

Overview on Emphysema Causes, Prevalence and Management

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Received: January 08, 2020; **Published:** January 16, 2021

Abstract

Background: Pulmonary emphysema is classified as a form of chronic obstructive pulmonary disease (COPD). COPD is defined by the global initiatives as "a common, treatable disorder of the respiratory system that is known by its persistent respiratory signs and blockage of the airflow because of the abnormalities that happens for the alveoli and airways, this happens mostly because of the exposure to harmful gases or particles.

Aim: In this review, we will look into the prevalence, causes, pathophysiology, diagnosis and management of emphysema.

Conclusion: Emphysema is a serious pulmonary disease; it is known to be form of COPD. As it affects mainly the lungs, smoking is considered the first leading cause to pulmonary emphysema, other causes such as coal workers and genetic factors can also be seen. Another type is the subcutaneous emphysema that occurs secondary to other causes once these causes are treated the condition will resolve by itself within 10 days. But the treatment of pulmonary emphysema requires usage of bronchodilators and corticosteroids. Early detection of the case can enhance the treatment and improve the quality of the patient's life.

Keywords: Pulmonary Emphysema; Epidemiology of Pulmonary Emphysema; Management of Emphysema; Causes of Pulmonary Emphysema

Introduction

The American thoracic society defined emphysema as abnormal and permanent enlargement of the air spaces in the lung that happens together with the damage of the bronchiole walls [1]. Pulmonary emphysema is classified as a form of chronic obstructive pulmonary disease (COPD). COPD is defined by the global initiatives as "a common, treatable disorder of the respiratory system that is known by its persistent respiratory signs and blockage of the airflow because of the abnormalities that happens for the alveoli and airways, this happens mostly because of the exposure to harmful gases or particles [2-4]. Although COPD is a separate disease it actually shows the symptoms of emphysema too, it is also classified as a disease that include patients with both chronic bronchitis and emphysema, in most cases patients who complain COPD, show other comorbidities, that makes the disease much more dangerous. COPD is said to be the 4th leading cause of death worldwide and WHO suppose that it will be the third one starting from 2020.

Pulmonary emphysema is characterized by absence of fibrosis, also destruction of lung parenchyma with loss of elasticity. Emphysema cause gas change interruption and damage the ventilatory units. Advanced emphysema could be life threatening as it causes chronic

respiratory failure [5]. High morbidity of emphysema makes it important to diagnose and treat this condition in the early stages. As the symptoms of emphysema are shared by other disease, fibrosis is the key factor to diagnose it as emphysema is distinguished from interstitial pneumonia by the lack of pulmonary interstitial fibrosis [6]. But it was documented that pulmonary fibrosis and emphysema (CPFE) existed in some patients as a separate disease [6].

Subcutaneous emphysema is characterized by infiltration of air to the subcutaneous layer of the skin. The skin layers are epidermis then dermis and finally subcutaneous tissue under the dermis layer, the expansion of air can affect the subcutaneous tissue, if the expansion is non-extensive it would not be of medical importance, however the presence of Subcutaneous emphysema suggest the existence of air in more serious tissues that cannot be seen by eyes, infiltration of air to other tissues may cause, pneumoretroperitoneum, pneumoperitoneum and pneumothorax [7]. The air passes from these regions across pressure gradients between both the intra-alveolar and perivascular interstitium, expanding through the connection of the fascial and anatomical planes to the head, neck, chest and abdomen [7]. In this case air prefer accumulation in areas with low pressure till the pressure increases then the air spread causing massive subcutaneous spread that can cause cardiovascular and respiratory collapse [8].

In this review, we will look into the prevalence, causes, pathophysiology, diagnosis and management of emphysema.

Participants and Methods

Study design: Review article.

Study duration: Data were collected between 1 June and 30 October 2020.

Data collection: Medline and PubMed public database searches have been carried out for papers written all over the world on the most notable advances in emphysema epidemiology and management. The keyword search headings included “pulmonary emphysema, epidemiology of pulmonary emphysema, management of emphysema, causes of pulmonary emphysema” and a combination of these will be used. For additional supporting data, the sources list of each research was searched.

Criteria of inclusion: The papers have been chosen on the basis of the project importance, including one of the following topics: pulmonary emphysema, epidemiology of pulmonary emphysema, management of emphysema, causes of pulmonary emphysema, etc.

Criteria for exclusion: All other publications that did not have their main purpose in any of these areas or multiple studies and reviews were excluded.

