Exploratory Analysis of Heart Rate Changes in Newborns to Investigate the Effectiveness of Bag-Mask Ventilation

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Abstract

Neonatal mortality due to birth asphyxia in low-resource countries is a global problem. During the first minutes immediately after birth, healthcare personnel need to resuscitate non-breathing babies by effective positive pressure ventilations. Currently, an increase in heart rate is thought to be the most important indicator of successful manual bag-mask ventilation. ECG and ventilation signals were detected and parameterized into relevant information to explore the relationship between changes in heart rate and different possible determinant factors for beneficial ventilation. A data analysis approach is proposed to identify the relationships between these signal characteristics and heart rate changes. Several associations between characteristics of ventilation parameters and changes in heart rate were identified.

1.   Introduction

It is challenging and time critical to ventilate newborns because of the complicated interaction between interventions and pathophysiological effects on the newborns. Therefore, it is desirable to understand the importance of the different ventilation parameters and corresponding characteristics and values in order to improve the quality of care, and hence increase the chance of survival among infants in need of resuscitation.

There are many publications regarding guidelines providing instructions for neonatal resuscitation (e.g., [3], [5]). Ramsden and Reynolds discussed the interaction between ventilator parameters and the physiology of the lung [1]. They concluded that it is difficult to determine the effective settings because of the diversity in the newborn population. The relationship between heart rate variability (HRV) and asphyxia was studied on 24 rats [2]. The work showed a correlation between HRV and asphyxia but needs to be validated on more data.

In this paper, we demonstrate a processing and parameterization of ventilation signals, and propose and illustrate how discriminative p-values can help to identify important ventilation parameters. The hypothesis is that characteristics of some ventilation parameters could relate to changes in heart rate.

2.   Material and methods

The data presented in this report is collected at Haydom Lutheran Hospital in rural Tanzania. Haydom is a referral hospital with a catchment area of more than 2 million people. Midwives predominantly perform the basic newborn resuscitations. This study is part of the "Safer Births" project which include continues observation of delivery management and neonatal characteristics and outcome, by local research staff.

2.1.   Material

The dataset used in our work was collected from Laerdal Newborn Resuscitation Monitors (LNRM) employed in the labor ward. The LNRM was developed by Laerdal Global Health and designed for research use in low resource settings where newborn resuscitations usually are performed by a single care provider. It can collect different physiological information such as heart rate (HR), airway pressure, flow, and CO_2 concentration. However, only HR is displayed to the caregiver using the LNRM at Haydom. There are 218 episodes recorded in the period from July 2013 through June 2014 with physiological signals and other clinical information of the babies.

2.2.   Methods

In this experimental work, we analyze three signals: the airway pressure, the flow and the ECG signal. Five ventilation parameters are defined: average ventilation

frequency, average peak inspiratory pressure (PIP), average expired volume, initial peak inspiratory pressure, and ventilation time percentage. Pressing of the ventilation bag creates a "ventilation event". One "ventilation event" is defined to start when the value of pressure increases from baseline and exceeds 5 mbar. The PIP of each ventilation event is the maximum value of the pressure signal. A continuous ventilation sequence is a series of ventilation events without "pause" in between. A pause is the period when the pressure signal value is lower than 5 mbar for more than 3 seconds. "Total ventilation time" is the time from the first to the last ventilation event performed on one baby.

Four of the five parameters are derived from the pressure signal and can be described as follows:

1. The average ventilation frequency ($f_{v_{av}}$) is the ratio of total number of ventilation events (n_{v_i}) over the sum of duration of each ventilation sequence (t_i).

$$f_{v_{av}} = \frac{\sum_i n_{v_i}}{\sum_i t_i}$$

2. The average PIP (PIP_{av}) is the "weighted average" of mean values of PIPs of each ventilation sequence ($\overline{PIP_i}$) and the weight is the duration of each ventilation sequence (t_i).

