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Dysphagia in Chronic Obstructive Pulmonary Disease

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1. Introduction

Swallowing is an array of synergistic interdependent movements initiated by complex set of sensory inputs that generate pressures and forces to propel ingested materials through the upper aerodigestive tract and simultaneously protect the upper airway. As seen in Figure 1, the oropharynx is common to both the swallowing and respiratory processes. This functional conflict, therefore, must require fine coordination at the neuronal level to ensure that the peripheral structures produce the intended target behaviour [1].

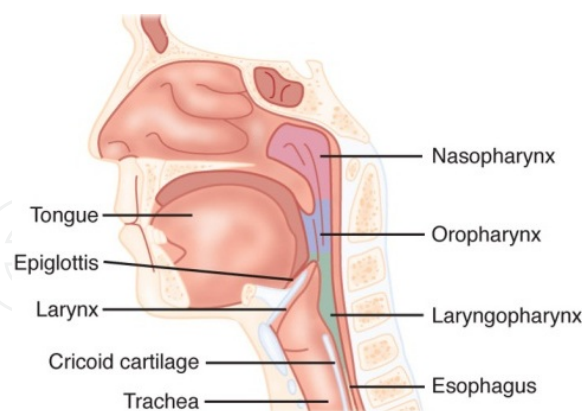


Figure 1. Simplified view of the structures related to swallowing and breathing. Note that the oropharynx is common to both the swallowing and respiratory processes.

Swallowing and breathing are closely related, and synergy of structures is needed for airway protection during the swallowing process to prevent the aspiration of food contents and thus prevent pulmonary complications. The swallowing apnea is described as an important

mechanism of airway protection. This may be altered in patients who have lung diseases such as chronic obstructive pulmonary disease (COPD) [2, 3]. COPD is a preventable and treatable disease characterized by progressive limitation of airflow that is usually associated with an abnormal inflammatory response of the lungs to noxious particles and gases [4, 5]. COPD is a major public health problem with high and increasing prevalence [4]. According to World Health Organization (WHO) estimates, 80 million people have moderate to severe COPD [6]. Pulmonary changes can be a detrimental factor to coordination between breathing and swallowing [2, 3, 7, 8]. Swallowing apnea requires a reorganization of the breathing pattern when swallowing. This can be limited by the typical respiratory changes observed in patients with COPD [9].

This chapter discusses the history and current state of our knowledge concerning dysphagia in chronic obstructive pulmonary disease. We also describe the development of instrumentation for the analysis of the swallowing apnea and preliminary results of this analysis in individuals with COPD. The main topics covered by this review will be as follows:

- First we will provide a brief description of dysphagia and the interaction between swallowing and breathing in section 2 and 3, respectively;
- In section 4, we describe the principles of the chronic obstructive pulmonary disease;
- Next, we describe the main results presented in the literature concerning the dysphagia in COPD;
- The development of instrumentation for analysis of swallowing apnea, performed in our laboratory, is presented in section 5;
- Preliminary results of the changes of swallowing apnea in individuals with COPD are described in section 6;
- Finally, we conclude by examining the potential role of the routine analysis of swallowing disorders in COPD in the clinical arena.

2. Dysphagia

Swallowing is a complex sensorimotor function that depends on the integrity of the mechanoreceptors and chemoreceptors for the sequential stimulation and inhibition of the upper aerodigestive tract; this coordinated process transports foods and liquids through the mouth and pharynx to the esophagus [10] and simultaneously protect the upper airway [1].

Biomechanical events that contribute to secure bolus transport and airway protective mechanisms include: closure of the introitus to the trachea by vocal cord adduction, approximation of the adducted arytenoids to close the laryngeal aditus, epiglottal descent, antero-superior displacement of the larynx away from the path of the bolus, and opening of the upper oesophageal sphincter [11]. During swallowing, the closure of the larynx and the respiratory pause during swallowing are vital protective mechanisms that prevent aspiration [12]. This phenomena is describes schematically in Figure 2.

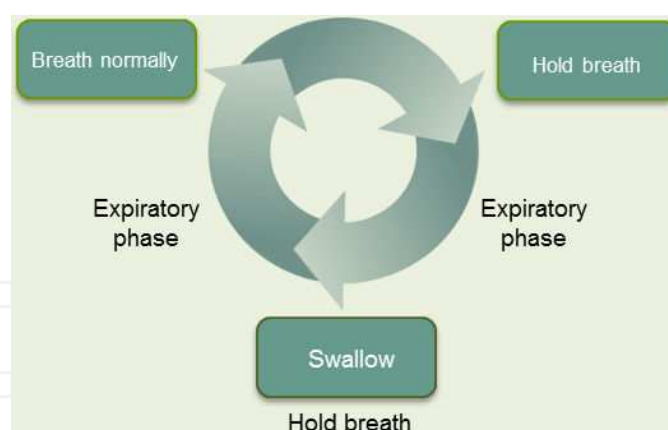


Figure 2. Simplified description of the usual swallowing pattern in healthy adults. Swallowing initiates during the expiratory phase of the breathing cycle. Swallowing interrupts exhalation (swallow apnea), and once the swallow has been completed, breathing resumes with exhalation.

Disordered swallowing, or dysphagia, can develop from lesions in certain areas of the cortex and brainstem that control the swallowing function, or damage to the associated cranial nerves. It is a common problem observed in patients with stroke and head injury [13]. Dysphagia affects at least 12% of patients in acute care hospitals and more than 50% of those in chronic care settings [14]. The presence of dysphagia is associated with aspiration induced chest infections and increases the risk of serious respiratory consequences such as pneumonia. Identification of the patient at risk of aspiration is important from a clinical view point. Due to the risk of aspiration, a significant number of dysphagic patients are fed with a nasogastric tube and /or intravenous fluids [13]. Dysphagia can significantly impact a person's quality of life as well as their health status [15].

3. Coordination of breathing and swallowing

Recent findings have delineated single neurons within medullary networks that demonstrate multifunctionality in the control of both the respiratory and swallowing behaviours [16]. The breathing cycle is not simply repressed during swallowing; it is substituted by a different well-controlled behaviour pattern. Variations in the bolus volume and viscosity characteristics will interfere with the breathing stop time duration [9, 17, 18]. The consistency of these observations has led to speculation that the precise coordination of breathing and swallowing may be an important mechanism to prevent aspiration [19]. The effect of bolus volume influences the swallowed-associated respiratory cycle [9, 20], and this observation notes that these neurological interference engrams may contribute to dyspnoea during meals in some patients with pulmonary disease.

Deglutition apnea is described as an important mechanism of airway protection. It consists of a respiratory pause that occurs involuntarily during each swallow, when the respiratory muscles are centrally inhibited and the airway closes. Breathing ceases just before and during the entire pharyngeal phase of deglutition [3]. The duration of this brief swallow apnea ranges

between 1 and 2 seconds in liquid swallows in most healthy adults, but there is a variability in the timing depending on the swallow task and bolus viscosity [1, 19, 21, 22].

Deglutition apnea occurs mainly during expiration and is followed by expiration [1, 2, 9, 18-25]. This pattern occurs more often in the presence of a bolus [9, 20]. A different pattern of this coordination of breathing and swallowing, for example, inspiration after swallowing, may increase the risk of aspiration and place patients at an airway protective disadvantage [1].

A modification to the stable respiratory-swallow occurs during advanced ageing. In healthy elderly aged individuals, the duration of deglutition is higher than in young groups [1, 18]. Studies have shown a greater occurrence of liquid swallow initiated and followed by the inspiratory phase of respiration [22, 26]. These pattern changes have not been associated with aspiration, however, they may cause implications on airway protection or bolus clearance in patients with already compromised swallowing function secondary to diseases and other conditions during old age, head and neck cancer, stroke and chronic obstructive pulmonary disease [1].

4. Chronic obstructive pulmonary disease

COPD is a preventable and treatable disease characterized by partially reversible airflow limitation [27, 28]. The limitation is often progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, especially cigarette smoke [27]. COPD increases mortality in worldwide each year, causing socio-economic damage. The total deaths from COPD are projected to increase by 30% over the next 10 years, unless urgent measures are taken to reduce the risk factors, particularly tobacco use. Estimates indicate that by 2030, COPD may become the third leading cause of death [6].

