

Is that asthma or something else?

Je li to astma ili nešto drugo?

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SUMMARY—The prevalence of asthma in adults varies widely around the world, ranging from 0.2% to 21.0%. Population-based studies suggest that from 20% to 70% of people with asthma in the community remain undiagnosed. On the opposite side of the spectrum, 30–35% of adults and children diagnosed with asthma do not have current asthma. Overdiagnosis of current asthma can occur due to various reasons: 1. Physicians' failure to confirm airflow limitation; 2. New signs and symptoms in patients with long-term clinical remission of previous asthma; 3. Alternative diagnoses that mimic signs and symptoms of asthma. The most common differential diagnosis of asthma in adults is vocal cord dysfunction, airflow obstruction (e.g. tumors and foreign bodies), congestive heart failure, chronic obstructive pulmonary disease (COPD), chronic sinusitis and infection of upper airways. The consequences of the overdiagnosis of asthma are: 1. Not diagnosing and treating the actual disease; 2. Prolonged use of medication for asthma treatment in patients without asthma leads to the occurrence of adverse effects and complications caused by medication; 3. Unnecessary costs of treatment or increased insurance rates.

KEY WORDS: asthma, overdiagnosis, differential diagnosis

SAŽETAK—Prevalencija astme odraslih u svijetu varira od 0,2 % do 21,0 %. Populacijske studije pokazuju da 20 – 70 % ljudi s astmom ostaje nedijagnosticirano. Na suprotnoj strani, 30 – 35 % odraslih i djece kojima je dijagnosticirana astma zapravo nemaju astmu koja im je dijagnosticirana. Prekomjerna dijagnoza trenutačne astme može se pojaviti iz različitih razloga: 1. neuspjeh liječnika da potvrdi ograničenje zračnog protoka; 2. novi znakovi i simptomi u pacijenta s trajnom kliničkom remisijom prethodne astme; 3. alternativne dijagnoze koje oponašaju znakove i simptome astme. Najčešća diferencijalna dijagnoza astme u odraslih su disfunkcija glasnica, mehanička opstrukcija dišnih putova (npr. tumori i strana tijela), kongestivno zatajenje srca, kronična opstruktivna plućna bolest (KOPB), kronični sinusitis i infekcije gornjih dišnih putova. Posljedice prekomjerne dijagnoze astme su: 1. nedijagnosticiranje i neliječenje stvarnog oboljenja; 2. produljena uporaba lijekova u liječenju astme u pacijenta bez astme čini apsolutnu pojavu nuspojava i komplikacija lijekova; 3. nepotrebni troškovi liječenja ili povišene stope osiguranja.

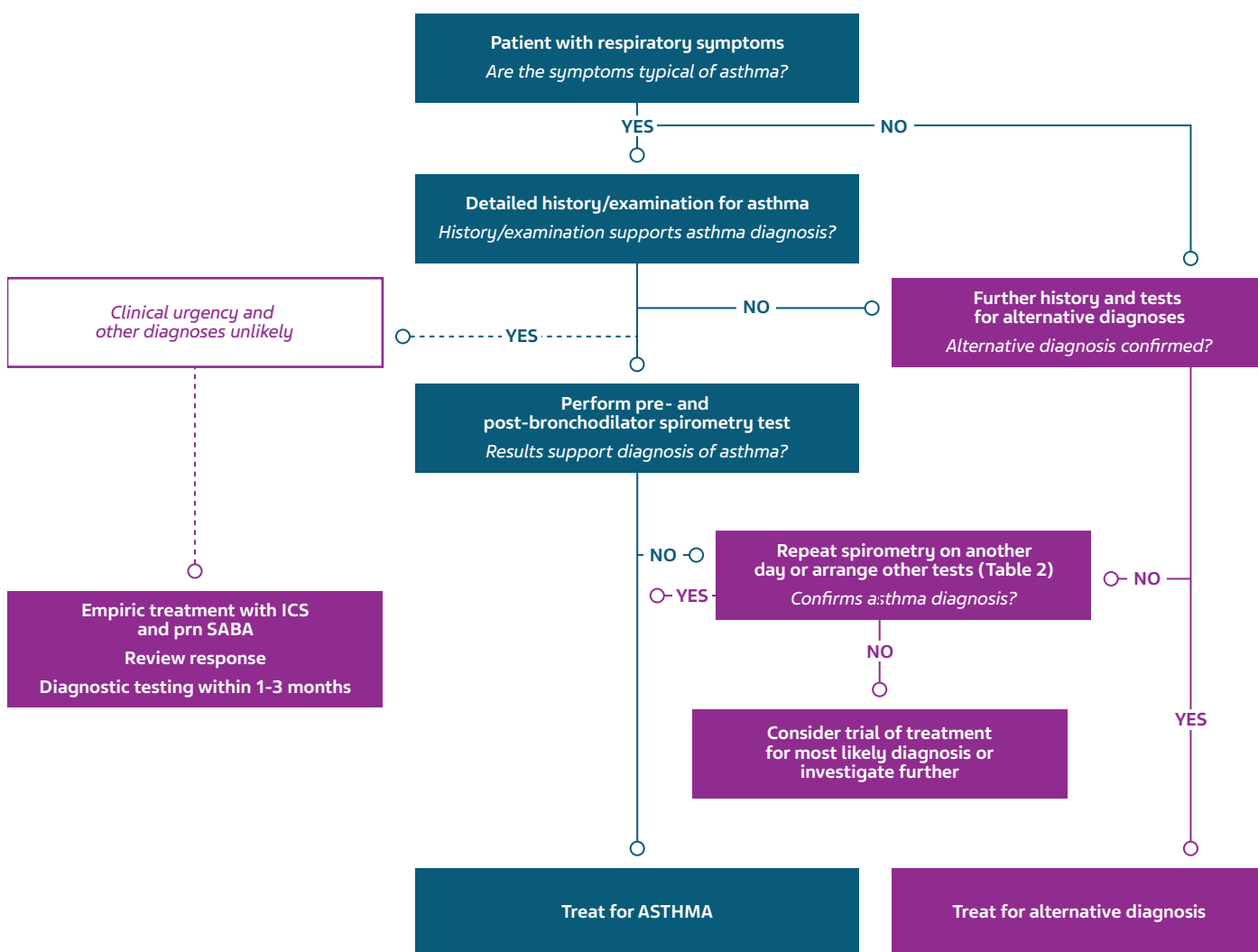
KLJUČNE REČI: astma, prekomjerna dijagnostika, diferencijalna dijagnoza



Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by a history of respiratory symptoms such as wheezing, shortness of breath, chest tightness, and cough that vary over time and intensity, together with variable expiratory airflow limitation (1). Past definitions of asthma were complex, but with growing evidence of the heterogeneity of asthma, the new GINA definition in 2019 reflected the view that the essential features are a history of variable symptoms and variable airflow limitation (2). The prevalence of asthma varies widely around the world, ranging from 0.2% to 21.0% in adults. Population-based studies in children, adults, and the elderly suggest that 20% to 70% of people with asthma remain undiagnosed and hence untreated. Underdiagnosis of asthma has been found to be associated with underreporting of respiratory symptoms by patients to physicians as well as poor socioeconomic status. On the opposite side of the spectrum, studies of patients with physician-diagnosed asthma suggest that 30–35% of adults and children diagnosed with asthma do not have current asthma, suggesting that asthma is also overdiagnosed (2).

Astma je heterogena bolest, karakterizirana kroničnom upalom dišnih putova. Definira je povijest respiratornih simptoma kao što su sviranja u prsima, kratkoća daha, stezanje u prsima i kašalj koji variraju u vremenu i intenzitetu, zajedno s promjenjivim ograničenjem ekspiracijskog protoka zraka (1). Dosadašnje definicije astme bile su složene, ali s rastućim dokazima heterogenosti astme. GINA definicija 2019. iznijela je mišljenje da su osnovna obilježja povijest promjenjivih simptoma i promjenjivo ograničenje protoka zraka (2). Prevalencija astme u odraslih vrlo je različita u cijelom svijetu, i to u rasponu od 0,2 % do 21,0 %. Populacijska istraživanja u djece, odraslih i starijih osoba sugeriraju da 20 – 70 % ljudi koji pate od astme ostaju nedijagnosticirani i stoga se ne liječe. Otkriveno je da je nedovoljno dijagnosticiranje astme povezano sa slabom prijavom respiratornih simptoma od strane pacijenata, kao i s lošim socioekonomskim statusom. S druge strane, druge studije daju izvješća da 30 – 35 % odraslih i djece kojima je dijagnosticirana astma uistinu nemaju ovo oboljenje i da je astma prekomjerno dijagnosticirana (2).

FIGURE 1. Diagnostic algorithm for confirming or ruling out asthma in a patient with respiratory symptoms



(source: GINA 2019.)

ICS = inhaled corticosteroids; SABA = short-acting β_2 -agonist

Asthma diagnosis

GINA 2019 suggests an efficient series of tests to diagnose asthma (Figure 1), starting with pre- and post-bronchodilator spirometry, and if spirometry is inconclusive, further tests can be ordered (1).

