Review article ■

Prognostic Mortality Factors of Community - Aquired Pneumonia in the Elderly

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SUMMARY

The geriatric population i.e. the elderly population is comprised of people older than 65, or, according to some authors, older than 75, which is relative, given the fact that there is often a mismatch between an individual's biological age and chronological age. Aging is a rather complex process during which various changes occur - both the physiological functions and composition of the human body undergo changes. Many are irreversible, inevitable and additive. Physiological changes that lead to the decrease in the function of the airways and the lungs occur as a person ages. Clinical characteristics of pneumonia in the elderly population have special markers. Several centuries ago, Osler described pneumonia in the elderly population as able to manifest itself without the shivers and elevated temperature, with a slight cough and expectoration. This description, although provided centuries ago, is still held valid. About 45% of elderly people exhibit high temperature with pneumonia. An altered mental status such as confusion is found in 70% of the elderly patients with pneumonia. Given the fact that the mortality rate from the community-acquired pneumonia in elderly patients is significantly higher than the rate in younger population, certain prognostic mortality markers have been examined.

Some of the most important prognostic mortality factors include: old age, associated diseases, high breathing frequency, the multilobular character of the pneumonic shadow, high levels of certain biochemical analyses, hypoxemia, hyponatremia, and the untimely application of the empirical antibiotic treatment.

Key words: community acquired pneumonia, elderly patients, prognostic mortality factor

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INTRODUCTION

Pneumonia is a common disease at all ages, especially in children and in the elderly population (1-4). Approximately 1% of the entire population i.e. 0.1 - 1.5% of middle-aged people acquire pneumonia per year. In the elderly population, i.e. persons 65 years old and over, as well as in people having associated diseases, the incidence of the appearance of pneumonia ranges from 2.5 to 4.5% (5).

According to the guidelines provided by the Infectious Diseases Society of America - IDSA and the American Thoracic Society - ATS from 2005, pneumonias can be divided into community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP) and ventilated-associated pneumonia (VAP), depending on the epidemiological circumstances of their onset (6).

In spite of the application of numerous and efficient antimicrobic drugs, the lethal outcome of community-acquired pneumonia (CAP) treated ambulatorily ranges from 0.6 to 1.5%. In patients who require hospitalization, mortality rate ranges from 5 to 13%. However, in case of development of complications and in artificially ventilated patients, the mortality rate rises up to 50% (2,7,8). Due to the structural and functional changes in the respiratory system as the human body ages, as well as due to the presence of certain associated diseases, the mortality rate in patients older than 65 is considerably higher - 12.5%.

Physiological changes in the lungs that occur due to aging

Geriatric population or the elderly population is comprised of people older than 65, or, according to some authors, older than 75, which is relative, given the fact that there is often a mismatch between an individual's biological and chronological age. According to the guidelines provided by the World Health Organization in this heterogeneous population, we can further recognize three subgroups:

- elderly people (aged 60 to 75)
- old people (aged 75 to 90) and
- very old people (more than 90 years of age).

Aging is a rather complex process during which both the physiological functions and the composition of the human body undergo serious changes. Many of these changes are irreversible, inevitable and additive, which signifies that their influence on the kinetics of the applied medicines, as well as on the treatment itself, is enormous. Physiological changes that lead to the decrease in the pulmonary function take place as the aging process advances. After a person turns 55, the respiratory muscles start to weaken. The thoracic wall becomes less elastic, probably due to the joint influence of kyphoscoliosis and aging, the calcification of the intercostal cartilage and arthritis of the costovertebral joints.

The size of the airway lumen also decreases with age and small airways collapsability increases proportionally. As a person ages, the diaphragm becomes weaker as much as by 25%, although this has little importance without the associated diseases. In the presence of pulmonary conditions such as pneumonia, when the demand for the minute ventilation is considerably higher, a weakened diaphragm predisposes elderly patients to numerous respiratory problems.

The forced expiratory volume in the first second is reduced by approximately 30 ml per year in males and 23 ml per year in females. The forced vital capacity decreases by 14 to 30 ml per year in men and 15 to 24 ml per year in women. It is not clear whether these decreases are directly influenced by aging or by the cummulative effect of respiratory illnesses, smoking and exposure to external toxins (9).

Aging linearly decreases the partial oxygen pressure (O_2) in the blood (PaO_2 =109 - (0.43x years of age). After a healthy non-smoker reaches 75 years of age, PaO_2 remains stable at 83 mmHg.

