Review Article

Community-acquired pneumonia: current data

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Abstract: A new term was introduced in 2005 from the American Thoracic Society and Infectious Diseases Society of America (ATS/IDSA): health-care associated pneumonia (HCAP) which seems to have been established in Greek medical society. Patients who are included in this subcategory of community acquired pneumonia (CAP) present increased rates of multi-drug resistant pathogens and as a result the initial empirical antibiotic treatment is often ineffective. This could be the cause of increased mortality and so, it is advised to provide broad-spectrum antibiotic treatment that covers multi-drug resistant pathogens. However there are many studies that object to this category and prove that the broad-spectrum management leads to overtreatment, resistance and increased mortality. In this review we refer to these studies leading to the questioning of this subcategory. It seems that the classic triad can include all pneumonia categories. However, there is certainly the need to include also new conditions that concern the great increase of elderly patients and the need for evaluation of the functional status and the aspiration that were not till now taken into account.

Keywords: Health-care associated pneumonia (HCAP); community acquired pneumonia (CAP); pneumonia

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Current data

Until recently, pneumonia categorization was based on the triad:

(I) Community-acquired pneumonia (CAP);

(II) Hospital-acquired pneumonia;

(III) Pneumonia in immunosuppressed patients.

Host's immune condition and the environment that pneumonia was acquired defined this classification which was clinically important for the microbial cause and treatment. According to this, the initial empirical antimicrobial treatment could be determined (1).

A new term was introduced in 2005 from the American Thoracic Society and Infectious Diseases Society of America (ATS/IDSA) (2): health-care associated pneumonia (HCAP). This new pneumonia category initially seemed to offer a new opportunity to treat patients who until now with the classic triad were not treated properly. Some patients

with CAP seemed to have been undertreated with the classic triad and to have increased mortality.

This new terminology exists as a separate pneumonia category in KEELPNO guidelines (Center of Diseases Control and Prevention) from 2007 (3-5), as well as at the National Action Plan "Procroustis" which was set up in October 2010 (6) for diseases' management and prevention. So, it seems that this new category has been established in Greek medical society as a possible measure to decrease mortality which can be an outcome of CAP. However there are voices that call for attention and support the idea that this subcategory has been established without evidence and may lead to unneeded overtreatment, resistance and even increased mortality.

According to ATS/IDSA, HCAP is defined as the pneumonia which appears in the following patient categories:

(I) Patients who were hospitalized in an acute care hospital for two or more days within 90 days of the current infection;
(II) Patients who have been resided in a nursing home or long-term care facility;
(III) Patients who received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection;
(IV) Patients who attended a hospital or hemodialysis clinic (2).

The members of ATS/IDSA committee recognized that many patients with HCAP (as well as patients with hospital-acquired and ventilator-associated pneumonia) are infected from multi-drug resistant pathogens and as a result, the initial empirical antibiotic treatment is often ineffective. This fact maybe suggests a cause of increased mortality. According to ATS/IDSA guidelines if there are risk factors for HCAP, broad-spectrum antimicrobial treatment that covers multi-drug resistant pathogens should be administered (2).

So, this new term not only refers to different patients' categorization, who until now belonged to CAP or hospital-acquired pneumonia, but also to different pharmaceutical treatment (2), similar to this for patients in risk for multi-drug resistant pathogens, with combination of broad-spectrum antibiotics (1). Thus: Antipseudomonal cephalosporin (cefepime, ceftazidime) or Antipseudomonal carbapenem (imipenem or meropenem) or Antipseudomonal β-Lactam/β-lactamase inhibitor (piperacillin-tazobactam) plus Antipseudomonal fluoroquinolone (ciprofloxacin or levofloxacin) or Aminoglycoside (amikacin, gentamicin, or tobramycin).

In suspicion of MRSA (methicilline-resistant staphylococcus aureus): plus Linezolid or vancomycin; in suspicion of legionella pneumophila: plus macrolide or fluoroquinolone (2).

As risk factors for multi-drug resistant pathogens were defined the following:

(I) Current hospitalization of 5 d or more;
(II) Antimicrobial therapy in preceding 90 d;
(III) Immunosuppressive disease and/or therapy;
(IV) High frequency of antibiotic resistance in the community or in the specific hospital unit;
(V) Presence of risk factors for HCAP (2).

