

Summaries of the scientific works of Dr. Valentina Dimitrova, MD
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for participation in the Competition for the academic position "ASSOCIATE
PROFESSOR"

Summaries of the following are presented:

- Dissertation for the award of educational and scientific degree "Doctor" (1 pc.)
- Monographs, textbooks and manuals (5 pcs.)
- Full-text publications in foreign and Bulgarian scientific journals and collections (26 issues, of which 2 in international scientific journals)
- Participation in forums in Bulgaria, with published abstracts (20 pcs.)
- Participation in international forums with published abstracts (13 pcs.)

• Dissertation for the award of educational and scientific degree "Doctor"

1. V.Dimitrova „Clinical and prognostic characteristics of patients with chronic post thromboembolic pulmonary hypertension“, Varna 2018, pages 130.

CTEPH is a life-threatening condition, where organized thromboembolic masses in the pulmonary vessels lead to increased pulmonary vascular resistance (PVR), progressive pulmonary hypertension (PH) and right-sided heart failure. CTEPH is associated with significant morbidity and mortality if untreated on time. CTEPH is the fourth subgroup in the classification of PH. It is connected with a past episode of acute PE i.e. thromboembolic material obstructing the branches of arteria pulmonalis (AP) at mean pulmonary arterial pressure (mPAP) ≥ 25 mm Hg at rest, pulmonary capillary wedge pressure (PCWP) ≤ 15 mm Hg, presence of segmental perfusion defect revealed in V/Q scintigraphy, computed tomography pulmonary angiography (CTPA) or pulmonary angiography after three months of effective anticoagulation.

Aim: To establish the prevalence and analyze the risk factors for the development of CTEPH after acute PE. To assess the short-term and long-term prognosis in patients with CTEPH. To establish the prevalence and major risk factors for CTEPH after acute or recurrent PE. To explore and monitor the parameters of cardiac function in patients with CTEPH. To study the prognostic factors in patients with diagnosed CTEPH. To assess the quality of life in

patients with CTEPH. To assess the survival in patients with CTEPH. To suggest an algorithm for diagnosis, monitoring, and follow-up of patients with CTEPH.

Patients and Methods: The study included patients hospitalized in the Clinic of Pulmonology at St. Marina University Hospital for an acute or recurrent PE for the period 2010 – 2016. The patients were divided into two groups with acute PE (n = 497) and recurrent PE (n = 80). A retrospective study evaluating risk factors, course, treatment, survival and mortality was performed in the patients with acute and recurrent PE. The prospective study included patients after acute or recurrent PE followed up for manifestations of PH and right-sided heart failure after at least 6 months of treatment with anticoagulants (Sintrom or NOAC) (n = 52). An outpatient screening was conducted, which included NT pro BNP, echocardiographic assessment of right heart cavities, measurement of systolic pressure and calculation of mean pressure in AP, as well as assessment of the systolic function of the right ventricle. CTPA was performed in patients, suspected of CTEPH, because of elevated systolic pressure in AP \geq 50 mm Hg.

Results : This retrospective study summarized our results and observations on patients with acute and recurrent PE in the last seven years and along with that, patients were examined and followed up prospectively for manifestations of right-sided heart failure and PH as a result of CTEPH.

We found that the mean age in women with acute PE is higher than in men. In both retrospective groups, men were more likely to suffer. Acute PE was more common in patients over 65 years of age and recurrent PE - in patients aged 40-65 years. The most important risk factor for PE is deep vein thrombosis (DVT), which is more common in males with acute PE and patients with recurrent PE. This risk factor is not related to the form of clinical manifestation of embolism. Other risk factors for acute PE are immobilization for more than 4 days, oncological disease, absolute arrhythmia, surgical or orthopedic intervention, trauma, etc. The risk of massive PE was twice higher in case of immobilization for more than 4 days. The risk factor profile of the recurrent PE includes DVT and absolute arrhythmia. The risk for recurrent PE was four times higher in the presence of metabolic diseases and 1.6 times higher in case of DVT. It is advisable to search for different blood coagulation disorders and thrombophilia, especially in young patients or in idiopathic PE cases as this is important for the duration of anticoagulation treatment as well as to reduce recurrence rates. The comorbidity in our population group was significant, with the largest share for cardiovascular diseases and diabetes mellitus. The female participants had greater comorbidity in the recurrent PE group, although the mean age by gender did not differ in a

statistically significant way in this group. The comorbidity in deceased and surviving patients differed by more than three points. The CCI index reliably assessed comorbidity in the retrospective and prospective groups. Mortality rate during hospitalization was not different in both groups as well as during the seven-year study period. The higher mortality rate compared to published data in the literature, we associate with the accompanying diseases.

The clinic of PE is well - known. The most common clinical symptoms in the retrospective group were dyspnea, chest pain, cough, syncope and hemoptysis. Syncope and hypotension were more common in men and adults over 65 years of age, while cough and hemoptysis were more common in women and younger patients. D - dimer was higher as an absolute value in patients with massive PE. The clinical course of acute and recurrent PE not always corresponded to the severity of the occlusions, found in the CTPA. There was a discrepancy with a rank of 16 to 50%. The selection of patients amenable to fibrinolysis should be done carefully due to the risk of serious complications. The patients with a clinic of massive PE with haemodynamic instability with the highest risk of relapse or death are suitable for thrombolysis.

The mean values of the right ventricle size and systolic pressure in AP were statistically significantly higher in patients with massive PE, who were treated with fibrinolysis in our group. The incidence of recurrences was not related to the use of a thrombolytic in acute PE cases. Male gender is a risk factor for the occurrence of relapsing PE and can be a determining factor for the duration of anticoagulation therapy. Right ventricular dysfunction during the acute event was a poor prognostic sign of early mortality during hospitalization in patients with recurrent PE in our group. Factors correlating with mortality in acute PE patients are DVT, ischemic heart disease, myocardial infarction, heart failure, absolute arrhythmia, cerebrovascular disease, diabetes mellitus and oncological disease, whereas in patients with recurrent PE, these are DVT, ischemic heart disease, myocardial infarction, heart failure, absolute arrhythmia. The use of Sintrom reduced death risk by 35% and the use of Dabigatran reduced death risk by 22%.

In the presence of clinical symptoms of CTEPH after experiencing acute or recurrent PE, it is advisable to look for signs of acute or chronic right ventricular burden by ECG, NT pro BNP test and, if necessary, echocardiography. The prospective group included patients after acute and recurrent PE who had anticoagulation treatment for more than 6 months. The risk factor profile in the prospective group includes DVT, absolute arrhythmia and oncological disease. It is similar to that of patients with recurrent PE. The prospective group included patients with AT III deficiency and Factor V Leiden genetic defect with no detected

signs of right ventricular dysfunction or elevated pressure in AP. The main clinical symptoms for which patients were actively interrogated were those of CTEPH. An assessment of the dyspnea degree can be made with mMRC and Borg scales. The six-minute walking test provides an objective assessment of the physical capacity of a patient with shortness of breath while exercising. In the prospective group we found a positive high statistically meaningful correlation between mMRC / Borg scales and the patient's perception of dyspnea at rest and while exercising. Secondly, a considerable positive statistically significant correlation was found between the dyspnea scales and NT pro BNP. An important positive statistically meaningful correlation was found from the echocardiographic indicators in the prospective group of patients between NT pro BNP values and the size of the right ventricle and systolic pressure in AP and a negative insignificant correlation with TAPSE. NT pro BNP can not be a stand-alone screening test for CTEPH, but its levels are an independent predictor of mortality. The prevalence we found for CTEPH in the study group is 1.39% (within the confidence interval of the published data in different studies). The mean age of patients is 73.38 ± 10.65 years, CTEPH being more common in men according to our study. There is no difference in the mean age by gender. Patients with CTEPH in our group are older and have more comorbidities. The calculated CCI index shows the same. The increased attention in the search for CTEPH may lead to a shortening of the time from the onset of the symptoms to diagnosis. The recurrent PE, DVT and major perfusion defects are risk factors for the appearance of CTEPH. Echocardiographic examination is a screening method for early objectification of the clinical symptoms of persistent right ventricular dysfunction and elevated systolic pressure in AP in patients after acute or recurrent PE. The mean systolic pressure values in AP in patients with CTEPH and deceased with recurrent PE were similar, so we believe that this indicator may be predictive of long-term survival. This also applies to the NT pro BNP values, which were 20 times higher in patients with CTEPH compared to the prospective group. A considerable positive statistically significant correlation was found between the levels of NT pro BNP and the systolic pressure in AP and the size of the right ventricle, and a negative statistically insignificant correlation with TAPSE. In this group, NT pro BNP correlated with the scales for the assessment of shortness of breath while exercising and at rest - mMRC and Borg. The systolic pressure values, echocardiographic indicators for right ventricular dysfunction, NT pro BNP and 6MWT in patients with CTEPH are prognostic factors for long-term survival.

CTPA and V/Q scintigraphy are the methods of choice from the imaging tests for objectification of CTEPH. The patients diagnosed with probable CTEPH should be directed to

specialized reference centers for RHC and decision-making for surgical treatment. PEA is the only treatment option that has been approved for operable patients and it improves the prognosis of this group of patients.

• **Monographs, textbooks and manuals**

2. V. Dimitrova *Pulmonary thromboembolism – a predictable mystery* Publisher – Medical University Varna, 2020; 144 pages, ISBN 978-619-221-272-8

The characteristics of patients hospitalized for treatment in the surgical and therapeutic wards of hospitals have changed radically in recent years. More and more elderly patients with predominant cardiovascular or oncologic concomitant diseases are admitted for treatment with the increase of life expectancy and aging of population. They undergo complex therapeutic or surgical interventions, sometimes requiring prolonged hospital stay and prolonged bed immobilization. All this increases the risk of venostasis, deep vein thrombosis and subsequent pulmonary or peripheral thromboembolism. Caution and adequate hospital and outpatient prevention of these complications are needed. Pulmonary thromboembolism is a multidisciplinary problem without a specific clinical picture, making it difficult for any clinician in the process of diagnosis, treatment and follow-up.

The present monograph summarizes information accumulated in the medical literature in recent years. It synthesizes modern recommendations and guidelines for faster assessment of clinical probability, diagnosis and decision-making for the most appropriate personalized treatment in patients with acute pulmonary embolism. In addition, the ten-year experience of the Intensive Respiratory Care unit (IRCU) /Intensive Care Unit and Non-invasive ventilation (ICUNIV) at the Clinic of Pneumology and Phthisiatrics of University Hospital "St. Marina" in the diagnosis and treatment of this socially significant disease has been summarized. There is no exact register of cases of deep vein thrombosis and pulmonary embolism in Bulgaria. It is a fact that a large percentage of cases are overlooked by clinicians and are detected only pathologically. Given that thromboprophylaxis is an opportunity to reduce the incidence of venous thromboembolism, a special place is occupied by the consideration of recommendations for the prevention of these complications. The book is intended for a wide range of readers - students, specialist doctors and specialists in all fields due to the difficulties in diagnosis and the possibility to prevent this sometimes life-threatening complication.

3. D. Petkova, V. Stratev, P. Atanasov, V. Dimitrova.

Home oxygen therapy. Patient Guide. Edited by Assoc. Prof. Dr. D. Paskalev. Publisher "Nira Communications", Varna 2017; ISBN: 978-954-92663-7-5

The guide is aimed at patients with chronic pulmonary diseases who need long-term home oxygen therapy. It presents in simple terms the main diseases that lead to the development of chronic respiratory insufficiency, the physiological role of oxygen and the consequences for the body of its decrease in blood and tissues. The guide focuses on the indications for oxygen therapy, various types of tests in patients with pulmonary diseases, where the main emphasis is on the use of different types of devices, supplying oxygen at home. Recommendations are given for proper use of oxygen concentrators and safety rules when working with them. There are advices described for active life of patients needing home oxygen therapy; advices for everyday life, travel and family life. There are presented answers of questions frequently asked by patients and an emergency plan is developed.