Asthma overdiagnosis

About one-third of adult patients diagnosed with asthma in the community do not have asthma and this diagnosis is overused. According to a Canadian study, 61 adults previously diagnosed with asthma have been assessed with the home peak flow, along with symptom monitoring, spirometry, and serial bronchial challenge tests. Asthma medications gradually tapered off over four study visits. Ultimately, current asthma was ruled out in 33% of study participants. After an additional 12 months of follow-up of all asthma medications, 30% of participants continued

Dijagnoza astme

GINA 2019. predlaže učinkovit niz testova za dijagnosticiranje astme (slika 1.), počevši od pre- i post-bronhodilatatorne spirometrije, a ako spirometrija nije uvjerljiva, mogu se provesti daljnji testovi (1).

Pretjerana dijagnoza astme

Otpriblike jedna trećina odraslih pacijenata u zajednici kojoj je dijagnosticirana astma nema astmu i ova dijagnoza je prekomjerno uporabljena. U kanadskoj studiji 61 odrasla osoba s ranije dijagnosticiranom astmom procijenjena je kućnim vršnim protokom, zatim praćenjem simptoma, spirometrijom i serijskim bronhoprovokacijskim probama. Lijekovi za astmu postupno su smanjivani tijekom četiri studijska posjeta. Konačno, isključena je dijagnoza astme u 33 % sudionika u studiji. Nakon dodatnih 12 mjeseci praćenja svih lijekova u liječenju astme, 30 % pacijenata i

FIGURE 2. Diagnostic serial testing algorithm to confirm or exclude asthma in patients who have previously been diagnosed with asthma and who are receiving asthma medications (source: Aaron *et al*, 2018.).



to exhibit no clinical or laboratory evidence of asthma. Authors of this study also suggested the algorithm to rule in or rule out asthma in patients who had been previously diagnosed with asthma (Figure 2) (2).

Similar results were obtained in other studies, where asthma diagnosis was excluded in 34%, or even 61% of patients (3).

Overdiagnosis of current asthma may occur for various reasons: 1. Physicians' failure to confirm airflow limitation; 2. New signs and symptoms in patients with long-term clinical remission of previous asthma; 3. Alternative diagnoses that mimic signs and symptoms of asthma; (2). Up to 68% of patients experience sustained clinical remission of asthma during their lifetime (4). Therefore, symptoms that mimic asthma in such adults do not necessarily mean the recurrence of asthma itself (2), and alternative diagnoses should be considered.

dalje nije imalo kliničkih ili laboratorijskih dokaza o astmi. Autori ove studije također su predložili i algoritam potvrde ili isključenja astme u pacijenata kojima je prethodno bila dijagnosticirana astma (slika 2.) (2).

Slični rezultati pokazali su se i u drugim istraživanjima, isključujući dijagnozu astme u 34 %, pa do čak u 61 % pacijenata (3).

Prekomjerna dijagnoza trenutačne astme može se pojaviti iz različitih razloga: 1. neuspjeh liječnika da potvrdi ograničenje zračnog protoka; 2. novi znakovi i simptomi u pacijenata s trajnom kliničkom remisijom prethodne astme; 3. alternativne dijagnoze koje oponašaju znakove i simptome astme (2). Trajnu kliničku remisiju rane astme iskusi i do 68 % pacijenata u nekom životnom razdoblju (4). Dakle, simptomi nalik astmi u ove odrasle osobe ne znače obvezatno i recidiv same astme (2), već bi trebalo uzeti u obzir i alternativne dijagnoze.

Consequences of asthma overdiagnosis

One of the most important consequences of asthma overdiagnosis may be a lost opportunity for detection and timely treatment of the real cause of patient's symptoms. Hence, about 6% of patients with asthma overdiagnosis actually had an unrecognized serious cardio-respiratory condition, critical disease of coronary arteries or subglottic stenosis (2). Furthermore, prolonged application of bronchodilators and inhaled corticosteroids in patients without asthma increases the risk of side effects and adverse effects of medication, as well as unnecessary costs of treatment and increased insurance rates (5).

Despite the availability of asthma diagnostics, there are still many potential pitfalls that can interfere with the correct diagnosis of asthma (2). In each suspected case, an alternative diagnosis should be sought.

Differential asthma diagnosis

The most common differential diagnosis of asthma in adults is vocal cord dysfunction, airflow obstruction (e.g. tumors and foreign bodies), congestive heart failure, chronic obstructive pulmonary disease (COPD), chronic sinusitis and infection of upper airways. The consequences of the overdiagnosis of asthma are: 1. Not diagnosing and treating of the actual disease; 2. Prolonged use of medication for asthma treatment in patients without asthma leads to the occurrence of adverse effects and complications caused by medication; 3. Unnecessary costs of treatment or increased insurance rates.

