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THE VOICE AND CYSTIC FIBROSIS: A DESCRIPTIVE CASE STUDY

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Bachelor of Speech and Hearing

Cleveland State University

December, 2013

Submitted in partial fulfillment of requirements for the degree

MASTER OF ARTS IN SPEECH-LANGUAGE PATHOLOGY AND AUDIOLOGY

at the

CLEVELAND STATE UNIVERSITY

May, 2016

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Student's Date of Defense: May 9, 2016

DEDICATION

I would like to dedicate this thesis to my cystic fibrosis pulmonologist, Dr. Robert Stern, the CF nurses at Rainbow Babies & Children's hospital, and all of my fellow cystic fibrosis fighters.

-to Dr. Stern, for his extreme dedication to his patients.

It was Dr. Stern's constant, never-ceasing hunger for knowledge that lit my fire for research.

-to my nurses at "Club Rainbow," for never failing to bring a little sunshine through even the heaviest of clouds.

-to my fellow fighters, for your perseverance. I may not know many of you personally, but knowing that we are all in this fight together is the best support system that anyone could ask for. Breathe easy, fighters.

ACKNOWLEDGEMENTS

I would like to take this opportunity to formally thank all those who have helped me to complete this thesis. I would like to thank my entire family for their love and support throughout my entire life, especially my education. I would especially like to thank my mom and dad for pushing me to always do my best and for reminding me that even the impossible is made possible with God. I am eternally grateful for their endless love, support, and prayers, I would not be where I am today without them

I would like to express my most sincere gratitude to Dr. Violet Cox for her continued support of my research, her enthusiasm, motivation, dedication, and especially her patience. I continue to thank her for sharing her immense wealth of knowledge with me and for opening my eyes to the world of voice therapy. I could not have asked for a better mentor in this monumental step toward completing my Master's degree. She truly inspired the researcher in me, and motivated me to always put my best effort forward, even during the most challenging moments. Thank you for your continued guidance and reassurance. I would also like to thank the members of my committee, Dr. Andrew Lammers and Dr. Myrita Wilhite, for always asking the challenging questions and offering insightful comments.

I would like to thank my supervisors from my off-campus clinical sites. Their patience, advice, and encouragement were key in my ability to complete this thesis while finishing my field experiences. I would like to thank and congratulate my entire cohort. In my graduate experience, I have met some of the most wonderful, dedicated, and intelligent people that continue to lift me up and inspire me in the field. I am indebted to all of my colleagues for providing an exciting environment in which to grow and learn. These ladies have truly shown me the best way for turning a frown upside down.

THE VOICE AND CYSTIC FIBROSIS: A DESCRIPTIVE CASE STUDY

VERONICA R. SMITLEY

ABSTRACT

Cystic fibrosis is a common autosomal recessive disease with severe effects on the respiratory, digestive, and endocrine systems. Symptoms include chronic cough and wheezing, frequent upper respiratory tract infections, and reflux disease. While most treatments for cystic fibrosis aim to mitigate the respiratory and gastrointestinal dysfunction, the potential adverse effects on an individual's voice has not been researched in a systematic manner. We hypothesized that individuals with cystic fibrosis may show physical signs of vocal fold damage, as well as common dysphonic symptoms. Given the impact voice disorders have on an overall quality of life, identification and management of cystic fibrosis-related dysphonia could be of great importance for assessment and treatment of this chronic illness. Four individuals participated, a male and female with cystic fibrosis, and male and female without cystic fibrosis. Each participant underwent videostroboscopy for vocal fold observation. Additionally, aerodynamic vocal parameters were measured using the *Visi-PitchTM*. Substantial structural changes were observed in the participants with cystic fibrosis. Significant differences in aerodynamic measures were also found, particularly in the area of vocal perturbation (jitter and shimmer). Participants with cystic fibrosis had markedly higher measures of jitter and shimmer. The observed differences may be a direct result of the phonotrauma experienced during day-to-day treatments and respiratory symptoms of the individual with cystic fibrosis.

TABLE OF CONTENTS

| | Page |
|--|------|
| ABSTRACT..... | v |
| LIST OF FIGURES..... | vii |
| LIST OF TABLES..... | viii |
| NOMENCLATURE..... | ix |
| CHAPTER | |
| I. INTRODUCTION..... | 1 |
| II. METHODS..... | 9 |
| Participant Selection and Ethics Statement..... | 9 |
| Consent Form..... | 10 |
| Objective Vocal Analysis..... | 10 |
| Videostroboscopy..... | 11 |
| Subjective Vocal Analysis..... | 11 |
| III. RESULTS..... | 13 |
| Videostroboscopy..... | 13 |
| Female Vocal Folds..... | 13 |
| Male Vocal Folds..... | 15 |
| Aerodynamic and Quantitative Vocal Parameters..... | 17 |
| Female Voice..... | 17 |
| Male Voice..... | 18 |
| Perceptual Self-assessment of Voice..... | 19 |
| IV. DISCUSSION..... | 21 |
| Conclusion..... | 24 |
| Limitations and Future Research..... | 25 |
| REFERENCES..... | 26 |
| APPENDICES..... | 28 |
| A. Instructions to Participants..... | 29 |
| B. Consent Form..... | 30 |
| C. Brief Screening Tool..... | 31 |
| D. Self-assessment Form..... | 32 |

LIST OF FIGURES

| Figure | Page |
|---|------|
| 1.1 Benign lesions of the vocal folds..... | 4 |
| 1.2 Normal abduction..... | 5 |
| 1.3 Paradoxical adduction..... | 5 |
| 3.1 Vocal folds of female participants..... | 15 |
| 3.2 Vocal folds of male participants..... | 17 |

LIST OF TABLES

| Table | Page |
|----------------------------------|------|
| 3.1 Female vocal parameters..... | 18 |
| 3.2 Male vocal parameters | 19 |