4. D. Petkova, V. Dimitrova. *Pulmonary arterial hypertension, Chapter in a textbook on Pulmonary Diseases 2, Chapter 34, pages 693-705, 2016, ISBN 78-619-90243-3-1*

The publication is intended not only for specialists in the field of internal medicine and pulmonary diseases, but for a wider range of physicians interested in the latest developments in the diagnosis and treatment of pulmonary diseases. The topic is presented in the light of the most recent guidelines published by ERS / ESC in 2015. The current changes in the classification, the latest data on the frequency, morbidity and mortality, diagnostic algorithm for Pulmonary Hypertension are presented. In recent years, great efforts have been made in the treatment of Idiopathic pulmonary arterial hypertension. On the one hand, this is due to new understandings of the pathophysiological mechanisms of pulmonary vascular diseases, and on the other hand to the growing number of new drugs. Understanding these mechanisms has made it possible to change the direction of therapy, which has shifted from a purely vasodilator therapy with calcium antagonists to a behavior aimed at changing the remodeling of the pulmonary vascular bed. This led to a revolution in the prognosis of the disease. Results from randomized and controlled studies in adults indicate that some treatment regimens can significantly alter the course of the disease. Today, it is possible to improve not only the symptoms and quality of life, but also the survival of patients with Idiopathic pulmonary arterial hypertension.

5. V. Dimitrova, D. Petkova. *Vascular diseases of the lungs. Pulmonary thromboembolism Internal Medicine for Healthcare Professionals, 2018, p. 81-87, ISBN 978-619-221-182-0*

The textbook can be used by both health care professionals and medical students, specialists and all outpatient and hospital care physicians: emergency physicians, general practitioners. The modern knowledge of semiotics, the main and additional diagnostic methods, the nosology and the modern therapeutic approach in the most common diseases are presented. Medical care in the XXI century requires modern knowledge of internal medicine nosology - etiology, pathophysiology and pathogenesis, clinical manifestation, diagnosis, therapy and prevention. Sufficient attention is devoted to the role, place and responsibilities of the healthcare professional. The textbook meets the modern high requirements for health care professionals and is a valuable tool in their clinical training.

The topic of Pulmonary Embolism is relevant because, despite advances in diagnosis and treatment, it is the third most common cause of cardiovascular morbidity and mortality worldwide. It is the third leading cause of death after myocardial infarction and stroke. Often patients with Pulmonary Embolism may remain asymptomatic or the diagnosis may be made accidentally, sometimes the first manifestation of the disease may be sudden cardiac death. As timely and rapid diagnostics play an important role and predetermine the decision for the most correct therapeutic behavior, the role of the health care specialist is significant. He must be well aware of the symptoms of the disease, to be able to recognize them and alert due to the risk of fatal complications.

6. V. Dimitrova, D. Petkova Pulmonary arterial hypertension, Internal medicine for health care professionals, 2018, p. 87-91, ISBN 978-619-221-182-0

Comparative epidemiological data on the prevalence of different groups of Pulmonary Hypertension are not widely available. Idiopathic pulmonary arterial hypertension is a relatively rare disease. Patients with this disease have an average life expectancy of about 40 years and limited physical capacity, which can significantly change their previous lifestyle. Information on the severity of the disease, which is available through various non-professional sources, can be confusing or insufficiently clear. As a result, patients suffer to varying degrees of anxiety and / or depression, which can have a significant impact on their lifestyle. Therefore, the advice given by health care professionals should be well thought out and based on knowledge of the clinic and the course of the disease.

• **Full-text publications in Bulgarian and foreign scientific journals and collections**

7. V. Stratev, D. Petkova, V. Dimitrova, J. Petev

Comorbidities of COPD in Bulgarian patients – prevalence and association with severity and inflammation. Folia Med (Plovdiv) 2018; 60(1):102-9. doi: 10.1515/folmed-2017-0078, ISSN: 1314-2143

Abstract:

Background: COPD is a disease with constantly rising economic and social burden; it is associated with multiple comorbidities which contribute to the disease severity.

Aim: To investigate the prevalence of co-morbidities in COPD patients and their association with the disease severity and CRP levels.

Patients and methods: We conducted a retrospective study among 338 COPD patients (mean age 65.2 ± 7.6 years) with assessment of comorbidities, spirometry measurements and serum levels of CRP. In 183 patients we found metabolic syndrome (MS) according to IDF criteria.

Results: We found prevalence of cardiovascular diseases (CVD) of 73.5% (hypertension 70.4%, CHF 47.4%, ischemic heart disease 37.5%, and cardiac arrhythmias 12.6%), with higher prevalence in patients with more severe disease. We found prevalence of type 2 diabetes of 21.1%, and 12.4% prevalence of bronchiectasis. In a subpopulation of the patients we found 48.1% prevalence of MS and the serum levels of CRP were significantly higher in patients with COPD and MS compared to those without the syndrome: 7.4 (3.14 – 11.54) mg/ml vs 4.06 (2.64 – 6.93) mg/ml, $p=0.006$.

Conclusion: The present study suggests high prevalence of CVD comorbidities in COPD patients and association with the disease severity. Metabolic syndrome is a common comorbidity and is associated with increased inflammatory response.

8.V. Stratev, V. Dimitrova, D. Petkova

COPD and comorbidities: Relating mechanisms and treatment. Current Respiratory Medicine Reviews Vol. 15, Issue 2, 2019, 90-101, DOI : 10.2174/1573398X14666181018101021

Abstract: Despite being a disease with constantly rising social burden and mortality, COPD is also associated with a number of other conditions known as comorbidities. COPD and other diseases often share similar risk factors, such as smoking and ageing which leads to increased prevalence of comorbidities. The key pathogenic mechanisms of COPD are chronic inflammation and oxidative stress and they also contribute significantly to the development of accompanying diseases. Through complex interactions COPD increases the risk for certain

comorbidities and they in turn have negative impact on health status and contribute to mortality in COPD patients. Proper treatment of comorbidities may have beneficial effect on COPD natural course and progression. Here we review the prevalence of the most common comorbidities of COPD; their interrelating mechanism and the current advances of the treatment in terms of co-existence.

9.T. Dobрева, D. Petkova, V. Stratev, V. Dimitrova.

Sleep-related Breathing Disorders: Upper Airway Resistance Syndrome. Medinfo issue 12, 2015, p. 20-28. ISSN: 1314-0345

Summary: Upper airway resistance syndrome (UARS) occurs in 8-20% of the population and is characterized by recurrent Upper Airway collapse, leading to limitation of inspiratory flow. The epidemiology of UARS, the pathogenesis and pathophysiology of the syndrome are described, as well as the main clinical characteristics and criteria for diagnosis. Optimal treatment of UARS is not yet available. Respiratory support methods (CPAP), reconstructive surgery, weight reduction and pharmacological strategies are used. Treatment options are limited due to low compliance or low efficacy, which requires a deeper understanding of pathogenic mechanisms and more precise monitoring before and after treatment.

10.V. Stratev, D. Petkova, T. Dobрева, V. Dimitrova.

New possibilities in the treatment of patients with Chronic Obstructive Pulmonary Disease (COPD). Medinfo Issue 12, 2015 p. 12-18. ISSN: 1314-0345

Summary: COPD is a disease that is a major cause of chronic morbidity and mortality worldwide. Due to the high social and economic burden of COPD, new drugs continue to be introduced to treat the disease. The effect of the dose frequency on adherence to therapy in patients with COPD, the various inhalation drugs available on the Bulgarian market, as well as the dose regimen of their administration are considered. An overview of innovative methods for the treatment of COPD is presented - regenerative therapy through stem cells. The new drugs provide a greater choice of dosage regimens, which improves adherence to treatment, leads to a reduction in exacerbations and better control of symptoms.

11.D. Petkova, V. Stratev, V. Dimitrova, P. Atanasov, V. Kostadinova, T. Dobрева

Sleep-related Breathing Disorders. Cardiovascular risk, GP news, Issue 11/2015, p.17-20, ISSN 1311-4727

Summary: Sleep-related breathing disorders can be considered a socially significant disease comparable to diabetes mellitus, arterial hypertension or other chronic pulmonary diseases. About 25% of the adult population in Europe suffers from sleep disorders. The

epidemiology, classification and diagnosis of these disorders are described, with an emphasis on objective examination and the gold standard for the diagnosis of “polysomnography”. The various patho-genetic relationships between Obstructive Sleep Apnea /OSA/ and increased cardiovascular risk, mainly through inflammatory mechanisms, are considered; effects on coronary vascular disease and the development of heart failure. The gold standard for the treatment of patients with respiratory disorders during sleep is the application of positive airway pressure through various modalities (APAP, CPAP, BiPAP, ASV). The effects of OSA treatment on the cardiovascular system, the improvement of left ventricular function and arrhythmias are indicated.

12.V. Kostadinova, V. Dimitrova, V. Stratev, T. Dobрева, D. Petkova.

Approach in lower respiratory tract infections in outpatient conditions, GP news Issue 11/2015, p.5-6, ISSN 1311-4727

Summary: Cough is among the five most common reasons for seeing a doctor. It is a major feature of lower respiratory tract (LRT) infections. These infections include influenza, acute bronchitis, exacerbation of chronic pulmonary disease (COPD, bronchiectasis) and pneumonia. The basic principles of behavior in LRT infections are considered, according to international guidelines and the specifics of outpatient treatment. Indications for inpatient treatment in certain groups of patients and risk stratification according to the CURB-65 scale are given. The prevention of LRT infections is carried out mainly by seasonal influenza vaccine and polyvalent antipneumococcal vaccine.

13.V. Stratev, Ts. Yordanov, T. Dobрева, V. Dimitrova, D. Petkova.

New biomarkers and metabolic profiling in patients with community-acquired pneumonia (CAP). Medicart Issue 5, 2016, p. 8-14. ISSN: 1312-9384

Summary: Society-acquired pneumonia remains the first most common severe infectious disease in Europe, with the course of the disease and its outcome highly variable. Different terms for clinical assessment of pneumonia severity and risk of death are considered. The importance of traditional inflammatory biomarkers is presented - CRP and procalcitonin, focusing on the new promising metabolic biomarkers for risk determination: proadrenomedulin, copeptin and cortisol, asymmetric dimethyl-arginine, kynurenine, lactate and glutathione. In patients hospitalized with CAP, risk stratification and early identification of high-risk patients are essential for behavior and therapy.

14.V. Dimitrova, D. Petkova, V. Stratev, T. Dobрева, V. Kostadinova.

Novelties in the epidemiology, diagnosis and treatment of pulmonary thromboembolism. GP news 2017, Issue 1 p. 5-9. ISSN: 1311-4727

Summary: The term venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and pulmonary embolism. It is the third most common cardiovascular disease. The new clinically significant aspects of VTE, published in 2014, as well as the main predisposing risk factors for the development of the disease are considered. The criteria for assessing the clinical likelihood of Pulmonary Embolism, according to internationally validated scales, are presented. The diagnosis of PE includes laboratory and imaging tests - multi-detector computed tomography, ventilatory perfusion scintigraphy and pulmonary angiography as the "gold standard". The current therapeutic possibilities and the risk assessment of recurrence are considered.

*15. T. Dobрева, N. Sapundzhiev, V. Stratev, V. Dimitrova, V. Kostadinova, D. Petkova
Upper respiratory tract infections. GP news 2017, Issue 1, p. 22-26. ISSN: 1311-4727*

Summary: The most common upper respiratory tract (URT) infections are rhinitis, rhinosinusitis, pharyngitis and bronchitis. They have a high frequency and cause a significant increase in direct and indirect medical costs due to temporary incapacity for work. The main causes of infections of URT, risk groups of patients, as well as the clinical picture of individual diseases are considered. Modern diagnosis and appropriate treatment are essential for reducing morbidity and limiting possible complications. The prevention of URT infections is carried out through vaccines, restorative and body-strengthening procedures.

*16.V. Stratev, D. Petkova, T. Dobрева, V. Kostadinova, V. Dimitrova.
COPD in primary outpatient practice - patients at risk. GP news 2017, issue 1, p. 26-30.
ISSN: 1311-4727*

Summary: COPD is a disease that affects nearly 400 million people worldwide; this represents prevalence of 11.4% among the population. COPD is the leading cause of morbidity and mortality in the world. The main risk factors for the development of COPD are described: smoking, socio-economic status, gender and age, occupational hazards, biofuel combustion, genetic factors, infections, asthma and bronchial hyperreactivity. The main symptoms that guide the diagnosis are shortness of breath, cough and sputum production. The role of GPs in the initial assessment of patients at risk is great and consists in the early identification of these patients and their referral to a pulmonologist, as well as in the prevention, assisting in quitting smoking and vaccinations of patients with established disease. The fight against this severely debilitating disease requires collaboration between GPs and pre-hospital and hospital care professionals.