$$PIP_{av} = \frac{\sum \overline{PIP_i} * t_i}{\sum t_i}$$

3. Initial peak inspiratory pressure (PIP_{init}) is the average PIP value of the first ventilation sequence.

4. Ventilation time percentage (VT_{PRC}) is the percentage of sum of duration of all ventilation sequences in the total ventilation time (T_v):

$$(VT_{PRC}) = \frac{\sum t_i * 100\%}{T_v}$$

The remaining parameter is computed from the volume waveform which is integrated from the flow signal measured by the hot-wire flow-sensor (Acutronic Medical Systems AG). The expired volume is the amount of air going back through the flow sensor after an inflation. The expired volume is the volume drop from the maximum value (on the volume curve) to zero - or to a non-zero value when there is mask leakage.

5. The average expired volume (ExV_{av}) is the average value of all expired volumes.

The physiological heart rate responses to different ventilation interventions are parameterized by the heart rate computed from the RR intervals of the detected QRS. The RR intervals longer than a threshold were considered as ectopic beats occurring in the interval $t_{k_e} < t_e < t_{k_e+2}$. Interval function ($d_{IF}$) over the interval $t_{k_e} < t < t_{k_e+2}$ can be replaced by linear interpolation as in the formula below [6].

$$d_{IF}^i(t) = d_{IF}(t_{k_e}) + \frac{d_{IF}(t_{k_e+2}) - d_{IF}(t_{k_e})}{t_{k_e+2} - t_{k_e}} (t - t_{k_e})$$

t_{k_e} is the time of QRS complex right before ectopic beat.

RR interval at a specific point of time was calculated by using piecewise cubic interpolation of three RR intervals surrounding that point. The instantaneous heart rates measured at the beginning and at the end of each ventilation sequence are the inverse of corresponding RR intervals.

We wanted to investigate if changes in heart rate are associated with certain characteristics of the mentioned ventilation parameters. The p-value approach for statistical significance test among groups of babies was done by using Wilcoxon rank-sum testing in MATLAB (Mathworks, Natick, MA) in an explorative manner. The p-values from such tests can be seen as a representation of the discriminative capability of different ventilation parameters. A low p-value indicates a difference in the means of the two groups implying that the corresponding ventilation parameter could be important to the result of the treatment. For each ventilation parameter, the set of values of that parameter are categorized into two groups depending on the corresponding delta heart rate (ΔHR). Group 1 has ΔHR <= 20 and group 2 has ΔHR > 20. First heart rate (HR_{first}) is average of three continuous valid heart rates before ventilation and last heart rate (HR_{last}) is the average of three continuous valid heart rates after ventilation. Because the QRS detection is considered to be valid if the quality of ECG signal is good. The detection of the HR_{first} moves forward from the point of the first ventilation event to the left within a time window of 30 seconds. If there is no valid QRS detection, the search moves from the point of the first ventilation event to the right. The same computation is applied for the HR_{last}. The detection of HR_{first} and HR_{last} is illustrated in figure 1.
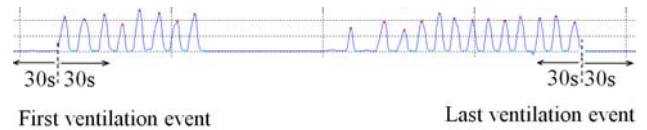

Figure 1: Detection of HR_{first} and HR_{last} within a time window of 30s.

$$\Delta HR = HR_{last} - HR_{first}$$

The effectiveness of the ventilation effort is evaluated by the heart rate changing. A threshold value is chosen to evaluate the effectiveness of ventilation. ΔHR that is greater than the threshold is assumed to represent a more effective ventilation effort and vice versa. Therefore,

group 2 is considered the one with positive outcome and group 1 is the one with negative outcome.

