A review of capnography in asthma: A new approach on assessment of capnogram

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ABSTRACT

Asthma is a chronic inflammatory disease of the bronchial tubes that occurs in about 3 to 5% of all people and continues to be a significant cause of morbidity and mortality. Traditionally, peak flow meter and spirometer is used to monitor the asthmatic patients which have lots of limitation. Nowadays, capnography is a new method used to monitor the asthmatic condition. It is able to show the different respiratory situation of patient including asthma. Unlike traditional methods, it is taken while the patient is breathing as comfortable as possible. Previous studies have shown significant correlation between the capnogram and asthmatic patient. However, all of them are just manual studies conducted through the conventional method. Manual analysis of capnogram is, however, time-consuming and led to erroneous due to human factor such as tiredness and lack of proficiency. Therefore, it is proposed here to develop a computerized system to detect the severity of airway obstruction by processing the capnogram signal using signal processing algorithms. The aim of this article is to give a review on methods for detecting the asthmatic conditions by using capnogram. This includes an investigation on capnography as a new approach for monitoring asthma and related researches. In the final section, we introduce our new method based on signal processing approach to detect severity of asthmatic patients automatically. This algorithm uses features of capnogram to characterize the asthmatic severity conditions. This developed algorithm is aspired to provide a fast and low-cost diagnostic system in handling increasing number of asthmatic patient, as it would be possible to monitor severity of asthma automatically and instantaneously.

Keywords: monitoring, asthma, capnogram, capnography, signal processing

INTRODUCTION

Asthma is caused by inflammation in the airways. When an asthma attack occurs, the muscles surrounding the airways become tight and the lining of the air passages swells. This reduces the amount of air that can pass by, and leading to variable and recurring symptoms, reversible airflow obstruction, and bronchospasm. A research showed that it is usually occurred in 3 to 5% of all people, showing its importance to be more investigated by the newly developed methods to improve the patient’s conditions [1]. There are many signs of asthma and the symptoms of an asthma attack include shortness of breath, chest tightness, trouble sleeping, whistling sound while exhaling, and coughing or wheezing attacks. These symptoms generally do not occur between asthma attacks, and asthma sufferers can live a normal, physically fit life in between their attacks [2]. Traditionally, one of the asthmatic tests is to make a record on a spirometer of the forced expiratory vital capacity (FVC) [3]. Spirometry involves a maximal inspiration followed by a rapid, forceful and complete exhalation until there is absolutely no more air to blow out. These results generally come with two different graphic displays in which the first is the spirogram and the second is the flow-volume curve. One of the information regarding the flow-volume curve is the point of maximal expiratory
flow, the same as the peak expiratory flow rate (PEFR). It is the expiratory flow at the moment that it is the fastest during the entire exhalation and the value that measured by peak flow meters [4].

Spirometry and peak flow meter are useful diagnostic tools, but there are some complications and contra indications. Both methods are mainly considered to study dizziness, chest pain, coughing, bronchospasm and oxygen desaturation due to the interruption of oxygen therapy. The reliable results cannot be obtained as the instruction for the patients are complicated and chest pain is the result of the tests. Hence, both tracings are derived from the same single manoeuvre that is taking a full, deep breath in, and then blast it out as hard and fast as patients can until they can empty no more air from their lungs. In addition, with a mouthpiece in the mouth normal breathing can be hardly achieved. Children under the age of 6 years are generally not able to perform an adequate test [4]. Nowadays, capnography is widely considered as a new method to monitor the asthmatic condition [5]. It uses the technology of infrared to determine the concentration of carbon dioxide and capnogram is the graphical display of instantaneous CO₂ concentration (mmHg) versus time (second). It is able to show the different respiratory situation of patient including asthma. Unlike peak flow meter or spirometer where the patient must follow a set of instructions, capnogram is taken while the patient is breathing as comfortably as able [6].

In this review, capnography as a new approach for detection asthmatic conditions is discussed. It contains researches that investigate the use of capnography in various medical diagnosis, and significant research that have been done to diagnosis bronchospasm and asthma by using capnogram signals. Finally, a new method based on digital signal processing techniques and artificial neural networks is proposed to cluster different states of asthmatic conditions.

