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Chronic Obstructive Pulmonary Disease and Occult Aspiration: A Review of the Recent Literature

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Abstract The World Health Organization has identified Chronic obstructive pulmonary disease (COPD) and lower respiratory infections as the 3rd most common causes of death worldwide. A better understanding of both of these conditions may lead to improved healthcare and help to lower the death rates. An underappreciated factor that links COPD and lower respiratory infection is occult aspiration. To obtain the current status about the contribution that dysphagia may have in relation to the morbidity and mortality of persons with COPD, a search and review of the literature covering the past 3 years was conducted. Overall, there is a strong evidence of swallowing dysfunction in COPD patients. The relationships between COPD exacerbation, lower airway infection, and swallowing impairments point to possible strategies that could be used to prolong and improve life in those afflicted by preventing aspiration and the subsequent sequelae.

Keywords Chronic obstructive pulmonary disease (COPD) · Deglutition · Aspiration pneumonia · Dysphagia · Swallowing · Exacerbation

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Introduction

The World Health Organization (WHO) has identified chronic obstructive pulmonary disease (COPD) and lower respiratory infections as the 3rd most common causes of death worldwide. While COPD prevalence, morbidity, and mortality may vary between countries and social groups, it is directly related not only to the prevalence of tobacco smoking but also, especially in low income countries, to occupational, outdoor, and indoor pollution [1]. As COPD prevalence is projected to increase in the coming decades, it is already a major economic burden and bound to increase across countries.

A better understanding of both of these conditions may lead to improved healthcare and help to lower the death rates. An underappreciated factor that links COPD and lower respiratory infection is occult aspiration. Because gross anatomic and neuroanatomic structures for the vital functions of breathing and swallowing overlap and interact, strategies that influence one function, have the potential to affect the other. Much more attention has been given to management of COPD and related lung infections than to swallowing ability in affected individuals. It is feasible that the death rates for COPD and lower respiratory tract infection reported by the WHO are partly the result of occult aspiration caused by dysphagia.

To obtain the current status about the contribution that dysphagia may have in relation to the morbidity and mortality of persons with COPD, a search and review of the literature covering the past 3 years was conducted. Scientific and review articles that were indexed with PubMed were identified using the term, chronic obstructive pulmonary disease and the following terms or combinations of terms: antibiotics, aspiration, aspiration pneumonia, cough, deglutition, drinking, dysphagia, eating, exacerbation,

gastroesophageal reflux, hypercapnia, lower respiratory tract infection, morbidity, mortality, obstructive sleep apnea, rehabilitation, speech pathology, swallowing, swallowing or dysphagia therapy, swallowing or dysphagia treatment, and tracheostomy. Both original research papers and review articles are included in this summary.

As defined by the GOLD (global initiative for chronic obstructive lung disease) program (2), COPD is a respiratory disease that is characterized by a chronic airway inflammation. It is associated with an enhanced chronic inflammatory response in the airways and the lungs to noxious gases or particles. This chronic inflammation is characterized by a persistent, slowly progressive narrowing of the airways leading to an airflow limitation. It can be associated with parenchymal destruction (emphysema) which loosens the alveolar attachment of the small airways and decreases the elastic recoil of the lung tissue. The relative contribution of both mechanisms varies individually, accounting for the heterogeneous presentation of the disease.

Chronic bronchitis (presence of cough and sputum for at least 3 months/year during 2 consecutive years) may precede or follow the limitation of airflow which defines the obstructive respiratory disease. The diagnosis of COPD may be considered clinically based upon dyspnea, sputum production, or chronic cough; but, spirometry is required to confirm the diagnosis defined as a post-bronchodilator $FEV_1/FVC < 0.7$. Assessment of disease severity, as proposed by the GOLD program in its updated version, takes into account breathlessness, exacerbation risk, and spirometry results. The classification of the disease is associated with treatment and management recommendations [2].

It is interesting to note that exacerbation risk has been integrated into the revised 2015 GOLD recommendations, distinguishing frequent exacerbators as the occurrence of 2 or more exacerbations per year. Indeed, exacerbations are defined as the acute enhancement of respiratory symptoms above the usual individual baseline symptoms of the patients, leading to modifications in treatment. While the factors leading to exacerbations may be multiple, the most common causes are upper and lower tract respiratory infections. The most frequent microbes involved in COPD exacerbations are Streptococcus pneumonia, *Haemophilus influenzae*, and *Moraxella catarrhalis* [3]. In severe patients, other pathogens may be encountered (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and enterobacteries).