Less common causes of chest wheeze include: pulmonary migraine, aortic arch anomalies, diffuse panbronchiolitis, gastroesophageal reflux disease, shortage of alpha 1-antitrypsin, aspergillosis, bronchiectasis, cystic fibrosis, pulmonary embolus, pulmonary eosinophilia, sarcoidosis, primary ciliary dyskinesia, obesity and use of some medication (2, 6, 7).

Vocal cord dysfunction may occur alone or with asthma and is caused by paradoxical vocal cord adduction during inhalation. It may occur during further breathing, speaking or laughing. Patients with chronic symptoms suggesting asthma, who have normal spirometry with poor reaction to medication for the treatment of asthma, should have their vocal cord dysfunction checked. The diagnosis can often be established by direct laryngoscopy, but only during symptomatic periods or after exercise. The flattening of the inhalation section of the spirometry flow-volume curve may also suggest vocal cord dysfunction, but it is observed only in 28% of patients at the onset of the disorder. Useful diagnostic examinations include video footage of the attack and laryngoscopy during the attack (7).

Tracheal and bronchial lesions, including tumors, may have symptoms and signs very similar to those

Posljedice prekomjerne dijagnoze astme

Jedna od najvažnijih posljedica prekomjerne dijagnoze astme može biti izgubljena prilika za otkrivanje i pravodobno liječenje stvarnog uzroka pacijentovih simptoma. Tako je oko 6 % pacijenata s prijedijagnosticiranom astmom imalo zapravo neprepoznato ozbiljno kardiorespiratorno stanje, kritičnu bolest koronarnih arterija ili subglotičnu stenozu (2). Nadalje, produljena primjena bronhodilatatora i inhalacijskoga kortikosteroidnog lijeka u pacijenata bez astme povećava rizik za pojavu nuspojava i neželjenih učinaka lijekova, zatim do nepotrebnih troškova vezanih uz liječenje, ali i povišene stope osiguranja (5).

Unatoč dostupnosti dijagnostike za astmu, još uvijek postoje mnoge potencijalne zamke koje mogu ometati ispravnu dijagnozu astme (2). U svakom sumnjivom slučaju uvijek treba tražiti alternativnu dijagnozu.

Diferencijalne dijagnoze astme

Najčešća diferencijalna dijagnoza astme u odraslih je disfunkcija glasnica, mehanička opstrukcija dišnih putova (npr. tumori i strana tijela), kongestivno zatajenje srca, kronična opstruktivna bolest pluća (KOPB), kronični sinusitis i infekcija gornjih dišnih putova.

Posljedice prekomjerne dijagnoze astme su: 1. nedijagnosticiranje i neliječenje stvarnog oboljenja; 2. produljena uporaba lijekova u liječenju astme u pacijenta bez astme čini apsolutnu pojavu nuspojava i komplikacija lijekova; 3. nepotrebni troškovi liječenja ili povišene stope osiguranja.

Rjeđi uzroci sviranja u prsima uključuju: plućnu migrenu, anomalije luka aorte, difuzni panbronhiolitis, gastroezofagealnu refluksnu bolest, manjak alfa 1-antitripsina, aspergilozu, bronhiektazije, cističnu fibrozu, plućnu emboliju, plućnu infiltraciju eozinofilima, sarkoidozu, primarnu cilijarnu diskineziju, gojaznost i uporabu nekih lijekova (2, 6, 7).

Disfunkcija glasnica može postojati sama ili s astmom, a prouzročena je paradoksalnom adukcijom glasnica tijekom udaha. Može nestati tijekom daljnjeg disanja, govorom ili smijehom. Pacijente s kroničnim simptomima što ukazuju na astmu, a koji imaju normalnu spirometriju uz slabu reakciju na lijekove za liječenje astme, trebalo bi pregledati na disfunkciju glasnica. Obično se dijagnoza može postaviti izravnom laringoskopijom, ali samo tijekom simptomatskih razdoblja ili nakon vježbanja. Prisutnost spljoštenosti udisajnog dijela spirometrijske protok-volumen krivulje također može sugerirati disfunkciju glasnica, ali to se primjećuje samo u 28 % pacijenata na početku oboljenja. Korisni dijagnostički pregledi su: videozapis napada i laringoskopija tijekom napada (7).

Lezije dušnika i bronhija, kao što su tumori, mogu imati simptome i znakove veoma slične astmi. To su najčešće

of asthma. These are most commonly endobronchial carcinoid and mucoepidermoid carcinoma, and also bronchocentric granulomatosis, subglottic stenosis, hamartoma of the trachea, bronchogenic cysts, leiomyoma and tracheobronchopathia osteochondroplastica. Useful diagnostic examinations include examination of pulmonary function (flattened exhalation section of the spirometry flow-volume curve), flexible bronchoscopy and dynamic computerized tomography (CT) (7).