The COPD is characterized by the presence of chronic bronchitis, obstructive bronchiolitis and emphysema [27, 28]. Chronic bronchitis is inflammation of the airways which deliver air to the lungs. This can lead to an increase in mucus production and consequent narrowing of the bronchi (Figure 3). In emphysema, the tissue that surrounds the smaller airways is damaged and air becomes trapped in the alveoli. These air sacs become overstretched and unable to function correctly causing shortness of breath. The disease process is directly related to an inflammatory response of the lungs, triggering the destruction of the lung parenchyma. Such changes are responsible for airflow limitation and air trapping. [27]. Pathological changes occur in four different regions of the lung: the larger calibre airway, the peripheral airways, the lung parenchyma and the pulmonary vasculature [27-29]. In the larger calibre airways, structural changes occur in the goblet cells and submucosal glands causing mucus hypersecretion and squamous metaplasia, as shown in Figure 3 [27-29].

In the peripheral airways (<2 mm diameter), we observed thickening of the airway wall, peribronchial fibrosis, exudate, narrowing of the airways (obstructive bronchiolitis) and increased inflammatory response. In the lung parenchyma, the structural changes involved destruction of the alveolar wall, apoptosis of epithelial cells and emphysema [27-29]. The main characteristic of COPD is airflow obstruction, which is not fully reversible. Spirometry is the gold standard technique used to assess this obstruction [28, 29].

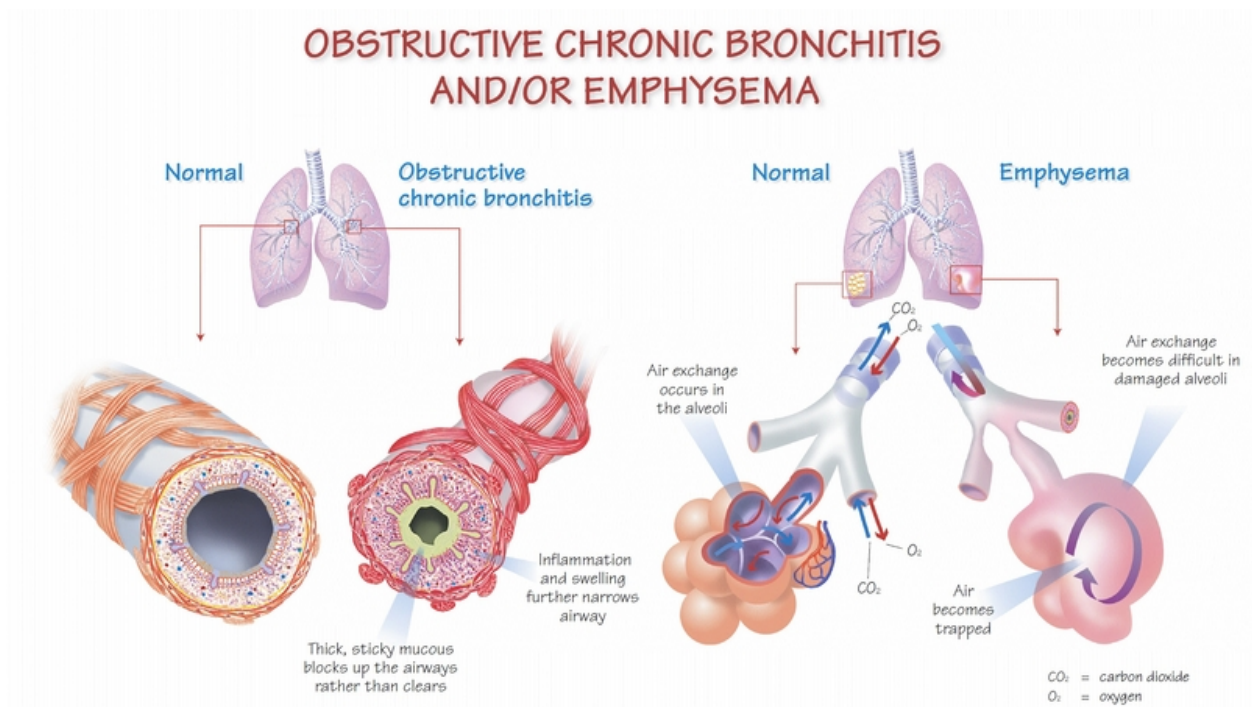


Figure 3. On the left, the effect of chronic bronchitis in which the inflammation of the airways can lead to an increase in mucus production and consequent narrowing of the bronchi. In emphysema (right), the tissue that surrounds the smaller airways is damaged and air becomes trapped in the alveoli. These air sacs become overstretched and unable to function correctly causing shortness of breath. (Source: <http://www.livingwellwithcopd.com/en/what-is-copd.html>).

The coordination between breathing and swallowing can be severely disrupted in patients with COPD due to their reduced ventilatory capacity. COPD also has the potential to disrupt the coordination of breathing and swallowing because of tachypnoea, an increased tendency to swallow during inspiration, reduced duration of apnea and changes in the mechanics of swallowing. The increase in the elastic and resistive respiratory loads, typical of these patients, is associated with a rapid shallow pattern of breathing that may increase the risk of aspiration [8].

5. Dysphagia in chronic obstructive pulmonary disease

This section focuses on a historically organized review of the main studies presented in the literature. To date, relatively little research has been conducted concerning dysphagia and other swallowing disorders in patients with COPD. The first studies begin in the 1980s, and few studies were conducted until the end of the past millennium. A significant increase was observed in this research area in the 2000s and 2010s.

5.1. The first studies in the 1980s and 1990s

The paper by Coelho [30] is believed to be the first that specifically deals with dysphagia in patients with COPD. The author studied 14 patients with a primary diagnosis of COPD. All

of the subjects but one had tracheostomy tubes, and five were ventilator-dependent. Bedside evaluation was performed to assess the oral phase of the swallow and videofluoroscopy was used to examine the pharyngeal phase. Subjects were presented with three consistencies of materials to swallow: liquid, paste and crackers coated with barium. The author observed that ten of the 14 patients demonstrated some degree of dysphagia. The COPD patients tired rapidly and often needed to rest in the midst of chewing foods. Their propensity for fatiguing rapidly is consistent with their performance on other basic activities of daily living. Consistent aspiration was noted in three of these patients and was attributed to a delayed swallowing reflex, decreased pharyngeal peristalsis and cricopharyngeal/oesophageal constriction. Dysfunctional swallowing with no aspiration was observed in 7 of the 14 COPD patients. These patients had difficulties with bolus formation and control, delayed swallowing reflexes and problems with lingual and pharyngeal peristalsis.

In the beginning of the 1990s, Stein et al. [31] performed videofluoroscopy in 25 patients with COPD and identified cricopharyngeal achalasia in 21 of them. In 17 patients, this was judged to be severe, and all were found to have some degree of symptomatic dysphagia. Ten patients had surgical correction and eight had improved pulmonary symptoms. The authors discussed that cricopharyngeal dysfunction may precede airway obstruction and contribute to subsequent progression and exacerbation of airway abnormalities. Alternatively, cricopharyngeal dysfunction may be secondary to COPD because it may increase gastroesophageal reflux by flattening the diaphragm; this reflux leads to cricopharyngeal achalasia, a mechanism that protects the larynx from aspiration of gastric acid.