Respiratory failure, often the result of a severe exacerbation, is the leading cause of death for persons with COPD, and the frequency of exacerbations increases with severe disease (GOLD 3 and 4). Exacerbation tends to lead to more exacerbations, increased morbidity and mortality, worsening of respiratory function, and decreased quality of life for patients [4–6]. Subsequently, there is also a significant impact on economic burden that contributes to skyrocketing health care costs. In the United States, the Center for Disease Control and Protection (CDC) predicts that costs related to the medical care of persons diagnosed with COPD will be approximately $90.6 billion by the year 2020 [7]. Therefore, the prevention of exacerbation is a major issue in the management of COPD.

Identifying and addressing factors that predispose patients to exacerbation may improve quality of life, reduce health care costs, slow the progression of the disease, and possibly, prevent some deaths. Unfortunately, the cause for exacerbation is often unknown, making strategies for prevention difficult to identify. As the most common cause of exacerbation is respiratory tract infection, the relationship between exacerbation and lower airway bacterial colonization has been widely investigated. However, the importance of swallowing impairment and occult aspiration in COPD patients is less known and explored. Indeed, aspiration of oral secretions and prandial aspiration as the result of untreated or unrecognized dysphagia may be a precipitating factor. Recognition of the role that dysphagia may play presents an opportunity for improved care and management and may lead to the prevention of some lung infections, primarily aspiration pneumonia.

A severe exacerbation is associated with increased mortality. In 2010, Hurst et al. reported some of their findings from a large longitudinal, observational study where one of the aims was to identify if there was a phenotype associated with frequent exacerbations [8]. They found that elevated white-cell counts and gastroesophageal reflux disease were the primary constituents. Ozyilmaz and colleagues recruited 107 COPD patients from in-patient and out-patient COPD clinics into their study that also sought to uncover precipitating factors in relation to frequent, severe exacerbations [9]. Patient questionnaires, clinic records, and spirometric measures were used to identify risk factors that could potentially be modified through medical intervention. Their analysis showed that poor adherence to inhalation therapy and low hematocrit values were correlated with frequent and severe COPD exacerbations. They postulated that low hematocrit could be an indication of poor nutrition. Although swallowing difficulty could be, in part, responsible for difficulty maintaining adequate nutritional status, it was not explored, nor considered, as a potential mechanism. Bassi et al. sought to identify risk groups for dysphagia in a sample of 32 in-patients who had no complaints of dysphagia [10]. They found that all of the COPD patients failed the risk screening for oral dysphagia by showing clinical signs of aspiration during controlled deglutition. In addition, nutritional compromise was present in nearly a

quarter of the COPD subset. While the study is limited by the small sample size, their findings are in agreement with previous reports linking dysphagia and malnutrition [11–13].

Many persons with COPD have bacteria present within the tracheobronchial tree. When the bacteria increase to high levels, exacerbation of COPD may occur. Approximately, 50 % of COPD exacerbations are treated with antibiotics. An increase in bacteria is thought to be related to aspiration of oral secretions and prandial aspiration; however, recent studies did not include dysphagia as a possibility, even when acknowledging the possibility of silent aspiration. For instance, Dixit and colleagues completed a comprehensive literature review on the management of the critically ill COPD patient to examine the evidence in relation to the use of antibiotics [14]. They found that antibiotic use significantly lowered hospital mortality; yet the authors did not consider the possibility that bacterial lung infections could be related to dysphagia and occult aspiration. While several strategies for preventing COPD exacerbation were also reviewed, dysphagia detection and management were not mentioned. Yet, should dysphagia be involved in the cause of exacerbation and left untreated, the patient is destined to repeat the cycle.

Aspiration syndromes refer to a wide array of diseases among which aspiration pneumonia is only one of the clinical manifestations. While all are characterized by the penetration of foreign material in the trachea and the lower respiratory tract, not all aspiration leads to pneumonia. They can be distinguished by the aspiration volume, or by the infectious nature of the inoculum. For example, gastroesophageal reflux disease may lead to chronic microaspiration of noninfectious inoculum; on the other hand, massive food aspiration, while initially noninfectious, may cause acute lung inflammation and respiratory distress and favor secondary infection. Upper airways bacterial colonization may also cause chronic infectious microaspirations, leading in some circumstances to lower tract infection with pneumonia. Swallowing dysfunction, altered mental status, esophageal motility disorders, oropharyngeal colonization, and enteral feeding are the identified predisposing factors of aspiration pneumonia. Over the past decades, the microbiology described in association with aspiration pneumonia has changed. While anaerobes used to describe the most common pathogens involved in the aspiration pneumonia, recent studies show a predominance of gram-negative bacilli (mostly enteric species, *Escherichia coli*, *Klebsiella pneumoniae*, *Haemophilus influenza*…) as well as other aerobes species (mostly streptococcus species and *Staphylococcus aureus*) [15–18].