Statistical analysis

No predictive analytics technology has been used. In order to evaluate the initial results and the methods of conducting the surgical procedure, the group members reviewed the data. The validity and minimization of error were double revised for each member’s results.

Pathophysiology

The clinical presentation and symptoms shown by the patients are due to the damage to airways distal to terminal bronchiole that include respiratory bronchiole, alveolar sacs, alveolar ducts, and alveoli totally known as acinus. The dilatation of air spaces is also accompanied with the action of protease enzyme shown as destruction of the walls, all the previous mentioned effects cause decrease in the alveolar surface area and subsequent impaired gas exchange. The disease is further classified as subtypes based on the part of the acinus affected into 3 main subtypes (1) proximal acinar: the most known subtype, found mostly in smokers and coal workers (2) Panacinar: common in alpha one antitrypsin deficiency. (3) Distal acinar: may occur alone or with the 2 previously mentioned subtypes, if alone it could be due to spontaneous pneumothorax [9].

Exposure to smoke and harmful gases cause recruitment of inflammatory cells such as neutrophils, macrophage and T lymphocytes. The cascade occur as the following steps the first is the activation of macrophages that cause release of chemotactic factors such as leukotriene B4 and interleukin-8 then recruitment of neutrophils together with macrophage cause release of proteinases and subsequent hypersecretion of mucous [9]. The integrity of lung parenchyma is maintained by the action of elastin, during emphysema Elastase/anti-elastase imbalance exists that increases the risk of lung damage. Neutrophil-derived proteases (such as elastase and proteinase) also cause damage of elastin and subsequent parenchyma damage. Beside the previously mentioned effects, smoking also cause inhibition of anti-proteolytic enzymes, the last known factor is AAT deficiency, alpha one antitrypsin (AAT) produced by parenchyma cells which act by inhibiting trypsinize and neutrophil elastase in the lung [9].

The pathophysiology of subcutaneous emphysema is different from the pulmonary one, as the subcutaneous emphysema is thought to be due to many factors as (1) Parietal pleura damage, which allows air to flow through the pleural and subcutaneous tissues. (2) The air in the mediastinum expands through the cervical viscera and other associated planes of tissue. (3) Air generated from external sources. (4) Locally produced gas through infections, in particular, necrotizing infections [7,10].

Causes

Although many causes were linked to emphysema, cigarette smoking is the first leading cause for it, 10 to 15% of cigarette smokers are known to have emphysema during their life and developing emphysema due to smoking depends on many factors such as the intensity of smoking, years of exposure and lung function. Genetic factors are also seen as those who have alpha-1 anti-trypsin (AAT) deficiency are suspected to develop emphysema, this happens mostly at young age and affects mainly lower lung lobes, in opposite to emphysema that happens due to smoking, arise mainly in late age and affect mainly upper lung lobes. Statistics shows that you need to smoke about 20 packs per years to develop emphysema [11]. Other factors such as passive smoking, specific chemicals, recurrent pulmonary infections and exposure to certain substances due to work were reported to cause emphysema [12]. Cooking using wood stove in developing countries also release smoke that can cause emphysema, Emphysema with marijuana smoking at young ages has also been recorded [13].

Surgical, traumatic, viral or spontaneous etiology may result in subcutaneous emphysema. Some common causes include damage to the thoracic cavity, sinus cavities, and facial bones, perforation of the intestine or pulmonary blebs. Due to malfunction or disruption of the ventilator circuit, improper closure of the pop-off valve, Valsalva manoeuvres which increase thoracic pressure, and trauma to the airway. During traumatic intubation, air may enter the subcutaneous spaces via minor mucosal injury to the trachea or pharynx [14]. During placement of the gastric tube, injury of the esophagus might occur where air may enter [15]. Entering of the air to the subcutaneous tissue can occur by many ways such as during tracheotomy affecting the cervical soft tissues, via industrial accidents that affect extremities, by the chest wall during arthroscopic shoulder surgery and by the female genital tract during a pelvic examination or during pregnancy as air could be blown into vagina.

The pressure exerted by ventilator inspiration will facilitate the expansion of the gas down the partial pressure gradient through the communicating fascial planes. Although non-invasive ventilation corresponds with less barotrauma rates, CPR ventilation of the bag mask and incorrect attachment of the oxygen mask that prevents exhalation can have damaging consequences [16]. A report of a case with epidural emphysema that happened due to usage of epidural catheters [17]. In another case a patient experienced massive bilateral subcutaneous emphysema with postoperative nausea and vomiting without signs of pneumothorax [14].