NOMENCLATURE

F₀ – fundamental frequency

NHR – noise-to-harmonic ratio

MPT – maximum phonation time

CF – cystic fibrosis

Phonotrauma – excessive vocal abuse

CHAPTER I

INTRODUCTION

Cystic fibrosis (CF) is a recessive genetic disease that affects approximately 30,000 individuals living in the United States, and 70,000 worldwide (Cystic Fibrosis Foundation, 2015). The defective gene causes the cystic fibrosis transmembrane conductance regulator (CFTR) protein in the body's cells to function poorly. The CFTR protein functions as a channel for the movement of chloride ions in and out of cells, which is important for the salt and water balance on epithelial surfaces, such as in the lungs or pancreas. Malfunctioning of this protein results in a build-up of thick, sticky mucus throughout the body. According to the Cystic Fibrosis Foundation (2015), there are over 1,800 different gene mutations, causing a wide variety of symptoms and severities. The most common symptoms include salty-tasting skin, persistent coughing, frequent lung infections including pneumonia or bronchitis, wheezing or shortness of breath, and poor growth or weight gain in spite of a good appetite. With the build-up of mucus, patients typically suffer respiratory complications. Due to the complexity and variations of the cystic fibrosis genotypes, most common treatments for patients with CF are designed for treating these respiratory components. However, it is known that respiratory dysfunction and persistent coughing can lead to significant trauma to an individual's vocal folds, therefore impacting overall vocal quality. The possibility of vocal fold damage or laryngeal dysfunction has not been thoroughly researched in CF.

In addition to respiratory distress, individuals with cystic fibrosis often suffer from various types of gastrointestinal disorders. Due to pancreatic insufficiency, patients with CF suffer from digestive tract dysfunction, which in turn can lead to acid reflux diseases such as gastroesophageal reflux disease (GERD) and laryngopharyngeal reflux disease (LPRD). According to Boone et al. (2014), GERD is defined as the passage of acid from the stomach back into the esophagus, and LPRD is the passage of acid from the stomach into the esophagus and superiorly into the larynx. Further research from Boone et al. (2014) showed that reflux diseases such as these can often compromise the individual's vocal folds and affect their ability to function properly.

A study conducted by Rozmanic, Dorian Tjesic-Drinkovic, Banac, Ahel, Duska Tjesic-Drinkovic, Persic, and Votava-Raic (2009) examined the presence of gastroesophageal reflux in patients with cystic fibrosis. Rozmanic et al. recruited twenty-five children with CF to undergo 24-hour esophageal pH monitoring. In their study, Rozmanic et al. (2009) defined an episode of acid reflux as an abrupt fall in intraesophageal pH less than 4 for at least 15 seconds. Standard variables used included the reflux index, which was the percentage of times when pH was less than 4, number of reflux episodes, and the number of reflux episodes lasting longer than 5 minutes. Rozmanic et al. considered a reflux index of >10% in patients under one year of age to be pathological, however an RI of >5% was considered pathological for other age groups. The study revealed that thirteen of the twenty-five patients showed pathological gastroesophageal reflux (Rozmanic et al., 2009). This study found that the prevalence of GERD increases with decreased lung function in the individual with CF. Lower lung function typically results in exacerbation of respiratory symptoms, which in turn leads to

extra treatments for the patient. All of these factors – severe acid reflux, excess cough, and extra treatments – can lead to damage of the laryngeal tissue.

The larynx has three main roles in daily living: biological, emotional, and linguistic. Biologically, the larynx protects the airway from foreign substances during eating and drinking. Emotionally, the larynx can offer changes in one's voice to signal happiness, sadness, anger, etc. In a linguistic function, the larynx offers movement in order to add various prosodic features to a person's voice. In other words, movement of the larynx accounts for vocal stress, pitch and volume changes, as well as respiratory regulation while speaking and eating. According to Boone, McFarland, Von Berg, and Zraick (2014), there are five aspects of voice that determine dysfunctionality. These are (1) loudness (volume of speaker's voice), (2) hygienic production (whether or not a speaker's voice sounds "healthy"), (3) pleasantness (smooth and easy or broken and harsh), (4) flexibility (ability to use appropriate intonation), and (5) representative (does the voice fit the speaker, such as man vs. woman). If a person's voice violates any one or more of these five aspects, a voice disorder exists.

According to Verdolini and Ramig (1998), voice disorders are generally characterized by an abnormal functioning in the mechanisms that control pitch, loudness, and/or vocal quality; that is, the larynx, respiratory system, and/or the vocal tract. Voice disorders can be considered of functional, organic, or neurogenic etiology. For the purpose of this study, the focus will be on voice disorders with a functional etiology. Functional voice disorders are those caused by phonotrauma, or an individual misusing, or abusing his or her voice. Examples of vocal abuse include screaming, continuously speaking at a high pitch, persistent throat clearing, or excessive coughing. Often times,

functional voice disorders can lead to physical damage of the vocal folds. Damage may occur in the form of benign lesions that grow forth from the tissue of the vocal folds. These lesions are typically classified into one of four descriptive categories: polyps, nodules, Reinke's edema, or cysts. See Figure 1.1 (Cipriani, 2011). As these injuries heal, they may result in a build-up of scar tissue and ultimately affect the function of the vocal folds.