17.V. Stratev, D. Petkova, V. Dimitrova.

Personalized approach in bronchial asthma - innovations in assessment and behavior. MedicArt "Pulmonology and Pediatrics" 2017, Issue 4, p. 4-8; ISSN: 1312-9384

Summary: Bronchial asthma is a heterogeneous disease defined by a history of respiratory symptoms and variable airflow limitation, which affects 1 to 8% of the world's population. Due to their heterogeneity, different phenotypes are defined that are stable over time and have different characteristics: allergic asthma, non-allergic asthma, late-onset asthma, asthma with obesity, asthma / COPD overlap syndrome, fungal hypersensitivity, bronchospasm caused by physical effort. Current diagnostic approaches are described, according to the leadership of the British Thoracic Society and the Global Initiative for Asthma (GINA 2017). The assessment of patients with bronchial asthma is based on two main components - control of symptoms and risk factors for worsening of the disease. The innovations in the treatment of asthma and the personalized approach to the individual phenotypes are described - treatment with monoclonal antibodies Mepolizumab, Reslizumab, Benralizumab, Dupilumab, which are used in patients with severe asthma.

18.V. Kostadinova, V. Dimitrova, V. Stratev, T. Dobрева, D. Petkova.

Outpatient treatment of acute infections of lower respiratory tract. Antibiotic resistance. GP news, issue 6/2017, p. 30-32; ISSN: 1311- 4727

Summary: Acute infections of lower respiratory tract in adult patients without chronic pulmonary disease are acute bronchitis and pneumonia. It is extremely important to distinguish between the two conditions, which is essential for the choice of treatment. The main causes of both diseases are considered, as well as the modern choice of antiviral and antibacterial drugs. The choice of medication for the treatment of acute bronchitis and pneumonia should be consistent with international recommendations and available data on resistance to certain antibiotic groups. When conducting outpatient treatment, close monitoring of the patient is important, especially in the first 2-4 days of treatment. In case of failure or deterioration, a change in treatment regimen or referral for hospitalization should be undertaken.

19.D. Miteva, J. Radkov, V. Kostadinova, V. Dimitrova.

Pulmonary and extra-pulmonary complications of patients with community-acquired pneumonia, MD Magazine, 2016, vol.91., Issue 1, p. 78-82, ISSN 1312-4471

Summary: To study the frequency of pulmonary and extra-pulmonary complications in the course of CAP. To reveal the risk factors for complications, as well as their influence on the outcome of pneumonia. 1203 patients were studied retrospectively, hospitalized on the occasion of CAP in the Clinic of Pneumology and Phtysiatry of the University Hospital "St.

Marina” for a 3-year period - 2012-2014. The studied patients were of average age 59.9 years \pm 17.3 years, 56.2% - men. Complications developed in 662 patients (55%). The most common pulmonary complications were: acute respiratory failure 413 (34.3%), pleural effusion 292 (24.3%), abscess -52 (4.3%). The most common extra-pulmonary complications were: reactive hepatitis-114 patients (9.5%) and acute renal failure 95 patients (7.9%). Less common extra-pulmonary complications include cardiac, endocrine, gastroenterological, and neurological manifestations. Complications associated with sepsis-septic shock were also observed in 63 patients (5.2%) and multiple organ dysfunction syndrome in 39 patients (3.2%). Risk factors for the development of complications are: multilobar involvement OR 4.97 (3.6-6.87 95% CI, $p < 0.001$), presence of comorbid diseases –Charlson comorbidity index ≥ 3 OR 3.02 (2.25-4.04 95% CI, $p < 0.001$) and age ≥ 65 years OR 1.42 (1.13-1.79 95% CI, $p < 0.01$). The average hospital stay in patients without complications is 7.3 ± 1.5 days, in the presence of complications it is increased to 8.8 ± 5.9 days, $p < 0.001$. In-hospital mortality was 11.7%, in the presence of at least one complication it is increased to 21.3%, $p < 0.001$. The presence of at least one complication prolongs the hospital stay and worsens the outcome of the disease.

20.P. Peneva, D. Petkova, V. Dimitrova

Influenza - something about the disease and prevention, Medcart issue 5/2017, p. 10-12, ISSN 1312-9384

Summary: Influenza infection is one of the most common infections in the winter months. Seasonal flu viruses circulate and cause annual epidemics. In rare cases, there may be a major change in the genetic material of an animal-specific strain, the so-called gene shift. This virus already has the ability to multiply in the human body, as well as the likely potential of a highly virulent strain. It is in such situations that a pandemic can occur. It affects people of all ages, mainly children, adults over 65 and those with chronic diseases. It occurs with varying severity, with different complications and often with an unpredictable course in high-risk patients. The best way to prevent flu viruses is to get vaccinated against the flu. Conducted on time, it has good effectiveness, prevents severe illness and serious complications.

21. V. Dimitrova, D. Petkova, V. Stratev, T. Dobрева

Place of NT pro BNP in the diagnosis and follow-up of patients with chronic thromboembolic pulmonary hypertension (CTEPH) Thoracic medicine 2018, vol.X /2018/Issue 1/p.26-40 ISSN 1313-9827

Abstract: Chronic thromboembolic pulmonary hypertension (CTEPH) is the only potentially curable form of pulmonary hypertension. Quick and accurate diagnosis is pivotal for successful treatment. Clinical signs and symptoms can be nonspecific. Risk factors such as history of venous thromboembolism may not always be present. Routine screening for CTEPH after pulmonary embolism is not supported by current evidence. Traditional methods of diagnosing CTEPH include echocardiography, ventilation/perfusion scintigraphy, computed tomography pulmonary angiography and right heart catheterization; Functional Class Assessment and 6 Minute Walk Test refer to the above mentioned as well. Biochemical markers have emerged in the last decade as a non-invasive method for assessment and monitoring of patients with right ventricular dysfunction. Natriuretic peptides are a marker of cardiac dysfunction, but are not specific to cardiovascular diseases alone. The level of NT pro BNP correlates with the degree of myocardial dysfunction and provides information both for diagnosis and follow-up of patients to assess the effect of treatment or after pulmonary endarterectomy. NT pro BNP is considered a strong predictor of survival. CTEPH is a serious complication in patients after acute or recurrent pulmonary embolism. Follow-up and monitoring of symptomatic patients predetermine early diagnosis and advanced treatment to increase patient survival.

22.V. Dimitrova, D. Petkova, V. Stratev.

Chronic post-thromboembolic pulmonary hypertension, GP News issue 10/2018, p. 21-27, ISSN 1311-4727

Summary: The clinical symptoms of CTEPH are nonspecific or difficult to recognize at the onset of the disease. When manifestations of right-sided heart failure are detected, the disease is already in an advanced stage. Early diagnosis remains a challenge with an average term of 14 months between the onset of symptoms and diagnosis at expert centers. The average age of patients diagnosed with CTEPH was 63 years and both sexes were equally affected. The diagnosis of CTEPH is made on the basis of the results of imaging and invasive tests, after at least 3 months of effective treatment with anticoagulants. One very important clinical question remains unanswered, and that is which patients after acute PE should be examined and monitored for CTEPH? The exact answer to this frequently asked question is not known, but it is possible to identify a group that is at relatively higher risk. This group includes: all patients with large thromboembolic defects located in the main and lobar branches of AP, patients with hemodynamically significant disorders and manifestations of right ventricular dysfunction, with documented thrombophilia or with permanent perfusion lung damage from imaging studies. Patients in these categories should be monitored for a

minimum of 2 years or at any time if symptoms of PH are detected. The majority of patients treated with anticoagulants after acute or recurrent PE normalize hemodynamics and only a small percentage of about 3.8% are diagnosed with CTEPH, but given the incidence of acute PE, this still represents a significant number of patients in absolute terms. CTEPH is associated with significant morbidity and mortality if not treated promptly. Early diagnosis and referral of operable patients improves long-term survival and prognosis because PEA restores pulmonary hemodynamics. The incidence of the disease in our country is not well studied and diagnostic approaches are not well standardized. This issue is interdisciplinary and not researched in Bulgaria. So far in our country there is no practice for identification of patients with CTEPH, there is no accepted algorithm for follow-up, evaluation and monitoring of their treatment, risk stratification, as well as established methodology and practice for selecting candidates suitable for surgical treatment.

23. V. Dimitrova, D. Petkova, V. Stratev.

Hospital-acquired pneumonia - guidelines for clinical practice, Medinfo 07/2019, p.50-56, ISSN 1314-0345

Summary: The ATS Guidelines are a document prepared by a group of international experts who make recommendations on key issues in diagnosis, empirical and definitive antibiotic therapy, and HAP / VAP prevention following the GRADE approach. The recommendations are a compromise between the need to provide early empirical antibiotic coverage and the avoidance of over-administration of these drugs, which can lead to unwanted side effects, Clostridium difficile infections, antibiotic resistance and increased cost.

24. V. Dimitrova, D. Petkova, V. Stratev.

Review of the novelties after the Sixth World Symposium on Pulmonary Hypertension, GP news, 07/2019, issue 7, p.5-8, ISSN 1311-4727

Summary: The Sixth World PH Symposium revised the definition, proposing a new level of mPAP to define as abnormal an increase above > 20 mm Hg, the need to measure PAWP ≤ 15 mm Hg and PVR ≥ 3 WU in Right Heart Catheterization, which characterize the presence of precapillary PH. The working group proposed to simplify the core of the clinical classification of PH by developing additional tables. The two main changes in group 1 included: 1) a subgroup of patients “responding to long-acting calcium channel blockers” and 2) the inclusion of a subgroup “PAH with venous / capillary involvement characteristics, which included patients with pulmonary vein occlusive disease / pulmonary capillary hemangiomatosis Group 5 PH with unclear and / or multifactorial mechanisms was simplified

by eliminating 1) splenectomy and thyroid disorders and 2) lymphangiomyomatosis associated with PH.

25. V. Stratev, D. Petkova, V. Dimitrova, T. Dobрева.

Chronic cough - assessment and behavior, GP news, 07/2019, issue 7, p.17-19, ISSN 1311-4727

Summary: Chronic cough is the most common persistent symptom in outpatients of all ages and is the most common reason for visiting a GP. The cough is acute lasting up to 3 weeks, subacute between 3-8 weeks and chronic if lasting more than 8 weeks. It can often worsen the quality of life and lead to vomiting, muscle aches, rib fractures, incontinence, fatigue and depression. This has a psychosocial effect and has a negative impact on the patient's social life. The article presents an algorithm for assessing chronic cough.

26. D. Petkova, V. Platikanov, V. Dimitrova, S. Andonova, V. Nestorova

Respiratory palliation in a patient with amyotrophic lateral sclerosis (ALS) and hypercapnic respiratory failure, "In Spiro", issue 2, 2009, pp.29-31, ISSN 1313-4329

Summary: Patients with amyotrophic lateral sclerosis (ALS) have a poor prognosis and need symptomatic treatment. Recent data show that active treatment of a patient with ALS with non-invasive ventilation improves quality of life and increases survival. The treatment of this group of patients is a challenge for physicians of different specialties and differs in nature from the treatment of any other disease. The reasons for this are the rapid progression of the disease, its unpredictability and the lack of causal medical treatment. A clinical case of a woman with ALS was presented, demonstrating 18 months of treatment with non-invasive and invasive ventilation at home. An important factor for the successful care of patients is the care by a multidisciplinary team of specialists. Both the data from clinical researches and our modest experience allow us to conclude that after proper assessment, the initiation and conduct of NIV and invasive mechanical ventilation at home is well tolerated by patients by improving their quality of life and survival. A necessary prerequisite for home ventilation is the training of the patient and his relatives, as well as the presence of a trained team of medical specialists, ensuring monitoring and control of treatment.

