

Do Greek doctors comply with guidelines for community-acquired pneumonia?

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ABSTRACT: *Background/aim.* Concordance with community-acquired pneumonia (CAP) guidelines remains suboptimal. The aim of this study was to assess the compliance of Greek physicians in public hospitals to the Greek National Guidelines concerning the use of CURB-65 index for the selection of patients who require hospitalization and the choice of empirical treatment.

Methods. This was a prospective multi-center study conducted in four pulmonary medicine and internal medicine departments. In patients hospitalized due to CAP, CURB-65, antibiotic regimen and aggravating factors (parapneumonic effusion, low oxygenation and previous antimicrobial therapy) were recorded.

Results. Out of 100 patients (mean age \pm sd: 69.41 \pm 17.34 years), 39 presented with a low (0-1), 37 with intermediate (2) and 24 with high (\geq 3) CURB-65 scores. Only 25% patients with a low CURB-65 index presented with none of the aggravating factors. Seventy five percent of the previously untreated patients were administered appropriate treatment.

Conclusions. Adherence of Greek physicians to CAP guidelines is rather poor. Despite the high percentage of low CURB-65 admitted patients, the coexistence of factors contributing to disease severity implies that this index should not exclusively dictate decision for admission. Identification of the patients who can be safely treated as outpatients may reduce the number of unnecessary hospitalizations

Key Words: Community-acquired pneumonia, Guidelines, CURB-65 index, Empirical antibiotic treatment.

INTRODUCTION

Despite continuous evolution of the antimicrobial armamentarium, until recently mortality due to community-acquired pneumonia (CAP) tends to remain in considerably high levels^{1,2}. Implementation of CAP guidelines has been consistently shown to result in improvements in clinically relevant outcomes and mortality²⁻⁶. Moreover, the Infectious Diseases Society of America and the American Thoracic Society (IDSA/ATS) guidelines for CAP strongly recommend the compliance with locally adapted guidelines².

Two important aspects in the implementation of such guidelines are the selection of patients that require hospitalization and the appropriate choice of

initial empirical treatment. As for the detection of patients who need to be admitted, several algorithms assessing the severity of the pneumonia and predicting the risk of death have been developed^{2,7-10}. CURB-65 index is a simple and attractive to routine clinical practice prognostic rule that was proposed by Lim et al⁷ in response to the previously introduced and more complex Pneumonia Severity Index (PSI)¹¹. CURB-65 consists of five easily measurable parameters (Confusion, Urea, Respiratory rate, systolic and/or diastolic Blood pressure and age over 65 years). According to CURB-65 score, patients with a score of 0-1, having very low mortality risk, can be treated safely as outpatients^{2,7,12}. Although CURB-65, as well as some other

severity assessing rules, has been repeatedly proposed by numerous guidelines^{2,13} as a valuable tool for the identification of low risk patients, multiple studies have demonstrated that 30-60% of such low-risk patients with CAP are admitted in hospitals, increasing tremendously the cost of therapy^{2,6,14-18}.

Several studies have provided convincing evidence that although guidelines-compliant treatment results in improved survival and reduced health-care costs, concordance with guidelines remains suboptimal¹⁹⁻²². The above conclusion applies also to the case of Greece^{23,24} where in addition, high-level macrolide-resistant *S. pneumoniae* is reported^{25,26}. Consequently, Greek national guidelines advise the use of respiratory fluoroquinolones or the combination of a beta-lactam with adequate anti-pneumococcal potency plus a macrolide for the treatment of CAP including both in- and outpatients²⁷.

The primary aim of this study was to assess the compliance of Greek physicians working in public hospitals to the Greek National Guidelines concerning the use of CURB-65 index for the selection of patients who require hospitalization. In addition we investigated whether the empirical antibiotic treatment administered to the patients was appropriately chosen.