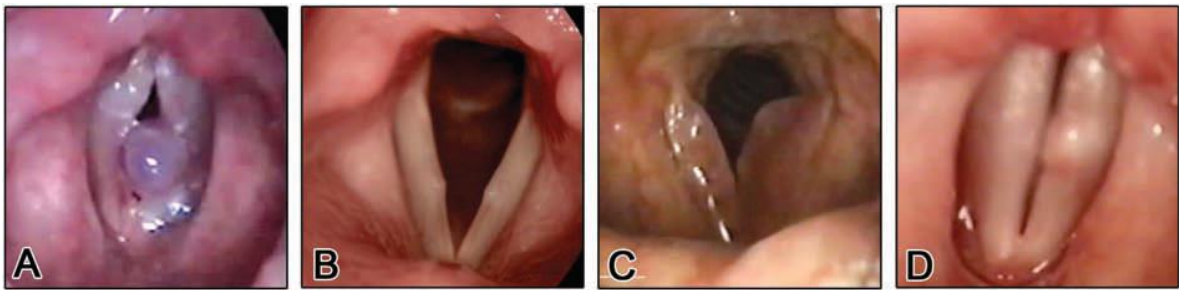


Figure 1.1 Benign lesions of the vocal folds. Variations of focal fold lesions due to phonotrauma. **A:** Polyps – unilateral, sessile, or pedunculated lesions of the anterior third of the vocal fold; blister-like appearance. **B:** Nodules – bilateral, symmetric swellings of the anterior to middle vocal fold; callus-like appearance. **C:** Reinke's edema – unilateral or bilateral swelling of the entire vocal fold. **D:** Cyst – discrete unilateral swellings clinically similar to foregoing 3 lesions. (Cipriani, 2011)

Paradoxical adduction of the vocal folds is another functional vocal fold disorder that may occur in CF patients. According to the American Speech-language and Hearing Association (ASHA) (2015), paradoxical vocal fold movement is when the vocal folds behave in a normal fashion almost all of the time (Figure 1.2), but inappropriately close during inhalation (Figure 1.3). A case study conducted by Shiels, Hayes, and Fitzgerald (1995) examined possible causes of this functional disorder. These authors studied a 17-year old female diagnosed with cystic fibrosis at birth. At 16 years of age, the girl had developed prominent hoarseness and noisy sounds in her throat. Upon observation, it was

also noted that she had considerable inspiratory stridor with minimal expiratory wheeze. While her lung functions appeared to be within functional limits, significant upper airway obstruction during inhalation was seen in interpretation of the flow-volume loop. Considerable paradoxical adduction of the vocal cords was found on bronchoscopy. The case study did not determine precisely what was causing this rare disorder, but the researchers concluded that the diagnosis of paradoxical vocal cord adduction should be considered in patients with cystic fibrosis and suggested that appropriate physiological and endoscopic assessments are needed in the general examination of individuals with CF (Shiels et al., 1995).



Figure 1.2 Normal abduction. Expected behavior of vocal folds during breathing (Galek, 2015)



Figure 1.3 Paradoxical adduction. Improper closure during inhalation (ASHA, 2014)

Lourenco, Costa, and Filho (2014) investigated aerodynamic measures in Brazilian individuals with cystic fibrosis. The study compared a female and male control group to a female and male test group using quantitative vocal parameters as well as subjective measures.

The quantitative parameters used were fundamental frequency (F_0), jitter, shimmer, and the harmonics to noise ratio (HNR). Fundamental frequency is defined as

the average rate at which an individual's vocal folds typically vibrate. It is measured by the number of vibratory cycles the vocal folds complete per second. F_0 can also be termed as a person's habitual pitch, the pitch that his or her voice has in a typical everyday setting. Jitter and shimmer are types of vocal perturbation, or variability in the output of voice. Jitter is the cycle-to-cycle variations of pitch that occur naturally. It often correlates with perceived vocal roughness. Shimmer is the index of variability in vocal intensity and is often measured both in decibels (dB) and percentages. When the mean shimmer is displayed in dB, it indicates the difference between sequential vocal amplitudes measured during sustained phonation. Mean shimmer in percent is the absolute cycle-to-cycle difference in amplitude and divided by the mean amplitude then multiplied by 100 in order to produce a percentage. Last, HNR is an index of glottal turbulence and noise.

In addition to the aforementioned quantitative measures, Lorenzo et al. (2014) used subjective measurements to analyze the subjects. Each participant was rated on a perceptual scale called the GRBAS (Grade, Roughness, Breathiness, Asthenia, Strain). The GRBAS is an assessment method used to evaluate the patients overall grade (G) of dysphonia through four subjective parameters – roughness, breathiness, asthenia, strain. Each of these four parameters is then rated as one (mild), two (mild alteration), or three (severe alteration) (Lorenzo et al., 2014).

Lorenzo et al. (2014) found that individuals with cystic fibrosis showed significant differences of vocal quality in the following quantitative factors: decrease in intensity, increase in jitter and shimmer, and a considerably lower HNR. In addition, the CF participants showed clear signs of vocal dysfunction in the GRBAS perceptual rating.

The GRBAS findings showed an overall increase in roughness, breathiness, and asthenia, as well as an increase in the general grade of dysphonia. The findings showed no significant differences in strain, according to the GRBAS rating (Lorenco et al., 2014).

Lorenco et al.'s (2014) study serves a guide for the current research. While the findings were considerable, some gaps and limitations exist that will be examined in the current study. Many voice specialists believe that the root of a voice disorder can be found in a visual examination of the vocal folds. In addition, physical examination will confirm the absence or presence of paradoxical adduction of the vocal folds. Physical damage caused by vocal abuse may include polyps or nodules and may lead to significant scar tissue. As previously stated, this type of damage may greatly alter an individual's vocal fold function. Visual examination of the vocal folds will also allow for observation of the mucosal wave. The mucosal wave is the movement of the mucous membrane of the vocal fold during phonation (Boone et al., 2014). Abnormalities or complete absence of the mucosal wave is significant in determining the presence of vocal fold pathology and a possible voice disorder. The hope is that physical examination of the vocal folds in conjunction with aerodynamic and perceptual measures may give a deeper explanation behind voice dysfunction in cystic fibrosis.

The present study will aim to extend the findings of Lorenco et al. (2014) by adding the components of vocal fold visualization and other aerodynamic measures such as S/Z ratio and maximum phonation time (MPT). The S/Z ratio measurement is a fairly simple procedure which measures the length of time a person can sustain the "s" sound and the length of time they can sustain the "z" sound, then divides the two figures to obtain a numerical ratio. The higher the figure the greater the possibility that the person is

experiencing difficulty with phonation. It is widely accepted in speech science that an S/Z ratio greater than 1.4 is indicative of laryngeal insufficiency; greater than 2.0 is considered symptomatic of vocal fold pathology and should be further assessed (Boone et al., 2014). This parameter is not typically used as a diagnostic tool by itself, but it may be used to determine the possibility of laryngeal malfunction.