### CAPNOGRAPHY: DEFINITION AND INTERPRETATION

Capnography is a non-invasive tool used to measure the concentration or partial pressure of carbon dioxide (CO₂) level during respiration. The output of the tool is presented as a graph of expiratory CO₂ plotted against time or expired volume. This monitoring tool has been primarily used by anaesthesiologist, cardiologist, critical care personnel, paediatricians, and emergency medicine practitioners [7]. A normal capnogram has four phases and an end-tidal point [8], as shown in figure 1. Each phase reflects the normal process of CO₂ elimination. The flat phase I (A-B) represents early exhalation that is relatively CO₂-free. As exhalation continues, alveoli containing CO₂ are increasingly recruited and exhaled with nonCO₂-containing gases. This creates a near vertical rising phase II (B-C). Near the termination of normal exhalation is a plateau phase III (C-D). At the end of the plateau phase is D, the point that the measured alveolar CO₂ levels best approximate PaCO₂. This sampled CO₂ level is known as PetCO₂. As inspiration occurs, a near vertical rapidly falling phase IV (D-E) is observed. When ventilation and perfusion function normally, PetCO₂ should read 2-5 mmHg higher than the PaCO₂ [9]. A variety of clinical causes can lead to incomplete alveolar emptying. Therefore, the true end tidal point was never reached. Figure 2b shows the capnogram of an asthmatic patient with an obstruction in tubing and other parts of the breathing circuit. It should be noticed that the ascending limb of the capnogram is prolonged and is not flat, as it should be normally as shown in figure 2a. These changes give rise to the so called ‘shark's fin’ morphology capnogram in patients with airway obstruction. However, there is more shape of abnormal capnogram that could be found depending on the patient’s condition [10].

### A REVIEW ON MEDICAL DIAGNOSIS USING CAPNOGRAPHY

Table 1 show a summary on medical diagnosis to date based on analyzing capnogram signal. Based on the findings in table 1, analysis of capnogram signal helps medical and clinical practitioners diagnose a variety of disease such as predicting suspected diabetic ketoacidosis (DKA) in children,
monitoring modality for nonintubated patients, and predicting survival from in-hospital cardiopulmonary resuscitation (CPR). Moreover, capnography has lots of clinical applications such as monitoring ventilation in unconscious patients, detecting the degree of metabolic acidosis in children with diabetes or acute gastroenteritis, assessing vital signs in critically injured patients, and tracking response to treatment in patients with acute respiratory distress. Therefore, based on these reported articles, it can be concluded that capnogram is a vital biosignal to many health conditions.

Table 1. Review on medical diagnosis associated with capnogram.

<table>
<thead>
<tr>
<th>Purpose</th>
<th>Findings</th>
<th>Reference</th>
</tr>
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<tbody>
<tr>
<td>To investigate the relationship between end-tidal carbon dioxide (ETCO₂) and cardiac output before cardiac arrest and during cardiopulmonary resuscitation (CPR)</td>
<td>A critical reduction in cardiac output is consequence of the increase in mixed venous carbon dioxide tension (PvCO₂) and the concurrent decrease in ETCO₂.</td>
<td>[11]</td>
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<tr>
<td>To determine the reliability and clinical value of end-tidal carbon dioxide (ETCO₂) by oral or nasal capnometry for monitoring paediatric patients presenting postictal or with active seizures</td>
<td>Continuous ETCO₂ monitoring provides the clinician with a reliable assessment of pulmonary status in paediatric seizure patients that can assist with decisions to provide ventilatory support.</td>
<td>[12]</td>
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<tr>
<td>To evaluate the relationship between measured serum bicarbonate (HCO₃) and ETCO₂ measured via nasal capnography in children with suspected diabetic ketoacidosis (DKA) and to assess the ability of capnography to predict DKA</td>
<td>ETCO₂ is linearly related to HCO₃ and is significantly lower in children with DKA. Hence, in conjunction with clinical assessment, may help discriminate between patients with and without DKA.</td>
<td>[13]</td>
</tr>
<tr>
<td>To evaluate the accuracy of a new low-flow side stream capnography technology and analyze components of the capnogram in mechanically ventilated newborns with and without pulmonary disease</td>
<td>The low-flow side stream capnography can accurately estimate PaCO₂ in intubated neonatal patients. Also, in the population without lung disease, the PetCO₂-PaCO₂ gradient was within normal limits, but in a heterogeneous population of neonates with lung disease was abnormal.</td>
<td>[14]</td>
</tr>
<tr>
<td>To review recent advances in the use of capnography as a diagnostic monitoring modality for nonintubated patients</td>
<td>Capnography is a non-invasive diagnostic monitoring that its clinical applications include assessing vital signs in critically injured patients, tracking response to treatment in patients with acute respiratory distress, monitoring ventilation in unconscious patients, and detecting the degree of metabolic acidosis in children with diabetes or acute gastroenteritis.</td>
<td>[15]</td>
</tr>
<tr>
<td>To determine the value of components of the continuous capnography trend-line for predicting survival from in-hospital cardiopulmonary resuscitation (CPR)</td>
<td>Computerized continuous capnography trend-lines may be used for early prediction of return of spontaneous circulation (ROSC).</td>
<td>[16]</td>
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</table>
In this section, a review on significant researches, those have been done to diagnosis bronchospasm and asthma by using signal processing of capnogram signals is presented [17-20].