Prevalence

Emphysema affects high number of people around the world. The Global Burden of Disease Study reported in 2016 that there are about 251 million patients with COPD worldwide. 90% of the deaths due to COPD happens in low-income regions [18,19]. The incidence of emphysema in United States is also high as there is about 14 million emphysema patient. 14% are smokers white males and 3% white

male nonsmokers. White females' smokers and African Americans are less affected. The prevalence of emphysema is supposed to increase within the upcoming years due to many factors such as the increase in the number of smokers worldwide, massive environmental pollutions, decreasing mortality from other causes, such as infectious and cardiovascular diseases and genetic factors. Coal worker show high incidence of emphysema, this is regardless of the smoking state of the workers [18,19].

The incidence of subcutaneous emphysema ranges between 0.43% - 2.34% everywhere. A study of subcutaneous emphysema over the last 10 years suggests that mean age of patients who are diagnosed with subcutaneous emphysema is 53 +/- 14.83 where 71% of the studied patients were males [20]. About 77% of patients who had laparoscopic surgery had subcutaneous emphysema even if it was not clinically detected or proven [21]. Children with asthma are also susceptible to subcutaneous emphysema as Pneumomediastinum which is very linked to subcutaneous emphysema happens in 1 of each 20000 children during the asthmatic attack. Children less than 7 years old have more incidences for the disease [22]. 1 women from each 2000 pregnant women develop subcutaneous emphysema in the second labor due to pushing that increases the intrathoracic pressure up to more than 50cmH₂O [23]. 3 to 10% of those who undergo mechanical ventilation may develop pulmonary barotrauma this percentage may vary depending on the cause of intubation [24]. While women and people aged more than 50 years old show more susceptibility to Tracheal injury when undergoing endotracheal intubation [25]. The incidence of the tracheal injury is .005%, tracheal tear can also happen due to Emergency intubation [26]. Single lumen ET tubes cause an incidence of injury that ranges from 1 in 20000 to 1 in 75000; this incidence increases up to 0.05 to 0.19% when using double lumen ET tubes [27].

Diagnosis

Pathological diagnosis is the main diagnostic way of emphysema, while laboratory and radiographic diagnosis are non-indicative. The main diagnostic test is pulmonary function testing (PFT) using spirometry. If the results are abnormal, further post-bronchodilator test could be done. COPD is known to be irreversible or partially reversible using bronchodilator, and post-bronchodilator FEV1/FVC, when the result is less than 0.07. The interpretation of the results is based on the following criteria [28,29]:

- FEV1 > or equal to 80% known to be mild condition.
- FEV1 < than 80% known to be moderate condition.
- FEV1 < than 50% known to be severe condition.
- FEV1 < than 30% known to be very severe condition.

Chest x-ray is useful in severe conditions to exclude other diseases, where it should show hyperinflation of the lungs and elongation of the heart. Arterial blood gases are another test also required in severe conditions where oxygen saturation is less than 92%, if the patient is young in age, genetic factors should be considered and tested for alpha 1 antitrypsin deficiency (AATD) [30,31].

Subcutaneous emphysema is detected by imaging through computed tomography (CT) and radiographic (X-ray). The disease on the radiograph is shown as fluffy appearance on the outside of abdominal and thoracic walls. While chest radiograph shows striation of the gas similar to that of ginkgo leaf [32]. It is recommended to perform laryngoscopy before extubation, if cervical or facial subcutaneous emphysema occurred during the intubation [33]. It is preferred to perform bronchoscopy to determine the site of injury if intubation injury occurred. Ultrasound can also be used by using ultrasound probe, that detects the lung sliding and A-lines with a sensitivity that reaches up to 95% [34].

The typical patient of emphysema are mostly 50 or more in age, heavy smoker for long time mainly come with productive cough and shortening of breath. While in advanced COPD, the case worsen that it would interfere the normal daily life of the patient. The patient

can look tired as unintentional weight loss is also common with emphysema. Cor pulmonale is a long-standing emphysema complication which could cause symptoms and signs similar to this of the right heart failure. The two main terms known in emphysema are “pink puffers” that describes patients with hyper-expanded chest which is not cyanotic while the term “blue bloaters” describes patients with chronic bronchitis which is cyanotic [35]. The two conditions are seen together in another condition called asthma COPD overlap syndrome (ACOS) [35]. So, history of the patient is important to distinguish the two medical cases. The family history is of great importance here as alpha-1 antitrypsin (AAT) deficiency is a hereditary disease that could be transmitted through the genes [36]. The habit of smoking also runs in the families as a cultural effect. Infections are a common cause of COPD exacerbation so information about contact with sick people is important; also the vaccination history should be included in the determination of the disease such as influenza vaccine.

