns with the *Initial HR (<100* bpm*)*. This post hoc analysis was motivated by the observation of rapid HR increases for this subgroup in the first two PPV sequences (Fig. 2). Thus, particularly for this group the association between HR, TV and PPV time is of high interest.

Data were analyzed using R (R core team 2013, Vienna, Austria) and SPSS Version 22.0. Results are shown as mean ± standard deviation (SD) with 95% Confidence Intervals (CI) in brackets unless otherwise stated.

## Results

### *General characteristics*

During the study period, 5914 newborns were delivered, and 459 (7.8%) received PPV. In 113 newborns, the monitor was not used. Newborns (n = 131) were excluded for the following indications: PPV initiated before application of HR sensor (n = 103), delay in initiating PPV for more than four minutes (n = 5), immediate outcome of death or fresh stillbirth on the resuscitation table (n = 18), other (n = 5). The remaining 215 newborns were included in the study. The included newborns had a GA of 37.3 ± 1.9 weeks and BW of 3115 ± 579 g. The 24-h outcome was "healthy and discharged home" (n = 165), "admitted to the neonatal area" (n = 40), and death (n = 10). Deliveries were via vaginal cephalic (n = 134), vaginal breech or vacuum (n = 13) and caesarean section (n = 68).

The mean first measured HR for *Initial HR* (<60) = 50.1 ± 9.5 (48.4, 51.8) bpm, *Initial HR* (60–100) = 77.1 ± 10.3 (75.6, 78.6)