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Mini Review
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Clinical Value of Audio Signal Processing and Machine Learning to Detect Cough Patterns: An Opinion Review

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Introduction

Cough is one of the most common reasons why patients consult their doctor. Cough due to common cold or upper respiratory infection is probably the most common cause of acute cough. Cough can be divided into the following three categories: acute, lasting <3 weeks; subacute, lasting between 3 and 8 weeks; and chronic, lasting >8 weeks [1]. In the majority of persons, cough that is acute and self-limiting is usually secondary to a viral upper respiratory tract infection. Cough can occasionally be associated with life-threatening conditions such as Heart Failure (HF), pulmonary embolism, and pneumonia [1]. In HF, the coughing or wheezing is due to the fluid accumulation or congestion, in the lungs, which increases the effort of breathing. Coughing can affect sleep quality and general quality of life. Definitive treatment of cough depends on the physician's assessment in determining its precise cause. Currently cough is assessed for its severity, frequency, intensity, associated urge, and its impact on quality of life [2].

Chronic Obstructive Pulmonary Disease (COPD) and Congestive Heart Failure (CHF) are progressive disorders, and often the terminal stage of pulmonary and cardiac disease leading to death. Cough is often regarded as a critical symptom of COPD and CHF, and listening to cough is still an important mechanism for physicians to gauge disease onset and severity.Since the publication of the 2006 American College of Chest Physicians (CHEST) cough guidelines, a variety of tools has been developed or further refined for assessing cough [3]. Acoustic cough counting to assess cough frequency but not cough severity has been recommended [3]. Although the guideline recommends assessing and monitoring cough severity, there is lack of evidence in the literature in assessing cough as a symptom of decompensation due to fluid buildup in lungs of patients with HF.

Current Assessment of Cough

In current practice, a range of subjective and objective measurements of cough are used. The initial clinical examination (history and physical) helps in developing a rapport with patients, identifying the severity of cough, determining prognosis, and monitoring therapy [4]. Respiratory assessment by nurses and clinicians include two key vital signs; respiratory rate and pulse oximetry that measures the oxygen saturation of arterial blood in a subject by utilizing a sensor attached typically to a finger, toe, or ear and listening to lung sounds. Nurses and clinicians ask subjective questions on cough including duration, character, sputum production, and color of the sputum [4]. There are validated tools to guide the assessment of cough severity in COPD and other respiratory conditions such as the Visual Analogue Scale (VAS), [5] cough-specific quality of life questionnaire, the Leicester Cough Questionnaire (LCQ), [6] and Cough-specific Quality of Life Questionnaire (CQLQ) [7,8]. These questionnaires are very subjective and are often completed by a family member or the parent of a child [9]. Other method that is often used in clinical practice to assess cough severity is the cough diary [10].

Significant progress has been made recently in the development of objective tools to assess cough. In addition to routine respiratory vital signs, airflow measurement at the mouth helps to obtain the flow dynamics of cough and measuring the physical character of the cough sound [11]. Researchers also used an accelerometer-based system by placing an accelerometer in the volunteer's chest wall to record cough events, but such system required researchers to count coughs manually [12]. Cough frequency evaluation is considered the gold standard along with the intensity of coughing, pattern of coughing, and the acoustic properties of cough sounds are helpful in determining clinical endpoints [13]. Counting cough events, cough frequency at specified intervals such as every 4-hours or 24-hours are used to quantify cough. Although, it is challenging to replicate the performance of the human ear to detect cough sounds and count them, recent advances in computer technology and the availability of portable digital sound recording devices using audio signal processing

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techniques have automated cough counting and classifying cough events seamlessly.

Cough Sound Basics

A deep inspiration usually starts a classical cough, followed by glottis closure. During the glottis closure, respiratory muscles contract against the closed glottis and then the sudden opening of the glottis occurs with transient and fast expiratory airflow accompanied by the typical cough sound [13]. Although, laryngeal structures and the resonance of the nasal and thoracic cavity are involved in cough, their roles are not clear. Cough sound is usually divided into three phases: (1) an explosive expiration due to the glottis suddenly opening, (2) the intermediate phase with the attenuation of cough sounds, and (3) the voiced phase due to the closing of the vocal cord [14]. In fact, there are a variety of patterns of cough that occur and some cough sounds may have only two phases (the intermediate phase and the voiced phase) and the explosive phase may be prolonged because of chronic diseases.

The frequency of cough events in patients with chronic lung diseases such as asthma, COPD and idiopathic pulmonary fibrosis depends on the prominence of cough as a symptom. Cough monitors are the best tools to discriminate patients with cough from healthy subjects. Sounds during an episode of coughing at the mouth is acoustically different from the sounds heard at the chest wall. Cough sounds at the mouth contain frequencies distributed widely from 200 to 2000 Hz, whereas breath sounds heard at the chest wall do not contain frequencies above 200 Hz as they are filtered off by the alveolar air and chest wall [15]. Thus, recording cough sounds to objectively measure cough frequency could be a valuable index of objective cough assessment. Manual counting of cough sounds remains the reference standard because compared with other tools, the human ear performs best in counting cough events [16]. Earlier version of cough recording used microphones and an MP3 recorder "VitaloJak", yet the cough is assessed and counted manually and accuracy of the monitor was dependent on the observer [17]. Therefore, researchers moved away from manually counting of cough events because it restricted feasibility in larger-scale studies and clinical application. Automatic monitoring and counting of cough sounds is feasible for use in large scale studies and clinical application. The first automatic cough counting monitor, Leicester Cough Monitor (LCM) comprised of a free-field microphone and an MP3 recorder with cough detection automated using specifically designed software [18]. The sensitivity and specificity for cough detection is very good with intra-class correlation coefficient at 0.9 [18]. The LCM has been used in single and multi-center clinical trials [19-21]. A meta-analysis of six-randomized control trials that assessed the efficacy of antitussive medication used a computerized system for identification of cough reported that the computerized tool wasconsistent and reproducible across the studies [22].