Shaker et al. [32] used concurrent respirography and submental surface electromyography to study the effects of ageing, tachypnea and bolus volume on the coordination of swallowing in patients with chronic obstructive pulmonary disease. Three groups were studied: 10 young healthy volunteers aged between 18 and 34 years, 11 healthy elderly volunteers aged between 63 and 83 years and 22 patients with COPD aged between 46 and 77 years. Dry and water swallows were observed at rest and during exercise (increased respiratory rate). A total of 2,331 analysable swallows were recorded and analysed for: 1) the respiratory phase in which the swallows occurred; 2) the respiratory phase during which respiration was resumed after swallowing; 3) and the duration of swallow-induced apnea. The author observed that at rest, in the young volunteers the majority of deglutitions were coupled with the expiratory phase of swallowing. The elderly generally initiated swallowing more often in the inspiratory phase compared with the young. Compared with the basal state, the advanced COPD patients swallowed significantly more in the inspiratory phase and resumed their respiration significantly more with inspiration. The reasons for this alteration were not determined; however, the authors noted that derangement in the acid-base balance present in COPD patients may conceivably influence the central coordination of the deglutitive centres. The results of this study indicated that tachypnea, ageing, bolus volume and COPD modify the coordination between deglutition and the phases of continuous respiration.

5.2. Studies performed in the 2000s

One of the first studies published in this decade was performed by Good-Fratturelli et al. [33]. It consisted of a retrospective study that described the swallows of 78 patients with a COPD

diagnosis who were seen for videofluoroscopy in 3 years and determined the prevalence of dysphagia in these patients. Patients were given a bolus containing barium in thin and thick liquid, puree, paste and cookie consistencies. Of these patients, 85% were found to have some degree of dysphagia. Bilateral vallecular stasis, bilateral pyriform sinus stasis, oral stasis and delayed pharyngeal swallow response were reported in 60% of the COPD patients. Aspiration was noticed in 42% and laryngeal penetration in 28% of these patients, which were evidenced substantially more with thin and thick liquids compared to semi-solid or solid textures. The authors suggested that the compromised respiratory system, such as the absence of a cough response, or use of quiet but ineffective coughs, may reflect their lack of respiratory strength to clear the airway, and consequently, explains the high prevalence of laryngeal penetration, the inability to expel material from the airway, and aspiration.

Martin-Harris [34] based a study on relevant articles and described the optimal patterns of care and care consideration in patients with COPD and swallowing disorders. The author emphasized that it has been historically reported that the laryngeal cartilage in patients with COPD is often seated more deeply in the neck compared with healthy adults. The lowered basal position of the larynx results in increased distance that the larynx must ascend to achieve maximal closure and facilitate pharyngoesophageal segment (PES) opening. Some patients have oral impairments such as slow bolus preparation and oral bolus transport, and these situations are consistent with their motor behavior in activities of daily living. The labored tongue movement and reduction in oropharyngeal sensation may also contribute to delayed initiation of the pharyngeal swallow. Patients attempting to maintain breathing activity as long as possible before the obligatory apneic pause, and trying to re-establish respiration quickly, while eating semisolids and solids, may present channeling of a bolus to the level of the pyriform sinuses and premature opening of the larynx during the latter stages of swallow. The habitual and sometimes necessary mouth-breathing characteristics of COPD patients, may lead to excessive dryness and adherence of thick and dry materials to the oropharyngeal tissues, with potential post-swallow aspiration.

Oxygen treatments and medications may also confound the problem with xerostomia. The authors suggested an eating and swallowing guideline to reduce the incidence of penetration/aspiration: small and frequent meals; appetite enhancement; environmental control; promotion of relaxation; pacing intake at mealtime; optimizing bolus volume and texture; avoiding sequential swallowing of large volumes of liquid; two swallows per bolus and reflux precautions.

Mokhlesi et al. [35] studied 20 patients with COPD and 20 healthy subjects matched for age and gender. The protocol consisted of swallowing two boluses each of 3 ml and 5 ml of barium liquid, drinking barium liquid from a cup, and swallowing 3 ml barium paste while performing videofluoroscopy. Of these patients, 20% reported dysphagia. The data from the study demonstrate that COPD is associated with abnormal swallowing physiology, including frequent spontaneous and protective manoeuvres and decreased laryngeal elevation during swallowing. A shorter duration of cricopharyngeal opening on three or four bolus types was also observed.

In a later work, Mokhlesi [36] noted that because there is a complex anatomical and functional relationship between the upper gastrointestinal tract and the respiratory tract, it is important

to elucidate if this harmonic relationship is disrupted when pulmonary function is compromised, as found in COPD. The aim of the author's article was to review the limited data concerning these important associations and to reinforce the need for additional clinical research in this area. A precise coordination of swallowing and respiration are necessary to avoid dysphagia and aspiration. The mechanisms of coordination between swallowing and airway protective reflexes have precise central and peripheral nervous system integration. COPD may interfere with the precise and complex coordination between swallowing and respiration. The aetiology of the exacerbation of COPD is often unclear. On many occasions, clinicians fail to demonstrate the conditions that are commonly known to cause COPD exacerbation, such as viral or bacterial infections, pulmonary embolism, pneumothorax or myocardial ischaemia. Tracheal aspiration has been suggested to be a cause of exacerbation in some patients with COPD, but there are few data supporting this relationship. In healthy individuals, swallowing interrupts the expiratory phase of respiration and induces an apneic pause of approximately 1 second followed by resumption of respiration with expiration. [21] [19]. However, patients with exacerbations of COPD swallow more often by interrupting the inspiratory phase and resume respiration significantly more with inspiration [32]. In a study of patients with severe COPD who experienced frequent exacerbations, cricopharyngeal dysfunction was diagnosed in 21 or 25 patients (84%). The majority had dysphagia, and eight patients who underwent cricopharyngeal myotomy had significant improvement in swallowing and a decrease in respiratory exacerbations [31]. In a retrospective study of 78 outpatient veterans with COPD referred for a videofluoroscopic swallow examination, the prevalence of dysphagia was 85%. Silent aspiration and laryngeal penetration were noted in 56% of patients. Patients with complaints of dysphagia or unexplained frequent exacerbation of COPD may benefit from detailed swallow evaluations and referral to a speech pathologist. The author (Mokhlesi, [36]) noted that further research was needed to evaluate the role of protective swallowing manoeuvres in stable COPD and their potential failure during acute COPD exacerbation. Additional studies should be performed to determine if occult aspiration is a cause or contributing factor to exacerbation of COPD and, conversely, whether patients with exacerbation are at even greater risk of aspiration.

The study by Kobayashi et al. [37] investigated 2 groups: the first was formed by 25 patients with COPD who had at least one exacerbation during the previous year, and the second group included 25 patients who were stable. They evaluated the swallow reflex by studying the latency of response to the onset of the swallowing action. It was injected 1ml of distilled water into the pharynx through a nasal catheter and the mean latent time of the swallowing reflex was significantly longer in the exacerbation group than in the stable group. Impairment of the swallow reflex was significantly associated with an exacerbation of COPD.

Gross et al. [3] elucidated the relationship between breathing and swallowing in patients with COPD during deglutition. In a prospective study with 25 patients with COPD and 25 healthy control subjects, swallows were analysed simultaneously by surface electromyographic measurements, respiratory inductance plethysmograph and nasal cannula. Patients were given portions of cookies and pudding. The data from that study demonstrated that participants with COPD swallowed the cookie (a bolus that requires mastication) during inhalation

significantly more often than normal subjects, and this pattern may increase the frequency of prandial aspiration. Post swallow inhalation occurred significantly more often in the COPD groups with the pudding texture when compared with control subjects. There was no difference in the duration of swallow apnea between the groups for either consistency. However, in the COPD group, the duration of swallow apnea of swallows that occurred during the inhalation phase was significantly longer for both food types. This prolongation could indicate the presence of a compensatory mechanism such as more time for recoil forces to generate higher swallow subglottic pressure or more time for the bolus to traverse the pharynx and enter the oesophagus.

Gross et al. [38] found that patients with stable moderate to severe COPD tend to swallow during inspiration and swallowing is often followed by inspiratory activity. Inspiration just before or just after a swallow increases the risk of inhaling pharyngeal contents. This may be caused because of the negative intrathoracic pressure. Fluoroscopic imaging of swallowing in patients with stable severe COPD and hyperinflation has shown reduced laryngeal elevation and a delayed pharyngeal response. The authors suggested that COPD is a significant risk factor for aspiration among nursing home residents. Alterations in respiratory rate and rhythm during exacerbations of COPD have been associated with an increased tendency for an inspiration-swallow-inspiration sequence when swallowing saliva spontaneously.