MPT is the maximum time (in seconds) for which a person can sustain a vowel sound when produced on one deep breath at a relatively comfortable pitch and loudness. Similar to the S/Z ratio, this is a quick and simple aerodynamic measure. Typically, with no laryngeal pathology, adult males can sustain vowel sounds for between 25-35 seconds and adult females between 15-25 seconds. As with the S/Z ratio, MPT is not diagnostic of laryngeal pathology, but it may be a precursor to vocal fold dysfunction. Research has shown that many voice disorders may stem from lack of respiration needed in order to produce voice. These parameters will give a better understanding of the individual's respiratory abilities as they relate to voice production.

Individuals living with CF may benefit from a confirmed diagnosis of voice disorder and a subsequent plan for voice therapy in order to further improve their quality of life. The purpose of this study is to further investigate through both perceptual and objective measures the presence of vocal fold dysfunction in individuals with cystic fibrosis.

CHAPTER II

METHODS

Participant Selection and Ethics Statement

The investigation, materials, and procedures for this study were approved by the Institutional Review Board (IRB) of Cleveland State University. Participants were recruited from the community by word of mouth through the student investigator who verbally contacted individuals with the diagnosis of cystic fibrosis and who are members of her support group. A total of four individuals participated in this study, one male and one female with a diagnosis of cystic fibrosis, and one male and female without cystic fibrosis. All participants reported that they have never been previously diagnosed with a vocal fold disorder and had never received voice therapy. There were no financial incentives for participation.

The participants with CF were diagnosed within the first year of life using the traditional sweat test and presence of pancreatic insufficiency. They were also diagnosed with Cystic Fibrosis-Related Diabetes (CFRD) and placed on an insulin regimen. They were receiving individual, regular treatment from a team of medical professionals, including physician, pulmonology, dietician, respiratory therapist, ENT, and endocrinologist. At the time of data collection, the participants were not experiencing an exacerbation of CF symptoms.

Consent Form

The investigator recruited, screened, and collected data for all participants. All data were collected in the voice lab of the Cleveland State University Speech and Hearing Clinic. All participants agreed and signed the consent form after discussing all procedures and associated risks with the examiner. Participants were also offered a reference copy of the consent form.

Objective Vocal Analysis

The following quantitative measures were collected on each participant using the *KayPentax Visi-PitchTM IV*, model number 3950B: fundamental frequency, jitter, relative average perturbation (RAP), shimmer (measured in dB and percentages), and noise-to-harmonic (NHR) ratio. The *Visi-PitchTM* is a computerized device that measures and stores vocal information. For this study, the participants were instructed (Appendix A) to phonate into a free-standing microphone attached to the machine. The microphone was positioned approximately two inches from each participant's mouth. The above-mentioned parameters have been extensively researched and validated as adequate objective measures for vocal quality. They are routinely used by specialists in the field as diagnostic tools. Abnormalities within these parameters are potential signs of dysphonia (Lorenco et al., 2014).

S/Z ratio and maximum phonation time were collected by the student investigator. To collect S/Z ratio, the patient was instructed to produce the “s” sound for as long as possible while they were timed. Next, the patient was instructed to produce the “z” sound for as long as possible. The investigator then divided the “s” time by the “z” time to calculate the ratio. Three trials were completed, and the lowest ratio reported for analysis.

To measure MPT, the investigator instructed the patient to produce the open vowel “ah” for as long as possible while being timed. The timer was stopped and time recorded when the patient’s voice began to waiver. Again, three trials were completed and the best time reported for analysis.

Videostroboscopy

KayPentax Rhino-Laryngeal StroboscopeTM model RLS 9100B was used to conduct videostroboscopy in order to complete a visual examination of the vocal folds. Videostroboscopy is a routine procedure used by ENTs and speech-language pathologists as a tool for assessment of vocal fold damage or dysfunction. A rigid endoscope attached to a camera from the videostroboscopy instrument was placed at the base of the tongue in the oral cavity while the participant was instructed to vocalize the open vowel /ah/. The investigator directly observed the participants’ laryngeal structures, as well as the vocal fold mucosal wave.

Subjective Vocal Analysis

In addition to the objective measures, each participant, with the investigator, completed a self-assessment of his or her own vocal quality. A perceptual assessment of vocal quality in CF participants was obtained using the *Clinical Voice Evaluation 2 (CVE2)* (2003), a paper and pencil self-assessment. The participant evaluated eight parameters of his or her own voice: quality, pitch, pitch range, loudness, nasal resonance, oral resonance, rate, and prosody. The ratings were based on a scale of 0 to 3: 0 = normal, 1 = mild, 2 = moderate, 3 = severe. The participant then provided a self-perception rating of his or her voice using the same rating scale. Professionals do not necessarily use this

particular self-assessment as a diagnostic tool, rather as a screening tool to determine the need for further voice evaluation.

CHAPTER III

RESULTS

Videostroboscopy

Female vocal folds. Still images from the videostroboscopy demonstrating abduction and adduction of the vocal folds in female participants are shown in Figure 3.1. In comparing the laryngeal structures of the female with CF to the same-age, non-CF participant, some significant structural differences were observed. The first noted difference is in the arytenoid cartilages, the structures that lie directly anterior to the vocal folds. As seen in the non-CF female participant (Figure 3.1A), the arytenoid cartilages are structures that have defined structural characteristics; this is to be expected. Upon examination of the female CF subject (Figure 3.1B), significant inflammation, swelling, and thickening of the tissue was noted to exist to the point where the arytenoid cartilages do not stand out as individual, distinct structures. Instead, these structures merely blend into the surrounding laryngeal tissue.

The second most notable difference was seen during adduction of the vocal folds. Typically, when adducted, the vocal folds come together and form a complete closure of the glottal space (Figure 3.1C). In the participant with CF (Figure 3.1D), incomplete glottal closure was noted upon adduction. The small opening, also called a posterior glottal “chink,” is not uncommon in females. In Figure 3.1D, the interarytenoid edema

was made even more obvious as the space that should exist between the arytenoid cartilages was significantly diminished.