Crepitus on palpation is the first sign of subcutaneous emphysema that could be seen during physical examination. Bloating could be found in the abdomen, chest, neck, or face that can result in visual disruption or phonation changes [37,38]. Crackling sound when palpating the diagnosed area can also be seen. Stethoscope can also be used to detect the emitted high-frequency acoustic sound; this technique is developed by Medeiros [39]. In late stages of subcutaneous emphysema, hemodynamic or respiratory compromise can be also detected, so detecting the cause of subcutaneous emphysema is the first step toward the right therapy. Knowing the stage of the disease could be done using grading system, although many systems are validated in some studies, these systems are not routinely used or applied universally [20]. Endotracheal intubation in patients who use inhalational corticosteroids can develop tracheal injury due to soft and thin mucosa [27]. So patient history is of great importance especially in those diagnosed with asthma or COPD.

Management

There is no definitive treatment of emphysema, however all treatments act mainly by modifying risk factors and managing symptoms, the goal of this treatment is to improve the quality of life and slow the progression of the disease.

Medical therapy: Using bronchodilators either alone or together with anti-inflammatory drugs. Bronchodilators are the first line of treatment found mainly as inhalation; they are divided into two groups anticholinergic and beta2 agonist drugs. They are given regularly and act by modifying the smooth muscles of the airways and thus decrease the incidence of hospitalization, symptoms and exacerbation. The short acting class of these drugs are used in intermittent dyspnea while long acting are used in case of severe dyspnea or more than occasional dyspnea. If one drug failed to treat the condition another drug could be added. Beta2 agonists cause relaxation of the smooth muscles of airways; examples of this group are short acting as SABA like albuterol, and long acting LABA as formoterol. The main side effects of this group are tremors, hypokalemia and arrhythmias so should be used with caution in patients with heart failure. The other groups Anticholinergics act by inhibiting acetyl-choline that causes bronchoconstriction [40-42].

Inhaled corticosteroid (ICS) is an additional therapy to bronchodilators, such as beclomethasone and budesonide; the side effects are cough, and pneumonia. The systematic type of it is used only in severe cases not in the mild ones due to severe side effects. Oral Phosphodiesterase-4 inhibitors can also be added in severe conditions to reduce inflammation. FDA recently approved the triple therapy (LABA+ LAMA+ ICS) and it is taken only once daily.

Supportive therapy: Such as oxygen therapy and ventilatory support, pulmonary rehabilitation, and palliative care. Continuous long-term supply of oxygen is recommended to maintain the oxygen saturation level above 90% aiming to increase the survival rate of patients with severe hypoxia. In acute respiratory failure Noninvasive positive pressure ventilation (NPPV) is recommended as it improves the mortality and morbidity of the patients as it improves gas exchange, reduces work of breathing and decrease hospitalization time. GOLD stages B, C and D are recommended to have pulmonary rehabilitation to decrease hospitalization and dyspnea.

Treatment of subcutaneous emphysema is based on treating the cause as the main factor, if the source was controlled, subcutaneous emphysema will resolve in less than 10 days [43]. Simple treatments such as abdominal binders can cause patient's comfort, if this did

not happen high-concentration of oxygen can be used to diffusion of gas particles in a patient [44]. During endotracheal intubation if injury occurred tracheostomy is necessary to prevent more emphysema, antibiotic can be also added to stop development of mediastinitis [27]. Minimizing the air trapping and bronchospasm is of great importance in improving the condition [45]. in a case study, a patient with severe subcutaneous emphysema after thoracotomy had active subcutaneous drain therapy positioned superficially at low suction to the pectoral fascia [46].

Conclusion

Emphysema is a serious pulmonary disease; it is known to be form of COPD. As it affects mainly the lungs, smoking is considered the first leading cause to pulmonary emphysema, other causes such as coal workers and genetic factors can also be seen. Another type is the subcutaneous emphysema that occurs secondary to other causes once these causes are treated the condition will resolve by itself within 10 days. But the treatment of pulmonary emphysema requires usage of bronchodilators and corticosteroids. Early detection of the case can enhance the treatment and improve the quality of the patient's life.