Ohta et al. [39] investigated the swallowing function before exacerbation of COPD when it was at a mild stage by performing the simple two-step swallowing provocation test (STS-SPT) and the repetitive saliva swallowing test (RSST). Sixty-four patients with COPD were divided into three groups: mild, moderate and severe. Fifteen healthy subjects were also recruited as a control group. In moderate to severe stages of COPD, the ratio of abnormal to normal swallowing patients estimated by the STS-SPT was higher than in the control group. In contrast, the RSST evaluated the ratio of abnormal to normal swallowing in patients at the mild stage of COPD as being higher than the control; this was also the case in the moderate and severe groups. This study suggests that both STS-SPT and the RSST can be used to evaluate swallowing dysfunction before the exacerbation of COPD occurs. It also suggests that the swallowing dysfunction in COPD may begin in the mild stage and, therefore, aspiration should be monitored from the mild stage in COPD patients. The RSST may be valid to evaluate swallowing at the mild stage.

5.3. Studies performed in the 2010s

Two studies were published in the beginning of this decade. Terada and collaborators [40] evaluated 67 patients with COPD and 19 age-matched controls, and observed that 23 of 86 subjects showed abnormal responses on the STS-SPT test. This behaviour was more frequent among subjects with COPD than controls. The swallowing abnormalities were associated with gastroesophageal reflux disease (GERD) symptoms, the existence of sputum bacteria, and serum C-reactive protein (CRP) levels in patients with COPD at the baseline and were related to an increased risk of frequent exacerbations.

As being part of educational sessions in a Pulmonary Rehabilitation Program, McKinstry et al. [41] discussed with COPD patients about normal swallowing and breathing, symptoms of dysphagia, consequences of aspiration and strategies to improve swallowing. Participants knowledge before and after these sessions was examined by a questionnaire. Of these, 383 patients with COPD underwent basic dysphagia screening and 104 were referred from screening for individual assessment and management of dysphagia. Participants were also asked to complete the standardized dysphagia-specific quality-of-life questionnaire (SWAL-QOL) survey, a dysphagia-specific quality-of-life questionnaire. Statistically significant improvement was found in participant's pre and post questionnaire results on knowledge of dysphagia and COPD. It was found that 27% of participants either exhibited or reported symptoms of dysphagia. Statistically significant improvement was found on 3 subscales of SWAL-QOL 3 months following initiation of treatment. The author concludes that dysphagia management and education of patients in pulmonary rehabilitation programs may contribute towards early identification and self-management of dysphagia and may enhance swallowing-related quality of life.

Cvejic et.al [2] studied 16 patients with COPD and 15 healthy control subjects that underwent videofluoroscopy while swallowing graduated volumes of barium liquid (5, 10 and 20 ml) and 100 ml (continuous cup drinking). Respiratory airflow was assessed using a combination of intranasal pressure measurement and respiratory inductive plethysmography. Electromyography was used to examine swallow timing. Transcutaneous oximetry was used to monitor oxygen saturation. After 36 months, respiratory health status was evaluated by telephone interview. The data of the study demonstrated that scores grading penetration/aspiration were significantly higher in patients with COPD and occurred almost exclusively during the 100 ml liquid swallow. Increased respiratory rates at rest were noted in 3/6 subjects in the COPD group with penetration/aspiration. Transient desaturation was noted after 100 ml liquid swallow in 13 subjects with COPD. The dominant respiratory-swallow pattern associated with smaller barium volumes was expiration-swallow-expiration. Swallowing of 100 ml elicited a different response. In COPD subjects, inspiration-swallow-expiration was observed in 60% compared to 20% of controls. All subjects who experienced penetration/aspiration used this pattern of breathing. The apnea intervals during 100 ml swallows were not different in COPD and controls. Predictive factors linked to impaired swallowing were reduced hyoid elevation and post-swallow pharyngeal residue. All subjects were assessed by telephone interview, and patients with COPD and penetration/aspiration appeared to have more serious adverse outcomes. The authors conclude that normal protective mechanisms during swallowing may be compromised in COPD and that penetration/aspiration may take place when drinking relatively large volumes of fluid.

Singh et al. [8] noted that lung disease including COPD has the potential to disrupt the coordination of breathing and swallowing. The authors suggest that it may happen because of tachypnoea, an increased tendency to swallow during inspiration, a reduced duration of apnoea and changes in the mechanics of swallowing.

The study of Cvejic et al. [2] provided convincing evidence of aspiration during swallowing in patients with stable moderate COPD. In this study, patients with COPD favoured an

inspiration-swallow-expiration pattern with larger boluses. Penetration or aspiration was associated with tachypnoea, reduced hyoid elevation, post-swallow pharyngeal residue and a trend towards increased hospitalizations and mortality over 36 months. The Editorial written by Singh [8] pointed out that these findings are important because aspiration may contribute to precipitating or aggravating exacerbations, and increase the morbidity in patient with COPD. Exacerbations of COPD are a major cause of reduced quality of life, reduced activities of daily living and increased health-care costs hospital admission and readmission, and morbidity and mortality [8].

Based on the responses from a self-perception questionnaire, Chaves et al. [7] identified symptoms of dysphagia by comparing 35 patients with COPD and 35 healthy volunteers. There were significant differences between the two groups, and pharyngeal symptoms, airway protection, oesophageal symptoms, history of pneumonia and nutritional symptoms were more common in participants with COPD.

Kobayashi et al. [42] noted that impairment of swallowing and cough reflexes leads to aspiration of oropharyngeal or gastric secretions and their bacteria, resulting in tracheobronchial inflammation and infection. Thus, impairment of these reflexes presents a potential risk factor for COPD exacerbations. The authors suggested that angiotensin-converting enzyme inhibitors can improve the swallowing reflex and protect against aspiration.

Tsuzuki et al. [43] studied sixty-five individuals with COPD during a 1-year follow-up. The repetitive saliva-swallowing test (RSST) and modified water-swallow test (MWST) were performed. The RSST counts the number of dry swallows in 30 seconds while sitting; fewer than three dry swallows was determined to be abnormal. Patients with abnormal RSST results had a significantly greater prevalence of exacerbations during the 1-year follow-up. Cold water (3ml) is placed on the floor of the mouth in the MWST. The MWST result was determined to be abnormal if the individual was unable to swallow, or experiences dyspnea, coughing, or wet-hoarse dysphonia after swallowing in either of two trials. The MWST results were not associated with exacerbations in participants with COPD. The small number of participants with abnormal results suggests that the MWST is not suitable for detecting dysphagia associated with COPD exacerbations. A cough peak flow (CPF) <270L/min was also associated with a higher frequency of exacerbations. The CPF results showed that the participants with dysphagia and a low CPF cannot eject residue in the pharynx or penetrated or aspirated boluses. The RSST is useful to detect dysphagia associated with exacerbations in individuals with COPD. The authors recommended that individuals with abnormal RSST results undergo videofluoroscopy or videoendoscopy to check their swallowing functions.

Clayton et al. [44] noted that relatively little research has been conducted on the prevalence of dysphagia and other swallowing disorders in patients with COPD until 2012. The authors suggested that COPD may weaken the strength of swallow and increase the prevalence of aspiration. The impaired ability to use expired air to clear the larynx and protect the airway, combined to weakening of swallow, may contribute to an increased risk for aspiration of pharyngeal contents and aspiration pneumonia. The authors suggested that one hypothesis is that a laryngopharyngeal sensory deficit exists. Thus, the primary goals of this study were to identify the prevalence of laryngopharyngeal sensory impairment as determined by the

laryngeal adductor reflex (LAR) threshold in patients with proven COPD and to characterize the relationship between laryngopharyngeal sensory impairment and the severity of COPD. The laryngopharyngeal sensory discrimination test (LPSDT) was performed. The study included 20 COPD patients and a control group with 11 volunteers. The study revealed that patients with COPD have a significantly worse level of laryngopharyngeal sensory impairment as defined by the LAR threshold. No relationship was identified between the severity of laryngopharyngeal sensory impairment and the severity of COPD (as defined by the FEV₁ testing). The diagnosis of COPD was strongly related to laryngopharyngeal sensory impairment, but the severity of COPD did not correlate with deterioration in laryngopharyngeal sensitivity. The presence of COPD itself is enough to predict impairment of laryngopharyngeal sensitivity.