**Measuring ‘S’ parameters**

One of the first and fundamental studies in analyzing capnogram has been conducted by You et al. [21] and the correlations between capnographic and spirometric indices were measured in 10 healthy subjects and 30 asthmatic patients. The usefulness of eight descriptive indices was assessed by measuring their reproducibility and their sensitivity to airway obstruction. Three indices measured the slope of the capnogram during the various phases of expiration (S1, S2 and S3). Next
index was slope ratio (SR) between the intermediate and the initial slopes was \((S2/S1) \times 100\). The area ratio (AR: \((A1/A2) \times 100\)) that the \(A1\) and \(A2\) were calculated above a threshold of 2.5% of CO\(_2\) between 0.2 and 1 second and three indices were used as the second derivative of the capnographic curve (SD1, SD2, and SD3). Their results showed that there exist large differences among the indices. According to their research, a high sensitivity to airway obstruction was seen for intermediate and terminal slopes (S2, S3, SR), followed by SD1, SD2, SD3 and the lowest ranges were seen with S1 and AR. This research introduced some basic and useful parameters, but it was in time domain and had a manual analysis of capnogram that lead to many irreversible mistakes due to human factors and lack of expertise. Also the thresholds to calculate the slopes and the area ratio are not accurate and are just a suggestion. In addition, measuring these indices manually comes with lots of errors. Figure 3 shows the eight shape indices tested.

![Figure 3. Description of the capnogram and its indices in normal and obstructive conditions. (a) The inspiratory (I1 and I2) and expiratory phases (E1, E2, E3) of a normal capnogram and (b) Schematic description of the capnographic indices measured on a normal (upper) and on an obstructive (lower) capnogram.](image)

**Calculating the dCO\(_2\)/dt of the plateau phase**

In 1996, Yaron et al. conducted a research on utilizing the expiratory capnogram in the assessment of bronchospasm [22]. They calculated dCO\(_2\)/dt of the plateau phase for five consecutive regular expirations and a mean calculated for each patient. They concluded that this parameter is an effort-independent, rapid, non-invasive measurement that indicates significant bronchospasm in adult patients with asthma. Their results for post-treatment show significant changes in percent predicted PEFR and dCO\(_2\)/dt. The pre-treatment and post-treatment percent predicted PEFR values were 58% and 74%, respectively (\(P<0.001\)). Also, dCO\(_2\)/dt values were 0.27% and 0.19%, respectively (\(P<0.005\)). However, their study was on just 20 adults with acute asthma and 28 normal adults. Like the previous study, this research defines a new parameter to analyse the capnogram for asthmatic patients. However, it is manual and difficult to calculate by a medical practitioner and physician to monitor the severity of asthma during monitoring the patients.

**Evaluating the slope of phase III from the volumetric capnogram**

Another research by Druck et al. [23] demonstrated that the slope of phase III from the volumetric capnogram as a non-effort dependent surrogate for changes in peak expiratory flow rate. The
patients breathed quietly for at least one minute through a combined CO$_2$/flow sensor and the best of three peaks expiratory flow rate measurements were then recorded. After that average values of the slope of phase III were computed over a 10-breath interval. Then percentage changes in slope measurements from the volumetric capnogram were compared to percentage changes in peak expiratory flow rates. The patient’s correlation coefficient was calculated. The mean pre- and post-treatment peak expiratory flow measurements were 252-99 and 310-107 l/min. Percent changes in the phase III slope were found to be correlated with the percent changes PEFR ($P<0.2$). This study has just suggested that changes in the volumetric capnogram slope of phase III may be useful as a non-effort dependent surrogate of peak expiratory flow rate and a measure of bronchospasm. Also, the patient needs to follow special instruction and breathes quickly for one minute. Definitely, it could be difficult for an asthmatic patient especially with chest pain. This process, nevertheless, needs lots of manual computing.

