Bronchopulmonary complications therapy

Pneumothorax in cystic fibrosis

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Background

Spontaneous Pneumothorax (PNX), a potentially life-threatening complication for people with CF (Mingora CM, Flume PA.2021), is characterized by the presence of air in the pleural space. Structural impairment and altered airflow dynamics in the lungs of CF patients are considered as the main predisposing factors, but also inhaled medications and non-invasive positive pressure ventilation (NIPPV) could increase the risk of pneumothorax (Kioumis IP et al. 2014). Its annual incidence is estimated at 0.64% according to US registry data, with a lifetime risk of 3.4%, and an incidence increasing proportionally with age and disease severity, as well as with the presence in sputum of Pseudomonas aeruginosa (PA), Burkholderia cepacia (BC), Aspergillus fumigatus (AF). In several cases the need for a feeding tube may represent a risk factor. Cysts, blebs and bullae are all commonly identified in the lungs of CF as risk factors. Spontaneous PNX is defined as recurrent when it occurs on the same side seven days or more after resolution of the first episode, or persistent if the air leak lasts for more than five days. In adults with CF (King CS et al. 2019) and severe lung disease pneumothorax occurs up to 72.4%. In the past (Diso D et al. 2013) a single-center longitudinal survey on 101 patients with CF and bilateral lung transplantation showed that PNX could be an additional risk factor for perioperative mortality. Clinical presentation could range from dramatic to very mild disease. The majority of people present clinical symptoms such as chest pain or breathlessness and on rare occasions respiratory failure, although pneumothorax may occasionally be asymptomatic. Generally PNX is associated with a higher morbidity and mortality in the two years following the clinical manifestation.

Diagnosis is based on clinical symptoms and imaging (CT scan). Recently (Dietrich CF. 2021) ultrasound (US) has been discussed by World Federation of Societies for Ultra-sound in Medicine and Biology (WFUMB) as a diagnostic tool for paediatric patients with pneumothorax, as discussed also in a recent review (Boni A et al. 2024).

Recently Artificial intelligence (AI) applications for chest radiography and chest CT are under development in radiology covering a wide range of abnormalities, including pneumothorax. Software could detect early changes of CF on chest CT (Schalekampe S et al. 2022) .

Cystic Fibrosis Pulmonary Guidelines for Pulmonary Complications (Flume PA et al. 2010) and a review (Flume PA et al. 2011) have been previously published to help clinicians to define how a PNX should be monitored. In CF spontaneous PNX therapy is a still a controversial issue and there are no standard treatments (Lord RW et al. 2016)). Management of spontaneous pneumothorax occurring to patients with CF is essentially similar to that for non-CF patients. Either medical or surgical interventions represent two options for acute or recurrent PNX therapy. While surgical interventions are felt to be more effective in pwCF, complications directly related to this procedure, as well as post-operative complications, make surgical interventions at higher risk in pwCF. Additionally, it is also debated whether these interventions make pwCF ineligible for lung transplantation in the future. No systematic reviews are available assessing both clinical efficacy and safety of different interventions for persistent PNX.

A report of the European Respiratory Society/European Cystic Fibrosis Society task force on the care of adults with CF (Elborn JS et al. 2016) outlined the relevance for respiratory physicians to be adequately trained in CF management of complications such as PNX. However, guidelines are unable to cover all aspects of this complication, as previously reviewed (Lord RW et al. 2016).

More recently (Bayomy OF et al. 2024) a dataset combining data from the CF Foundation Patient Registry and the Organ Procurement and Transplantation Network (2005-2019) was performed in order to evaluate the frequency of LAS (lung allocation score) exceptions in PwCFs listed for lung transplantation and assess whether LAS exceptions are associated with improved waitlist outcomes for PwCFs compared with similarly "at-risk" individuals without LAS exceptions, including PNX. LAS exceptions resulted in a similar time to transplantation for PwCFs compared with similarly at-risk individuals. By the new lung allocation score used to determine transplant priority in USA these LAS-based results could improve the risk of stratification among PwCFs being considered for lung transplantation.

Recently (Haider S et al. 2025) it has been suggested a higher incidence of post-ERCP pneumothorax (0.93%) in patients with CF requiring endoscopic retrograde cholangiopancreatography (ERCP) than the patients in the non-CF group (0.15%).

Issues

To evaluate both benefits and side effects or disadvantages for surgical and non-surgical treatments of persistent and recurrent PNX in people with CF.

What is known

Only one CDSR (Amin R et al. 2012) has been published many years ago to compare the use of chemical pleurodesis by quinacrine, silver nitrate, talc or tetracycline derivatives with surgical interventions, including open thoracotomy or video assisted thoracoscopic surgery (VATS) for pleurodesis in recurrent and persistent PNX. No RCTs have been found on this topic.

Recently (Bhagat M et al. 2024) a systematic review searching from PubMed, Cochrane, Embase, Web of Science, and clinical trials.gov was performed with the aim to compare the efficacy of doxycycline, tetracycline, and minocycline to other pleurodesis agents in the resolution of pnx and reduction of recurrence of pnx in adults with persistent air leaks following secondary spontaneous pnx. After

screening, three studies were selected which includes 2 randomized controlled trials (RCTs) and 1 prospective study with a pooled sample size of 168 adults including COPD, tuberculosis TB, HIV, cystic fibrosis , and history of smoking. The mean age and standard deviation of the study participants was 50.57±13.23 years. The success rate of autologous blood patch pleurodesis (ABPP) was reported as 94.70% followed by doxycycline with 84.20%, talc with 84% and tetracycline 63%. The mean time of cessation of air leaks was lowest with doxycycline (11 and 36 hours) and ABPP (24 and 27 hours). Furthermore, ABPP is reported having fewer complications when compared with other agents.

Unresolved questions

There is no consensus on the agent which should be used for pleurodesis in people with CF, when applicable, neither what surgical intervention is more effective.

While the choice of sclerosing agents, as well as the ideal dose and technique of administration, remains variable in clinical practice for medical intervention, limitations of sclerosant instillation procedure mainly include prolonged pleural drainage and unequal deposition, resulting in incomplete pleurodesis. In particular, talc results in more systemic inflammation and its use is a relative contraindication for lung transplantation in people with CF.

On the other hand, up to now clinicians have no sufficient data showing whether surgical interventions, primarily including open thoracotomy, pleurectomy and resection, electrocautery or laser ablation of a bleb or bullae, could be the most effective way for treating or preventing PNX.

As previously outlined multi-centered RCTs mainly designed to explore the optimal management strategy for spontaneous and persistent PNX in people with CF aimed at evaluating recurrence of PNX as primary outcome, and length of hospitalization and adverse events as secondary outcomes are still missing. Besides the need of RCTs, ethical issues make very difficult to design clinical trials studies and draw the appropriate conclusions. So clinicians must make an individual choice of intervention for each patient (Lord RW et al, 2016).

Keywords

Pneumothorax;