PATIENTS AND METHODS

Patients

This is an observational prospective multi-center study conducted at three General Hospitals in Thessaloniki, a city with a population greater than 1.000.000 inhabitants, in Northern Greece. We analyzed the data of patients hospitalized due to CAP in two departments of pulmonary medicine in «G. Papanikolaou» General Hospital and two departments of internal medicine in «Papageorgiou» and «Hippokraton» General Hospitals. Recording was performed from January 2011 to January 2013, one week per month by the same group of physicians, who were independent of the physicians deciding the patients' admission to the hospital and antimicrobial treatment.

Patients eligible for the study were adults admitted through the ED with a new infiltrate or consolidation on their chest-radiograph, along with at least one of the following signs or symptoms of lower respiratory tract infection: acute illness with cough, fever > 3

days, dyspnea, new focal chest signs. Exclusion criteria were: age < 18 years, hospital-acquired pneumonia (development of symptoms > 48 h after admission or discharge from an acute care facility < 2 weeks prior to admission), healthcare associated pneumonia, immunosuppression and previously known bronchiectasis. The study design was approved by the Ethics Committees of the participating hospitals and written informed consent was obtained from all study participants.

For each patient CURB-65 was assessed within 24 hours of admission based on data recorded at the time of admission. As previously described⁷, CURB-65 consists of five easily measurable parameters and the final score is build after charging one point for each of the following: Confusion, serum Urea > 7 mmol/l or 42 mg/dl, Respiratory rate \geq 30/ min, systolic Blood pressure < 90 mmHg and/or diastolic Blood pressure < 60 mmHg and finally, age \geq 65 years.

In addition aggravating factors not included in CURB-65 were assessed. The following parameters were recorded: age, gender, prior antimicrobial therapy, blood gas analysis (pH, pO₂, pCO₂, HCO₃), oxygen saturation, supplementary oxygen administration, presence of pleural fluid, number of pulmonary lobes infected, antimicrobial therapy upon admission and outcome at hospital discharge.

Appropriateness of empirical treatment

In order to evaluate the appropriateness of empirical treatment administered upon admission, we assessed empirical antibiotic treatment agreement with Greek guidelines for CAP. According to the Greek National Guidelines released by the Hellenic Centre for Control and Prevention of Infectious Diseases and the ATS/IDSA Guidelines treatment was considered appropriate (depending on the severity of CAP and risk factors for pneumococcal resistance) for the patients requiring hospital admission when 1) monotherapy with a respiratory quinolone 2) anti-pneumococcal beta-lactam/macrolide combination or 3) a proper beta lactam/fluoroquinolone combination, were administered^{2,27}. Appropriateness was assessed only for patients without previous treatment.

Statistical Analysis

Data comparison between pulmonary and internal

medicine departments concerning CURB-65 scores and antibiotic treatment was performed by χ^2 test.

RESULTS

Curb-65 index

109 patients admitted to hospital due to CAP were identified. Six patients were excluded due to immunosuppression and three patients due to incomplete data. Finally, 100 patients were included in the study. Patients' demographics and pneumonia localization are shown in Table 1. CURB-65 score was 0 in 15 patients, 1 in 24, 2 in 37, 3 in 13, 4 in 10 and 5 in one, as presented in Table 2. No difference was detected in CURB-65 index distribution between patients hospitalized in pulmonary and internal medicine departments ($\chi^2 = 3.739$, $p = 0.689$, $f = 5$).

Aggravating factors not included in CURB-65

Parapneumonic effusion was evident in 4 patients with a CURB-65 score of 0, 2 patients with a score of 1, 1 with a score of 2 and 2 with a score of 4. Arterial blood pH was assessed in 81 patients and respiratory acidosis was detected in 6. Hypoxemia was present in 49 out of 84 patients (47 in pulmonary departments). Out of these patients, 6 had a CURB-65 score of 0 (12.2%), 9 a score of 1 (18.4%), 17 of 2 (34.7%), 9 of 3 (18.4%) and 8 a score of 4 (16.3%). Only 13 patients hospitalized for CAP with a CURB-65 index of 0-1 had all of the following: sufficient oxygen saturation, no evidence of pleural effusion and no record of previous treatment for the same condition. Four of these patients had significant co morbidities and advanced age (>75 years).