**Hjorth parameters**

One of the recent studies on capnogram to detect asthma was conducted by Tan Teik Kean [24]. This study extracted the Hjorth parameters from the capnogram signal. Hjorth parameters use information from the curves and slopes of capnogram to produce 3 different parameters which are activity, mobility, and complexity [25]. The Hjorth parameters were extracted from the capnogram for two conditions. Firstly, it was extracted from the whole cycle of capnogram, named as HP1. Secondly, the Hjorth parameters were extracted from capnogram cycle ranging from beginning of phase II to time at the end tidal peak, named as HP2. The author also has extracted features proposed by You et al. [21] to compare their performance against Hjorth parameters in differentiating asthma and non-asthma capnogram.

In his study, a total of 13 features have been extracted from capnogram and according to their results, the slope ratio (SR) of the capnogram is the best among the parameters investigated to differentiate the asthmatic and non-asthmatic conditions. Furthermore, the Hjorth parameters have shown good performance through the HP2-mobility for monitoring asthmatic patients using capnography. This research presented a computerized method to detect the different parts of capnogram signals besides introducing Hjorth parameters as the new features to detect the severity of asthma. However, it is again a time domain analysis with the idea that the capnogram is a stationary signal. Moreover, the author just used 34 samples that it could not be enough for confirming the reliability of the procedure.

**A NEW METHOD TO DETECT SEVERITY OF ASTHMA**

All researches mentioned above shows significant correlation between the capnogram and asthmatic patient. However, all of them are just manual study conducted through the conventional time domain method. In addition, they are based on assumption that the capnogram is a stationary signal, while most physiological signals are non-stationary. Therefore, the analysis based on assumption that capnogram is stationary has limitations and requires further analysis based on concrete facts. In addition, manual analysis of capnogram is time-consuming and led to erroneous due to human factor such as tiredness and lack of proficiency. As such, it is proposed here to develop a computerized system to detect the severity of airway obstruction by processing the capnogram signal using digital signal processing techniques. Figure 4 shows the overall flowchart of the proposed technique in tracking asthmatic patients utilizing capnography technique.
Data collection

The capnogram data were collected from patients with complaints of asthma and breathing difficulties at the Emergency Department of Penang Hospital. First, the capnography sensor was attached on the mouth or nose of the patients. Mainstream capnography method was used in the process of data collection because this method has higher accuracy [5]. After attaching the sensor on the patient’s nose or mouth, the continuous capnogram was recorded using the capnography patient monitor, Capnostream™20 Model CS08798. The capnogram data in the patient monitor was transferred to a personal computer for analysis. Throughout the study, a total of 20 non-asthmatic capnogram, and 31 asthmatic capnogram were successfully collected. The capnogram for each patient was recorded around five minutes at a sampling frequency of 200Hz. Then, a continuous and complete part of recorded data with the length of five breathing cycles and without any artefact (approximately 20 seconds; according to the patient’s respiratory rate) was extracted for further analysis. Figure 5 shows the block diagram of data collection in brief. In our database, each sample has an ID which is used in this review. This ID consists of 3 alphabet letters and a number. The alphabet letter is either CAP (Capnogram of Asthmatic Patient) or CNP (Capnogram of Non-asthmatic Patient) and a number right after the letters which indicates the sample number, e.g. CAP2 means the second asthmatic sample and CNP6 means the sixth non-asthmatic sample.

Preprocessing

Data pre-processing was carried out to eliminate unnecessary noise in the recorded capnogram signals. Figure 6 shows the capnogram of non-asthmatic patient (CNP2) before pre-processing. In this review, the moving average filtering method was used to smooth the curve. This method smoothes data by replacing each data point with the average of neighbouring data points defined within a specific span. This process is equivalent to lowpass filtering with the response of the smoothing given by the difference equation as given follow:

\[
y_s(i) = \frac{1}{2N+1} (y(i+N) + y(i+N-1) + \ldots + y(i-N))
\]

where \( y_s(i) \) is the smoothed value for the \( i^{th} \) data point, \( N \) is the number of neighbouring data points on either side of \( y(i) \), and \( 2N+1 \) is the span. Indeed, the span defines a window that moves across the data set as the smoothed response value is calculated for each predictor value. A large span increases the smoothness but decreases the resolution of the smoothed data set, while a small span decreases the smoothness but increases the resolution of the smoothed data set. The optimal span value depends on the data set and usually requires some trial and error to determine [26]. In this study, we used the span as 13, because it produced the best results for both smoothness and resolution. Furthermore, the correlation coefficients calculated for each signal after filtering justified this span width, e.g. the correlation coefficient for the CNP2 after filtering was 0.9924. Figure 7 shows the capnogram of non-asthmatic patient (CNP2) after smoothing.