In addition to the incomplete glottal closure, it was noted that the vocal folds of the female patient with CF are substantially thicker than the non-CF female. The vocal folds were not as elongated compared to those of the female without CF.

In reviewing the videostroboscopy, vocal fold movement was considered functional for the female patient with CF. The mucosal wave for this patient was observed to be slower than that of the female without CF. Furthermore, there was abnormal movement of the arytenoid cartilages and false vocal folds. Typically, these structures move slightly toward midline upon phonation, but do not move together completely as the vocal folds do. For the patient with CF, the arytenoid cartilages complete vibratory cycles in a near-spastic manner. This anomaly does not occur regularly, but rather at random intervals.

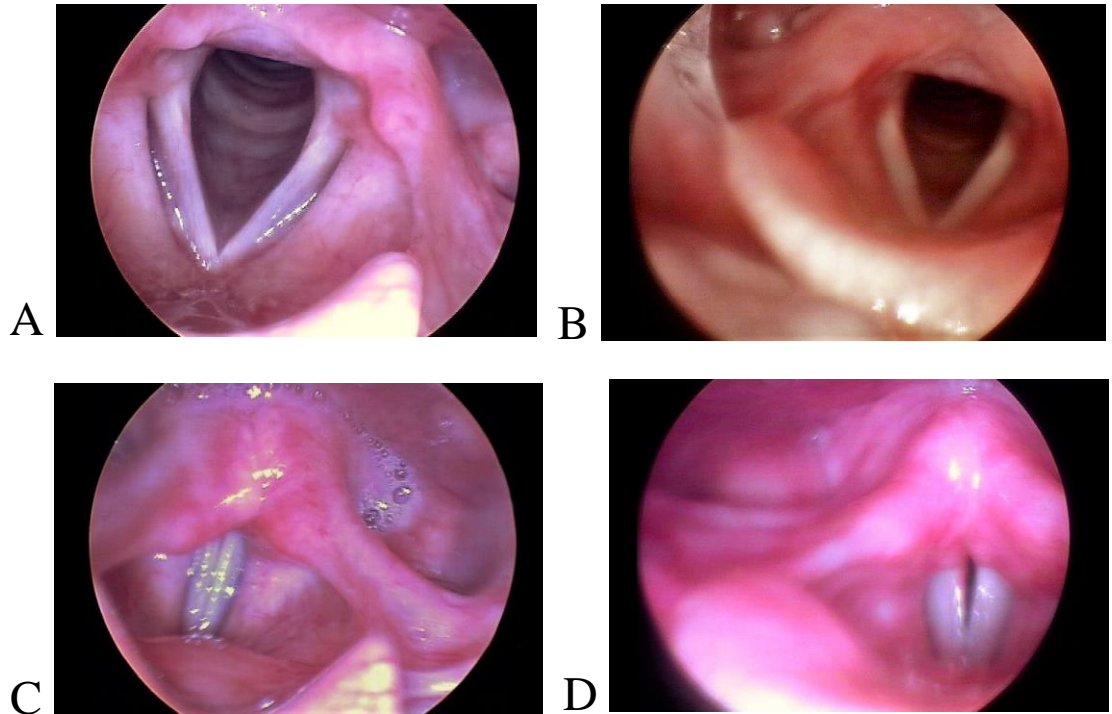


Figure 3.1. Vocal folds of female participants. Shown in abducted and adducted position. **A:** Abducted vocal folds of female without CF. **B:** Abducted vocal folds of female with CF, notice the swollen arytenoids. **C:** Adducted vocal folds of female without CF. **D:** Adducted vocal folds of female with CF; note the thickness of the vocal folds as well as incomplete glottal closure.

Male vocal folds. Figure 3.2 shows comparative images of the vocal folds of the male participants, both CF and non-CF. Structural changes of the vocal folds were most noticeable in the male CF participant (Figures 3.2B and 3.2D). Upon examination, the CF male's left vocal fold is of the most interest. The medial aspects of the left vocal fold in this same participant appeared as if the tissue was torn. This gave the impression of two separate vocal folds on the left side. Additionally, there appeared to be a blister-like mass on the posterior edge of the left vocal fold. Both of these anomalies are most evident upon vocal fold abduction shown in Figure 3.2B.

Glottal closure seems adequate for both male participants. In the male with CF, there appears to be a double opening due to the tear in the left vocal fold. In observing the

motion of the vocal folds, this tear does not significantly impact the mucosal wave or closure of the glottis. However, the blister like mass of tissue on the posterior aspect of the left vocal fold seemed to be a slight barrier to achieving full glottal closure during phonation.

The laryngeal tissue surrounding the vocal folds appears to be slightly swollen and inflamed in the male with CF, though not to the extent observed in the female with CF. In particular, there is a section of swollen tissue directly anterior to the subject's right vocal fold; it is most clearly seen in Figure 3.2B, during abduction. In Figure 3.2D, the tissue appears to come to midline during adduction and nearly cover the posterior portion of the right vocal fold. There is a similar anomaly on the patient's left vocal fold that is more clearly seen when the vocal folds are adducted (Figure 3.2D).

Finally, the videostroboscopy did not reveal any significant differences in the movement or function of the laryngeal tissue. The vocal fold mucosal wave was observed to be fully functional for the male CF patient, despite having the appearance of a double left vocal fold and subsequent double glottal opening.