Bibliography

1. American Thoracic Society. "Chronic bronchitis, asthma and pulmonary emphysema: a statement by the Committee on Diagnostic Standards for Nontuberculous Respiratory Diseases". *The American Review of Respiratory Disease* 85 (1962): 762-768.
2. Rustagi N., et al. "Efficacy and Safety of Stent, Valves, Vapour ablation, Coils and Sealant Therapies in Advanced Emphysema: A Meta-Analysis". *Turkish Thoracic Journal* 2.1 (2019): 43-60.
3. Fernandez-Bussy S., et al. "Bronchoscopic Lung Volume Reduction in Patients with Severe Emphysema". *Seminars in Respiratory and Critical Care Medicine* 39.6 (2018): 685-692.
4. Dunlap DG., et al. "Bronchoscopic device intervention in chronic obstructive pulmonary disease". *Current Opinion in Pulmonary Medicine* 25.2 (2019): 201-210.
5. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015". *The Lancet Respiratory Medicine* 5.9 (2017): 691-706.
6. Alsumrain M., et al. "Combined pulmonary fibrosis and emphysema as a clinicoradiologic entity: Characterization of presenting lung fibrosis and implications for survival". *Respiratory Medicine* 146 (2019): 106-112.
7. Maunder RJ., et al. "Subcutaneous and mediastinal emphysema. Pathophysiology, diagnosis, and management". *Archives of Internal Medicine* 144.7 (1984): 1447-1453.
8. Dixit R and George J. "Subcutaneous emphysema in cavitary pulmonary tuberculosis without pneumothorax or pneumomediastinum". *Lung India* 29.1 (2012): 70-72.
9. Pahal P., et al. "Emphysema" (2020).
10. Abu-Omar Y and Catarino PA. "Progressive subcutaneous emphysema and respiratory arrest". *Journal of the Royal Society of Medicine* 952 (2002): 90-91.
11. Thomson NC. "Challenges in the management of asthma associated with smoking-induced airway diseases". *Expert Opinion on Pharmacotherapy* 19.14 (2018): 1565-1579.
12. Peiffer G., et al. "[COPD: think about occupational exposures!]" *Rev Prat* 68.1 (2018): 74-78.

13. Chardon ML, et al. "[Pneumothorax in young cannabis smokers: A propos of three cases]". *La Revue des Maladies Respiratoires* 35.5 (2018): 556-561.
14. Sullivan TP and Pierson DJ. "Pneumomediastinum after freebase cocaine use". *American Journal of Roentgenology* 168.1 (1997): 84.
15. Schumann R and Polaner DM. "Massive subcutaneous emphysema and sudden airway compromise after postoperative vomiting". *Anesthesia and Analgesia* 89.3 (1999): 796-797.
16. Newton NI and Adams AP. "Excessive airway pressure during anaesthesia. Hazards, effects and prevention". *Anaesthesia* 33.88 (1978): 689-699.
17. Dolinski SY, et al. "An unusual case of subcutaneous emphysema". *Anesthesia and Analgesia* 89.1 (1999): 150-151.
18. Zhang H, et al. "Epidemiology of chronic airway disease: results from a cross-sectional survey in Beijing, China". *The Journal of Thoracic Disease* 10.11 (2018): 6168-6175.
19. Mouronte-Roibás C, et al. "Influence of the type of emphysema in the relationship between COPD and lung cancer". *International Journal of Chronic Obstructive Pulmonary Disease* 13 (2018): 3563-3570.
20. Aghajanzadeh M, et al. "Classification and Management of Subcutaneous Emphysema: a 10-Year Experience". *The Indian Journal of Surgery* 77.2 (2015): 673-677.
21. Ott DE. "Subcutaneous emphysema--beyond the pneumoperitoneum". *Journal of the Society of Laparoendoscopic Surgeons* 18.1 (2014): 1-7.
22. González García L, et al. "Severe subcutaneous emphysema and pneumomediastinum secondary to noninvasive ventilation support in status asthmaticus". *Indian Journal of Critical Care Medicine* 20.4 (2015): 242-244.
23. Berdai MA, et al. "Spontaneous Pneumomediastinum in Labor". *Case Reports in Obstetrics and Gynecology* (2017): 6235076.
24. Anzueto A, et al. "Incidence, risk factors and outcome of barotrauma in mechanically ventilated patients". *Intensive Care Medicine* 30.4 (2004): 612-619.
25. Lim H, et al. "Tracheal rupture after endotracheal intubation - A report of three cases". *Korean Journal of Anesthesiology* 62.3 (2012): 277-280.
26. Ghosh I, et al. "Subcutaneous emphysema after endotracheal intubation: A case report". *Saudi Journal of Anaesthesia* 12.2 (2018): 348-349.
27. Ovári A, et al. "Conservative management of post-intubation tracheal tears-report of three cases". *The Journal of Thoracic Disease* 6.6 (2014): E85-E91.
28. Harrison R, et al. "Surgical Emphysema in a Pediatric Tertiary Referral Center". *Pediatric Emergency Care* 36.1 (2020): e21-e24.
29. Buttar BS and Bernstein M. "The Importance of Early Identification of Alpha-1 Antitrypsin Deficiency". *Cureus* 10.10 (2018): e3494.
30. Cheng T, et al. "Emphysema extent on computed tomography is a highly specific index in diagnosing persistent airflow limitation: a real-world study in China". *International Journal of Chronic Obstructive Pulmonary Disease* 14 (2019): 13-26.
31. Bhatt SP, et al. "New Spirometry Indices for Detecting Mild Airflow Obstruction". *Scientific Reports* 8.1 (2018): 17484.
32. Medeiros BJDC. "Subcutaneous emphysema, a different way to diagnose". *Revista da Associação Médica Brasileira* (1992). 64.2 (2018): 159-163.