Aspiration may often go undiagnosed. Hu et al. recently pointed out the there is increasing evidence showing that, frequently, aspiration is not suspected in patients with pulmonary syndromes because aspiration pneumonia is often not distinguished from community-acquired or hospital-acquired pneumonia [19]. To illustrate this point, Yomiya et al. used the combination of risk factors for aspiration (such as a neurologic disorder) with computed tomography (CT) evidence of "gravity-dependent" opacity to categorize patients who were diagnosed with community-acquired pneumonia (CAP) and Healthcare-Associated pneumonia (HCAP) as having aspiration pneumonia [20•]. Among the 188 patients with risk factors for aspiration, CT findings consistent with lower airway opacity were present in 116 patients (62 %). In addition, the researchers determined that aspiration pneumonia was a strong and independent predictor for mortality. They noted that a possible reason for the increased mortality of the aspiration pneumonia group was that the patients may have continued to aspirate while hospitalized.

These observations support the current problem of underappreciated prandial aspiration and the link to lower respiratory infection. Noting that the most common basis for exacerbation is likely bacterial respiratory tract infection, Yamauchi et al. compared the characteristics of CAP and aspiration pneumonia in COPD patients [21•]. Using the nationwide data of in-patients in Japan, they identified 87,330 persons with COPD over the age of 40 who were admitted for pneumonia, among which approximately 20 % were diagnosed with aspiration pneumonia. When compared to CAP, the mortality rate of the aspiration pneumonia group was nearly twice that of the CAP group (22.7 vs. 12.2 %). COPD patients with aspiration pneumonia were also sicker and required more frequent intensive care admission and mechanical ventilation.

In a European survey of 14,111 patients who were admitted for COPD exacerbation, Saleh and colleagues reported evidence of consolidation on chest radiographs in 19.2 % of the patients [22•]. When compared to patients with COPD exacerbation who did not have radiographic evidence of consolidation, patients with radiographic consolidations were significantly more likely to require mechanical ventilation ($p \leq 0.001$) and to be treated with antibiotics ($p \leq 0.001$). They also had a poor prognosis and more frequent exacerbations. While aspiration was not diagnosed in this study, it seems probable that prandial aspiration is a likely cause for radiographic evident consolidations. Nonetheless, since not all persons who aspirate go on to develop aspiration pneumonia, it is becoming clearer that the diagnosis of COPD is among the conditions that place patients at increased risk for aspiration and subsequent aspiration pneumonia [23]. While the

significance of dysphagia in relation to exacerbation is often not considered, COPD has been identified as a significant risk factor for dysphagia and aspiration [24].

Multiple factors contribute to probability of increased aspiration risk in persons with COPD. Impaired breathing and swallowing coordination [25, 26] and reduced laryngopharyngeal sensitivity [32••] are thought to be primarily responsible. In an attempt to better understand possible relationships between exacerbation and impaired swallowing function, Steidl et al. recently conducted a review of the past, pertinent literature [27••] and reviewed 19 studies on the topic of COPD exacerbations and dysphagia. Overall, the conclusion was that swallowing impairment with aspiration appeared to be one of the precipitating factors for exacerbation. The reviewers also felt that "there seems to be a consensus among authors" that COPD exacerbations are frequently related to aspiration as a result of disorganized breathing and swallowing coordination. In addition, other swallowing impairments such as cricopharyngeal dysfunction and aspiration have been identified in stable COPD patients [28–30]. Although few, there have been recent additions in the scientific literature that have attempted to further characterize swallowing impairments in persons with COPD.