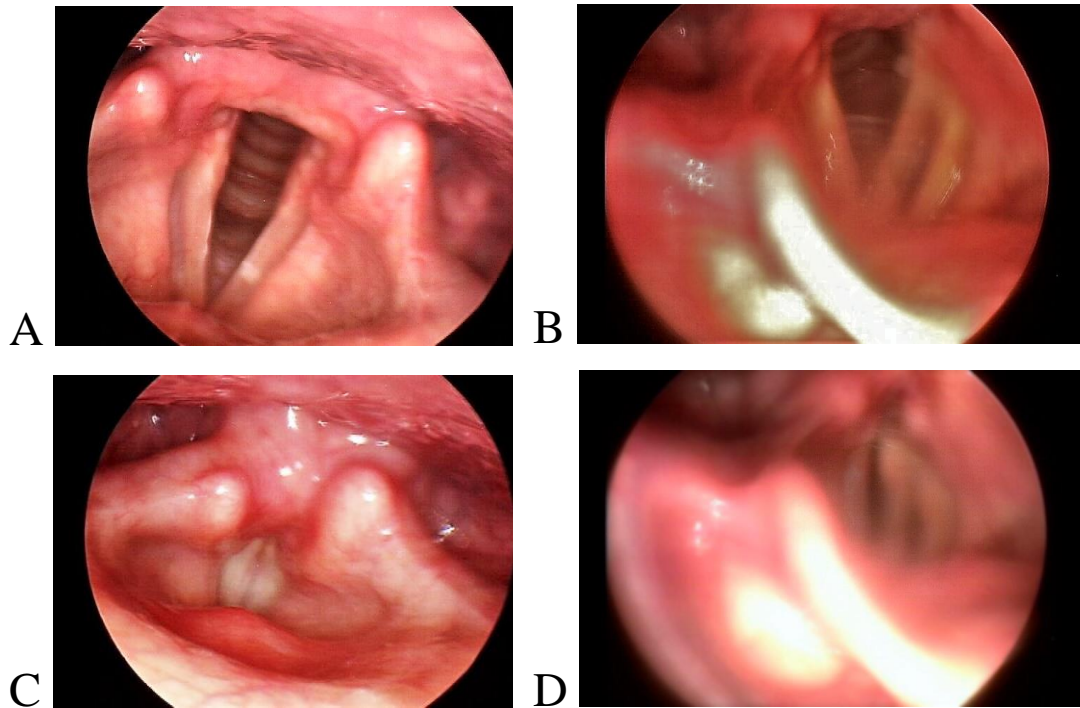


Figure 3.2 Vocal folds of male participants. Shown in abducted and adducted position. **A:** Abducted vocal folds male without CF. **B:** Abducted vocal folds of male with CF, notice the swollen arytenoids and structural changes. **C:** Adducted vocal folds of male without CF. **D:** Adducted vocal folds of male with CF; note the thickness of the vocal folds as well as incomplete glottal closure.

Aerodynamic and Quantitative Vocal Parameters

Female voice. The CF patient demonstrated differences in many of the quantitative parameters that were measured. The female patient with CF showed a marked decrease in the parameters of MPT, F_0 , percent of jitter and RAP. Additionally, the female CF patient showed higher numbers in the areas of S/Z ratio, shimmer, and noise-to-harmonic ratio (NHR). The CF patient displays vocal parameters that are considered to be outside the range of normal in nearly all that were examined. The following vocal qualities were measured to be two standard deviations (SD) from the mean: F_0 , shimmer, and NHR. These values are displayed in a comparative layout in Table 3.1.

| | Female Norms* | Non-CF Female | CF Female |
|----------------------|----------------------|----------------------|------------------|
| Age (years) | | 23 | 24 |
| s/z ratio | 0.8-1.2 | 0.85 | 1.167 |
| MPT (seconds) | 20 (5) | 26 | 18 |
| Fo (hertz) | 244 (17.45) | 295 | 192 |
| Jitter% | 0.633 (0.351) | 0.878 | 0.494 |
| RAP% | 0.378 (0.214) | 0.545 | 0.276 |
| Shimmer dB | 0.176 (0.071) | 0.197 | 0.443 |
| Shimmer% | 2.00 (0.791) | 2.26 | 4.99 |
| NHR | 0.112 (0.009) | 0.097 | 0.141 |

Table 3.1. Female vocal parameters. Vocal parameters of female participants compared to expected vocal norms.

*Norms reported for females age 20-30 years. Standard deviation (SD) reported in parentheses.

Male voice. The quantitative measurements for the male patients revealed less differences than the female measures between the CF and non-CF patients. The male patient with CF showed a minor decrease in the parameters of MPT and Fo. The remaining measurements were higher than the non-CF male counterpart. The most notable differences were revealed in the amount of perturbation in the CF participant. The CF patient's measured shimmer values are more than three SD from the mean. Exact values for each of these vocal attribute are displayed in a comparative layout in Table 3.2.

| | Male Norms * | Non-CF Male | CF Male |
|----------------------|---------------------|--------------------|----------------|
| Age (years) | 20-30 | 26 | 29 |
| s/z ratio | 0.8-1.3 | 0.956 | 0.933 |
| MPT (seconds) | 30 (5) | 38 | 26 |
| Fo (hertz) | 145 (23.406) | 121 | 111 |
| Jitter% | 0.59 (0.535) | 0.223 | 1.61 |
| RAP% | 0.345 (0.333) | 0.108 | 0.969 |
| Shimmer dB | 0.219 (0.085) | 0.217 | 0.86 |
| Shimmer% | 2.52 (0.997) | 2.588 | 10.01 |
| NHR | 0.122 (0.014) | 0.098 | 0.143 |

Table 3.2. Male vocal parameters. Vocal parameters of male participants compared to expected vocal norms.

* Norms reported for males age 20-30 years. Standard deviation (SD) reported in parentheses.

Perceptual Self-assessment of Voice

Upon review of each person’s self-assessment, no significant factors stand out. The two CF patients perceived themselves to have some qualities that they did not consider to be “normal.” Perceptually, the female participant rated the following qualities to exist mildly (rating of 1): hoarseness, huskiness, and low pitch. She rated moderate (2) in the restricted pitch quality. In addition, she rated herself to have phonation breaks as well as fluctuations in overall vocal quality. Her overall perceptual rating of vocal quality was a 1, meaning mildly out of normal.