In a recent study, Terzi et al. [45] evaluated fifteen consecutive chronic obstructive pulmonary disease patients with exacerbations requiring ICU admission and non-invasive ventilation (NIV). The objectives of this study were to evaluate swallowing during NIV in COPD patients with acute respiratory failure and, if appropriate and based on the results, to develop and evaluate a simple alteration in the ventilator design to eliminate ventilator insufflations during swallowing. Swallowing and breathing interactions were investigated noninvasively by chin electromyography, cervical piezoelectric sensor, and inductive respiratory plethysmography. Two water volumes (5 and 10 ml) were tested in random order. The results indicated that swallowing during NIV is feasible in patients with COPD experiencing acute exacerbations, swallowing efficiency and the breathing-swallowing pattern improve with NIV compared with spontaneous breathing and dyspnea decreases during swallowing when using NIV.

The work recently published by Chaves et al. [46] emphasizes that previous studies have indicated consistent aspiration in COPD patients. It is believed that this phenomenon was mainly related to delayed swallowing reflex and problems with lingual and pharyngeal peristalsis as a result of bilateral weakness and incoordination of the related muscles. When combined with an impaired ability to use expired air to clear the larynx and protect the airway, a weak swallow may contribute to an increased risk for aspiration of pharyngeal contents and may consequently lead to aspiration pneumonia. This work discusses that although the cause of impaired laryngopharyngeal sensitivity remains unclear, a few hypotheses have been introduced: (1) the use of inhaled corticosteroids and anticholinergics may have an effect on the sensory mucosa of the laryngopharynx; (2) laryngeal edema caused by smoking and the presence of chronic cough commonly reported in COPD patients may contribute to reduced sensation. The purpose of the study by Chaves et al. [46] was to evaluate swallowing transit times and valleculae residue characteristics of stable COPD patients who have no swallowing complaints. The population included 20 patients with COPD and 20 healthy controls. Swallows were assessed through videofluoroscopy. The protocol included swallows of 3, 5 and 10 ml of liquid consistency; swallows of 7 ml of paste consistency, and swallows of a solid biscuit. The data of the study indicated that stable COPD patients and healthy controls did not present any signs of penetration-aspiration for any tested consistency. Patients with COPD presented longer pharyngeal transit time (PTT) during the ingestion of 10 ml of the liquid consistency and during the ingestion of the paste consistency. In cases of exacerbation, patients are more likely to have difficulties in prolonging swallowing events, so this manoeuvre might be

difficult to execute. Regarding the duration of the tongue base contact (TBC) with the posterior pharyngeal wall, COPD patients also presented longer durations for liquid and paste consistencies. The authors concluded that the risk for aspiration in the COPD population is not limited to the presence of valleculae residue, and this cannot be seen as an isolated factor in an attempt to explain swallowing alterations in this population. Stable COPD may present physiological adaptations as a protective swallowing manoeuvre to avoid aspiration/penetration of pharyngeal contents.

Table 1 summarizes the studies conducted on the prevalence of dysphagia and other swallowing disorders in patients with COPD to date.

Reference	Subjects	Reference test	Oral impairment	Pharyngeal impairment	Presence of aspiration	Coordination of breathing and swallowing
Coelho (1987)	14 COPD patients	Videofluoroscopy and bedside evaluation	Difficulties with bolus formation and control	Delayed swallowing reflex, decreased pharyngeal peristalsis and cricopharyngeal and esophageal constriction	3 of 14 patients (21%)	Not tested
Stein et al. (1990)	25 COPD patients with cricopharyngeal dysfunction	Videofluoroscopy	Not tested	Cricopharyngeal achalasia	Not tested	Not tested
Shaker et al. (1992)	21 healthy subjects and 22 COPD patients	Electromyography and respirography	Not tested	Not tested	Not tested	Swallowing occurred during inspiration in exacerbation of COPD
Good-Fraturelli et al. (2000)	78 COPD patients	Videofluoroscopy	Oral stasis	Bilateral vallecular and pyriform sinus stasis, delayed pharyngeal swallow response.	42% of patients evidenced aspiration with thin and thick liquid, more than with semi-solid or	Not tested

Reference	Subjects	Reference test	Oral impairment	Pharyngeal impairment	Presence of aspiration	Coordination of breathing and swallowing
					solid textures.	
Martin-Harris et al.(2000)	Review of literature, no subjects were tested	Review of literature and care guidelines based on clinical deductions from experience in the evaluation and treatment of patient with COPD and dysphagia	Altered oropharyngeal sensation, slow lingual motility, slow and effortful chewing and bolus preparation, oropharyngeal xerostomia	Delayed laryngeal closure, prolonged laryngeal ascent and descent, premature laryngeal opening, pharyngeal residue, channeling of food to pyriform sinuses	Post-swallow aspiration may occur with thick and dry materials	Not described
Mokhlesi et al.(2002)	20 COPD patients and 20 healthy subjects	Videofluoroscopy	Reduced tongue control, reduced antero-posterior tongue movement, reduced tongue stabilization, reduced tongue strength, and reduced tongue base retraction.	Frequent spontaneous and protective maneuvers, delayed pharyngeal swallow, decreased laryngeal elevation, shorter duration of cricopharyngeal opening	Not observed	Not tested
Kobayashi et al.(2007)	25 stable COPD patients, and 25 that had one exacerbation during the previous year	Injection of 1 ml distilled water into pharynx	Not tested	Mean latent time of swallowing reflex was longer in exacerbation group of COPD	Not tested	Not tested
Gross et al. (2009)	25 COPD patients and 25 control subjects	Electromyography, nasal cannula and respiratory inductance plethysmography	Not tested	Not tested	Not tested	Swallowing during inhalation, and post swallow inhalation were observed more often in COPD

Reference	Subjects	Reference test	Oral impairment	Pharyngeal impairment	Presence of aspiration	Coordination of breathing and swallowing
						than in normal subjects
Ohta (2009)	64 COPD patients	STS-SPT and RSST	Not tested	Impairment of triggering of the swallowing response and the frequency of saliva swallowing, may begin in the mild stage of COPD	Not tested	Not tested
Terada et al. (2010)	67 COPD patients and 19 healthy subjects	Simple Two-Step Swallowing Provocation Test (STS-SPT)	Not tested	Impairment of triggering of the swallowing response was more frequent in COPD than in normal subjects	Not tested	Not tested
McKinstry et al. (2010)	55 COPD patients	Dysphagia screening and Swal-QOL	Not tested	Not tested	Not tested	Not tested
Cvejic et al. (2011)	16 COPD patients and 15 control subjects	Videofluoroscopy, eletromyography, and respiratory inductive plethysmography	Not tested	Reduced hyoid elevation and post-swallow pharyngeal residue	4 of 16 patients(2 5%) in 100ml liquid barium	Inspiration-swallow- expiration pattern was observed more often in COPD than in control subjects
Kobayashi et al. (2011)	25 stable COPD patients, and 25 that had one exacerbation during the previous year	Simple Two-Step Swallowing Provocation Test (STS-SPT)	Not tested	Not tested	Not tested	Angiotensin-converting enzyme inhibitors protect against aspiration tracheobronchitis and exacerbations of COPD.
Chaves et al. (2011)	35 COPD patients and 35 healthy subjects	Self perception questionnaire	Not tested	Airway protection and pharyngeal symptoms were common in	Not tested	Not tested

Reference	Subjects	Reference test	Oral impairment	Pharyngeal impairment	Presence of aspiration	Coordination of breathing and swallowing
				participants with COPD		
Tsuzuki et al. (2012)	65 COPD patients	Repetitive Saliva Swallowing Test (RSST) and Modified Water-Swallow Test (MWST)	Not tested	Reduced number of swallows in RSST, and dyspnea, coughing or wet-hoarse dysphonia after swallowing in MWS in patients with COPD	Not tested	Not tested
Clayton et al. (2012)	20 COPD patients and 11 healthy subjects	Laryngeal sensory discrimination test (LPSD)	Not tested	COPD patients have a worse level of laryngopharyngeal sensory impairment	Not tested	Not tested
Terzi et al. (2014)	15 COPD patients	Electromyography and respiratory inductive plethysmography during noninvasive ventilation	Not tested	Not tested	Not tested	Swallowing efficiency and the breathing-swallowing pattern improve with NIV compared with spontaneous breathing
Chaves et al. (2014)	20 COPD patients and 20 healthy controls	Videofluoroscopy	Longer duration of the tongue base contact with the posterior pharyngeal wall	Longer pharyngeal transit time	Not observed	Not tested

Table 1. Summary of the studies that evaluated the prevalence of dysphagia and other swallowing disorders on patients with COPD.