However, it was made clear that the establishing of all these risk factors for multi-drug resistant pathogens could lead to overuse of antibiotics and probably to unneeded overtreatment (7). Moreover, ATS/IDSA recognizes that the increased frequency of drug resistant pathogens is mainly due to excessive and thoughtless use of antibiotics (2).

Support of HCAP concept

Earlier prospective studies showed positive cultures for resistant pathogens and increased mortality in patients with HCAP in comparison with CAP and thus they carried forward the use of broad-spectrum antibiotic therapy (7).

Kollef *et al*. analyzed 2-year data from 59 US hospitals, from 4,543 patients with pneumonia, non-immunosuppressant, with cultures collected the first 5 days of admission. In HCAP were categorized patients: (I) in chronic hemodialysis; (II) being transferred from health-care institution or (III) with history of hospital admission the last 3 months. The study resulted that HCAP is frequent, with increased mortality and great proportion of patients with positive cultures for Enterobacteriaceae and multi-drug resistant pathogens. Moreover, hospital residency and cost were greatly increased in comparison with CAP. However, in the study some important data where not taken into account. Initially, the definition of facility care was not made clear. Additionally, the number of Enterobacteriaceae and multi-drug resistant pathogens was indeed unexpectedly high (26.5% MRSA, 25.3% P.aeruginosa, 2.6% Acinetobacter, 25.8% Enterobacteriaceae) but with respectively unusually increased rates for CAP (8.9% MRSA, 17.1% P.aeruginosa, 1.6% Acinetobacter, 21.3% Enterobacteriaceae). Such rates had not been previously reported for CAP and they lead to the need of rethinking CAP treatment. Moreover, in

the study analysis only patients with positive cultures were included (1,8).

Micek *et al*. analyzed data from a US medical center for 3 years based to the patients' positive cultures from the first 2 days of admission. In this study immunosuppression was also included to the criteria for HCAP (including cancer chemotherapy as well). Particularly, the criteria for HCAP were: (I) outpatient hemodialysis, peritoneal dialysis or intravenous therapy which requires frequent clinical visits; (II) residency at rehabilitation hospital, nursing facility or other long-term stay in a nursing institution; (III) admission to hospital the past 12 months; (IV) corticosteroid treatment (≥5 mg/day) or HIV infection or organ/bone marrow transplant, or radiotherapy/chemotherapy for cancer the last 6 months, or hereditary/acquired immunosuppression. The study results were that HCAP is frequent, differs from CAP in the microbiological causes and often correlates to inadequate initial antimicrobial treatment and increased mortality. However, this analysis also included only patients with positive cultures. Additionally, there was not qualitative evaluation of the microbiological results and finally, patients at all immunosuppression categories were included, which normally constitutes a separate pneumonia category (1,9).

However, newer prospective studies for HCAP patients showed smaller rates of resistant pathogens and lack of increased mortality. According to these studies the use of HCAP definition for providing antimicrobial treatment seems to lead to broad-spectrum therapy in many patients who do not need one (7).

Additionally, there is evidence which shows unfavorable results for patients who were treated with broad-spectrum treatment. One multicenter study of Kett *et al*. in USA, dealing with the management of possible multidrug-resistant pneumonia in intensive care, showed increased mortality of HCAP which was correlated with the adjustment of broad-spectrum therapy. More specifically, in the above study the guidelines of ATS/IDSA for the management of hospital-acquired pneumonia, HCAP and ventilator-acquired pneumonia were fully applied; thus, use of empirical antimicrobial treatment in patients with possibly multi-drug resistant pathogens. The patients' follow-up lasted until their discharge from the hospital or the 28th day or death. In the study were included as a total of 303 patients with risk factors for pneumonia from multi-drug resistant pathogens. From these patients, 129 were treated with empirical treatment according to the guidelines, whereas the rest 174 were treated with antimicrobial treatment without following guidelines. From the first group 44 patients died (33%) while the respective number at the second group was 35 (20%). The Kaplan-Meier survival estimate for the 28 days was 65% at the adherent group and 79% at the non-adherent group (P=0.0042). This difference remained and after the adjustment of pneumonia severity. In the non-adherence was included the non-usage of double treatment for Gram (–) pathogens in 154 patients as well as the non-coverage for MRSA in 24 patients. For patients where the pathogens were identified, the empirical treatment was effective at the 81% of the adherence group (79 from 97 patients) and 85% at the non-adherence group (109 from 128 patients) (10).