The male participant perceived his voice as being relatively normal. He gave a mild rating of 1 in the areas of high pitch and fast rate. A moderate rating was also given in the category labeled “too loud.” Overall, he rated a zero, meaning he perceived himself as having a relatively normal voice.

CHAPTER IV

DISCUSSION

Our results show that individuals living with CF have some significant differences in both laryngeal structures, as well as quantitative vocal parameters. To our knowledge, this area of research has not yet been explored in detail within the United States, therefore allowing for this purely descriptive study. The descriptions given are highly suggestive of possible dysphonia in CF patients, and help lay the groundwork for further studies to be conducted.

In the objective measures, a significant difference is noted when comparing the CF patients to those without CF in the measurement of MPT. Lower MPT is typically indicative of a compromised respiratory system, meaning there is not enough breath support for the individual to sustain voice for the expected length of time (Boone et al., 2014). Given the nature of cystic fibrosis and the severe adverse effects it has upon an individual's lung function, a decrease in MPT is not surprising. However, even while the CF patients experience a lower MPT than the non-CF, the times of 18 and 26 seconds still fall within average range for females and males, respectively.

The second notable difference is seen in the Fo of the female patient with CF when compared to her non-CF counterpart, as well as the expected Fo for females. The subject presented with a Fo of 192 Hz, 52 Hz below that of the expected 244 Hz. A decreased fundamental frequency perceptually correlates to a low pitch when the individual is speaking. As mentioned previously, the Fo is the number of vibratory cycles

completed in one second during phonation. The lower the number of cycles, the lower the person's pitch will be. A low habitual pitch is symptomatic of the vocal folds' inability to move properly. Slowed movements are caused by decreased pliability, or vocal fold stiffness.

Stiffness in the laryngeal tissue could be caused by many things, including vocal fold scarring, which is caused by phonotrauma, or vocal abuse, and is typically indicative of possible reduction in pitch range and a decrease in vocal fold elasticity. In the case of a patient with CF, we would expect to see some vocal stiffness due to the excessive chronic coughing. In addition, inhaled medications could cause dehydration of the vocal folds, which would then result in the slowed rate of vibration and roughness upon vibration.

The last most notable variation of the acoustic measures exists when comparing the amount of perturbation in the participants' voices. Both the female and male CF participants have significantly higher levels of vocal perturbation, particularly in the amount of shimmer that exists. The male CF patient has shimmer values nearly five times that of the expected and the female nearly twice the amount of shimmer than typically expected. Excess amount of shimmer correlates with the perception of vocal hoarseness. Research states that excess shimmer can have biomechanical causes. Biomechanical etiology is a term meaning it was caused by misuse of a particular mechanism within the body, in this case we are talking about phonotrauma to the larynx and vocal folds. Again, given the respiratory distress, excessive coughing and possible GERD, it would be expected that a patient with CF may have this excess amount of vocal perturbation.

In addition to the measured vocal qualities, the participants with CF showed marked differences in their laryngeal structures and functions. These difference could

have several different etiologies behind them. The female patient showed significant swelling and redness in the entire laryngeal cavity, particularly in the arytenoid cartilages. These types of changes typically result from reflux disease. The participant reported during data collection that she had been diagnosed with GERD and only recently began taking medication to treat it. The posterior pharyngeal wall presented in a red, bumpy manner, and the arytenoid cartilages appeared similarly. These findings are consistent with previous research as well as subject report. Additionally, she presented with thickening of the vocal folds and a slowed mucosal wave. These changes are consistent with research findings involving trauma to the laryngeal area. However, the vibratory motion of the arytenoid cartilages is an anomaly that is rarely seen in humans and cannot, at this time, be definitively connected to any factors related to CF.

Likewise, the male with CF had minor swelling and inflammation of the laryngeal tissue, as well as thickening of the vocal folds. Report from this participant revealed that he had been intubated approximately one year prior to data collection. He also reported that he had a nasogastric (NG) tube placed following surgery. Due to these reported complications, the presence of a posterior lesion on his left vocal fold is neither surprising nor of major concern. It is believed that this lesion has not diminished over time due to his bouts of excessive coughing, however, only a time-lapse trial would definitively prove such hypotheses. The presence of a “split vocal fold” is a risk faced by those who are intubated at some point. Due to the subject’s reported intubation and subsequent complications, this structural change cannot be linked directly to CF at this time.

Additionally, research has stated that some medications can cause changes to the vocal fold tissue. Patients with CF are typically placed on an intense treatment regimen that often includes use of aerosolized medications to be used two or three times daily. These medications may play a role in the tissue changes seen in the subjects of this study. The most researched of these aerosols is hypertonic saline. While this added routine has proven helpful for alleviating symptoms of CF, it may be creating the structural changes seen in this study. However, given the small case study design, we cannot completely generalize the possible cause of structural changes to the entire population of patients with CF.

Conclusion

We have shown in this case study that individuals living with cystic fibrosis demonstrate changes in vocal quality as well as in the laryngeal structures. The changes seen are comparable to individuals who are considered to have a diagnosis of dysphonia. Consistent with Lorenzo et al. (2014), our findings revealed more pronounced alterations in the female voice than in the male, with the exception of the shimmer in the male voice. The CF-related changes to laryngeal tissue that were hypothesized in the beginning of this study were demonstrated very clearly in the female patient. It cannot be said with any measure of certainty, that the laryngeal and aerodynamic changes in the CF participants are directly due to CF. Since individuals with CF are routinely on various medications for respiratory difficulties, it may also be speculated that the changes may be directly related to the medication rather than to the disease itself. Whatever the case, the results suggest further investigation of the vocal parameters in individuals with CF is necessary. The

results of this study also suggest that patients with CF may benefit, to an extent, from voice therapy.

Limitations and Future Research

While our findings were substantial, some limitations exist that impede a definitive conclusion. The most obvious limitation to this study was the small sample size. Unfortunately, the ability to recruit patients with CF diminishes as the target age increases. Many CF patients are already participating in research studies for medications that will result in direct benefit. In order to remain in those studies, they may be prevented from participating in any other sort of extraneous medical procedures, such as videostroboscopy, due to the risk of exposure to infections because of an already compromised immune system.