Aging further reduces sensitivity of the peripheral and central chemoreceptors. The ventilatory response is decreased by 50% in healthy individuals aged 64 to 73 when compared to that of healthy individuals aged 22 to 33. The ventilatory response to hypercapnia is decreased by 40% in the old age. This reduction increases the risk for the development of a disease that causes a decrease in PaO_2 such as pneumonia, COPD or sleep apnea (10).

Aging causes the defense mechanisms of the airways to decrease; it also reduces the efficacy of the mucocilliary clearance. More importantly, there is a decrease in the efficacy of the cough reflex. This occurs in more than 70% of elderly patients with community-acquiered pneumonias, considerably more when compared to 10% in the younger and middle-aged population. All the aforementioned factors influence the characteristics of the clinical picture, duration of the treatment, duration of recovery, increase in mortality and morbidity by pneumonia in the elderly patients.

The term pneumonia in elderly patients is fairly recent. The first one to use was William Osler, who wrote: "A physician who treats an elderly patient with pneumonia and waits for the fever to appear will lose that patient." That was the first attempt to differentiate between pneumonias in older people and pneumonias in younger population.

Epidemiological data show that pneumonia is the most common disease resulting in death when talking about elderly patients (200 per 100.000). Data based on various studies conducted in the USA show that every 18th person older than 65 contracts pneumonia. Risk factors for the appearance of pneumonia in elderly patients are numerous. They include anatomical changes connected to aging, decreased cough reflex, the decrease in the mucocilliary clearance and an increased colonization of Gram-negative bacteria. Apart from these

physiological changes, other conditions are of great importance: alcohol abuse, asthma, chronic obstructive pulmonary disease (COPD), heart disease, diabetes, neurological conditions, the use of immunosupressive therapy or the application of a large number of medicines (especially hypnotics and sedatives). Additional risk factors include hypoalbuminemia, excessive use of antibiotics, especially in viral infections (because of the development of resistant strains) (11-13).

Clinical characteristics of pneumonia in elderly patients can have special markers. Osler maintained that pneumonia could be latent, and appear without fever in elderly patients. He further mentioned that cough and expectoration were poor, and that high temperature need not occur. He added that the body temperature was higher in healthy people than in older patients and alcoholics. This description is still held valid, despite the fact that it was provided several centuries ago. Younger people with pneumonia typically exhibit symptoms such as: an elevated temperature, productive cough, heavy breathing and chest pain, which rarely occur in old patients with pneumonia. Only 43% (33-60%) of older patients have high temperature with pneumonia. An altered metal status such as confusion is found in 70% of the old patients with pneumonia. Delirium and acute states of confusion have been registered in 25% of the old patients with pneumonia. This is why it is completely justified to request a chest radiography when treating old patients with an altered mental status (12).

Prognostic pneumonia mortality factors in elderly patients

A precise, objective model of pneumonia prognosis could help doctors estimate the risk for a particular patient, as well as help them reach the decision regarding hospitalization. Mortality is used as the criterium for the outcome of the disease. Factors that influence the *increase in pneumonia mortality* are: age over 50, diabetes mellitus, malignity, mental status alteration, multilobar infiltrates or radiological progression, leukopenia, tachypnea, hypotension, abnormal hemodynamic status, bacteriemia, high-risk pathogens (12,14).

Factors that can *reduce the speed of pneumonia resolution* are: old age, alcohol abuse, associated diseases, severe pneumonia, multilobar changes, smoking, persistent leukocytosis, bacteriemia, febrility.

Having in mind that pneumonia in elderly population is characterized by a distinctive clinical picture, a more complicated course of the disease and that it often results in fatality, prognostic score systems that are currently used in pulmological practice are not precise enough to predict the mortality risk in this part of the population. This is the reason why there is a need to determine distinctive prognostic mortality factors in elderly people in order to estimate the severity of the disease with greater precision (15-17).

Old age

Bacteriemia as a part of pneumococcal pneumonia is much more frequent in elderly people than in younger and middle-aged population. The mortality rate is around 40% in patients aged ≥85. In severe forms of pneumonia which require treatment in the intensive care unit, the mortality rate is extremely high - over 40% (18,19). In patients aged 65-69 who are treated in hospital, mortality of CAP is 7.8% and is doubled in older patients (in patients aged ≥90, it is 15.4%).