Foreign body aspiration may cause not only localized wheezing but also generalized wheezing. Aspirated foreign bodies may be radiolucent and therefore not be visible on a chest radiograph. However, radiography may show unilateral hyperinflation of the lung parenchyma, infiltrate, or may be normal. Even 25% of patients can never remember the aspiration event, therefore the suspected foreign body aspiration always requires a bronchoscopy (7).

Congestive heart failure causes the clogging of pulmonary vessels and interstitial pulmonary edema, which reduce pulmonary compliance and contributes to the feeling of heavy breathing and wheezing. So-called cardiac asthma is characterized by wheezing caused by secondary bronchospasm, and is associated with paroxysmal nocturnal dyspnea and nocturnal cough (8).

Chronic obstructive pulmonary disease (COPD) most often shows fixed obstruction of airflow, while most of the patients with asthma demonstrate variable obstruction of airflow. However, variable obstruction of airflow is observable in up to 25% of patients with COPD, while on the contrary, some patients with asthma show fixed obstruction of airflow (9). Lung diffusing capacity (DLCO) is often reduced in patients with COPD, while it is normal (or even slightly increased) with asthma. High resolution CT scan shows air trapping or emphysematous changes in patients with COPD. FeNO, which is usually normal in patients with COPD, is often increased with asthma (10).

Sinus disease is often associated with asthma and chest wheezing. Although such association is not strong in patients with CT evidence of slight sinus mucosal thickening, the grading system developed by Newman and associates showed that the comprehensive sinus disease is associated with a significantly higher degree of chest wheezing (11).

Upper respiratory tract infections, including pertussis, may cause a prolonged coughing period and are often misdiagnosed as a newly developed asthma (12). Acute obstructive laryngotracheobronchitis, usually caused by parainfluenza viruses, with inhalation and exhalation chest wheeze, often mimic asthma (6).

Pulmonary migraine consists of combined recurring asthma, cough with thick mucus sputum, pain in lower back reflected to shoulders, subtotal or total atelectasis of segment or lobe, and occasionally, nausea with vomiting.

endobronhijalni karcinoidni i mucoepidermoidni tumor, ali i bronhocentrična granulomatoza, subglotična stenoza, hamartom dušnika, bronhogene ciste, leiomiom i osteohondroplastična traheobronhopatija. Korisni dijagnostički pregledi su: ispitivanje funkcije pluća (spljošten izdisajni dio spirometrijske protok-volumen krivulje), fleksibilna bronhoskopija i dinamična kompjutorizirana tomografija (CT) (7).

Strano tijelo u bronhijama može prouzročiti ne samo lokalizirano već i generalizirano sviranje. Aspirirana strana tijela mogu biti radiolucentna i zato nevidljiva na radiografiji prsnog koša. Međutim, radiografija može pokazati jednostranu hiperinflaciju plućnog parenhima, infiltracij, ali može biti i normalna. Čak 25 % pacijenata se nikada ne može sjetiti događaja aspiracije, stoga sumnja na aspiraciju stranog tijela uvijek zahtijeva bronhoskopsku pretragu (7).

Kongestivno zatajenje srca uzrokuje začepjenje plućnih žila i intersticijski plućni edem koji smanjuju plućnu komplijansu i doprinose osjećaju otežanog disanja i sviranja u prsima. Takozvanu srčanu astmu karakterizira sviranje u prsima, prouzročeno sekundarnim bronhospazmom, a povezano je s paroksizmalnom noćnom dispnejom i noćnim kašljem (8).

Kronična opstruktivna plućna bolest (KOPB) pokazuje najčešće fiksnu opstrukciju protoka zraka, dok većina pacijenata s astmom demonstrira promjenjivu opstrukciju protoka zraka. Međutim, varijabilna opstrukcija protoka zraka može se vidjeti i u do 25 % pacijenata s KOPB-om, dok na drugoj strani neki pacijenti s astmom pokazuju fiksnu opstrukciju protoka zraka (9). DLCO se često smanjuje u pacijenata s KOPB-om, dok je normalan (ili čak blago povišen) u astmi. CT skeniranje visokom rezolucijom pokazuje zarobljavanje zraka ili emfizematozne promjene u pacijenata s KOPB-om. FeNO, koji je uobičajeno uredan u pacijenata s KOPB-om, često je povišen u astmi (10).

Oboljenja sinusa često su povezana s astmom i sviranjem u prsima. Iako ta povezanost nije jaka u pacijenata s CT dokazima blagog zadebljanja sluznice sinusa, sustav bodovanja koji su razvili Newman i suradnici je pokazao da je opsežna bolest sinusa povezana sa znatno višim stupnjem sviranja u prsima (11).