Future research would benefit from an increase in the number of participants. Likewise, screening individuals before data collection in order to get a full report on current medications would allow for a cause-effect study to take place. If a certain medication is being used by one group, but not another, there may be further information to gain simply from differentiating the groups taking a potentially damaging medication. Furthermore, the wide variations that exist across patients with CF make it difficult to confirm that abnormal voice or structural changes are a direct result for all patients. There is always the possibility that the dysphonic qualities seen in one patient may not exist in a second patient of the exact same age with the exact same diagnosis. This is the challenge in conducting research within the world of medicine.

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APPENDIX

APPENDIX A



Instructions from the investigator to the participant for measuring S/Z/ ratio:

I need you to take a breath and say “sss” for as long as you can. Next I need you to take a breath and say “zzz” for as long as you can. We are going to complete this cycle a total of three times. You will have time to rest between each cycle.

Instructions from the investigator to the participant for measuring MPT:

I need you to take a breath and say ‘ah’ for as long as you can. You are going to complete this task a total of three times. You will have time to rest between each task.

Instructions from the investigator to the participant for use of the *Visi-Pitch*TM:

You are going to stand with the microphone approximately two inches from your mouth. When I tell you to go, you will say “ah” in your normal speaking voice until I tell you to stop. It will only be a couple of seconds. We are going to do this twice.

Instructions from the investigator to the participant for videostroboscopy:

I am going to spray a light topical numbing spray into the back of your mouth. We will wait approximately ten minutes for it to take affect before beginning with the scope. I need you to relax and stick your tongue out. I will slide the scope back in your mouth along the base of your tongue. Once the camera is where it is needed, I will ask you to say either “ah” or “ee.”

APPENDIX B



Effects of Cystic Fibrosis on Vocal Fold Function
Informed Consent Form

Dear Participant:

We are Dr. Violet Cox and Veronica Smitley, faculty member and graduate student, respectively, in the Department of Speech and Hearing at Cleveland State University. We would like you to participate in a research study. The study is about vocal fold function in people with cystic fibrosis (CF). We will look at vocal folds during production of a vowel sound. We will use a tiny camera and light source placed over your tongue. We hope that this study will help to contribute to improving voice quality for people with CF.

The data collected will be confidential. Your name and other identifying information will not be linked with the data collected. Every effort will be exerted to maintain privacy. Results of this study will not be traced back to you.

You will be tested at the Cleveland State University Voice and Swallowing lab located in CIM 211. We will provide you with directions to the University. Participation in this study is voluntary. You may withdraw at any time. There is no reward for participating, or consequence for not participating. Outside of risks associated with those of daily living, there is a very slight possibility that you may experience gagging during the oral examination. To reduce this gag a light numbing spray may be applied to the back of your throat. If you are allergic to nova-caine routinely used by your dentist then this spray will not be used. You will not have to participate in this study. This study will take about 60 minutes to complete.

For further information regarding this research please contact Dr. Violet Cox at (216) 687-6909, email: v.cox@csuohio.edu. If you have any questions about your rights as a research participant you may contact the Cleveland State University Institutional Review Board at (216)687-3630.

There are two copies of this letter. After signing them, keep one copy for your records and return the other copy to me. I thank you in advance for your cooperation and support. Please indicate your agreement to participate by signing below.

“I am 18 years or older and have read and understood this consent form and agree to participate.”

Signature: _____

Name: _____ (Please Print)

Date: _____

APPENDIX C



BRIEF SCREENING TOOL

AGE _____

GENDER: [] Male [] female


Answer all questions that follow:

1. Have you ever been given Nova-caine by your dentist? **Yes** **No**
2. Are you allergic to Nova-caine? **Yes** **No**
3. Are you a smoker? **Yes** **No**
4. Do you have a history of any chronic respiratory illness? **Yes** **No**
5. Are you currently on medications? **Yes** **No**. If yes list all medications below.

6. Are you on oxygen? **Yes** **No**. If yes, state how many liters.

7. Have you ever had a history of a voice disorder? **Yes** **No**

APPENDIX D

| SCREENING ASSESSMENT | |  | | | |
|-----------------------------|-------------------------|---|------|-------------|-----|
| Name: | | dob: | | | |
| Address: | | | | | |
| Assessor: | | Screening date: | | | |
| | | normal | mild | mod | sev |
| QUALITY | breathy | 0 | 1 | 2 | 3 |
| | hoarse | 0 | 1 | 2 | 3 |
| | husky | 0 | 1 | 2 | 3 |
| | whispered | 0 | 1 | 2 | 3 |
| PITCH | too high | 0 | 1 | 2 | 3 |
| | too low | 0 | 1 | 2 | 3 |
| PITCH RANGE | restricted | 0 | 1 | 2 | 3 |
| LOUDNESS | too loud | 0 | 1 | 2 | 3 |
| | too quiet | 0 | 1 | 2 | 3 |
| NASAL RESONANCE | hypernasal | 0 | 1 | 2 | 3 |
| | hyponasal | 0 | 1 | 2 | 3 |
| ORAL RESONANCE | throaty | 0 | 1 | 2 | 3 |
| RATE | fast | 0 | 1 | 2 | 3 |
| | slow | 0 | 1 | 2 | 3 |
| PROSODY | inadequate variability | 0 | 1 | 2 | 3 |
| | excessive variability | 0 | 1 | 2 | 3 |
| AERODYNAMICS | S/Z ratio | | | | |
| | MPT | (seconds) | | | |
| RELATED OBSERVATIONS | glottal fry | present | | not present | |
| | diplophonia | present | | not present | |
| | phonation breaks | present | | not present | |
| | fluctuations in quality | present | | not present | |
| CLIENT PERCEPTION | (self-rating scale) | 0 | 1 | 2 | 3 |

(Severity: 1 = mild deviation 3 = moderate deviation 5 = severe deviation)