Mortality rate that rises almost exponentially with age shows a tendency to decrease in very old individuals due to the slow development of the disease. Such an influence of the old age on the mortality rate refers only to pneumonia as the cause of death (20, 21).

The analyses regarding the influence of sex on the mortality rate have shown that mortality rate of CAP in elderly people is higher in men than in women (22).

Associated diseases

Patients suffering from CAP that also suffer from COPD as an associated disease exibit a more serious tachichardia, a high degree of respiratory acidosis and hypoxemia, which, as a result, leads to cardiac decompensation and death. The aforementioned parameters which, according to the pneumonia severity index (PSI), represent prognostic factors for the unfavorable course and outcome of the disease, point to the importance of COPD as a significant prognostic mortality factor (23).

Due to a number of pathophysiological changes, especially due to the reduced function of the alveolar macrophages, a decreased pathogen elimination and the development of more severe chemodynamic disorders that occur on the level of the lungs in patients with CAP with associated *congestive coronary insufficiency*, the clinical course and the outcome of pneumonia are often unfavorable (24).

A *stroke* is a commonly associated neurological disease that represents a considerable risk factor for the prediction of mortality in both younger and older patients (24).

The development of azothermia and metabolic acidosis as a part of an associated chronic renal insufficiency also has negative effects on the clinical course and the outcome of pneumonia (25). Due to the supression of cellular immunity in people with renal insufficiency, there is a colonization of upper airways with Gram-negative bacterial flora, which often leads to the development of more severe forms of pneumonia with the unfavorable outcome (26).

Chronic liver insufficiency, although seldomly associated with pneumonia, as well as *malignity* represent considerable prognostic mortality markers (27). Liver cirrhosis, diastolic hypotension and hypoxemia are important prognostic factors in the early stages of pneumonia, while alcohol abuse, malignity, hypoalbu-

minemia and renal complications strongly influence the mortality rate, even in the period of one year after the hospitalization.

Community acquired pneumonia in people with associated *diabetes mellitus* are characterized by the more frequent development of pleural effusion, which further complicates the course of the disease and considerably increases the mortality rate (28). Moreover, diabetes mellitus, together with age >65, alcoholism, chronic bronchopulmonary diseases, immunodepression or/and renal damage predicts a bad clinical course with staphylococcal pneumonia as the outcome.

Bad habits (smoking, alcohol abuse)

Smoking and alcohol abuse represent major and most common risk factors for the development of pneumonia in elderly patients. These bad habits also influence the clinical course of pneumonia - complications occur more often, there is a radiological progression of pneumonic infiltrates and very often the disease takes an unfavorable course (29). Alcohol reduces the cough and swallow reflexes, which makes the alcohol-abusing patients more prone to the aspiration of microorganisms from the upper airways. Smoking incessantly chafes the airways and causes an increased production of sputum, which is a good prerequisite for the growth and multiplication of bacteria. Apart from these bad habits, using drugs can also predispose a patient to pneumonia. This is partially due to the way drugs are used, especially with those used parenetrally. The development of septicemia and pneumonia are frequent in these patients (although these habits are not typically present in elderly patients).

ABSENCE OF PRE-HOSPITAL ANTIBIOTIC TREATMENT

Despite the fact that the excessive use of antibiotics is blamed for the appearance of resistent strains of bacteria and the increase in mortality rate, when talking about elderly patients, the timely treatment of pneumonia is a matter of life and death. The absence of antibiotic treatments prior to hospitalization influences the development of more severe forms of pneumonia in older patients, and often accounts for a complicated course of the desease and the unfavorable outcome (30). In case of untimely administration of the antimicrobic therapy, the mortality rate can reach 73.7%. This is why it is strongly advised that all patients with pneumonia, especially old ones, be given antimicrobic medicines, even at the beginning of the diagnostic process and early treatment, i.e. 8 hours after the arrival at the hospital at the latest.