27. D. Petkova, J. Yotov, V. Dimitrova.

Pulmonary hypertension - diagnosis, screening, follow-up, "In Spiro", Issue 1,2010, p.17-25, ISSN 1313-4329

Summary: This article comments on key points in the diagnosis of PAH, discussing in the context of the guidance document of the three scientific societies the main steps and instrumental research in the diagnostic algorithm of 2009. The diagnosis of PAH and in

particular idiopathic PAH are diagnoses of "exclusion", therefore the diagnostic algorithm proposed by experts should become a starting position for any patient with suspected PAH. If suspected, the pressure in the AP should be determined by Doppler echocardiography. If there is evidence of clinically significant pulmonary hypertension, sources are sought that could be removed and treated. This includes diseases of the connective tissue, lungs, left heart, liver and other diseases. To rule out chronic thromboembolic pulmonary disease it is necessary to perform ventilator perfusion scintigraphy, spiral CT, respectively MRT or MR, angiography. The severity of pulmonary hypertension is clinically determined by WHO class and by submaximal or maximal loading before and after starting treatment. Right cardiac catheterization with a reactivity test is the standard for the diagnosis of pulmonary hypertension and a method that monitors the effectiveness of treatment. It is recommended to make early contact with a center specialized in the diagnosis and treatment of pulmonary hypertension.

28.D.Petkova, Y.Yotov, Br. Kanazirev, V.Dimitrova

Idiopathic pulmonary arterial hypertension: diagnosis clinical efficiency of target treatment, problems "Thoracic medicine" vol. IV, 2012, Issue 4, p. 43-48, ISSN 1313-9827

Abstract: We present a single center experience in problems of the diagnosis, monitoring and clinical efficacy of the target treatment and survival of patients with idiopathic pulmonary arterial hypertension. Pulmonary hypertension is a progressive and fatal disease with high mortality and delayed diagnosis. These are the problems in Europe and worldwide and patients at our center are no exception to the general trend. Despite the limitation of the small number of reported patients, our results suggest that IPAH remains a serious life threatening disease, despite new developments in awareness, therapeutic options and improvement in health care structures including our country too. Our conclusions are that despite significant progress in this field the diagnosis comes late, the disease has a poor prognosis and further efforts are needed to build structured support for timely diagnosis and improvement of prognosis in these patients.

29. V.Dimitrova, M.Peneva, Y.Radkov, K.Yankov

Pathomorphosis of pulmonary TBC – a real fact. A clinical case. Heart-Lung (Varna), vol.19, 2013, Issue 3-4, p. 43-48

Abstract: Tuberculosis is one the most ancient diseases known mankind. Despite the success achieved in the field of infectious diseases pathology, it has preserved its significance and still presents a serious challenge. Pathomorphosis is a concept introduced by Helpach in 1929 and it represents a sum of the changes in the course of a pulmonary tuberculosis,

resulting from the influence of the environment or the application of the a drug therapy. In clinical aspect it is divided into two types: spontaneous (idiopathic) and induced (therapeutic). Its expression consists of higher frequency of cases with atypical symptoms, unusual localization of the changes in the lungs with an expression of uncharacteristic radiographic image, decreased or concealed infectious stage, some classic differences between pulmonary TBC and non -specific inflammatory pulmonary diseases disappear, which brings the level of diagnostic errors to 30%.

30. V.Dimitrova, M.Peneva, Y.Radkov, D.Petkova, A.Atanasova

Clinical cases of pulmonary tuberculosis as a results of TNF antagonist therapy, Heart-Lung (Varna), vol.18, 2012, Issue 1-2, p. 30-37

Abstract: During the past 12 years TNF antagonists have been successfully used for the treatment of many patients suffering from chronic inflammatory diseases. This treatment increases the risk of tuberculosis up to 25 times. This is due to the fact that TNF and TNF-receptors play an important role in mediating the immune response in acute and chronic inflammation. Therefore all patients undergoing such treatment should be subject to rigorous assessment to exclude active and latent tuberculosis infection. In 2010 a TBNET consensus was published entitled "The risk of tuberculosis related to TNF therapies." In this article we present two cases of pulmonary tuberculosis, which were observed in the course of an ongoing treatment with TNF antagonists in patients with proven inflammatory bowel disease.

31. V. Dimitrova, K. Yankov, D. Dimitrov, St. Nenkova, Tz. Yordanova

Clinical analysis of the patients treated by mechanical ventilation in intensive respiratory care unit, Thoracic medicine, vol.VI,2014, Issue 2, p. 91-98, , ISSN 1313-9827

Abstract

Aim: To analyze the indications, duration, complications and outcome of mechanical ventilation in patients, treated in Intensive Respiratory Care Unit.

Material and methods: A retrospective analysis of the patients, treated by artificial pulmonary ventilation in the Intensive Respiratory Care Unit during the last 5 years (2007-2011) was performed. 191 patients (10,33%) from the total number of patients (1848), treated in the Intensive Respiratory Care Unit during this period, needed mechanical ventilation.

Results: The proportion of patients, treated by mechanical ventilation, does not differ significantly in the monitored years – from 10,81% in 2007 to 11,68% in 2011. The largest number of patients on mechanical ventilation belongs to the age group 60 to 69 years – 60 patients (31,42%). The most common cause of severe respiratory failure, demanding mechanical ventilation, is pulmonary pathology (81,67%) as the greatest percentage belongs

to COPD exacerbation and its complications (pneumonia) – 134 patients (85,90%). The most common reasons from the non-pulmonary pathology are alveolar hypoventilation in extreme obesity, chest deformations and left-sided congestive heart failure. The usual duration of mechanical ventilation is 15 days as there are no significant differences in the monitored years – from 77,14 % to 87,10 %. 7 of the patients (3,66 %) have ventilator – associated pneumonia as a verified diagnosis. The total number of deceased patients is 66 (34,50 %) as there is no significant difference in the studied years.

Conclusion: An average of about 10,33% of the patients, treated in the Intensive Respiratory Care Unit, need mechanical ventilation as the most common pulmonary pathology is COPD. Problematic microbial flora, most often Gram - negative strains, is isolated from tube secrets, which significantly worsens the prognosis and leads to lethality in 34,50 % of the cases.

32. A.Tsonev, S.Nenkova, D.Dimitrov, V.Dimitrova, D.Miteva, K.Kisyova

Our ten year experience with the diagnosis and treatment of pulmonary embolism, Heart-Lung (Varna), vol.12, 2006, Issue 3, p. 48-54

Summary: The main diagnostic methods and therapeutic schedules recently used in the patients with pulmonary thromboembolism who are hospitalized in the Second Clinic of Pulmology with Intensive Respiratory Care Unit at Sv. Marina University Hospital of Varna are presented. The diagnostic achievements relate with the application not only of conventional laboratory, clinical and apparatus methods but also of the perfusion scintigraphy and pulmonary angiography. Contemporary fibrinolysis with rtPA Alteplase and Reteplase possesses a high effectiveness. Both catheter fragmentation and embolectomy are some of the most reliable methods for treatment of the massive pulmonary thromboembolism.

Participation in national scientific forums, with published abstracts

33. V. Dimitrova, D. Petkova, V. Stratev, T. Dobрева

Comorbidity and survival in patients with acute pulmonary embolism Thoracic medicine vol. X/2018/Issue 1/ p.32 ISSN 1313-9827

Abstract

Introduction: Data from a number of studies show that the clinical features of the course, age and comorbidity have an impact on the long-term prognosis in patients with acute pulmonary embolism (PE).

Aim: To show co-morbidity, short-term and long-term survival in patients with acute PE.

Patients and methods: A seven-year retrospective study was conducted in 577 patients who survived acute PE. Comorbidity is calculated using the Charlson Index (CCI). The mean age of the participants was $64,23 \pm 14,60$ years; 53,03% were men and 46,97% were women.

Results: Acute PE is more common in polymorbid patients over 65 years (50,96%). CCI in deceased patients with acute PE was $5,35 \pm 3,17$ ($p < 0.0001$). Comorbidity in patients with massive and non-massive acute PE did not differ in a statistically significant way ($p = 0,228$). The use of fibrinolytic agents reduced mortality in patients with massive PE by 35% (OR = 0,65, 95% CI 0,25-1.42, $p = 0,24$). The analysis of comorbidities in deceased patients with acute PE found a positive statistically significant correlation between the incidence of ischemic heart disease, myocardial infarction, cerebrovascular disease, diabetes mellitus type 2, hemodialysis and mortality. The risk factors for death with the highest significance in acute PE patients were deep venous thrombosis ($\beta = 0,225$, $p = 0,0001$); ischemic heart disease ($\beta = 0,144$; $p = 0,002$); and cerebrovascular disease ($\beta = 0,114$, $p = 0,009$). The mortality rate during hospitalization was 11,8% and 41,1% for the follow-up period from 2010-2016. There is no statistically significant difference in gender mortality rate (Independent Samples T-test; $t = 1,29$; $p > 0,05$).

Conclusions: The follow-up of patients after acute PE detects high mortality rate. Age and cardiovascular diseases are determinants of the prognosis and survival in patients with acute PE.

34.D.Petkova, T.Dobрева, V.Dimitrova, B.Balev, Y.Yotov, M.Cenova, Pl.Panayotov

Dissection of the pulmonary artery, chronic recurrent pulmonary embolism and pulmonary arterial hypertension in a patient with diffuse interstitial lung fibrosis – clinical case. V

congress of the Bulgarian respiratory societyq Thoracic medicine , vol. VI, June 2014, suppl.1 p.23-24, ISSN 1313-9827

Abstract

Aim: To show a clinical case of an young man with a diffuse interstitial fibrosis and progressive dyspnea during minimal physical exertion in the past 2 months.

Case presentation: Male age 39 with proved diffuse interstitial fibrosis 7 years ago treated with steroids and Imuran is admitted with a history of dyspnea during minimal physical exertion, with a duration of 2 months, cough and fever. When admitted clinical signs of respiratory failure, EKG signs for right ventricular overload, EchoCG data for extremely dilated right cavities, pressure in the pulmonary artery 70 mm Hg and suspected thrombus in the right ventricle were seen. From the MRI protocol AX FIESTA dyn, COR FIESTA dyn, SAG FIESTA dyn, obl 2D FIESTA dyn, AX FIESTA with dissection of the left branch of the pulmonary artery, pulmonary hypertension, right cavities dilation, pericardial effusion and lung infarction. From the HRCT of the thorax: chronic pulmonary embolism, idiopathic lung fibrosis, cylindrical bronchiectasias, right ventricular thrombus, pulmonary hypertension.

Conclusion: After the multidisciplinary discussion, the patient was assessed indicated for conservative treatment as an outpatient.

35. V.Dimitrova, D.Petkova, Y.Yotov, Sv.Georgiev, T.Dobreva.

Quality of life in patients with pulmonary arterial hypertension, V congress of the Bulgarian respiratory society, Thoracic medicine , vol. VI, June 2014, suppl.1 p.50-51, ISSN 1313-9827

Abstract

Aim: To assess quality of life in patients with pulmonary arterial hypertension (PAH) by means of Short Form Health Survey (SF-36) before and after initiation of treatment with target medicines.

Material and methods: The study included 7 patients with idiopathic or scleroderma - associated PAH at an average age of 51, 4 men, 3 women with symptoms of right heart failure, II or III functional class according to NYHA, undergoing treatment with target medicines in combination or as a monotherapy for the period 2008-2014. Quality of life (QoL) was assessed before and after initiation of treatment. SF-36 is a questionnaire for subjective assessment of QoL in eight domains: 1. Physical activity, 2. Limitation in physical capacity as a result of physical health problems, 3. Bodily pain, 4. General health perceptions, 5. Vitality, 6. Social function, 7. Limitation in functions as a result of emotional problems, 8. Mental health. Calculation of results was performed by standardized methodology.

Results: Significantly improved quality of life was found in the studied domains in patients on target treatment, which correlates with improvement in 6MT, performance of echocardiography and right heart catheterization in all patients after the start of treatment with target medicines.

Conclusion: Therapy with target medicines improves the quality of life in patients with PAH. The SF-36 questionnaire is an intelligible tool for assessing the quality of life and the disease course in patients with PAH.

36. A.Dyakova, V.Dimitrova, D.Petkova, D.Miteva, M.Tsenova

Lung cancer in women – four years assessment, V congress of the Bulgarian respiratory society, Thoracic medicine , vol. VI, June 2014, suppl.1 p.51-52, ISSN 1313-9827

Abstract

Aim: To evaluate the most common type of women's lung cancer and to present the possible diagnostic methods.