6. Development of instrumentation for the analysis of the coordination between respiration and swallowing in COPD patients

This section briefly describes the development of a configurable system that may be used for ambulatory and/or home analysis of swallowing using telemedicine and internet data

exchange developed in our laboratory [24]. The general architecture of the instrument is described in Figure 4.

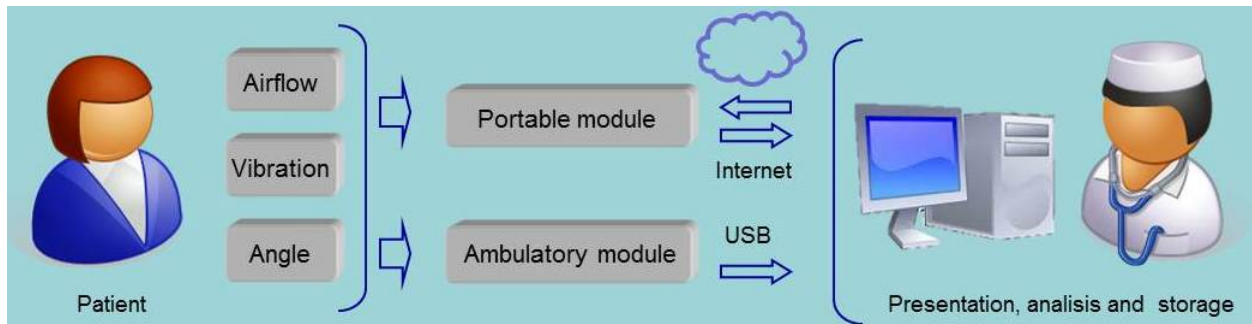


Figure 4. Simplified block diagram of the configurable instrument for the analysis of swallowing disorders.

The instrument allows an unobtrusive monitoring of respiration during feeding using a nasal airflow measurement system based on a nasal cannula attached to a sensitive pressure transducer (176PC; Honeywell Inc., New York, U.S.A.) through a long and flexible connection tube (100 cm length, 4 mm, i.d.). Intranasal air pressure recordings yield minimally intrusive and accurate information about the direction of airflow in real time.

Also included in the basic instrument is a system used to monitor the elevation of the larynx. This movement prevents the entering of the material in the tracheal airway and gives rise to a characteristic vibration pattern that can be used to detect the pharyngeal phase of the swallowing mechanism [47]. This mechanical vibration was measured using an electret microphone (CZN-15E; Ningbo Yuelong Electronics Co., Zhejiang, China) which was placed on the throat at the level of the thyroid cartilage by an apparatus similar to a collar.

The angle of the glass used to drive water was used to non-invasively monitor the beginning of water entering the mouth of the volunteer. To this end, inclinometry data have been obtained from a dual axis accelerometer (ADXL213, Analog Devices Inc., Norwood, MA, U.S.A.). The resulting analogue output value is then used in conjunction with a lookup table to determine the corresponding glass angle relative to the line of gravity.

The module dedicated to telemonitoring applications is battery operated. This subsystem also includes a Palmtop iPAQ HP hx2490 with 520 MHz, 64 Mb of RAM and 192 Mb of ROM, with operational system Microsoft® Windows Mobile® 5.0. For ambulatory application, a data acquisition system was developed using an 18F4550 microcontroller (Microchip, Arizona, USA).

Regardless of the method used for data acquisition (ambulatory or telemonitoring), the final analysis of the airflow, mechanical vibration and glass angle signals is performed by a dedicated software (Figure 5). It allows the user to automatically calculate the time in the course of the swallowing apnea (s) and the phase in which the swallowing apnea started and stopped in the respiratory cycle (inspiration or expiration).

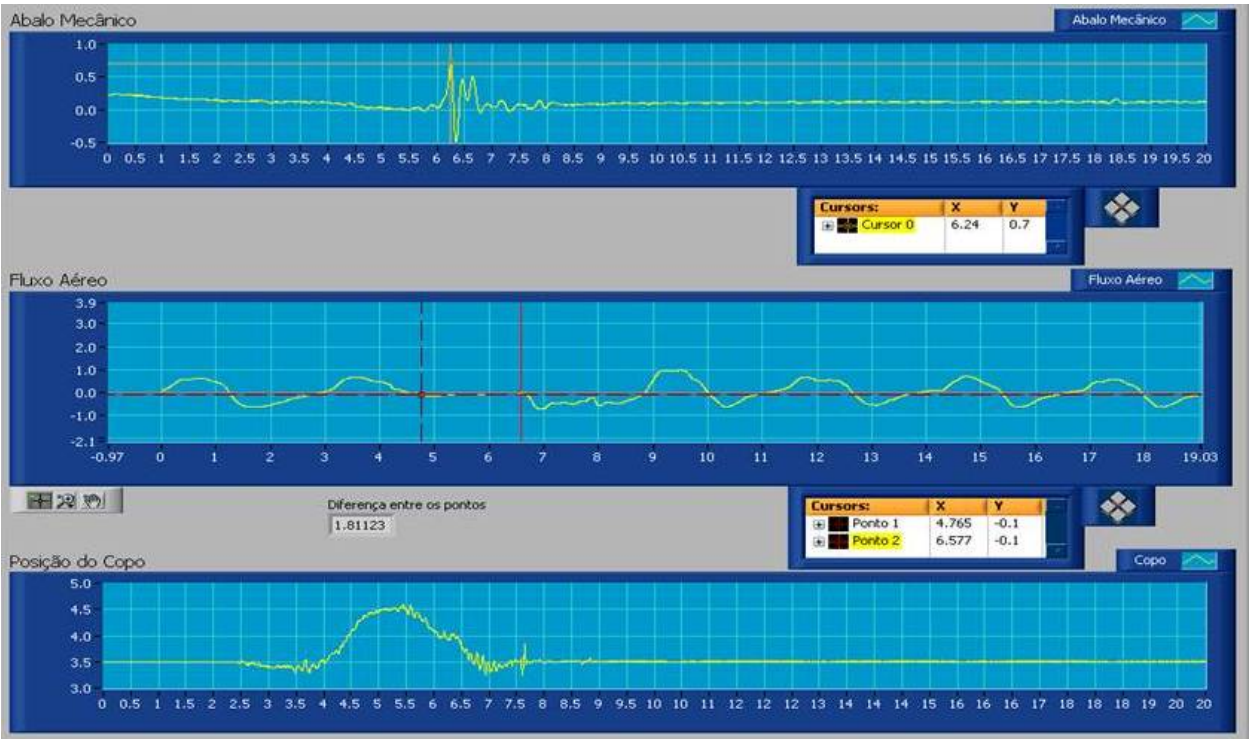


Figure 5. Front panel of the program used to automatically calculate the time in the course of the swallowing apnea (s) and the phase in which the swallowing apnea started and stopped in the respiratory cycle (inspiration or expiration).

Representative examples of the typical morphology of the nasal airflow, mechanical vibration and glass angle signals obtained during a swallowing of 20 mL of water in a normal subject and a dysphagic patient are presented in Figure 6.