33. Chien GL and Soifer BE. "Pharyngeal emphysema with airway obstruction as a consequence of laparoscopic inguinal herniorrhaphy". *Anesthesia and Analgesia* 80.1 (1995): 201-203.
34. Husain LF, et al. "Sonographic diagnosis of pneumothorax". *Journal of Emergencies, Trauma, and Shock* 5.1 (2012): 76-81.
35. Kim M., et al. "Association between asthma/chronic obstructive pulmonary disease overlap syndrome and healthcare utilization among the US adult population". *Current Medical Research and Opinion* 35.7 (2019): 1191-1196.
36. Hazari YM, et al. "Alpha-1-antitrypsin deficiency: Genetic variations, clinical manifestations and therapeutic interventions". *Mutation Research* 773 (2017): 14-25.
37. Abu-Omar Y and Catarino PA. "Progressive subcutaneous emphysema and respiratory arrest". *Journal of the Royal Society of Medicine* 95.2 (2002): 90-91.
38. Ahmed Z, et al. "High negative pressure subcutaneous suction drain for managing debilitating subcutaneous emphysema secondary to tube thoracostomy for an iatrogenic post computed tomography guided transthoracic needle biopsy pneumothorax: Case report and review of literature". *International Journal of Surgery Case Reports* 26 (2016): 138-141.
39. Medeiros BJDC. "Subcutaneous emphysema, a different way to diagnose". *Revista da Associação Médica Brasileira* (1992). 64.2 (2018): 159-163.
40. Campo ML, et al. "Emphysema Quantification On Simulated X-Rays Through Deep Learning Techniques". *Proc IEEE Int Symp Biomed Imaging* (2018): 273-276.
41. Storre JH, et al. "Home noninvasive ventilatory support for patients with chronic obstructive pulmonary disease: patient selection and perspectives". *International Journal of Chronic Obstructive Pulmonary Disease* 13 (2018): 753-760.
42. Press VG, et al. "Screening for Chronic Obstructive Pulmonary Disease". *The Journal of the American Medical Association* 17 (2017): 1702-1703.
43. Balaji SM. "Subcutaneous emphysema". *Journal of Oral and Maxillofacial Surgery* 14.2 (2015): 515-517.
44. Ahmed AH and Awouda EA. "Spontaneous pneumomediastinum and subcutaneous emphysema in systemic lupus erythematosus". *BMJ Case Reports* (2010).
45. Wang HS, et al. "Tracheal injury characterized by subcutaneous emphysema and dyspnea after improper placement of a Sengstaken-Blakemore tube: A case report". *Medicine* 97.30 (2018): e11289.
46. Tran Q, et al. "Management of extensive surgical emphysema with subcutaneous drain: A case report". *International Journal of Surgery Case Reports* 44 (2018): 126-130.

Volume 17 Issue 2 February 2021

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