Antimicrobial treatment

Twenty seven patients were already on antimicrobial therapy before admission whereas for the remaining 73 patients treatment was initiated after admission. Out of the 27 patients already on treatment five were receiving a beta-lactam/macrolide combination, four a quinolone, eight a macrolide, five a beta-lactam, two an aminoglycoside and the remaining three were under clindamycin, doxycycline or unknown medication (one case in each category). The regimen that was administered to the patients during their hospitalization is shown in Table 3. No difference in the choice of treatment was detected between pulmonary and in-

ternal medicine departments ($\chi^2 = 6.353$, $p = 0.385$, $f = 6$). In addition, 12 patients (8 in pulmonary and 4 in internal medicine departments) received anti-influenza treatment.

Appropriateness of treatment

Fifty five (75,3%) out of the 73 previously untreated patients were administered appropriate treatment. More specifically 37 out of 48 patients in pulmonary and 18 out of 25 patients in internal medicine departments were given appropriate first-line treatment ($\chi^2 = 0.037$, $p = 0.848$, $f = 1$). Out of the remaining 18 patients (11 in pulmonary and 7 in internal medicine departments), 17 were undertreated receiving antimicrobial agents that did not appropriately cover the spectrum of possible pathogens (11 received a beta-lactam, 3 received a macrolide, 2 ciprofloxacin/clindamycin combination and 1 ciprofloxacin/macrolide combination). One patient was over-treated receiving a combination of beta-lactam, macrolide and doxycycline. Three patients died (with CURB-65 index 3, 4 and 5) and one was admitted in intensive care unit (ICU) and recovered (CURB-65 index 2).

DISCUSSION

The main findings of the present study are: 1) Almost 40% of hospitalized patients with CAP in Greek hospitals present at the Emergency Department with a CURB-65 score of 0-1, 2) 25% of patients hospitalized in common hospital wards due to CAP suffer in fact from severe CAP (CURB-65 ≥ 3) but are not admitted to ICU and 3) 25% of admitted to the hospital patients with CAP are undertreated in terms of appropriate coverage for common CAP pathogens.

The implementation of guidelines considering admission for CAP is overlooked quite often, since multiple studies had constantly demonstrate that low-risk patients tend to be admitted in hospitals^{2,6,14-18,23}. Hospitalization increases time to normal activity restitution, risk of thromboembolic events and superinfection². In addition, the substantial increase of health-care cost is of particular concern, since inpatient care is 25 times more expensive than outpatient management^{2,23,28}. In that setting, unnecessary hospitalizations represent a significant financial burden to the national health systems.

A possible explanation for the hospitalization of

low-risk patients may be that severity indexes are under-utilized in routine clinical practice at EDs²⁹. Our results are in agreement with those by Triantafyllidis et al²³ who concluded that almost one out of two hospitalized patients with CAP in Greek hospitals could have been treated as outpatients.

However, it is undisputedly clear that the final decision about hospital admission should take in account a variety of criteria not included into any proposed severity assessment rule, such as the mental and social status of the patients and availability of outpatient support^{2,14,29,30,31}. In the case of Greece, the outpatient support services are underdeveloped, thus, the hospital-supervised follow-up of the acutely ill outpatients is uncertain. Moreover, the decision for admission is frequently dictated by the need for further investigation, failure of appropriate previous treatment, and the presence of additional severity markers such as hypoxemia or clinically substantial pleural effusion that are not included in CURB-65^{29,32}. Indeed, in the present study oxygen treatment was necessary for 58% of patients, the majority of whom were treated in departments of pulmonary medicine. Noteworthy, 15 of these patients presented with a CURB-65 score of 0-1. Although the present study was not designed to identify the reasons behind guideline non-adherence, our findings are in agreement with previous investigations^{29,32} that consider failure of previous treatment, hypoxemia and pleural effusion as significant explanations for the admission of low-risk patients. Indeed out of the 39 patients with a CURB-65 index of 0-1, only 13 did not present with at least one of the above factors. Out of these 13 patients, 4 were older than 75 years and suffered from significant co-morbidities. For the remaining 9 patients (i.e 25% of patients with a CURB-65 of 0-1), no medical or social reason for admission could be identified. Similarly Choudhury et al in a large prospective trial concluded that approximately 20% of patients hospitalized due to CAP despite a low CURB-65 index had no clear reason for admission²⁹.