Material and methods: For the period of 2010 -2013, 1060 patients (870 men and 190 women) suspected of having lung cancer were hospitalized. The average age of the woman was 66 years. The diagnosis and staging of the lung cancer was realized by standard methods.

Results: The morphological type of lung cancer in women is: non-small cell lung cancer (NSCLC) in 128 cases (67.36%) small cell cancer 26 (13.68%) carcinoid in 2 (1.05%). From NSCLC with adenocarcinoma are 49 patients (25,7%) NSCLC undetermined type – 45 (23,6%), squamous cell carcinoma 22 (11,57%) bronchoalveolar carcinoma 3(1,57%) mucoepidermoid carcinoma 3 (1,57%), large cell carcinoma 3 (1,57%), adenosquamous cell carcinoma 3 (1,57%). In four patients (2,10%) was determined Non –Hodgkin lymphoma, Hodgkin lymphoma in 1 (0,52%), mesothelioma in 2 (1,05%), lung metastases 8 (4,21%), and metastatic pleural effusion from other primary oncological disease in 5 cases (2,63%). In 14 patients (7,36%) the morphology was not determined. Most of the patients (92 - 57%) were diagnosed with stage four. Diagnostics Methods are fibrobronchoscope 47,3%, transthoracic needle aspiration biopsy 27,3%, other methods 25,4%.

Conclusion: Adenocarcinoma is a major histologic type of lung cancer in women. The diagnosis was obtained in final stage. Therefore the lung cancer should be included in screening programs, similar to breast and cervical cancer.

37. A.Dyakova, V.Kostadinova, V.Dimitrova, D.Miteva

Clinical case of pulmonary Langerhans cell histiocytosis, V congress of the Bulgarian respiratory society, Thoracic medicine, vol. VI, June 2014, suppl.1 p.49-50, ISSN 1313-9827

Abstract

Aim: To report a clinical case of pulmonary Langerhans cell histiocytosis (LCH) and to follow up the development of the disease after treatment with Prednisolon and Metotrexat.

Material and methods: This study reports a clinical case of a 30 years old male smoker with pulmonary LCH, diagnosed by open lung biopsy. For assessment of the patient's condition high resolution computed tomography, pulmonary function test, blood gases and echocardiography were performed after one year of treatment.

Results: In this case study the first clinical manifestation of the disease was spontaneous pneumothorax. Computed tomography of the lung revealed diffuse fibrosis findings, subpleural cysts and nodules predominantly in the upper lung fields. Although the sweat test for suspected cystic fibrosis was positive, a genetic analysis failed to confirm this diagnosis. Surgical lung biopsy confirmed pulmonary LCH. The patient was treated with 30mg (initial dose) of Prednisolon for one year. 20 mg of Metotrexat was added to regime 3 months after the initiation of the treatment. During this period no worsening of the symptoms, radiological findings, pulmonary functional test and blood gases was observed.

Conclusion: Pulmonary LCH should be included in the differential diagnosis of the interstitial lung disease. After smoking cessation a spontaneous regression is possible occur.

38. A.Dyakova, D.Miteva, V.Kostadinova, V.Dimitrova

Clinical case of pulmonary alveolar proteinosis, V congress of the Bulgarian respiratory society, Thoracic medicine, vol. VI, June 2014, suppl.1 p.49-50, ISSN 1313-9827

Abstract

Aim: To present the challenges in diagnosis of pulmonary alveolar proteinosis (PAP) and to follow up patient condition after whole lung lavage.

Material and methods: We report a case of a 56 years old male patient, nonsmoker with a history of progressive dyspnea. After the bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBB) PAP was diagnosed. The patient was followed over a period of three years, during which a whole – lung lavage was performed once.

Results: Based of the results from pulmonary functional test, blood gases, high resolution computed tomography (HRCT) and from insufficient fibrobronchoscopy lung biopsy (lack of lung parenchyma) we supported the primary diagnosis of idiopathic pulmonary fibrosis. Initially the patient was treated with corticosteroids (Medrol) and subsequently with purine analogue (Imuran).The presence of modest clinical symptoms and rich radiological findings imposed a reassessment of the case after two years of observation. Repeated the fibrobroncho scopy with BAL and TBB confirmed the diagnosis of PAP.As a result the patient was sent for WLL. One year after the treatment the pulmonary functional

test, blood gases, high resolution computed tomography (HRCT) showed an improvement. The forced vital capacity increased with 1,05 L and the blood oxygen with 1,63 kPa.

Conclusion: The slow progression of the disease and nonspecific clinical and physical manifestations make the diagnosis of PAP difficult and complex. It appears that WLL should be first line treatment for idiopathic PAP.

39. V.Kostadinova, D.Miteva, Y.Radkov, I.Mircheva, A.Dyakova, V.Dimitrova

Role of CRP in the clinical assessment of community acquired pneumonia, V congress of the Bulgarian respiratory society, Thoracic medicine, vol. VI, June 2014, suppl.1 p.37, ISSN 1313-9827

Abstract

Aim: To analyze the value of CRP (C-reactive protein) according to clinical characteristics in hospitalized patients with community acquired pneumonia (CAP)

Material and methods: Retrospective study for a period of three years. It includes 1278 patients with CAP men 57,4% (n=734), age 60,3±16.9 years.

Results: Factors associated with significantly higher levels of CRP on the day of hospitalization were: multilobar pneumonia (t= -6.368 ,p <0,01), comorbidities (t= -3,173, p <0,01),pleural effusion (t= -3,575, p <0,01), hypoxemia (t =-9,071, p <0,01), severe pneumonia according to the criteria of the IDSA/ATS (t =-11,205, p <0,01), males (t= 3,244, p <0,01). Patients treated in the intensive care unit (t= -8,685 ,p =0,04) and patients who died (t= -6,078 ,p <0,003) had higher CRP levels on admission than those treated in general ward and survived patients, respectively. There is no difference in the value of this inflammatory marker in patients on mechanical ventilation (MV) and those without MV (t =-0,458, p = 0.648, NS), and among patients who died within the first 72 hours and those who died later (t =-0,531, p <0,569 NS). Patients with high mortality risk according to CURB 65 have higher CRP levels on admission (183,4mg/L) comparing with low risk patients (115,4mg/L).

Conclusion: Elevated CRP levels are associated with more severe pneumonia, a higher risk of death presence of co-morbidities, more frequent complications.

40. D.Miteva, Y.Radkov, I.Mircheva, V.Kostadinova, A.Dyakova, V.Dimitrova

Influence of comorbid diseases on the severity and prognosis of hospitalized patients with community acquired pneumonia, V congress of the Bulgarian respiratory society, Thoracic medicine, vol. VI, June 2014, suppl.1 p.40, ISSN 1313-9827

Abstract

Aim: To investigate the role of comorbid diseases on the severity and outcome of hospitalized patients with CAP.

Material and methods: 408 patients hospitalized with CAP in the Clinic of Pneumology and Phthisiatrics at the University hospital „St. Marina“ – Varna in 2013 were retrospectively studied.

Results: The mean age of the patients is 61.31, 59, 6% were male, 40, 4% female. 74,75% had comorbidities. The most common are ischaemic heart disease 29,65%, diabetes mellitus 26,23%, heart failure 19,85%, cerebrovascular disease 19,6%. For each patient Charlson comorbidity index (CCI) was calculated. The average value was 1,72 (от 0 до 10 points). Patients were divided into four groups according to their level of comorbidity low (0 points) -36,8% moderate (1-2 points) 36,5% high (3-4 points) 16,7% and very high 10%. Patients with acute respiratory failure in different levels were respectively – 16%, 28,9%, 54,4%, 65,9%. The incidence of acute respiratory failure increased with the level of comorbidity (55,5 p < 0,001). The non survivors are distributed according to the different levels of CCI as follows 0 points -3,3%, 1-2 points 6,0%, 3-4 points 22,1% and very higher 41,5%. CCI of the deceased is higher than that of survivors 3,24 v/s 1,41 (p< 0,001).

Conclusion: Comorbid conditions assessed by CCI have significant impact on the severity and inhospital mortality of CAP.

41. V.Stratev, D.Petkova, T.Dobрева, V.Dimitrova

Echocardiographic evaluation of the right heart and pulmonary arterial hypertension in COPD patients, VI congress of the Bulgarian respiratory society, Thoracic medicine, vol. VIII, 2016, Issue 1, suppl.1 p.44, ISSN 1313-9827

Abstract

Aim: The aim of the present study echocardiographic evaluation of the right heart and presence of PAH in COPD patients as well as their association with the disease severity.

Patients and methods: We performed a retrospective study of 154 patients with COPD (mean age 66,8 ±10,04 years, 64,9% males), hospitalized in pulmonary clinic for 4 year period. We performed dopler EchoCG of the right heart with measuring the systolic pressure in the pulmonary artery (sPAP). We performed spirometry, blood gas analysis and biochemical investigations.

Results: The mean size of the right ventricle in the investigated group was 32,4 ± 6,65 mm, and the size of the right atrium was 38 ± 14,14 mm. The mean systolic pressure in PA was 49,3±14,3 mm Hg without significant difference between males and females. 54,7% of the patients showed increased systolic pressure >35 mm Hg in PA with significant higher values in GOLD spirometry stages 3 and 4 (p<0,5). The sPAP correlated positively with the

CRP levels ($p=0,034$, $r=0,456$) and negatively with oxygen saturation ($p=0,029$, $r=-0,381$) and FEV1 predicted ($p=0,035$, $r=-0,324$).

Conclusion: The present study suggests that there is significant right heart burden in COPD patients, as well as high prevalence of PAH. There is association of sPAP levels and COPD severity, oxygen uptake and inflammatory markers.

42. A.Angelov, T.Dobreva, V.Stratev, V.Dimitrova, D.Petkova

New opportunities for screening of subclinical atherosclerosis in patients with OSA – a pilot study, VI congress of the Bulgarian respiratory society, Thoracic medicine, vol. VIII, 2016, Issue 1, suppl.1 p.44, ISSN 1313-9827

Abstract

Introduction: Coronary arterial calcium (CAC) is a marker for the presence of coronary atherosclerosis and the biological age of the vessels. Quantitative assessment of CAC is performed by measurement of the coronary arterial calcium score (CACS).

Aim: To investigate CACS in patients with OSA without known cardiovascular diseases (CVD).

Patients and methods: We investigated five males with mean age $52,2\pm 10,4$ years with OSA and without CVD. All patients had arterial hypertension and metabolic syndrome according to IDF criteria. The 10 years risk for ischaemic heart disease was defined using the Framingham Risk Score (FRS). CACS measurement was performed using CT scanner Siemens Somatom Definition (Dual Source 2x64)

Results: According to FRS three of the patients were classified as low risk ($FRS<10\%$), and two were with intermediate risk ($FRS 10-20\%$). CAC was found in all five patients (mean score $44,1\pm 68,7$ AU). Three of the patients were below 50 years of age and had three risk factors for coronary disease but the factor age indicated low FRS. In young patients slightly increased values of CACS may be higher from the 75-th percentile for sex and age. When applying this criterion for reclassification and not the classical $CACS \geq 400$, two of the young patients were reclassified in the high risk category.

Conclusion: In young patients with OSA without known CVD, measurement of CACS may overcome the risk underestimation, typical for the classical risk models like FRS.

Finding $CACS >75$ th percentile for sex and age places the subject into the high risk category which allows individual approach when choosing protective medications.

43. D.Petkova, V.Stratev, Y.Petev, V.Dimitrova, T.Dobreva

Home oxygen therapy (HOT) clinical features of the patients (six years of experience of Varna pulmonary league) VI congress of the Bulgarian respiratory society, Thoracic medicine, vol. VIII, 2016, Issue 1, suppl.1 p.44, ISSN 1313-9827

Abstract

Introduction: The increasing number of patients with chronic diseases, who are suitable for HOT, demands better understanding of the clinical indications, the main disease and active follow up of this group patients.

Aim: To investigate the epidemiological and clinical features of the using HOT.

Patients and methods: We performed a retrospective study among 75 patients (mean age $70,9 \pm 8,62$ years, 65,8% males) from August 2010 to March 2016. All patients are referred for treatment after hospitalization in specialized clinic, assessment of indications by pulmonologist and oxygen dose titration in the hospital.