In the same way, one study of Attridge *et al*. showed increased mortality at patients who were given broad-spectrum antimicrobial treatment in comparison with those who received the classic treatment for CAP. Specifically, the study compared, in more than 150 hospitals in USA, the mortality (in 30 days) of HCAP patients, under treatment for HCAP according to the guidelines, with HCAP patients, under treatment for CAP according to the guidelines. Patients were included who had at least one risk factor for HCAP and they received antimicrobial treatment within 48 hours from their admission excluding from the study the severe patients. The study criteria were fulfilled from 15,071 patients. Eight percent received treatment for HCAP, 75.7% treatment for CAP and 16.3% treatment non-adherent with the guidelines. The most important risk factors for mortality within 30 days were recent admission to the hospital and treatment for HCAP. Providing treatment for HCAP to non-severe patients was not connected with increased survival in comparison with those who received treatment for CAP (11).

Studies for HCAP that took place in Europe and Japan did not manage to prove the validity of this categorization. There is not constant presence of drug-resistant microbes and the excessive mortality cannot be attributed to ineffectiveness of initial empirical antimicrobial treatment. Additionally, broad-spectrum initial antimicrobial treatment usually is not selected for those patients due to expected unfavorable prognosis (e.g., for patients with severe comorbidity-elderly). Possible explanations include treatment ceiling in patients due to expected unfavorable prognosis, the presence of greatly increased frequency of aspiration pneumonia and patient's functional status (1).

Shorr and colleagues compared the proportion of resistant infections' isolation in patients with HCAP. They were included 639 patients who fulfilled any criterion for HCAP. From those only 289 (45.2%) were presenting

drug-resistant pathogens. Also, they investigated the concept's components: recent admission to the hospital, residency in a facility care, long-term hemodialysis and immunosuppression. Each one of the above components was more possible to be encountered at patients with drug-resistant pathogens. However, HCAP as a total was only encountered at 48.6% of patients with drug-resistant pathogens (1,12).

Brito and Niederman recognize that HCAP concept needs revision. In their last review concluded that a few only of the patients that are included in HCAP are in danger of multi-drug resistant pathogens and so, not all patients need broad-spectrum antibiotic treatment for suitable and effective treatment. Patients in danger of multi-drug resistant pathogens were those with: severe disease or other risk factors, including admission to hospital the last 90 days, antimicrobial treatment the previous 6 months, poor functional status (as it is defined from ADL score—Activities of Daily Living score) and immunosuppression (1,13).

However, based to the risk factors that are described from the writers maybe there is not really the need of an additional pneumonia category. The patients with a recent admission to the hospital can belong to the category of hospital-acquired pneumonia, with the need to reevaluate the limit from 1 to 3 months. Antimicrobial treatment the last 3–6 months is an important risk factor for resistance and change of treatment is demanded (observation that is however already included in the last revision of CAP guidelines). The immunosuppression cannot be a part of any pneumonia category (community or hospital-acquired) since it constitutes a separate category and such it should be approached. The only important factor for treatment evaluation, which is not included in any pneumonia category, is the patient's functional status (1).

Additionally, one recent study [2013] of Shindo *et al*. dealing with the risk factors for drug-resistant pathogens in HCAP and CAP suggested the presence of six risk factors for pneumonia from pathogens resistant to the treatment suggested from ATS/IDSA guidelines:

(I) Stay in the hospital for at least 3 days the last 90 days;
(II) Antibiotic treatment the last 90 days;
(III) Non-ambulatory status;
(IV) Tube feeding;
(V) Immunosuppression status;
(VI) Use of gastric acid suppressive agents (6,14).

The above risk factors for pneumonia with drug-resistant pathogens have been reported in other studies too and lead to the result that recent antibiotic treatment or admission to hospital and the poor functional status are more important risk factors for prediction of resistant pathogens than the residency in an institution alone (7).