Different instrumental techniques that are typically employed in the evaluation of swallowing have been used in research protocols to identify and describe swallowing characteristics of persons with COPD and to evaluate the risk for lower airway infections from prandial aspiration. Fiberoptic endoscopic evaluation of swallowing (FEES) enables clinicians to directly observe pharyngeal and laryngeal structures during mastication, during the early onset of the pharyngeal swallow, and immediately post-swallow. An advantage of the technique is that it does not impose time limitations or require special foods since there is no radiation involved. However, it does not allow the observation of the oral cavity, biomechanics, and bolus transit during the pharyngeal phase, nor any portion of the esophageal phase. Nevertheless, many important observations can be made using FEES. For example, the location of the bolus during mastication can be viewed. Typically, the majority of the material should remain within the oral cavity; however, it is considered to be within normal limits for a portion to be transferred into the vallecular space. Observation just prior to swallow onset and determination as to whether or not material enters the deep pharyngeal recesses or airway before the pharyngeal swallow is elicited can also be made easily using this method. After the swallow, aspirated material can be identified below the true vocal folds. Additional residua remaining in the laryngeal vestibule, on the true vocal folds, or within the pharynx can also be seen.

Macri et al. used FEES to identify correlations between swallowing characteristics and COPD severity in 19 COPD patients [31•]. A variety of liquid viscosities were given (thin, nectar, honey) along with a pudding consistency and a solid. Despite all of the patients showing clinical signs of aspiration (coughing), FEES examination revealed no tracheal aspiration in any of the subjects. However, food items entered the pharynx prior to swallow onset in 10.5 % of the participants with liquid and pudding consistencies and in 21 % of the subjects with the solid consistencies. There were no estimates as to the amount of escaped material, although the associated risk factor for aspiration, related to the airway remaining open at this time, was acknowledged. The authors pointed out the need for instrumental assessment of swallowing function because of the disparity between the clinical findings and FEES.

Clayton et al. used standardized clinical assessments of swallowing and FEES to characterize swallowing function in persons with COPD [32••] The same group of investigators had previously demonstrated that persons with COPD have significantly greater thresholds for laryngeal adductor reflex using air pressure during laryngopharyngeal sensory discrimination testing (LPSDT) than healthy controls [33]. Based upon those findings, they hypothesized that the reduction in laryngopharyngeal sensitivity (LPS) could increase the risk for aspiration. Using a prospective, case series design and fixed protocol, sensory testing and FEES examinations were completed on 22 COPD patients. Participants also received clinical evaluation using the Mann Assessment of Swallowing Ability (MASA) [34]. In contrast to the clinical observations of Macri's work, the MASA findings were within normal limits; yet, FEES results showed significant findings that were consistent with dysphagia. For example, 90 % of the participants had post-swallow residue with all consistencies and greater than 50 % made no attempt to clear the material. Laryngeal penetration and/or aspiration was found in 25 % of the group, with only 10 % sensing the aspiration as indicated by cough or throat clearing, while 15 % silently aspirated thin liquid.

Videofluoroscopy is a second technique that is often used to evaluate swallowing function. The evaluation was originally called the "modified" barium swallow (MBS); but, many now use the term videofluoroscopic swallowing study, or VFSS. This method employs the use of videofluoroscopy for the purpose of directly observing barium-laced consumable consistencies being swallowed. VFSS is typically done using a lateral view of the oral cavity, pharynx, larynx, and upper 1/3 esophagus and enables direct observation of the interaction between bolus transit and swallowing structures. The primary limitation is that the patient is exposed to ionizing radiation, and therefore,

exam time and the number of presentations of food consistencies must be limited. VFSS enables researchers to make temporal measures, and two recent studies have revealed that persons with COPD appear to be able to make compensatory adjustments to avoid aspiration.

VFSS was used by Cassiani et al. to examine swallowing physiology in 16 stable COPD patients who were compared to a control group of healthy volunteers [35]. Durational measurements were made in both groups who swallowed 5 and 10 ml boluses of liquid along with paste and solid consistencies. Nine different temporal measures were calculated for each swallow. They found that pharyngeal transit time, duration of laryngeal vestibule closure, and hyoid movement were significantly longer in the COPD subjects for both the 5 and 10 ml liquids. No aspiration was observed in either group. The investigators postulated that, in persons with COPD, afferent signaling from the respiratory system, such as low subglottic pressure, may have inducted compensatory adjustments to the efferent output, thus preventing aspiration [36, 37].