Infekcije gornjega dišnog trakta, poput pertusisa, mogu prouzročiti produljeno razdoblje kašlja i često su pogrešno dijagnosticirane kao novonastala astma (12). Akutni opstruktivni laringotraheobronhitis, obično prouzročen virusima parainfluenze, uz udisajno i izdisajno sviranje u prsima često simulira astmu (6).

Plućna migrena se sastoji od kombinirane ponavljajuće astme, kašlja s gustim mukoidnim iskašljajem, bolovima u donjem dijelu leđa koji zrače u rame, subtotalnom ili totalnom atelektazom segmenta ili reznja i, povremeno, mučninom s povraćanjem. Simptomi su često usko

The symptoms are often accompanied by focal headache (13).

Aortic arch anomalies may emerge in adulthood, and may mimic asthma caused by exercise. This condition may cause bronchoconstriction during exercise when the need for lung blood flow, oxygen and airflow is increased in the trachea, and intra-thoracic pressure is reduced, with the turbulence of air current distally from trachea, all during physical effort. In combination with those factors, chest wheeze occurs, accompanied by the feeling of heavy breathing (14).

Diffuse panbronchiolitis may mimic bronchial asthma with chest wheeze, cough, heavy breathing during physical exertion and sinusitis. High resolution CT scan results include centrilobular nodules and linear shadows, which are usually more prominent than multifocal bronchial impactions, seen with asthma (7).

Gastroesophageal reflux disease (GERD) is often associated with cough, recurring bronchitis, pneumonia, chest wheeze and asthma as well. Although the frequency of GERD in patients with asthma is in the range of 48%, no causal link has been established between GERD and asthma. However, evidence suggest that increased pulmonary resistance occurs with reflux symptoms during acid challenge testing because the lesions may be sufficiently significant to produce clinically obvious bronchoconstriction (15).

Alpha-antitrypsin deficiency (AATD) with or without COPD has symptoms and signs very similar to those of asthma. Furthermore, AATD itself predisposes hyper reactivity of airways, which is crucial for reversible obstruction of airflow. In the absence of well characterized markers which would differentiate between COPD and asthma in a potential AATD patient, the clinical diagnosis leads to cough in recognition that asthma symptoms, like chest wheeze, may be an early manifestation of COPD in AATD. COPD in AATD often has panlobular emphysema (16).

Aspergillosis may mimic asthma or pneumonia. Actually, most patients with allergic bronchopulmonary aspergillosis also have asthma. Positive skin prick tests and highly specific serum immunoglobulin E (IgE) to *Aspergillus* (17) may show benefits.

Bronchiectasis, especially in its early course, manifests itself with obstructive ventilation disorder. Chest CT is considered a golden standard in bronchiectasis diagnosis (18).

Cystic fibrosis (CF) may not be presented with the conventional gastrointestinal malabsorption, and in some patients it does not occur with clinical symptoms until adolescence or early adulthood. This disease should be suspected when signs of airways disease appear despite the high doses of systematic corticosteroids. The most important clinical characteristics are persistent productive cough, recurring infections of the chest, recurring sinusitis

popraćeni i žarišnom glavoboljom (13).

Anomalije aortalnog luka mogu se pojaviti i u odrasloj dobi, a mogu simulirati astmu prouzročenu vježbanjem. Ovo stanje može prouzročiti bronhokonstrukciju kada se tijekom vježbanja pojača plućni protok krvi, potreba za kisikom i protokom zraka u dušniku te smanjen intratorakalni tlak, uz turbulenciju zračne struje distalno od dušnika, a sve u tijeku fizičkog napora. U kombinaciji s tim čimbenicima nastaju i sviranje u prsima i osjećaj otežanog disanja (14).

Difuzni panbronhiolitis može oponašati bronhijalnu astmu sa sviranjem u prsima, kašljem, otežanim disanjem prilikom napora i sinusitisom. Nalazi CT-a visoke rezolucije uključuju centrilobularne nodule i linearna zasjenjenja, koji su obično više izraženi negoli multifokalne bronhijalne impakcije, koje se viđaju u astmi (7).

Gastroezofagealna refluksna bolest (GERB) je često povezana s kašljem, ponavljajućim bronhitisom, upalom pluća, sviranjem u prsima, ali i astmom. Iako se učestalost GERB-a u pacijenata s astmom kreće do 48 %, nije utvrđena uzročno-posljedična veza između GERB-a i astme. Ipak, dokazi sugeriraju da se pojačana plućna rezistencija javlja sa simptomima refluksa tijekom testiranja provokacijom kiselinom jer promjene mogu biti dovoljno značajne da proizvedu klinički očitu bronhokonstrukciju (15).