The incidence of multi-drug resistant pathogens is not considered greatly increased except if there are three or more risk factors. However the MRSA is an exception: the presence of one special for MRSA risk factor (previous infection or colonization with MRSA, long-term hemodialysis or cardiac failure) and one special for pneumonia risk factor may justify the coverage for MRSA (7).

Questioning HCAP concept

At a recent study of Baum *et al*., with 5,130 patients with CAP, the pathogens Enterobacteriaceae and P.aeruginosa were isolated in 72% and 55% of patients respectively, while the mortality of the patients was similar to those of the general population in whom these pathogens were not isolated (1). Moreover, even for patients with risk factors, who based to the ERS (European Respiratory Society) guidelines are treated for P.aeruginosa as well in the initial empirical antibiotic treatment, some are against to this aspect thinking of Pseudomonas as colonization and not pathogen (15). Conclusively, in many cases the isolated pathogens probably cannot be considered causes of the disease (1). Increased mortality in HCAP cannot be justified by an increased number of resistant pathogens (16). Moreover an equally increased number of MDR-pathogens have been detected in community acquired pneumonia (CAP) (17).

In a study in Germany which included for 2 years all the adults who have been hospitalized with CAP, from the patients who died in hospital only 15.7% have entered intensive care unit (ICU) which shows the presence of restrictions in treatment escalation. The aspiration pneumonia seems to be affected from the functional status (just as this is expressed from ADL score). A study showed that enteral tube feeding, as well as the functional status and aspiration, omen drug-resistant pathogens, while the functional status (as assessed by ADL score) constitutes the most definite risk factor for drug-resistant pathogens (1).

However the most obvious change of the last years is the increasing number of the patients who are elderly and live in health-care facilities. The above mentioned 2-year study in Germany showed that the elderly constitute now the main group of patients with pneumonia, 81% being

≥60 years old and 28.4% 80–89 years old. The group also of the elderly is connected greatly with the previously mentioned risk factors for resistance: aspiration and poor functional status (1).

Thus a group of elderly patients (>65 years old) with pneumonia is created which requires special attention. The age on its own does not constitute risk factor for drug-resistant pathogens neither the comorbidity nor the heath-care facilities are a homogeneous condition and should be evaluated individually for each case since all residents have not the same functional status (1).

Additionally the immunosuppression and the admission to the hospital cannot be included in any pneumonia category except for those that belong to the classic triad—thus pneumonia in immunosuppressed patients and hospital-acquired pneumonia respectively (1).

Conclusions

All the pneumonia cases can be included in the classic triad of pneumonia. The health-care in a facility or home from personnel belongs to CAP, and the previous admission to a hospital is categorized to hospital-acquired pneumonia and the immunosuppression to pneumonia in immunosuppressed patients.

HCAP concept promotes excessive broad-spectrum empiric therapy and overtreatment leading to resistance while having little evidence of successfully detecting resistant pathogens (17,18).

In order to avoid abuse of broad-spectrum remedies new scoring systems must be used in CAP in order to evaluate risk for MDR pathogens (19). HCAP concept seems not to be enough. An attempt has been made with a new evaluating tool, ARUC score, trying to predict pneumonia from community due to resistant pathogens (17).

However a new approach is also required for CAP for the admission to the hospital of patients over 65 years old, who constitute now the core group, as well as of patients with great disability where the unfavorable prognosis and the severe condition restrict the increase-maximization of the treatment. It is also required evaluation of the functional status (with ADL score) as well as additional risk factors for multi-drug resistant pathogens: health-care in a facility or at home (where should be yet the type/conditions of care and the functional status strictly defined) and the aspiration risk. It is also good that the epidemiology is co-assessed just as it is determined by the differences of multi-drug resistant pathogens among countries (1).

So finally CAP maybe could be subdivided in CAP: (I) in younger patients (18–64 years old); (II) in elderly patients (≥65 years old) with medium-good functional status (ADL score <14); (III) in elderly patients (≥65 years old) with severe disability/poor functional status (ADL score ≥14) who constitute and the risk group for multi-drug resistant pathogens (1).

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Footnote

Conflicts of Interest: The authors haves no conflicts of interest to declare.

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