Results: The main disease resulting in chronic respiratory failure and necessity of HOT were as follows: COPD 34,7%, pulmonary fibroses 30,1%, palliative care for lung carcinoma 15,1%, CHF 11%, obesity hypoventilation syndrome 4,1% and pulmonary hypertension 1,4%. The mean values of blood gas indices at initiation of oxygen treatment were $5,9 \pm 1,32$ kPa for PaO₂, $6,2 \pm 1,9$ kPa for PaCO₂, $7,38 \pm 0,078$ for pH and the mean oxygen saturation was $77 \pm 10,6$ %. The mean oxygen flow used for HOT was $2,25 \pm 0,95$ l/min. 41,1% of the patients who started HOT are deceased. The main duration of HOT was $7,8 \pm 9,05$ (range 1-48) months and it showed negative correlation with the values of partial pressure and saturation of oxygen ($p < 0,05$).

Conclusion: HOT is an integral part of the complex care of disabled patients. The delayed referral and lack of sufficient monitoring are current issues. In indicated patients HOT improves survival and lessens the number of hospitalizations.

44. V. Dimitrova, K. Yankov, P. Peneva, S.Nenkova, D.Dimitrov, C.Yordanova, I.Hristova Effectiveness of noninvasive ventilation in patients treated in respiratory ICU MHAT "St. Marina "Varna, VI congress of the Bulgarian respiratory society, Thoracic medicine, vol. VIII, 2016, Issue 1, suppl.1 p.18, ISSN 1313-9827

Abstract: Noninvasive ventilation used for the treatment of chronic and acute respiratory failure is one of the greatest achievement in the field of respiratory medicine last years. Patients treated with NIV in ICU were investigated for the period of time 2013-2015. The whole number of the patient was 203: 31 (15,27%) with acute respiratory failure and 172 (84,73 %) with chronic respiratory failure. Patients with chronic respiratory failure were separated into four groups: COPD 68 (33.5%). obesity hypoventilation 48 (23.65 %), overlap

syndrome 31 (15.27 %) and others 25 (12.31 %). The type of NIV, ventilation pressures, length of ventilation, PaCO₂ and pH at the beginning and at the end of ventilation, trend of SpO₂ during treatment very calculated for all the patient. The number of the patient classified as treatment failure who needed invasive ventilation was also recorded.

Conclusion: NIV is an affective and reliable therapeutic approach in patients with acute and chronic hypercapnic respiratory failure. The ventilation improves hypoxemia in both groups of patients. The level of PaCO₂ is decreased statistically in patients with hypercapnic respiratory failure.

45. V. Dimitrova, D. Petkova, K. Yankov, V. Stratev, T. Dobрева

Prevalence of relapses and CTEPH in patients followed-up after acute pulmonary embolism VI congress of the Bulgarian respiratory society, Thoracic medicine, vol. VIII, 2016, Issue 1, suppl.1 p.44, ISSN 1313-9827

Abstract

Introduction: Chronic thromboembolic pulmonary hypertension is a disease, resulting from proximal or distal thromboembolic obstruction, which leads to remodeling of pulmonary vascular system, increased pulmonary vascular resistance and manifestations of right heart failure despite the adequately carried out anticoagulant therapy.

Aim: To investigate the prevalence of relapses and CTPEH in patients followed-up after acute PE.

Patients and methods: We performed a retrospective study among 493 patients with acute PE, hospitalized in the Clinic of pulmonary diseases of Varna University Hospital within the period 2010-2015. The mean age of the patients involved in the study is 64.76 ± 14.34 years (54,76% men vs 45,24% women).

Results: The prevalence of PE relapses in the study group was 13.99 % (69 patients). Forty-two patients (60.87%) were followed up for a mean period of two years and four months (range from 3 months to 6 years). The mortality rate in the follow-up group was high 21.43 %. At the moment of relapse, 57,14% of the patients were receiving treatment with Sintrom or NOAC. 47,62% of the patients in the study group had a relapse within 1 year as relapses in men are statistically significantly registered more frequently more than 1. Charlson co-morbidity index in the study group was 1.48. The prevalence of CTEPH in the study group was 4.06 %.

Conclusion: CTEPH is a serious complication in patients with acute or relapsing PE. Patients surviving acute PE are not followed up prospectively. The discovery and monitoring of patients at high risk is an important step for early diagnostics and treatment.

46. M. Peneva, S. Nenkova, V. Dimitrova, D. Dimitrov, Tz. Yordanova.

Clinical features of severe pneumonia treated in the intensive respiratory care unit of 'St. Marina' Hospital in Varna, Bulgaria during the influenza A(H1N1) epidemic wave at the end of 2009. III congress of the Bulgarian respiratory society, Thoracic medicine, vol. II, 2010, Issue 1, suppl.1 p.65, ISSN 1313-9827

Abstract: The influenza A (H1N1) pandemic provided many challenges toward pulmonologists in our country.

Objectives: To determine the clinical characteristics of severe pneumonias in patients treated in the period when influenza A H1N1 epidemic occurred.

Method: Retrospective analysis of the clinical, laboratory records, imaging and pathological features in patients with severe pneumonia (Group A) treated in the period from November to December 2009. Data were compared to these for patients with severe pneumonia treated in the same institution for the period from January to October 2009 (Group B).

Results: Eighty seven patients have been hospitalized in our IRCU with severe pneumonia in 2009, 43(49,4%) of them (Group A) - in the epidemic period and 44(50,6%) in the remaining months. For the entire 2009 year 17 patients with pneumonia needed mechanical ventilation. 11 (64.7%) of them were from Group A (in 6 patients Influenza A H1N1) was confirmed. Bacterial pathogens were isolated only in 16% in Group A and 60.5% from Group B. The most frequent manifestation of multi organ failure in Group A consisted of hematological changes, changes in liver function, increased serum levels of CPC, neurological symptoms. In Group B changes in liver function and renal failure were dominant. Mortality rates were 32,5% in Group A and 18,42% in Group B.

Conclusions: Significantly higher incidence of severe pneumonias including the cases requiring mechanical ventilation has been observed for the period of Influenza A (H1N1) epidemic.

47. D. Petkova, V. Dimitrova, M. Peneva, S. Nenkova, Y. Yotov, D. Dimitrov, B. Drumev

Incidence and prevalence of chronic thromboembolic pulmonary hypertension: from acute to chronic pulmonary embolism III congress of the Bulgarian respiratory society, Thoracic medicine, vol. II, 2010, Issue 1, p. 49 ISSN 1313-9827.

Abstract: Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare disease that results from obstructive of the major pulmonary arteries by incompletely resolved or organized pulmonary emboli that have become incorporated into the pulmonary artery wall eventually causing an increase in pulmonary vascular resistance. From 0,1 to 4,0% of patients

recovering from acute pulmonary embolism develop CTEPH. In Bulgaria there is no epidemiological data about incidence and prevalence of CTEPH.

Aim: of the study is to establish the occurrence of CTEPH in patients diagnosed with acute pulmonary embolism.

Patients and methods: 184 patients (96 male и 88 female with mean age of $62,55 \pm 13,46$ years) with diagnosed acute pulmonary embolism participated the study. The study population was analyzed from 2007-2009. 40 patients (21,74%) were with symptoms for CTEPH. 22 patients (11,96%) had history and clinical data for acute pulmonary embolism in the past. Ten patients were rehospitalized with symptoms of CTEPH 1 year after the acute pulmonary embolization, 3 patients after 2 years, 1 patients after 3 years, and 5 patients and above. There was limited data for the rest of the study population about history of the first thromboembolic events, hospitalizations and verification of pulmonary hypertension. None of the patients were actively monitored about the presence of CTEPH.

In conclusion: Patients with acute pulmonary embolism are not being followed up closely in order to verify and to treat CTEPH. Further prospective epidemiologic studies are needed to better define the incidence and prevalence of CTEPH.

48. K. Yankov, St. Nenkova, D. Dimitrov, V. Dimitrova, Ts. Yordanova, P. Peneva
Pulmonary thromboembolism - risk factors, diagnosis and clinical significance.

IV National Congress of Bulgarian respiratory society. , Thoracic Medicine, Volume IV, 2012, Issue 1, suppl.1 ISSN 1313-9827.

49. D. Petkova, J. Yotov, V. Dimitrova, B. Kanazirev, St. Georgiev

Idiopathic pulmonary hypertension-diagnosis, clinical efficacy of targeted treatment and problems. IV National Congress Bulgarian respiratory society , Thoracic Medicine, Volume IV, 2012, Issue 1, suppl.1 ISSN 1313-9827.

50. D. Petkova, V. Dimitrova, Kr. Kisova, M. Peneva

Home oxygen therapy: clinical results, problems and prospects. Eighteen months of experience in the lung league in Bulgaria. IV National Congress of Bulgarian respiratory society , Thoracic Medicine, Volume IV, 2012, suppl.1, ISSN 1313-9827.

51. V. Dimitrova, M. Peneva, K. Yankov

Clinical analysis of patients treated with mechanical ventilation in an Emergency Respiratory Ward, IV congress of the Bulgarian respiratory society Thoracic medicine, 2012, vol 4, p.65 ISSN 1313-9827

Abstract

Aim: To make analysis of indications, duration, complications and outcome of the mechanical ventilation in patients treated in the Emergency Respiratory Ward.

Data and methods: A retrospective analysis of the patients in the Emergency Respiratory Ward treated with mechanical ventilation during the last 5 years (2007-2011) has been made. 191 patients (10,33%) from the total number of patients (1848), treated in the Emergency Respiratory Ward during this period, needed mechanical ventilation.

Results: The percentage of patients, treated with mechanical ventilation, does not differ substantially during the studied years – from 10,81% in 2007 to 11,68% in 2011. The most common reason for heavy respiratory insufficiency, demanding mechanical ventilation, is pulmonary pathology (81,67%) as the greatest percentage belongs to COPD exacerbation and its complications (pneumonia) – 134 patients (85,90%). The most common reasons from the non-pulmonary pathology are alveolar hypoventilation in case of extreme obesity, chest deformations, left - side cardiac insufficiency. The usual duration of mechanical ventilation is 15 days as there are no significant differences in the studied years – from 77,14 % to 87,10 %. 7 of the patients (3,66 %) have a verified diagnosis ventilator – associated pneumonia. The total number of patients with lethal outcome is 66 (34,50 %) as there are no significant differences in the studied years.

Conclusion: About 10 % of the patients, treated in Emergency Respiratory Ward, need mechanical ventilation as the most common pulmonary pathology is COPD. Problematic microbial flora, most often Gram negative strains are isolated in tube secrets, which significantly deteriorates the prognosis and leads to lethality in 34,50 % of the cases.

52. V. Dimitrova, K. Yankov, D. Dimitrov, Y. Radkov, A. Dyakova

Bronchogenic carcinoma: verification, staging and choice of therapeutic approach, IV congress of the Bulgarian respiratory society Thoracic medicine, vol. IV 2012, p.65, ISSN 1313-9827

Abstract

Aim: To make analysis of the verification methods and therapeutic approach in patients with bronchogenic carcinoma during the period 2010 - 2012.

Materials and methods: A retrospective analysis of the cases with proved bronchogenic carcinoma has been made by sex, age, method of morphological verification and histological type of the tumor, stage and therapeutic behaviour.

Results: Out of the total number of patients treated at the clinic during the analyzed period (6949), 1698 patients (24,42 %) are suspected to have bronchogenic carcinoma. The diagnosis has been confirmed in 987 patients (58,12%). The men - women ratio is 4,1:1. The

most affected age group is 60-69 – 377 patients (38,19%) and 50-59 – 271 patients (27,46%). The morphological diagnosis has been proved in 523 patients (52,98 %) by bronchoscopic sample material – brush, forceps, needle biopsy and BAL, and in 369 patients (37,39%) – by TTAB. The most common morphological type is non-small cell bronchogenic carcinoma – 596 patients (57,46%) followed by adenocarcinoma - 202 patients (20,47%) and small cell carcinoma – 142 patients (14,38%). Bronchogenic carcinoma, diagnosed in IV clinical stage, has the greatest percentage – 581 patients (58,87%). 125 patients (12,66%) are directed to surgical treatment, 785 patients (79,53%) – to chemotherapy and 69 patients (6,99%) – to palliative care.

Conclusion: Pulmonary carcinoma is a common disease in pulmonary practice, which is diagnosed at a late stage - the most common morphological type being non-small cell carcinoma with limited chances for radical surgical treatment.