Despite the possible overtreatment of low-risk patients, 21 out of 24 patients with severe CAP (CURB-65 \geq 3) were successfully treated in hospital wards. The only patient who was transferred to the ICU and recovered presented with a CURB-65 score of 2. With

the exception of those patients which satisfy the major IDSA/ATS criteria² and require emergent transfer to the ICU, most Greek clinicians prefer to admit less critically ill patients in common wards, possibly due to the limited availability of ICU beds. Moreover it is generally accepted that most of the proposed severity scores have low discriminative performances in identifying patients requiring ICU admission^{6,33}. In concordance to this, Marrie et al have demonstrated that up to 14% of patients with a PSI of IV and V can be safely treated on an ambulatory basis^{34,35}.

Interestingly, empirical treatment was compliant with Greek National Guidelines in 75% of cases. This percentage, although far from perfect, corresponds to previously reported compliance^{36,37}. In a recent report from Greece²³ the observed compliance was reported to lower (60%), however the exact treatment options that were considered as compliant to the relative guidelines were not specified. Although the impact of guideline adherence on mortality has been debated^{38,39}, several studies have shown that guideline-compliant empirical treatment leads to reduced mortality^{19-22,37}. Factors that are associated with adherence are specialty of the attending physician and the severity of pneumonia^{37,40}. In the present study the impact of pneumonia severity on adherence was not assessed due to the small sample size. Moreover, no significant difference in the selection of the antimicrobial regimen between pulmonary physicians and internal medicine specialists was observed. Despite the fact that non-adherence was not higher than expected it is clear that almost 25% of hospitalized patients with CAP receive treatment that does not adequately cover the common respiratory pathogens and the possible resistance patterns. The majority of these patients (11/18) did not receive treatment for "atypical" bacteria. Although this practice is not in accordance with international and Greek guidelines, a recent meta-analysis has not found any benefit of survival or clinical efficacy in hospitalized patients with CAP receiving additional empiric coverage of «atypical» pathogens, compared to those without such coverage⁴¹. It is therefore possible that this discordance with guidelines did not have any negative consequences on patients' outcome.

The present study is one of the few reports about CAP management in Greece. Limitations that should

be addressed are the low number of patients, the unavailability of 30-day mortality and the fact that non-hospitalized patients were not included. Despite these limitations our results are in accordance with previous Greek studies^{23,24} suggesting that there is still a necessity for more efficient medical education, particularly in this field. Furthermore outpatient support and readily access to public primary care facilities are critical aspects of CAP management in order to reduce unnecessary hospitalizations, especially in countries suffering from economic recession, like Greece.

In conclusion adherence of Greek physicians working in public hospitals to international and Greek guidelines concerning selection of patients with CAP who require hospitalization and empirical antibiotic treatment is rather poor and should be addressed. However concerning decision for admission, the non-adherence may not be entirely wrong, since CURB-65 index should not dictate need for hospitalization

but rather be used as an adjunct to clinical judgment. The present study provides further evidence that only a proportion of patients with low CURB-5 index can actually be safely treated as outpatients. Identification of this group and enhancing outpatient support may effectively reduce the number of unnecessary hospitalizations in Greece, thus reducing the financial burden of CAP.

CONFLICT OF INTEREST

None declared.

Abbreviation list

CAP: community-acquired pneumonia

IDSA/ATS: Infectious Diseases Society of America and the American Thoracic Society

PSI: Pneumonia Severity Index

ICU: intensive care unit

Table 1. Patients' demographics and pneumonia localization.

Gender: men/women	62/38
Age (mean \pm sd)	69.41 \pm 17.34 years
Comorbidities	
arterial hypertension	32%
diabetes mellitus	21%
chronic heart disease	41%
neurologic/psychiatric disease	21%
chronic obstructive pulmonary disease	17%
Pneumonia localization	
right/left/bilateral (n = 94)	58/28/14

Table 2. Distribution of CURB-65 scores in patients hospitalized in Pulmonary and Internal Medicine departments.