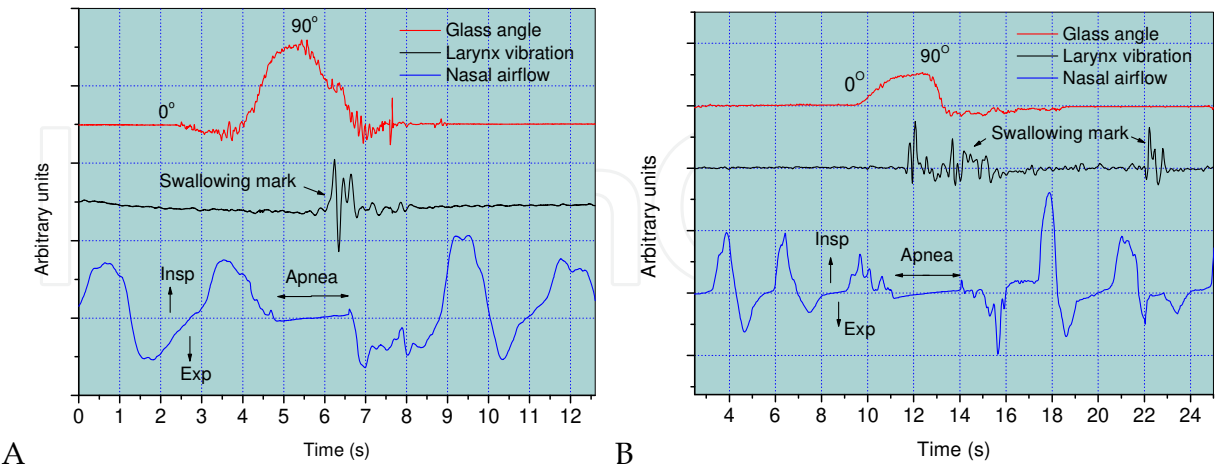


Figure 6. Typical glass angle, larynx mechanical vibration and nasal airflow normal signal morphology during swallowing of 20 mL of water in a normal (A) and a dysphagic patient (B).

As seen in Figure 6A, the movement necessary to drive water into the mouth of the volunteer is described by the increase in the glass angle. When the angle is near 90° and water is beginning

to enter the mouth of the volunteer, the swallowing apnea begins. The absence of airflow, which can be observed in the end of the inspiration cycle, demarks the beginning of the deglutition process (near 4.8 s). After the beginning of this event, Figure 6A shows the presence of the mechanical vibration signal indicating the action of protective mechanisms including the movement of the larynx-hyoid complex. Note a small delay between water entering the mouth (glass angle = 90°) and the movement of the larynx-hyoid complex. After a period of approximately 1.5 s, the apnea reaches its end, and an expiration phase is initiated. Meanwhile, the returning of the glass to the initial position is described by a correspondent gradual reduction of the associated signal to zero.

A representative recording in a patient with dysphagia is shown in Figure 3B. Water entering the mouth of the patient (near 11 s) is accompanied by a first swallowing mark (larynx vibration signal) which lasted approximately 4 s. The corresponding apnea period also lasted approximately 4 s. Note that these periods were higher than that presented by the normal volunteer. An important characteristic of this patient is the constant presence of coughing during liquid swallowing. This is related to a clinical history of three cerebral vascular accidents (CVA). This behaviour is in conformity with the hypothesis of an adaptation mechanism in which the patient increases swallowing times to protect itself from aspiration. While similar to the normal subject, the apnea was followed by expiration and a transitory hyperventilation. Figure 3B also shows a second swallowing mark and a second apnea event ($\cong 22$ s), which was preceded by an expiratory event. This occurs because the patient was not able to swallow all of the 20 mL of water in the first swallowing, therefore, a second swallowing event was necessary. The detailed description presented in Figure 3B confirms the potential of the proposed instrument in the analysis of abnormal swallowing events.

7. Preliminary results of the analysis of swallowing apnea in individuals with chronic obstructive pulmonary disease

This section presents new results concerning the evaluation of swallowing apnea in patients with COPD. This analysis was performed using the instrument described in the previous section. The primary hypothesis is that swallowing apnea in COPD patients is altered during liquid swallowing compared with age-matched healthy subjects.

7.1. Patients and methods

The study included a control group formed by eleven healthy subjects and twelve outpatients with COPD. The volunteers initially were analysed using spirometry and plethysmography [48]. This study was approved by the Ethics Committee of the State University of Rio de Janeiro. Informed consent was obtained from all volunteers before inclusion in the study.

The variables studied were: forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), the ratio of forced expiratory volume to forced vital capacity (FEV1 / FVC), forced expiratory flow between 25 and 75% of the FVC curve (FEF 25-75%), total lung capacity (TLC), functional residual capacity (FRC), residual volume (RV) and the ratio of residual

volume and total lung capacity (RV / TLC). The exams were performed by swallowing saliva and water at volumes of 5, 10 and 20 mL. Patients were instructed to swallow each volume three times. Twelve swallows of each patient were studied (276 total swallows).

7.2. Results

Table 2 shows the biometric, spirometric and plethysmographic characteristics of these volunteers. Volunteers in the two groups were comparable considering age, weight and height, showing no statistically significant differences. In general, the pulmonary function parameters were highest in normal subjects and lower in patients.

	Control n=11	COPD n=12	p-value
Age (years)	69.8 ± 6.8	71.3± 6.1	ns
Weight (kg)	69.98 ± 10.3	61.4 ± 17.4	ns
Height (cm)	160.8 ± 9.9	156.9 ± 9.0	ns
IMC (kg/m²)	24.7 ± 5.5	27.0 ± 2.8	ns
FEV ₁ (%)	106.8 ± 12.7	69.9 ± 29.7	0.001
FVC (%)	103.9 ± 13.0	95.0 ± 24.1	ns
FEV ₁ /CVF	81.2 ± 4.00	56.1 ± 16.1	<0.0001
FEF25-75(%)	117.0 ± 24.5	34.3 ± 24.9	<0.0001
TLC (%)	100.7 ± 6.5	114.0 ± 9.4	<0.0001
FRC (%)	86.3 ± 14.1	112.7 ± 2.2	0.003
RV (%)	98.9 ± 14.1	148.5 ± 38.6	<0.0001
RV/TLC	39.9 ± 6.40	52.9 ± 10.8	0.0003

Table 2. Biometric and pulmonary function characteristics of the investigated subjects. Ns: non-significant.

Figure 7 shows that, in contrast with the control subjects (p=ns), the increase of the offered volume resulted in a longer duration of swallowing apnea in patients with COPD (p<0.05).

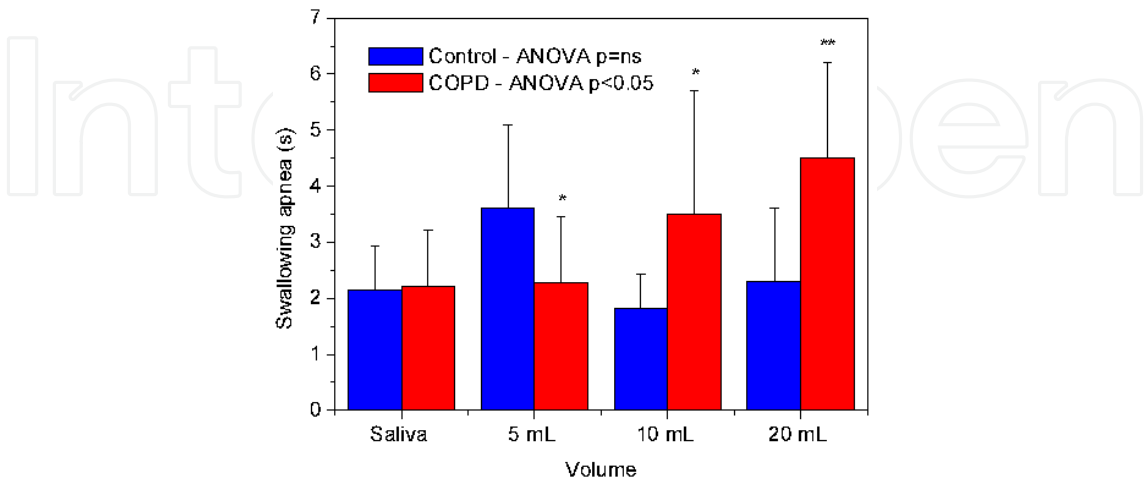


Figure 7. Time interval of swallowing apnea in healthy subjects and patients with COPD for different volumes of water. * p < 0.02; ** p < 0.002 in comparison with the control group.