We divided our data into different subsets based on the range of the HR_{first} value of each baby. For example, a set of babies who have HR_{first} in the range from 100 to 150 beats per minute (bpm) is one of the possible subsets. For each ventilation parameter, we calculated a p-value grid which is a plot with x and y axes representing the lower and upper boundaries HR_{first}. One point on the grid corresponds to a subset of patients with the HR_{first} in the range defined by the two coordinate values (x, y). The purpose of dividing data into subsets with various range of HR_{first} is to investigate the effect of ventilation parameters on many subsets of patients with different heart rates at the start of the ventilation. Using Wilcoxon rank-sum test, we computed the p-value for each point on the grid and assign a color to that point according to the p-value color map next to the grid. To more clearly illustrate the subsets with low p-values, we use triangles for the points with p-value < 0.05, otherwise, we use circles. The colors represent different range of p-values. The pointing direction of triangles depends on the median value of ventilation parameters of group 2 in comparison with group 1. For instance, for points with low p-value, if the median value of group 2 is greater than group 1, upward triangles will be used, otherwise, downward triangles are used. To represent the size of the samples in the comparisons, the size of each point in the grid is proportional to the number in the smallest of the two groups.

3.   Experiment and results

The experiments presented in this paper all used ΔHR threshold of 20. Each ventilation parameter has 1 p-value grid. Figure 2a shows one example of a p-value grid presenting associations between "ventilation time percentage" and a ΔHR change below or above 20 bpm. Figure 2b shows the corresponding box plot for the red circle point in the p-value grid. The downward pointing triangles indicate that in the cohort of infants with a first HR ranging from 50 – 180 bpm, the babies with a subsequent increase in HR > 20 bpm (Group 2), had a lower median "ventilation time percentage" compared to those with an ΔHR ≤ 20 bpm (Group 1). Grids of p-values of the other parameters are illustrated in figure 3. The upward pointing triangles in figure 3b indicate that in the cohort of infants with a first HR ranging from 70 – 190 bpm, the babies with a subsequent increase in HR > 20 bpm (Group 2), had a higher average "expired volume" compared to those with an ΔHR ≤ 20 bpm (Group 1).
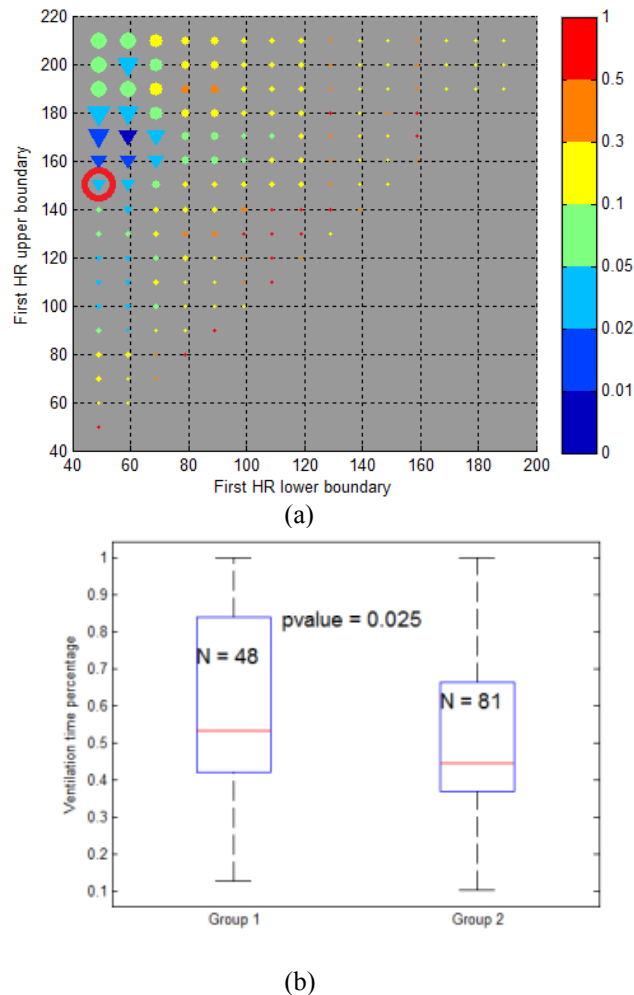

(a)

(b)

Figure 2: (a) Grid p-values of ventilation time percentage (VT_{PRC}). (b) Box plot of the corresponding red circled point which has HR_{first} in the range from 50 to 150 beats per minute. Group 1 represents the bag mask ventilated babies with a ΔHR ≤ 20 bpm (n=48) and Group 2 represents the bag mask ventilated babies with a ΔHR > 20 bpm (n=81).