CURB- 65 score	Dpt of Pulmonary Medicine (n, %)	Dpt of Internal Medicine (n, %)	Total
0	11 (16.2)	4 (12.5)	15
1	16 (23.5)	8 (25)	24
2	23 (33.8)	14 (43.8)	37
3	8 (11.8)	5 (15.6)	13
4	9 (13.2)	1 (3.1)	10
5	1 (1.5)	0	1
Total	68	32	100

Dpt: Department.

Table 3. Antibiotic treatment in patients hospitalized in Pulmonary and Internal Medicine departments.

Antibiotic therapy	Dpt of Pulmonary Medicine (n, %)	Dpt of Internal Medicine (n, %)
respiratory quinolone	20 (29.4)	10 (31.3)
beta-lactam/macrolide	27 (39.7)	13 (40.6)
macrolide	1 (1.5)	2 (6.2)
beta-Lactam	9 (13.2)	4 (12.5)
ciprofloxacin/clindamycin	3 (4.4)	0
beta-lactam/quinolone	5 (7.4)	0
other	3 (4.4)	3 (9.4)
Total	68	32

Dpt: Department.

Συμμόρφωση των Ελλήνων γιατρών στις οδηγίες για την αντιμετώπιση της πνευμονίας της κοινότητας.

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ΠΕΡΙΛΗΨΗ: Σκοπός. Η τήρηση των οδηγιών για την πνευμονία της κοινότητας (ΠΚ) είναι μικρότερη από το επιθυμητό. Σκοπός της παρούσας μελέτης είναι η εκτίμηση της συμμόρφωσης των γιατρών στα Δημόσια Νοσοκομεία με τις Ελληνικές οδηγίες όσον αφορά αφενός τη χρήση του δείκτη CURB-65 για την επιλογή των ασθενών με ΠΚ που χρήζουν νοσηλείας και αφετέρου την εμπειρική αντιμικροβιακή θεραπεία.

Μέθοδοι. Πρόκειται για μία προοπτική πολυκεντρική μελέτη σε τέσσερις πνευμονολογικές και παθολογικές κλινικές. Σε ασθενείς που νοσηλεύονταν λόγω ΠΚ καταγράφηκαν ο δείκτης CURB-65, το αντιβιοτικό σχήμα και οι επιβαρυντικοί παράγοντες (παραπνευμονική συλλογή, χαμηλή οξυγόνωση και προηγούμενη αντιμικροβιακή θεραπεία).

Αποτελέσματα. Από το σύνολο 100 ασθενών (μέση ηλικία \pm sd: 69,41 \pm 17,34 έτη), οι 39 εμφάνισαν χαμηλό (0-1), οι 37 μέσο (2) και οι 24 υψηλό (\geq 3) δείκτη CURB-65. Μόνο 25% των ασθενών με χαμηλό δείκτη CURB-65 δεν είχαν κανέναν από τους προαναφερθέντες επιβαρυντικούς παράγοντες. Το 75% των ασθενών χωρίς προηγηθείσα θεραπεία έλαβαν κατάλληλη αγωγή στο νοσοκομείο.

Συμπεράσματα. Η συμμόρφωση των Ελλήνων γιατρών με τις οδηγίες για τη ΠΚ είναι μάλλον φτωχή. Παρά το υψηλό ποσοστό των νοσηλευόμενων ασθενών με χαμηλό δείκτη CURB-65, η συνύπαρξη επιβαρυντικών παραγόντων συνηγορεί στο ότι ο δείκτης αυτός δεν θα πρέπει να αποτελεί το μοναδικό κριτήριο για τη νοσηλεία των ασθενών. Η αναγνώριση των ασθενών που μπορούν να αντιμετωπιστούν με ασφάλεια εξωνοσοκομειακά θα μπορούσε να ελαττώσει τον αριθμό των περιττών νοσηλείων.

Λέξεις Κλειδιά: Πνευμονία της κοινότητας, Οδηγίες, Δείκτης CURB-65, Εμπειρική αντιμικροβιακή αγωγή.

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