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Streszczenie w języku angielskim

Evaluation of the role of chest imaging tests in the diagnostics of chronic cough in adults.

Chronic cough (CC), lasting more than 8 weeks, is a frequent complaint for which patients seek medical attention. It affects both children and adults, but the diagnostic and therapeutic procedures in children and adults are different. According to epidemiological data, it affects about 4-10% of the world's population.

The most common cause of CC is cigarette smoking and related with it chronic bronchitis and chronic lung diseases (chronic obstructive pulmonary disease (COPD), chronic infections, bronchiectasis, interstitial lung diseases, lung cancer). It also often occurs as a side effect of therapy with angiotensin converting enzyme inhibitors (ACEi). The most frequent causes of CC in non-smoking patients, who are not treated with ACEi and have normal chest radiograph (CXR) are asthma, gastroesophageal reflux disease (GERD) and upper airway cough syndrome (UACS).

The cough reflex begins with stimulation of receptors of the vagus nerve endings located in the mucous membrane of the lower and upper respiratory tract, as well as of the esophagus, middle ear or pericardium. Patients with CC often develop hypersensitivity of the cough reflex, i.e. coughing in response to low intensity stimulation (speaking, cold or dry air, tickling in the throat) which in healthy subjects does not induce cough. Hypersensitivity of cough reflex leads to two clinical situations- unexplained chronic cough (UCC), when we are unable to determine the cause of the cough and refractory chronic cough (RCC), when the cause of cough is established but the treatment is ineffective.

The diagnosis of CC in adults begins with taking a thorough history and physical examination of the patient. History taking should include assessment of exposure to cough-provoking substances (smoking, drugs, allergens, irritants at home and at work), coexisting symptoms (shortness of breath, wheezing, heartburn, regurgitation, nausea, grunting, chronic runny nose, impaired nasal patency, sense of smell, headache), characteristics of cough

and assessment of response to previous treatment. Current recommendations of the *European Respiratory Society* (ERS) regarding the management of CC recommend CXR and spirometry as obligatory diagnostic tests. Further investigations depend on the symptoms and signs presented by the patients. However, chest computed tomography (CT) is not routinely recommended. The authors of the ERS guidelines as justification pointed out that so far there is no convincing data to link the changes revealed in chest CT scan with the actual causes of cough and better response to treatment. Moreover, the authors of the recent ERS guidelines emphasized the increased risk of cancer due to exposure to ionizing radiation associated with the CT scan. On the other hand, chest CT is currently a key imaging test in the diagnosis of many respiratory diseases, including those where one of the symptoms may be CC.

The thesis consists of three publications related thematically, the objectives of which were:

1. Analysis of the diagnostic accuracy of CXR in relation to the results of chest CT as the "gold standard" of imaging diagnostics of chest diseases in adults with CC.
2. Evaluation of the impact of the results of chest CT on further management in adults with difficult to treat CC.
3. Determining the group of diseases in which performing chest CT in the course of CC diagnostics is particularly useful.
4. Evaluation of the impact of the presence of hiatal hernia (HH) demonstrated in chest CT on the severity, severity and efficacy of treatment of CC associated with gastroesophageal reflux (GER).

The research was conducted by analysing retrospective clinical data of adults admitted to the Department of Internal Medicine, Pulmonary Diseases and Allergy of the Medical University of Warsaw between 2010 and 2021 due to CC. All patients underwent diagnostics of the causes of CC in accordance with the current recommendations of ERS 2004 and 2020, *British Thoracic Society* (BTS) 2006 and *American College of Chest Physicians* (ACCP) 2006 and 2018. CXR and chest CT images were evaluated by experienced radiologists. The study protocol was approved by the Institutional Review Board of the Medical University of Warsaw (KB/101/2009 and KB/20/A2021) as part of a larger project analysing the effectiveness of CC management. All patients gave informed consent for their data to be used for analysis.

First study, *Is a normal chest radiograph sufficient to exclude pulmonary abnormalities potentially associated with chronic cough?* doi:0.5603/ARM.2018.0018, included 59 non-smoking patients who had a normal CXR and in whom chest CT was performed. Evaluation of the results of the chest CT made it possible to distinguish two groups of patients with 1) true negative CXR and 2) false negative CXR, in whom significant abnormalities were found in CT. Negative predictive value (NPV) was calculated as the ratio of the number of patients with a true negative CXR to the number of all patients with a normal CXR result and chest CT performed. In 21 patients (21/59, 35.6%), significant abnormalities were found in CT, despite the normal result of the CXR. The NPV for a CXR in the diagnosis of the causes of CC was calculated as 64%, which is a relatively low value. In conclusion, the CXR seems to be insufficient to rule out important causes of CC.

In the second study, *Diagnostic yield of chest radiograph in management of adults with difficult-to-treat chronic cough—retrospective study.* doi: 10.21037/jtd-22-111, there were 189 adults with CC included who underwent both a CXR and a chest CT. Statistical analysis was performed, calculating the sensitivity, specificity, negative and positive predictive value (PPV) and diagnostic accuracy of the CXR based on the results of CT as the "gold standard". In addition, the impact of revealed changes significant for the cause of cough in CT on the modification of further diagnostic and therapeutic management was assessed. CXR showed abnormalities in 23 patients (23/189, 12.2%), and it was normal in 166 (166/189, 87.8%). CT confirmed a normal CXR in 141 patients (141/166, 84.9%), while in 25 (26/166, 15.1%) changes that may be a significant cause of CC were found and in these patients further management was modified due to the result of CT. Based on the CT result, HH was found in 8 patients, bronchial wall thickening with parenchymal opacities in 1 patient, deformation of the trachea and bronchial wall in 1 patient, multiple pulmonary nodules (MPN) in 1 patient, ground glass opacities in 1 patient, bronchiectasis coexisting with MPN with parenchymal opacities and mediastinal lymphadenopathy in 1 patient, bronchiectasis in 2 patients, reticular opacities with honeycomb pattern and traction bronchiectasis in 1 patient, nodule with a spiculated margins with diameter >10 mm was found in 1 patient, and injury of the diaphragm with secondary hernia in 1 patient. Sensitivity, specificity, PPV, NPV and diagnostic accuracy were 24.2%, 90.4%, 34.8%, 84.9% and 78.8%, respectively. Based on the above results, it can be concluded that CXR shows limited diagnostic usefulness in CC and that

chest CT may provide additional important data that may influence further diagnostic and therapeutic procedures in patients with CC.

The third study, *Does hiatal hernia impact gastroesophageal reflux-related chronic cough?* doi: 10.1183/23120541.00669-2022, involved 45 patients with CC and gastroesophageal reflux (GER), in whom the presence and size of HH was assessed in CT and the effectiveness of anti-reflux treatment was documented. HH was diagnosed in 26.6 % of patients (12/45). There was no difference in clinical features, cough duration and severity on the visual analogue scale (VAS), and cough-related quality of life as assessed by the Leicester Cough Questionnaire (LCQ). A moderate positive correlation was found between the maximum sagittal dimension of the hernia and cough severity ($\rho=0.692$, $p=0.013$) and cough duration ($\rho=0.720$, $p=0.008$). In addition, in patients without HH, a greater effectiveness of anti-reflux therapy was found, with a significant increase in LCQ. A strong negative correlation was found between the maximum dimension of the hernia gate and the increase in LCQ ($\rho= -0.764$, $p=0.004$), which indicates that the size of the hernia gate may affect the lack of effectiveness of CC treatment in this group. In conclusion, the presence of HH demonstrated in chest CT may affect the severity and duration of cough, as well as the response to anti-reflux therapy in patients with GER-related CC.