4.   Discussion

By using DHR threshold 20, low p-values were found for varying initial heart rate ranges for two parameter average expired volume (ExV_{av}) and ventilation time percentage (VT_{PRC}). This could imply that adequate ExV_{av} is important for effective ventilations. However, a lower median VT_{PRC} is difficult to interpret in the absence of additional clinical information (e.g. stimulation/suction).
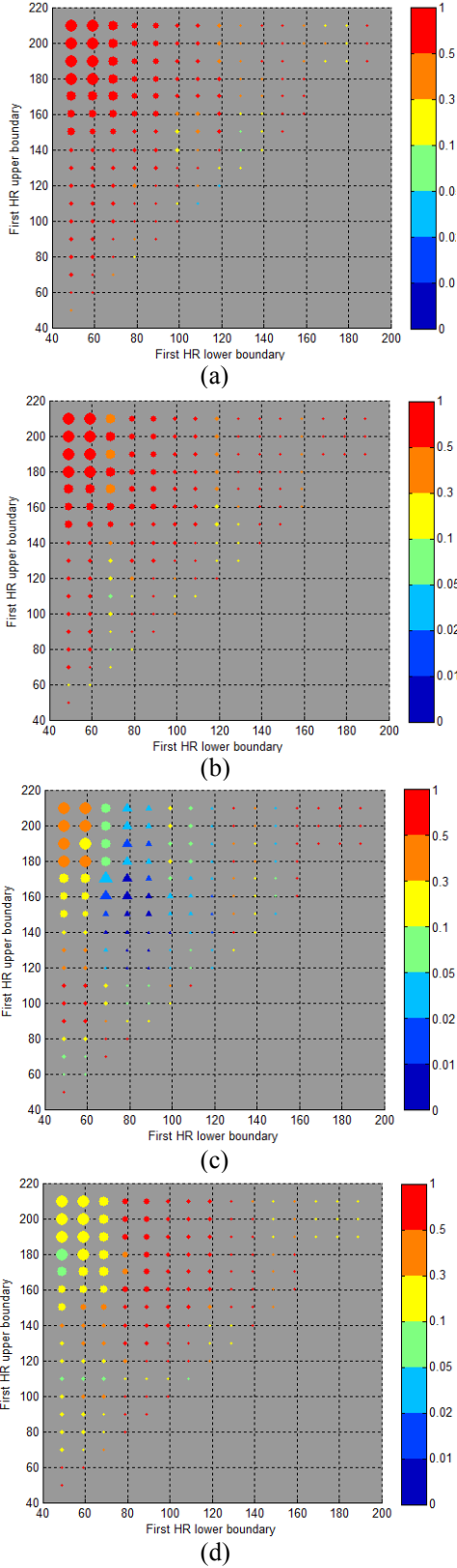
Figure 3: (a) P-value grid for $f_{v_{av}}$. (b) P-value grid for PIP_{av} (c). P-value grid for ExV_{av}. (d) P-value grid for PIP_{init}.

5.   Conclusion and future work

The main contributions of this work are: the processing and defining of ventilation parameters describing the given interventions and corresponding heart rate responses of the babies, proposal of a framework for exploring data using a statistical approach to search for determinant factors in changing heart rates of newborns. Low p-values were found for (ExV_{av}) and ventilation time percentage (VT_{PRC}) parameters.

To possibly provide relevant clinical conclusions this work needs to be extended by looking at combinations of ventilation parameters, the pattern of the pressure and flow curves, and associations with other clinical variables describing additional treatments and outcomes.

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