Rationale to Use Mobile Technology to Assess Cough

The World Health Organization has estimated that the proportion of persons over 60 years of age will double to 22% in 2050 from 11% in 2000 [23]. Thus over 2 billion people will require additional medical support, even assisted living, as they will be more prone to health related issues [23]. The aging society can be served by satellite based medical diagnosis and care from their homes. Mobile health (mHealth) technology is undergoing rapid evolution. The level of exuberance for mHealth is driven by the unsustainability of current health care spending and the recognition of the need for disruptive solutions; the rapid and ongoing growth in wireless connectivity with more than 3.2 billion unique mobile users worldwide; and the need for more precise and individualized medicine [24]. There are nearly 7 billion mobile subscriptions worldwide and this is equivalent to 95.5 percent of the world population [25]. Although, cough monitors are available, they have been used in research but their use has not been translated into clinical practice. There has been a consensus that a combination of subjective and objective assessment is necessary to assess cough comprehensively in clinical practice.

Application of Audio Signaling Process to Assess Cough

Smart-phones today come with advanced microphones and provide options to record audio data sensed by their in-built microphone. The Digital Signal Processing (DSP) has been used to calculate characteristic spectral coefficients of sound events, which are then classified into cough and non-cough events by the use of a Probabilistic Neural Network (PNN). Parameters such as the total number of coughs and cough frequency as a function of time can be calculated from the results of the audio processing [26,27]. While recognition of a single cough event is relatively easy, evidence of calculating episodic and nocturnal cough event is lacking. Particularly cough frequency over a long period of time remains difficult both for clinical and research purposes among population who have COPD or CHF.

Automatic recognition and counting of coughs solely from sound recordings of cough includean extraction of the audio features of the cough for subsequent classifications including: a) Minimum Value - This is minimum value or the deepest trough of the audio signal; b) Maximum Value - This is minimum value or the peak of the audio signal; c) Mean/ Median/ Variance - The average, median and variance of the entire audio signal; d) Zero Crossing Rate - Rate at which the signal changes from positive to negative and *vice versa*; e) Signal to Noise Ratio - Ratio of the signal power to noise power; f) RMS power - Root Mean Square Power of the Signal; and g) Entropy - Uncertainly or unpredictability of the audio signal [28].

The final step used in the development of an algorithm for automatic recognition of cough include the application of Machine Learning. Machine learning is a method of data analysis that automates analytical model building. Using algorithms that iteratively learn from data, machine learning allows computers to find hidden insights without being explicitly programmed where to look [28]. Most scientist use random forest based algorithm for classification that are suited for audio signal processing. Random forests are general technique of random decision forests that are an ensemble learning method for classification, regression and other tasks, that operate by constructing a multitude of decision trees at training time and outputting the class that is the mode of the classes (classification) or mean prediction (regression) of the individual decision trees [28,29]. Random decision forests correct for decision trees' habit of over fitting to their training set, both deterministic and randomness in data samples for superior classification.

Review of Current Smartphone Applications

The SymDetector, a smartphone based application to unobtrusively detect the sound-related respiratory symptoms occurred in a user's daily life, including sneeze, cough, sniffle and throat clearing. The SymDetector uses a number of time and frequency domain features, followed by Support Vector Machine (SVM) based Algorithms of machine learning [30]. The authors report an accuracy of 82% for detecting respiratory events, and 99.1% for non-respiratory events [30]. Similar methods to classify cough from other noises have been developed such as an automatic diagnosis of pertussis [31] differentiate wet and dry cough using digital signal processing of cough [32,33] and differentiate pneumonia from asthma in children [34]. An Automated System for Asthma Monitoring (ADAM) was developed based upon standard speech recognition and machine learning paradigms for children with asthma [35]. Recently, Australian researchers developed a smartphone app that could analyze the sound of a child's cough to distinguish and diagnose asthma with 97% sensitivity and pneumonia at 87% sensitivity [36].

Efficacy of a fully automated Internet-linked, tablet/computer-based system of monitoring and self-management support for COPD patients (EDGE' sElf-management anD support proGrammE) demonstrated significant improvement in quality of life in the EDGE group (0.076, 95% CI 0.008-0.14, P=.03) [37]. More recently, researchers in Australia has designed aMH-COPD program to integrate an mHealth system within a clinical COPD care service; in which participants will use a mHealth application at home to review educational videos, monitor COPD symptoms, use an electronic action plan, modify the risk factors of cigarette smoking and regular physical activity, and learn to use inhalers optimally [38]. A randomized clinical trial to test this mHealth program is currently underway [38].

Clinical Implication

Cough monitoring, more specifically, cough detection from audio recordings has been thoroughly investigated in literature as outlined in the related work section. No cough monitor, however, is currently the gold standard. As technology evolves, more accurate cough detection may be a possibility in the near future. The management of COPD requires a multidisciplinary approach. A system for the automatic, objective, and reliable detection of cough events is important and very promising to detect pathology severity in chronic cough disease. To avoid inaccuracies of patient self-reports and to reduce the patient's burden of data collection, automatic cough detection systems have been proposed to count coughs from audio recordings. The tool can be mainly designed for elderly patients with COPD using a user friendly interface to collect data which will be easily accessible to health care professionals and provide feedback to the patients. Understanding patients' and providers' perception in the use of such automated tool is vital to avoid false positives.

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