De Deus Chaves et al. also used VFSS to compare swallowing function between stable COPD patients and healthy controls [38•]. They measured specific swallowing transit times and documented vallecular residue in asymptomatic patients with COPD. Both groups swallowed standardized volumes of liquid and puree as well as a solid consistency. Duration measures for pharyngeal transit time and base of tongue to posterior pharyngeal wall contact were taken. In addition, estimates of pharyngeal residue were calculated using a ratio between the area of residue and area of valleculae. The Penetration/Aspiration (Pen–Asp) scale was also used to compare the groups [39]. Consistent with several of the recent investigations of stable COPD patients, no aspiration or penetration was observed in either group. Also, in agreement with the Cassiani et al. report, significantly longer pharyngeal transit time and longer base of tongue contact with the posterior pharyngeal wall occurred in the COPD group with liquids, but in this study, the significant difference extended to the paste consistency. These investigators also surmised that the lack of aspiration may result from a protective mechanism at work in the patients. In summary, it may be that stable COPD patients have the ability to compensate for their dysphagia; however, this may not be the case when comorbidities are present or in the setting of acute exacerbation, where increased respiratory drive may interfere with the breathing swallowing interaction. For instance, stroke patients with the comorbidity of COPD have been shown to have statistically higher Pen-Asp scores and to aspirate at a higher rate that stroke patients without COPD [40]. In a study of 103 stroke patients (with 30 COPD patients), Park et al. used VFSS, while each subject swallowed a 20 ml liquid bolus. Aspiration was observed in 40 % of the stroke patients with COPD and 12.3 % of the patients without COPD ($p = 0.002$). Accordingly, COPD patients with other comorbidities may be more likely to experience chronic occult aspiration. Overlap syndrome is the combination of obstructive sleep apnea (OSA) and COPD [41, 42], while OSA has been linked to increased risk of dysphagia [43], no study has examined swallowing function in patients with overlap syndrome. In addition, gastroesophageal reflux disease (GERD) is associated with dysphagia and aspiration and is also a common comorbidity in COPD [44]. Recently, there has been some investigation into the consequences of GERD in patients with COPD.

Egyptian researchers showed a high prevalence of motility disorders in 40 COPD subjects [45] and found that 15 % of the participants also had dysphagia. Sakae et al. completed a meta-analysis that revealed that COPD patients with GERD had a significantly higher risk for exacerbation [46] and Hu et al. linked esophageal motility disorders to aspiration [19]. Consistent with previous reports, GERD has been recently identified as an independent risk factor for exacerbation, although anti-acid medications use did not lower the risk of exacerbation [47]. Overall, link between GERD and aspiration in patients with COPD is an area that deserves more investigation. In addition, other factors such as lack of mobility and poor oral hygiene are known to increase the risk for aspiration pneumonia, and their association with COPD exacerbation should be considered.

Most of the studies previously described explored stable COPD patients. However, in the acute exacerbation stage with respiratory failure, swallowing disruption may worsen, jeopardizing breathing and swallowing coordination, and potentially lead to an increased aspiration risk. In a noninvasive evaluation of breathing and swallowing interaction in 15 COPD patients hospitalized in ICU for acute exacerbation, Terzi et al. observed a significant improvement in swallowing parameters and perceived dyspnea when the patients swallowed while noninvasively ventilated [48]. In all patients, improved breathing and swallowing coordination was observed, as indicated by a decrease in the percentage of swallows followed by an inspiration. The authors surmised that the use of noninvasive ventilation reduced the load on the respiratory muscles and contributed to improved coordination. Because swallowing movements are liable to trigger the ventilator and lead to unwanted insufflation, and expose patients to aspiration if bolus swallowing is not complete, special attention needs to be given to the synchronization between the ventilator and the patient. In their study, the use of a prototype ventilator allowed the patients to withhold and resume ventilation as they wished. However, as recent evidence showed an improved survival with the use of

noninvasive ventilation in severe COPD patients [49], this type of approach may be of interest in the future for the management of ventilated COPD patients.

Conclusions

Overall, there is strong evidence of swallowing dysfunction in COPD patients. The relationships between COPD exacerbation, lower airway infection, and swallowing impairments point to possible strategies that could be used to prolong and improve life in those afflicted by preventing aspiration and the subsequent sequelae. As such, instrumental assessment of swallowing function in order to identify prandial aspiration and risk for occult aspiration should be included as part of an overall exacerbation prevention strategy. Esophageal dysphagia is an important area that should be evaluated as increasing the risk for aspiration in patients with COPD.

Compliance with Ethics Guidelines

Conflict of Interest Roxann Diez Gross and Hélène Prigent declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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