Alfa-antitripsinski nedostatak (AATD) s ili bez KOPB-a je vrlo sličan simptomima i znacima astme. Nadalje, sam AATD predisponira hiperreaktivnosti dišnih putova, a što je ključno za reverzibilnu opstrukciju protoka zraka. U nedostatku dobro karakteriziranih markera koji bi razlikovali KOPB od astme u mogućeg AATD pacijenta, klinička dijagnoza dovodi do kašnjenja u prepoznavanju da simptomi astme, poput sviranja u prsima, mogu biti rana manifestacija KOPB-a u AATD-u. KOPB u AATD-u često ima panlobularni emfizem (16).

Aspergiloza može oponašati astmu ili upalu pluća. Zapravo, većina pacijenata s alergijskom bronhopulmonalnom aspergilozom ima i astmu. Od koristi mogu biti pozitivni ubodni kožni test i visoko specifični serumski imunoglobulin E (IgE) na *Aspergillus* (17).

Bronhiektazije, osobito u svom ranom tijeku, prezentiraju se opstruktivnim poremećajem ventilacije. CT prsnog koša smatra se zlatnim standardom u dijagnozi bronhiektazija (18).

Cistična fibroza (CF) može ne biti prezentirana klasičnom gastrointestinalnom malapsorpcijom, a u nekih pacijenata se niti ne javlja s kliničkim simptomima sve do adolescencije ili rane odrasle dobi. Na ovu bolest treba sumnjati kada se pojave znaci bolesti dišnih putova, unatoč visokim dozama sustavnim kortikosteroidima. Najvažnije kliničke karakteristike su uporni produktivni kašalj, ponavljajuće infekcije prsnog koša, ponavljajući sinusitisi i zadebljanja prstiju. Zlatni standard za dijagnozu je test na kloride

and finger thickening. The golden standard for diagnosis is the sweat chloride test. An early CF diagnosis is important for the improvement of long-term clinical results (19).

Pulmonary embolus (PE) may cause bronchoconstriction with chest wheeze which may be so obvious to establish the asthma diagnosis (20). The chest wheeze in acute pulmonary embolus may be more frequent in patients with previous cardiopulmonary disease, and may be a sign of severity in acute pulmonary embolus (21).

Pulmonary infiltrate with eosinophilia (PIE) is a heterogeneous group of chest diseases associated with the presence of an increased number of eosinophils in periphery blood or lungs, together with abnormalities at a chest roentgenogram. It seems that some forms of PIE develop as complications of the previously existing asthma. These are allergic bronchopulmonary aspergillosis, chronic eosinophil pneumonia and allergic granulomatosis with angiitis. Many patients with steroid-dependent asthma are also diagnosed with allergic bronchopulmonary aspergillosis. Asthmatic chest wheeze is present in many forms of PIE, and the combination of chest wheeze with eosinophilia may lead to a wrong conclusion that a patient has asthma (6).

Sarcoidosis and asthma often share many same symptoms. Chest radiography scan should be performed in asthmatic patient when pulmonary sarcoidosis is suspected or when the asthma presentation is atypical or the patient does not react to standard asthma treatment. In patients with ruled in pulmonary sarcoidosis, the diagnosis of the concurrent asthma is problematic. The demonstration of hyper reactivity of airways cannot differentiate these disorders, because it is common both in sarcoidosis and asthma. On the contrary, serum IgE, angiotensin converting enzyme level in serum, eosinophilia of sputum and measuring of exhalation of nitrogen oxide may be helpful (22).

Primary ciliary dyskinesia (PCD) usually affects the lower airways. One of the commonest PCD manifestations is the obstruction of airflow, which mainly does not react to asthmatic treatment. The history of unresolved respiratory problems at birth, recurring otitis, infection of the lower and upper respiratory system require further medical tests. Measuring of nasal nitrogen oxide (nNO) is a useful screening test for PCD diagnosis. nNO levels are significantly low in PCD. Otherwise, there is no single golden standard diagnostic test for PCD. A complete diagnostic procedure, including rapid analysis of microscopy, transmission electronic microscopy, immunofluorescence, sinus and chest CT, is mandatory when patients are highly suspected to PCD (7).

Obesity itself may complicate the existing asthma. However, despite previous beliefs that overdiagnosis of asthma may be more frequent in obese adults, it has been observed that

žlijezda znojnica. Rana dijagnoza CF je važna za poboljšanje dugoročnih kliničkih rezultata (19).

Plućna embolija (PE) može prouzročiti bronhokonstrikciju sa sviranjem u prsima, koje može biti tako očito da se postavi dijagnoza astme (20). Sviranje u prsima u akutnoj plućnoj emboliji može biti češće u pacijenata s prethodnom kardiopulmonalnom bolešću, a može biti i znak ozbiljnosti u akutnoj plućnoj emboliji (21).