53. V. Dimitrova, M. Peneva, J. Radkov, K. Yankov

Pathomorphosis of pulmonary tuberculosis - a real fact, 18th Heart-Lung Conference, April 27, 2013, Varna, presentation

Summary: The presentation presents two cases of hematogenously disseminated tuberculosis, which once again confirm the diversity in the course of this infection. Under the influence of various external and internal causes at the present stage there are significant changes in the nature and course of pulmonary tuberculosis, which create differential diagnostic problems.

• **Participation in international scientific forums, with published abstracts**

54.M. Peneva, S. Nenkova, V. Dimitrova, D. Dimitrov, Tz. Yordanova.

Clinical features of severe pneumonia treated in the intensive respiratory care unit of 'St. Marina' Hospital in Varna, Bulgaria during the influenza A(H1N1) epidemic wave at the end of 2009. European Respiratory Journal, 2009; vol.34: Suppl. 53, 534s, ISSN 0903-1936

Abstract :The influenza A (H1N1) pandemic provided many challenges toward pulmonologists in our country.

Objectives: To determine the clinical characteristics of severe pneumonias in patients treated in the period when influenza A H1N1 epidemic occurred.

Method: Retrospective analysis of the clinical, laboratory records, imaging and pathological features in patients with severe pneumonia (Group A) treated in the period from November to December 2009. Data were compared to these for patients with severe pneumonia treated in the same institution for the period from January to October 2009 (Group B).

Results: Eighty seven patients have been hospitalized in our IRCU with severe pneumonia in 2009, 43(49,4%) of them (Group A) - in the epidemic period and 44(50,6%) in the remaining months. For the entire 2009 year 17 patients with pneumonia needed mechanical ventilation. 11 (64.7%) of them were from Group A (in 6 patients Influenza A H1N1) was confirmed. Bacterial pathogens were isolated only in 16% in Group A and 60.5% from Group B. The most frequent manifestation of multi organ failure in Group A consisted of hematological changes, changes in liver function, increased serum levels of CPC, neurological symptoms. In Group B changes in liver function and renal failure were dominant. Mortality rates were 32,5% in Group A and 18,42% in Group B.

Conclusions: Significantly higher incidence of severe pneumonias including the cases requiring mechanical ventilation has been observed for the period of Influenza A (H1N1) epidemic.

55.V. Dimitrova, M. Peneva, K. Yankov, S. Nenkova, D.Dimitrov.

Clinical analysis of patients treated with mechanical ventilation in an Emergency Respiratory Ward. ERJ, September 2012, vol. 40 / supplement 56 /, 352s

Abstract

Aim: To make analysis of indications, duration, complications and outcome of the mechanical ventilation in patients treated in the Emergency Respiratory Ward.

Data and methods: A retrospective analysis of the patients in the Emergency Respiratory Ward treated with mechanical ventilation during the last 5 years (2007-2011) has

been made. 191 patients (10,33%) from the total number of patients (1848), treated in the Emergency Respiratory Ward during this period, needed mechanical ventilation.

Results: The percentage of patients, treated with mechanical ventilation, does not differ substantially during the studied years – from 10,81% in 2007 to 11,68% in 2011. The most common reason for heavy respiratory insufficiency, demanding mechanical ventilation, is pulmonary pathology (81,67%) as the greatest percentage belongs to COPD exacerbation and its complications (pneumonia) – 134 patients (85,90%). The most common reasons from the non-pulmonary pathology are alveolar hypoventilation in case of extreme obesity, chest deformations, left - side cardiac insufficiency. The usual duration of mechanical ventilation is 15 days as there are no significant differences in the studied years – from 77,14 % to 87,10 %. 7 of the patients (3,66 %) have a verified diagnosis ventilator – associated pneumonia. The total number of patients with lethal outcome is 66 (34,50 %) as there are no significant differences in the studied years.

Conclusion: About 10 % of the patients, treated in Emergency Respiratory Ward, need mechanical ventilation as the most common pulmonary pathology is COPD. Problematic microbial flora, most often Gram negative strains are isolated in tube secrets, which significantly deteriorates the prognosis and leads to lethality in 34,50 % of the cases.

56.V. Dimitrova, D. Petkova, V. Stratev, T. Dobрева.

Prevalence of relapses and chronic thromboembolic pulmonary hypertension (CTEPH) in patients with pulmonary embolism“ ERJ September 2016, vol. 48,/ supplement 60 / PA 2432

Abstract:

Introduction: New evidence suggests that the prevalence of CTEPH after acute and relapsing PE is increasing.

Aim: To investigate the prevalence of relapses and CTPEH in patients followed-up after acute PE and their mortality rate.

Patients and methods: We performed a retrospective study among 493 patients (mean age 63.56 ± 14.34 years) with acute PE hospitalized in the pulmonary clinic of Varna University hospital for six year period (2010-2015). We assessed the demographic data and clinical presentation of the patients. Echocardiography, MDCT angiography and VP scan were performed. CTEPH was defined as elevated SPAP > 25 mm Hg at rest in the presence of mismatched perfusion defects in the vascular filling-up, found on the imaging studies.

Results: The prevalence of PE relapses in the study group was 13.99 % (69 patients) with a significantly higher rate among men (53.62% males vs. 46.38% females, $p > 0.05$). Forty-two patients (60.87%) of the latter were followed for a mean period of two years and four

months (range from 3 months to 6 years). In the follow-up group, 85.71% of the patients had a relapse in 1 year. The prevalence of CTPEH in the whole study group was 4.06%. Comorbidity, assessed with the Charlson index was 1.48. The mortality rate among the patients with relapse was 21.43%.

Conclusion: CTEPH is not a rare complication in patients with acute or relapsing PE. Patients with relapses of PE are at high risk and early diagnose and strict follow-up is very important for improving survival.

57.V. Stratev, V. Dimitrova, T. Dobрева, D. Petkova.

Pulmonary artery dissection (PAD) in a patient with diffuse interstitial lung disease and chronic thromboembolic pulmonary hypertension (CTEPH) ERJ September 2016, vol. 48, /supplement 60/ PA 2491

Abstract:

Introduction: PAD is an extremely rare condition. Over the past two centuries, around 70 cases of pulmonaryartery dissection have been described, of which only nine were diagnosed during lifetime.

Case report: A 39 year old man presented in the pulmonary clinic with notable exertional dyspnea, cough and occasional fever, which lasted for a month before admission. Blood gas analysis showed severe hypoxemia (PaO₂ 4.3 kPa). The patient was diagnosed 7 years ago with diffuse interstitial lung disease-desquamative pneumonia using transbronchial biopsy. The patient received corticosteroid and immunosuppressive treatment. Echocardiography displayed increased mean pulmonary artery pressure (PAP) >70 mm Hg, TAPSE 17 mm. The HRCT imaging showed signs of chronic pulmonary embolism of the left pulmonary artery with infarction formation, which was confirmed with VP scan. MRI showed marked enlargement of the right heart (ventricle 64.2 mm, atrium 57 mm), pericardial effusion and dissection of the left branch of the pulmonary artery with flap formation. The patient was assessed eligible for anticoagulant treatment, which led to improvement of the dyspnea. Surgical treatment was discussed, but assumed not appropriate due to severe hypoxemia. He was discharged with recommendation for home oxygen treatment and oral anticoagulant therapy. Patient follow up for 5 years showed stable condition (PAP ~100 mm Hg) and no further progression of PAD on control MRI. The co-existence of interstitial lung disease with CTEPH and PAD is very rare and physicians should be aware of this possibility. There should be multidisciplinary approach to these patients.

58.V. Stratev, T. Dobрева, V. Dimitrova, D. Petkova.

*Co-morbidities and pulmonary arterial hypertension (PAH) in COPD patients , ERJ
September 2016, vol. 48,/ supplement 60/PA 1131*

Abstract:

Introduction: COPD is a systemic disease with significant co-morbidities. PAH is known to develop in mild to severe COPD and is associated with disabling course of the disease.

Aim: To assess the incidence of co-morbidities and PAH in COPD patients and their association with disease severity.

Patients and methods: We performed a retrospective study of 161 COPD patients (mean age 67.7 ± 10.8 years, 67.4% males), hospitalized due to COPD exacerbations in pulmonary clinic of the University hospital for four year period. Spirometry, blood gas analysis and biochemical investigations were performed. Co-morbidities were assessed using patient's medical records. Systolic pulmonary arterial pressure (SPAP) was measured using dopler echocardiography.

Results: The incidence of co-morbidities was: hypertension (83.1%), ischaemic heart disease (40%), cardiac arrhythmias (12.6%), chronic left heart failure (47.4%), diabetes mellitus (21.1%) and bronchiectasis (8.4%). The mean SPAP of the study group was 49.3 ± 14.3 mm Hg with no significant difference between males and females. 53,2% of the patients showed increased SPAP > 35 mm Hg with significantly higher values in GOLD spirometry stages 3 and 4 ($p < 0.05$). SPAP correlated positively with the presence of hypertension, ischaemic heart disease, chronic left heart failure and the levels of CRP ($p < 0.05$) and negatively with oxygen saturation ($p = 0.029$, $r = -0.381$) and FEV1% ($p = 0,035$, $r = -0.324$).

Conclusion: The present study suggests significant burden of cardiovascular co-morbidities and increased incidence of PAH in COPD patients. There was association of PAH with lung function, oxygen uptake and inflammation.

59.V. Stratev; J. Petev; V. Dimitrova; T. Dobрева; D. Petkova.

Levels of antioxidant enzymes and CRP in patients with COPD and metabolic syndrome (MS) and their association with obesity, 3 rd International workshop on lung health, Monaco 15-17 Jan 2016, Abstract book page 28 P18a.

Abstract:

Introduction: Patients with metabolic syndrome (MS) have been recently recognized as a distinct phenotype in the COPD population. Antioxidant enzymes and CRP play key role in the pathogenesis of both COPD and MS.

Aim: The aim of the present study was to investigate the levels of CRP and antioxidant enzymes superoxidedismutase (SOD) and glutathione-peroxidase (GPx) in patients with COPD and MS, compared to those without the syndrome and their association with the indices of overall and abdominal obesity.

Patients and Methods: A cross-sectional study was performed among 183 COPD patients (mean age 65.6±7.3) and 103 subjects without respiratory diseases served as a control group (mean age 52.97±6.3). The presence of MS was identified by the IDF criteria. BMI and waist circumference were calculated and the levels of SOD, GPx and CRP were measured.

Results: The prevalence of MS was 48.1% in COPD cohort vs. 39% in the control group. COPD patients had significantly higher BMI and WC compared to the control group ($p<0.001$). The levels of antioxidant enzymes were significantly lower in COPD patients presenting MS (GPx 37.1±6.1 U/gHb; SOD 1203.3±149.5 U/gHb), compared to those without the syndrome (GPx 38.5±7.8 U/gHb; SOD 1220.2±175.5 U/gHb) and the control group (GPx 40.4 ± 38 U/gHb; SOD 1264.5 ± 120.5) ($p<0.05$). In obese patients (BMI >35) the levels of SOD and GPx were significantly lower compared to overweight patients and those with normal BMI ($p<0.05$). The levels of CRP were significantly higher in patients with COPD and MS, compared to COPD patients without the syndrome and the control group ($p<0.05$). Linear regression analysis showed significant negative association between antioxidant enzymes and waist circumference (WC) ($\beta=-0.243$, $p<0.001$ for SOD; $\beta=-0.191$, $p=0.002$ for GPx) and BMI ($\beta=-0.143$, $p=0.016$ for SOD; $\beta=-0.149$, $p=0.012$ for GPx).

Conclusion: The present study demonstrates decreased antioxidant defense and increased inflammation in patients with COPD and MS and association between antioxidant enzymes and the indices of overall and abdominal obesity.

60. V. Dimitrova; D. Petkova; N. Usheva; V. Stratev; T. Dobрева.

Clinical features of patients with pulmonary embolism (PE). 3rd International workshop on lung health, Monaco 15-17 Jan 2016, Abstract book page 5, P03a.

Abstract:

Aim: To analyze the incidence, co-morbidity, risk factors, relapses and mortality in patients with PE.