Clinical status after admission, laboratory blood tests and degree of radiological progression of pneumonic infiltrates

The presence of cough, expectoration and pleural pain have a protective effect in patients suffering from pneumonia, since they point towards the appropriate response of the body to the pneumonic infection. In other words, these signs represent the proper immune response (25). This is why it is possible to expect the deadly outcome in those patients suffering from pneumonia who exhibit an atypical clinical picture of the disease, which is the consequence of the patient's decreased immune system. What is more, in patients with the respiratory frequency of >25 breaths/minute, SpO_2 <90%, pH <7.35; PaO_2<60 mmHg, mental status disorder and hemodynamic instability, a result in death should be expected (31). The given facts point to the necessity to determine the gas status of those suffering from CAP, as hypoxemia, acidosis and mental confusion are clear indicators or tissue hypoperfusion caused by insufficient oxygenation, which results in an unfavorable clinical course of the disease and death.

Other considerable prognostic mortality factors include the presence of pleural effusion (parapneumonic effusion) and/or bilateral pneumonic infiltrates on the chest radiogram, hyperphosphatemia and hypotension, reduced physical activity - being tied to bed, creatinine value >1,2 mg/dl and PaO_2/FiO_2 <200 (32).

Functional status, hyperkaliemia and lymphopenia have high sensitivity and specificity in the prediction of the unfavorable outcome of pneumonia in the first 5 days of hospitalization in patients suffering from CAP (12).

However, in patients older than 65 who have a special clinical presentation of the disease, other prognostic mortality factors have been recognized. These include body temperature <37^0C, respiratory frequency >24 breaths/minute, the value of sodium in the serum <135 mmol/l, the concentration of urea in blood >19.6 mg/dl and the presence of pleural effusion on chest radiograph. A research conducted on 120 old patients with CAP identified mental status disorder, bilateral pneumonic infiltrates on the chest radiograph and respiratory frequence >23 breaths/minute as the most important prognostic mortality factors. The importance of this prognostic model of mortality is in its 100% specificity, 57.89% sensitivity and 93.33% accuracy (33).

Certain measures preventing the occurence of pneumonia in elderly patients include vaccines against *Influenza, Streptococus Pneumoniae* and *Haemophylus influenzae* (20).

CONCLUSION

In the recent years, pneumonia in elderly patients has become a separate clinical entity. The reason for this is that the human lifespan is constantly increasing and there is a growing number of old people in the majority of the world's countries. The presence of physiological failure of body functions in the elderly, as well as the possibility of having associated illnesses, makes forms of pneumonia in old patients ever more complex. The characterisics include: the absence of high temperature, a slow onset of the disease, a slight cough and the production of sputum, as well as mental confusion. Prognostically important mortality factors in pneumonia include: old age, associated illnesses, multilobilarity of pneumonia, high levels of certain biochemical analyses (urea), hypoxemia, hyponatremia and the untimely application of the empirical antibiotic treatment.

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PROGNOSTIČKI FAKTORI MORTALITETA VANBOLNIČKI STEČENE PNEUMONIJE KOD STARIJIH OSOBA

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Sažetak

Gerijatrijsku populaciju ili "osobe visokog životnog doba" čine osobe starije od 65 godina ili, prema nekim autorima, starije od 75 godina, što je relativno, s obzirom na to da se biološka starost često ne poklapa sa hronološkom. Starenje je veoma složen proces tokom koga se menjaju i fiziološke funkcije i sastav organizma. Mnoge od ovih promena su ireverzibilne, neizbežne i aditivne. Fiziološke promene koje dovode do smanjenja funkcije disajnih puteva i pluća nastaju tokom starenja. Kliničke karakteristike pneu-monije kod starijih osoba imaju posebna obeleža. Osler je pre više vekova opisao pneumoniju kod starijih osoba da je bez drhtavice i temperature sa slabijim kašljem i ekspektoracijom. Ovaj opis dat pre više veko-va je još uvek aktuelan. Oko 45% starijih osoba ima povišenu temperaturu kod pneumonije. Izmenjen mentalni status, poput konfuzije, nalazi se i kod 70% starijih bolesnika sa pneumonijom. S obzirom da je mortalitet vanbolnički stečene pneumonije kod bolesnika starije životne dobi značajno veći u odnosu na mlađe osobe, proučavani su mogući prognostički faktori mortaliteta.

U najvažnije prognostičke faktore mortaliteta spadaju: starije životno doba, pridružene bolesti, viso-ka frekfenca disanja, multilobularnost pneumonične senke, visoke vrednosti nekih biohemijskih analiza, hiposkemija, hiponatremija i neblagovremeno aplikovanje empirijske antibiotske terapije.

Ključne reči: vanbolnički stečena pneumonija, starije osobe, prognostički faktori mortaliteta