The COPD patients had longer swallowing apnea with volumes of 10 mL ($p<0.02$) and 20 mL ($p<0.002$). A higher number of swallows in the pattern of inspiration-apnea-inspiration was observed in the COPD group, especially in the volumes of 10 and 20 mL (Figure 8).

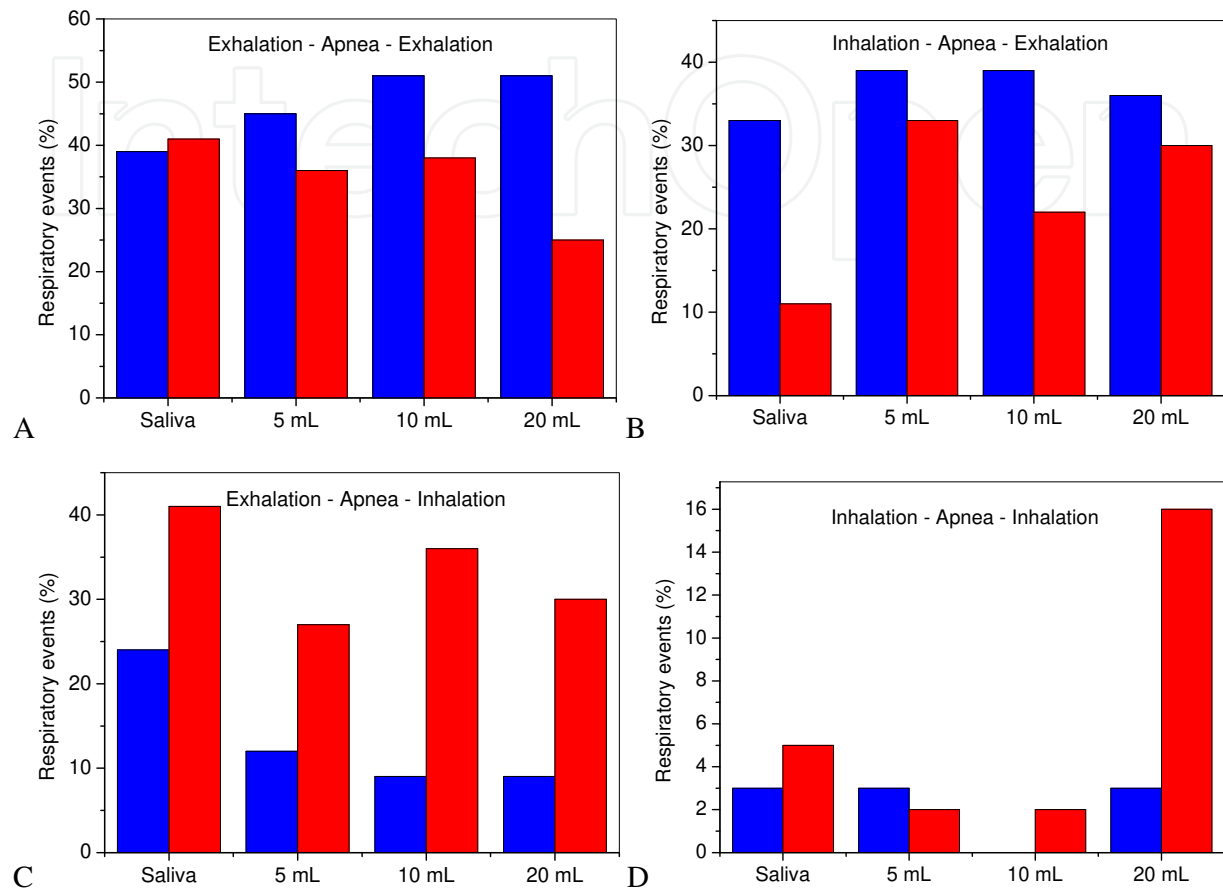


Figure 8. Percentage of exhalation-apnea-exhalation (A), inhalation-apnea-exhalation (B), exhalation-apnea-inhalation (C) and inhalation-apnea-inhalation (D) events in healthy (blue) and COPD patients (red) for different water volumes. 276 swallows were studied.

7.3. Discussion

Leslie et al. [49] suggested that the apnea time significantly increases with volume in normal elderly subjects. In contrast, Esteves and colleagues [24] found no increase in apnea time and swallowing with volume in normal young subjects. In the results described in Figure 7, the increase in volume did not result in increased swallowing apnea time in elderly individuals. Note that, in the volume of 5 mL, individuals of the control group had significantly longer apnea times than that observed in the swallowing of saliva, 10 and 20 mL of water ($p<0.02$). This result may be related to the relatively small number of individuals analysed.

In contrast with that observed in normal volunteers, the presence of COPD resulted in increased apnea time with the bolus volume (Figure 7). We can also observe that patients with COPD had apnea times significantly higher during conditions of higher volume (10 mL and

20 mL). These findings disagree with those described in the study by Gross [38], which observed no difference in apnea time between the COPD and control group. These authors note, however, that in the swallows of COPD patients in which apnea occurred in inspiration time, the apnea interval was longer. Physiologically, the presence of longer periods of apnea in COPD could indicate a compensatory mechanism for airway protection against aspiration of food residuals.

The control group presented an increased number of swallows in the standard-expiration apnea-expiration (EE) pattern in all studied volumes (Figure 8). This is in close agreement with previous studies [9, 20, 22, 50]. This finding supports the theory that swallowing during the expiratory phase represents less risk of aspiration and therefore may be considered a protective mechanism of the airways. Swallowing during the inspiratory phase may facilitate the entry of food and saliva into the airways during and after swallowing [22]. Other patterns were also observed in this group. In order of increasing frequency: inspiration-apnea-expiration (IE), expiration-apnea-inspiration (EI), and inspiration-apnea-inspiration (II). This result is consistent with that reported by Martin-Harris [22]. The pattern II presented the smallest frequency in all volumes, which agrees with previous results [9, 20, 22].

COPD patients more frequently showed the EE and EI patterns (Figure 8). Similar findings were reported in the study conducted by Cjevic [2]. The pattern II occurred less frequently compared with other patterns. Comparing the swallowing of COPD patients with control subjects, it can be observed that the pattern EI (Figure 8C) occurs more frequently in COPD patients compared to control subjects. This phenomenon was observed in all studied volumes. Considering the pattern II (Figure 8D), we observe that this also occurs more frequently in COPD, particularly in exams using 20 mL. In agreement with the present work, the study by Gross [38] describes that patients with COPD had pre and post inspiration swallowing apnea more often than the control subjects. These results are consistent with the observation that the inspiration after swallowing facilitates aspiration of food and saliva.

8. Conclusions

This chapter initially provided a brief overview of dysphagia, coordination of breathing and swallowing, and COPD. This was followed by a historical review that described the research through the decades on swallowing in COPD. In addition to these previous studies, new results were presented. This analysis provides evidence that (1) the apnea interval increases with the swallowed volume in COPD; (2) COPD patients had higher swallowing apnea time compared to controls in larger volumes; (3) the occurrence of inspiratory patterns after swallowing increases in COPD, which may facilitate the occurrence of aspiration in these patients, and (4) the prototype that was described in section 6 is suitable for clinical studies.

Routine clinical evaluation of swallowing disorders in COPD has yet to gain full acceptance, but the evidence of the importance of these analyses is growing fast. The results of the present study, together with the results described in the historical review, provide additional evidence that patients with COPD might present modifications in deglutition and a specialized evaluation is necessary for safe deglutition, especially in case of acute exacerbation.

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