Patients and methods: We performed a retrospective study of 415 patients with pulmonary embolism (mean age 63.5 ±14.3 years) and cases of relapses, hospitalized in the clinic of pulmonary diseases at UMHAT “St. Marina” Varna for a 5 year period (2010-2014).

Results: Females with PE were with higher mean age than males ($p<0.001$). Co-morbidity scored with Charlson index was 1.55. The incidence of massive PE for the 5 year

period was 30.4% and the incidence of relapses was 32.2%. There was no significant difference between the two groups ($\chi^2=6.5$; $p=0.164$). The risk of massive PE is twice higher in the presence of immobilization for more than four days ($p>0.05$). The risk of lethal outcome in patients with massive PE is 3 times higher than those with non-massive forms. (OR=3.15; CI 95% 1.71- 5.82). The mortality was significantly higher in females ($\chi^2=9.69$; $p=0.04$). The mortality in the group without relapse is 12.4% versus 8.5 % in the relapse group without reaching significance ($p= 0.23$). The use of fibrinolytic therapy reduces the mortality in massive forms of PE with 35% (OR=0.65; 95%CI 0.25-1.42; $p=0.24$). The incidence of relapses does not differ during the investigated 5 year period ($\chi^2=2.39$; $p=0.66$). 67.8% of patients with relapse of PE have been treated with oral anticoagulants. At the time of the relapse 49.15 % of them are on current treatment with oral anticoagulants.

Conclusion: Pulmonary embolism is a common cause of death. The risk is higher in patients with prolonged immobilization and increased co-morbidity score. The mortality is higher in females and the use of fibrinolysis reduces the death rate. Appropriate oral anticoagulant treatment and follow up can prevent the onset of relapse.

61. D. Petkova, A. Angelov, V. Stratev, T. Dobreva, V. Dimitrova.

New opportunities for screening of subclinical atherosclerosis in patients with obstructive sleep apnea (OSA) a pilot study ERJ September 2017, vol. 50 /supplement. 61/ PA2323

Abstract:

Introduction: Coronary arterial calcium (CAC) is a marker of the presence of coronary atherosclerosis and the biological age of the vessels. Quantitative assessment of CAC is performed by measurement of the coronary arterial calcium score (CACS).

Aim: To investigate CACS in patients with OSA without known cardiovascular disease (CVD).

Patients and methods: We investigated 12 males with mean age 52.2 ± 10.4 years with OSA and without CVD. All patients had arterial hypertension and metabolic syndrome according to IDF criteria. The 10 years risk for ischemic heart disease was defined using the Framingham risk score (FRS). CACS was measured using CT scanner Siemens Somatom Definition (Dual source 2x64).

Results: According to FRS five of the patients were classified as low-risk (FRS<10%) and seven were with intermediate risk (10-20%). CAC was found in all twelve patients (mean score 44.1 ± 68.7 AU). Five of the patients were below 50 years of age which indicated low FRS, although having three risk factors for coronary disease. In young patients slightly increased values of CACS may be higher form the 75th percentile for sex and age. When

applying this criterion for reclassification and not the classical CACS>400 AU, four of the patients were reclassified in the high risk category.

Conclusion: The present study suggests that in young patients with OSA without known CVD, CACS may overcome the risk underestimation of classica

62.V. Dimitrova, D. Petkova, V. Stratev, T. Dobрева.

Efficacy of noninvasive ventilation in patients with acute and chronic respiratory failure. 4th International workshop on lung health, Budapest 19-21 January, 2017. Abstract book P06, page 7.

Abstract:

Introduction: NIV is a contemporary and reliable method for treatment of patients with acute and chronic hypercapnic respiratory failure.

Aim: To analyze the frequency of usage, NIV regimen modalities and mean duration of NIV in patients with respiratory failure.

Patients and methods: We performed a retrospective study of patients on NIV, hospitalized due to exacerbation of respiratory failure in intensive care unit of pulmonary clinic at MHAT "St. Marina" for 3 years period (2013-2015). We analyzed 203 patients with mean age 63.17 ± 12.58 years (52.2% males). All the patients received medication treatment and NIV was started according to international criteria and after admission in ICU.

Results: Treatment with NIV received 170 (83.7%) of the patients with chronic hypercapnic respiratory failure and 33 (16.3%) of the patients with acute respiratory failure. 68(33.5%) of the patients receiving NIV had underlying COPD, 48 (23.65%) had obesity hypoventilation syndrome and 31 (15.27%) had overlap between this conditions. We used pressure control ventilation (PCV) in 62.1 % of the cases, pressure support ventilation (PSP) in 24.1% and AVAPS in 13.8 % of the cases. NIV succeeded significant decrease of PaCO₂ from mean 8.38 kPa range (3-14 kPa) to 7.41 kPa range (3-12 kPa) ($p < 0.0001$) and significant increase of SaO₂% from mean 56.76% range (19-88%) in the first hour of NIV, to 80.27% range (43- 96%) ($p < 0.0001$) on the fourth day of treatment. Mean duration of NIV was 4.47 ± 3.4 days and it correlated positively with the PaCO₂ values ($r = 0.356$, $p = 0.023$). In 25 (12.3%) of the patients NIV was stopped due to treatment failure and invasive ventilation was introduced.

Conclusion: NIV is an efficacious and useful treatment method in patients with acute and chronic hypercapnic respiratory failure.

63.V. Stratev, T. Dobрева, B. Balev, V. Dimitrova, M. Gospodinova, D. Petkova.

A case of pulmonary cysticercosis. Differential diagnosis of pulmonary nodules. 4th International workshop on lung health, Budapest 19-21 January, 2017, Abstract book P23, page 28.

Abstract:

Introduction: The differential diagnosis of multiple pulmonary nodules is wide and includes congenital, acquired, infectious and non-infectious granulomatoses, malignomas and others. Extra-pulmonary symptoms and findings help for their discrimination.

Aim: We describe a case of multiple pulmonary nodules and brain involvement of nodules with characteristic image morphology.

Patients and methods: An 81 years old male, who breeds swine and cattle presented at the pulmonary clinic with acute onset of fever, cough and neurological symptoms. At admission he was with stable vital signs and normal reflexes, there were crackles at lung basis on auscultation. During hospital stay the patient developed neurological symptoms and his condition deteriorated rapidly. We performed biochemical and hematological tests, urine analysis, fecal probes, serological tests for toxoplasmosis, echinococcosis, cysticercosis and liquor analysis. We performed CXR, CT of the lung and abdomen, MRI of central nervous system.

Results: The serological tests were negative for parasites. All of the image techniques showed characteristic features of scolices, which are pathognomonic for cysticercosis. The unique morphology is not seen in other diseases with multiple nodules.

Conclusion: Cysticercosis is an infectious disease of the larva stage of the measles-T. solium. The disseminated form is rare. Unlike brain involvement (neurocysticercosis), lung involvement is extremely rare. The presence of one absolute criterion according to Del Brutto's scale (cystic lesions with scolices) is sufficient for the diagnosis. Enzyme and serological tests may remain negative when scolices are dead or in the presence of calcifications.

64.V. Dimitrova, D. Petkova, V. Stratev, T. Dobrova.

Prevalence of chronic thromboembolic pulmonary hypertension (CTEPH) in patients after pulmonary embolism ERJ September 2018, vol. /supplement / poster 3780

Abstract:

Introduction: CTEPH is a rare and debilitating disease caused by chronic obstruction of the large pulmonary arteries. The exact morbidity and prevalence are not known.

Aim: To investigate the prevalence of CTEPH after acute and recurrent pulmonary embolism (PE).

Patients and methods: A retrospective study of 577 patients, who survived PE over a 7 year period and a prospective study of 52 patients (61,5% after acute PE and 38,5% after recurrent PE), treated more than 6 months with anticoagulants, evaluated and analyzed: echocardiographic variables, NT pro BNP, 6 MWT, MDCT angiography of patients with raised systolic pressure in arteria pulmonalis (AP) ≥ 50 mm Hg. The mean age of the participants was $65,71 \pm 12,32$; 53,8% were men and 46,2% were women.

Results: The data were collected from 8 participants (1,39%) with CTEPH. A major risk factor in 62,5% was deep venous thrombosis; 50 % had concomitant heart failure and absolute arrhythmia. Comorbidity rate calculated by the CCI index was $3,63 \pm 1,06$. Half of the patients with CTEPH experienced acute PE and the rest of them recurrent PE. NT pro BNP in patients with CTEPH was $6265,38 \pm 5947,07$ pg/ml. According to the obtained results, the level of NT pro BNP correlated with the echocardiographic markers for right ventricular dysfunction and systolic pressure in AP (Pearson Correlation $r = 0,751$, $p = 0,032$), mMRC and Borg scales for dyspnea severity assessment (Pearson Correlation $r = 0,5$; $p = 0,001$).

Conclusions: CTEPH is a serious complication in patients after acute or recurrent PE. The follow-up and monitoring of symptomatic patients predetermine early diagnosis and advanced treatment to increase patient's survival.

65.V. Dimitrova, D. Petkova, V. Stratev, T. Dobрева.

Tuberculosis infection during treatment with TNF - α antagonists. A report of three cases. 5th International workshop on lung health, Berlin 2018. Abstract book P14, page 9.

Abstract:

Introduction: Treatment with new biological drugs is proved to be effective in the management of wide spectrum of systemic inflammatory diseases. The use of TNF- α antagonists increases the risk of infectious diseases including Mycobacterium tuberculosis infection.

Cases: We describe three cases of severe tuberculosis infection: haematogenously disseminated and infiltrative pulmonary form occurring in the course of treatment of inflammatory bowel disease with infliximab and adalimumab. Two of the patients were males aged 21 and 31 years, diagnosed with Crohn's disease and were treated with adalimumab for 29 and 8 months resp. The third patient is 38 years old female, diagnosed with chronic ulcerative colitis and treated with infliximab for 6 months. All patients performed chest X-ray, tuberculin skin test and IGRA test for latent TB screening before starting the biological drugs. 3 to 4 months after onset of lung symptoms the diagnosis of active tuberculosis was confirmed on culture and histologically in one of the cases. When the diagnosis of TB was

established all patients disrupted the biologicals and started treatment with the standard four drug regimen. During the treatment the female patient had progression of the disease – tuberculosis of soft tissues, which was managed surgically. In all patients the eradication of the bacilli occurred late after initiating anti-tuberculosis drugs and required extended treatment regimens.

Conclusion: treatment with TNF- α antagonists puts the patients at risk of TB infection. Candidates for biological treatment should be carefully screened and monitored.

66.D. Petkova, D. Stefanova, I. Kotzev, V. Stratev, B. Balev, P. Genev, D. Kostadinov, V. Dimitrova.

A case of nontuberculosis mycobacterial lung disease in a patient with chronic eosinophilic colitis and malabsorption syndrome. 5th International workshop on lung health, Berlin 2018. Abstract book P09, page 19.

Abstract:

Introduction: NTM have non-specific clinical presentation in immunocompetent patients and are difficult to diagnose in the presence of other chronic inflammatory conditions.

Case report: A 67 years old female presented in the pulmonary clinic with occasional non-productive cough, fever and loss of weight. After a period of food intolerance and detected blood eosinophilia (12%) she was performed colonoscopy showing lymphoplasmocytic and eosinophilic infiltrates in the mucosa. PET CT demonstrated focal ventrally located opacity in the left lung with honey-combing structure and slight uptake of the FDG. On a subsequent HRCT this opacity was larger and there was additional finding of granuloma adjacent to the pleura and two nodules with 6-16 mm size in the left lung. The suspected diagnosis was eosinophilic granulomas. T-SPOT TB and HIV tests were negative. In the pulmonary clinic we performed true cut biopsy of the lesions with results displaying non-caseous granulomas, small areas of necrosis, possible sarcoidosis. A subsequent bronchoscopy with BAL showed cytology consistent with allergic alveolitis or Churg-Strauss syndrome. Though, c-ANCA and p-ANCA were negative. Microbiology of BAL showed positive cultures on MGIT and Lowenstein Jensen media. Molecular testing for Mycobacterium tuberculosis complex was negative and for Mycobacterium avium complex – positive. This was confirmed by lung biopsy with histological result: infectious-type granulomatous disease; morphologic picture is most consistent with mycobacterial infection. Treatment with clarithromycin, rifampicin and ethambutol was started with general improvement of the patient condition.