Plućni infiltrat s eozinofilijom (PIE) je heterogena skupina prsnih bolesti povezana s prisutnošću povećanog broja eozinofila u perifernoj krvi ili plućima, zajedno s abnormalnostima na rentgenogramu prsnog koša. Čini se da se neki oblici PIE razvijaju kao komplikacije ranije postojeće astme. To su alergijska bronhopulmonalna aspergiloza, kronična eozinofilna pneumonija i alergijska granulomatoza s angitisom. Mnogim se pacijentima sa steroidno-ovisnom astmom dijagnosticira i alergijska bronhopulmonalna aspergiloza. Astmatično sviranje u prsima je prisutno u mnogim oblicima PIE, a kombinacija sviranja u prsima s eozinofilijom može dovesti do pogrešnog zaključka da pacijent ima astmu (6).

Sarkoidoza i astma često dijele mnoge iste simptome. Radiografski snimak prsa treba obaviti i u astmatičnog pacijenta, kada se posumnja na plućnu sarkoidozu ili kada je prezentacija astme netipična ili pacijent ne reagira na standardno liječenje astme. U pacijenata s potvrđenom plućnom sarkoidozom, dijagnoza istodobne astme je problematična. Demonstracija hiperreaktivnosti dišnih putova ne može razlikovati ove poremećaje jer je ona uobičajena i u sarkoidozi i u astmi. Na drugoj strani, serumski IgE, razine angiotenzin konvertirajućeg enzima u serumu, eozinofilija sputuma i mjerenje izdisajnoga dušikovog oksida mogu biti od pomoći (22).

Primarna cilijarna diskinezija (PCD) obično utječe na donje dišne putove. Jedna od najčešćih manifestacija PCD-a je opstrukcija protoka zraka koja uglavnom ne reagira na astmatski tretman. Povijest nerazjašnjenih respiratornih tegoba pri rođenju, ponavljajući otitisi, infekcije donjega i gornjega dišnog sustava zahtijevaju daljnje pretrage. Mjerenje nazalnoga dušikovog oksida (nNO) koristan je test probira za dijagnozu PCD-a. Razine nNO iznimno su niske u PCD-u. Inače, ne postoji niti jedan zlatni standardni dijagnostički test za PCD. Kompletna dijagnostička obrada, uključujući brzu analizu videomikroskopije, transmisijsku elektronsku mikroskopiju, imunofluorescenciju, CT sinusa i prsnog koša, obvezatna je kada su pacijenti visoko sumnjivi na PCD (7).

Gojaznost sama po sebi može komplicirati postojeću astmu. Međutim, unatoč prethodnom vjerovanju da preveliko dijagnosticiranje astme može biti učestalije u pretilih odraslih osoba, primijećeno je da više od jedne trećine pretilih pacijenata s prethodnom dijagnozom astme uistinu

more than one-third of obese patients with previous asthma diagnosis actually do not have bronchial hyper reactivity (23). In 41% of morbidly obese persons with previous asthma diagnosis, no elements of this disease have been found (24). Also, asthma overdiagnosis is not significantly more frequent in obese persons than in persons of normal weight (2).

Some medication, such as carvedilol and other non-selective beta-adrenergic blocker (β_1 , β_2) receptors, as well as aspirin and other non-steroid anti-inflammatory drugs, may cause chest wheeze (25, 26).

Alternative diagnoses should always be considered in all patients, especially patients above 30 years of age, and those below two years of age with new symptoms suggesting asthma. An absence of airways obstruction in initial spirometry results should lead to consideration of alternative diagnoses and further testing (2).

nema bronhijalnu hiperreaktivnost (23). U 41 % morbidno gojaznih osoba s prethodnom dijagnozom astme nisu pronađeni elementi ovog oboljenja (24). Također, preveliko dijagnosticiranje astme nije značajno učestalije u pretilih osoba nego u osoba normalne težine (2).

Neki lijekovi, poput karvedilola i drugih neselektivnih blokatora beta-adrenergičkih (β_1 , β_2) receptora, kao i aspirin i drugi nesteroidni protuupalni lijekovi, mogu uzrokovati sviranje u prsima (25, 26).

Uvijek treba razmotriti alternativne dijagnoze u svih pacijenata, osobito u onih starijih od 30 godina, kao i mladih od dvije godine s novim simptomima, koji ukazuju na astmu. Nepostojanje opstrukcije dišnih putova u početnim nalazima spirometrije trebalo bi potaknuti razmatranje alternativnih dijagnoza i dodatnih ispitivanja (2).

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PRIMLJENO/RECEIVED:

17. travnja 2020./April 17, 2020

PRIHVAĆENO/ACCEPTED:

27. travnja 2021./April 27, 2021