Feature extraction

After that, features of capnogram were extracted to characterize the airway obstruction severity conditions. In time domain, features based on the shape of capnogram will be extracted. This includes the linear predictive coding (LPC) coefficients because these parameters are suitable for capnogram which has slope changes for a lot of airway abnormalities [9,10]. In frequency domain, the classic Fast Fourier Transform (FFT) is used to identify the spectral components of capnogram.
This will then lead to differentiation in frequency content of capnogram for different conditions. It is important to note that, until today, there is no study to analyse the capnogram in frequency domain. Therefore, it is proposed to use FFT to investigate the spectral components of capnogram signals. Figure 8 and 9 show the FFT of a non-asthmatic and an asthmatic capnogram, respectively, using Blackman window with length of 128 point.

**Feature evaluation**

The effectiveness of extracted features is assessed by Receiver Operating Characteristic (ROC) curve analysis. ROC curves can be used to compare the diagnostic performance of two or diagnostic tests [27]; in our case the asthmatic and non-asthmatic conditions. When the variable under study cannot distinguish between the two groups, i.e. where there is no difference between the two distributions, the area under the ROC curve will be equal to 0.5, so the ROC curve will coincide with the diagonal. When there is a perfect separation of the values of the two groups, i.e. there is no overlapping of the distributions, the area under the ROC curve equals 1, so the ROC curve will reach the upper left corner of the plot. Also the P-value is the probability that the sample area under the ROC curve is found when the true population area under the ROC curve is 0.5 (null hypothesis: area = 0.5). If P is low (P<0.05) then it can be concluded that the area under the ROC curve is...
significantly different from 0.5 and that therefore there is evidence that the capnogram test does have an ability to distinguish between the two groups [27].

Figure 6. The capnogram signal of CNP2 before filtering.

Figure 7. The capnogram signal of CNP2 after filtering.
Figure 8. The FFT of a non-asthmatic capnogram (CNP2) using Blackman window.

Figure 9. The FFT of an asthmatic capnogram (CAP9) using Blackman window.
Designing artificial neural network

A radial basis function (RBF) neural network is designed to automatically cluster and classify the patients with different asthmatic severity. The RBF networks have benefits such as easy design, good generalization, strong tolerance to input noise, and online learning ability [28]. Figure 10 shows the architecture of a standard RBF network. Artificial neural networks have been successfully applied to hosts of pattern recognition and classification tasks, time series prediction, data mining, function approximation, data clustering and filtering, and data compression. It can be used to solve a wide variety of problems while being robust to error in training data. Hence, the developed RBF network will help the medical practitioners and physicians to monitor severity of asthmatic patients. Since, manual analysis of capnogram is time-consuming and leads to erroneous due to the human errors such as tiredness and many other related faults, it is proposed that a computerized system should be developed to detect the severity of airway obstruction by processing the capnogram signal using digital signal processing techniques. The proposed computerized method is an innovative idea that is useful for healthcare professionals involved in respiratory care as it would be possible to automatically monitor severity of airway obstruction and asthma.

![Architecture of a standard RBF network](image)

Figure 10. Architecture of a standard RBF network ($x_1$ to $x_5$ are extracted features from LPC and FFT analysis, and $y$ is output index to detect severity of asthma).

CONCLUSION

Current methods of assessing asthma are limited for many reasons as mentioned earlier. Furthermore, monitoring asthma condition has not become part of clinical practice. Capnogram is a vital representation of the respiratory system. Therefore, analysis of this physiological signal could lead to the development of the computerized methods to differentiate airway disorders, which could benefit the healthcare professional involved in respiratory care. This chapter gives a review on this new method to detect asthmatic conditions. However, previous studies conducted were based on the
fact that capnogram is a stationary signal, and this assumption leads to limitations in its signal processing approach. As such, in this chapter, we propose a new computerized automated way to monitor and differentiate severity of asthmatic conditions. In future, this developed algorithm is expected to help healthcare professional involved in respiratory care as it would be possible to monitor severity of asthma automatically and instantaneously.

REFERENCES