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Low CURB-65 is of limited value in deciding discharge of patients with community-acquired pneumonia☆

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KEYWORDS
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Summary
Background: The relationship between clinical judgment and indications of the CURB-65 score in deciding the site-of-care for patients with community-acquired pneumonia (CAP) has not been fully investigated. The aim of this study was to evaluate reasons for hospitalization of CAP patients with CURB-65 score of 0 and 1.
Methods: An observational, retrospective study of consecutive CAP patients was performed at the Fondazione Cà Granda, Milan, Italy, between January 2005 and December 2006. The medical records of hospitalized patients with CAP having a CURB-65 score of 0 and 1 were identified and reviewed to determine whether there existed a clinical basis to justify hospitalization.
Results: Among the 580 patients included in the study, 218 were classified with a CURB-65 score

Abbreviations: AMI, acute myocardial infarction; ATS, American Thoracic Society; BTS, British Thoracic Society; CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; CPAP, non-invasive continuous positive airway pressure; CURB-65, confusion, blood urea nitrogen, respiratory rate, blood pressure, and age ≥65 years; ER, emergency room; FiO_2, fraction of inspired oxygen; LOS, length of stay in the hospital; N, number; NIV, non-invasive ventilation; $PaCO_2$, partial pressure of carbon dioxide in arterial blood; PaO_2, partial pressure of oxygen in arterial blood; PSI, pneumonia severity index; SAPS, simplified acute physiology score; SD, standard deviation; USA, United States of America.

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of 0 or 1. Among those, 127 were hospitalized, and reasons that justified hospitalization were found in 104 (83%) patients. Main reasons for hospitalization included the presence of hypoxemia on admission (35%), failure of outpatient therapy (14%) and the presence of cardiovascular events on admission (9.7%). Used as the sole indicator for inappropriate hospitalization, the CURB-65 score had a poor positive predictive value of 52%.
Conclusions: Although the CURB-65 has been proposed as a tool to guide the site of care decision by international guidelines, this score is not ideal by itself, and should not be regarded as providing decision support information if a score of 0 and 1 is present. In CAP patients with CURB-65 scores of 0 or 1, further evaluations should be performed and completed by clinical judgment.
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Introduction

Community-acquired pneumonia (CAP) is the leading cause of death from infectious disease in western countries, as well as a major burden on healthcare resources. The major impact on the cost of its care is determined by whether or not a patient is admitted to the hospital.[1] Up to 20% of all patients with CAP are hospitalized in the USA and dollars spent on these patients account for 90% of the total cost of care for the disease.[2] In view of these considerations, hospital admission decision represents a cornerstone in the management of CAP patients and should be based on an objective assessment of severity of illness, and stratification of patients on the basis of their mortality risk.[3]

In clinical practice, physicians have the availability of models of prognosis for patients with CAP to quantify severity of illness and to guide their clinical judgment. One of most widely accepted and used tools is the CURB-65 score developed by the British Thoracic Society (BTS).[4] The CURB-65 score uses five clinical and laboratory characteristics (confusion, blood urea nitrogen, respiratory rate, blood pressure, and age $\geq$65 years) and stratifies patients into three risk groups for mortality: patients with none or one of these characteristics are considered at low risk for mortality (0%—2.1%), those with two characteristics at intermediate risk (9.2%), while those with more than two characteristics are considered at high risk for mortality (up to 22%). The CURB-65 score is particularly attractive since it is easy to remember, simple to compute and, thus, cost-effective. Two recent systematic reviews and meta-analysis validated the ability of the CURB-65 in predicting 30-day mortality in patients with CAP.[5,6] Moreover, authors found that CURB-65 performs well at identifying patients with pneumonia who have a low risk of death.[6]

Based on its ability in predicting mortality, the CURB-65 has been adopted internationally as a tool in deciding the site of care for CAP patients, and is now recommended by a large number of national and international guidelines.[3,7,8] Among those, the BTS suggests outpatient management for patients with a low mortality risk, as well as hospitalization for patients with intermediate-high mortality risk.[8]

The relationship between clinical judgment and indications based on the CURB-65 score in deciding the site-of-care for patients with CAP has not been yet investigated. The CURB-65 score could be, thus, used as a quality improvement tool in order to assess inappropriate hospitalizations for CAP patients with low risk for mortality.

The aim of this study was to evaluate reasons for hospitalization of CAP patients with CURB-65 score of 0 and 1.

Methods

Study design and subjects

This was an observational, retrospective study of consecutive adult patients who were referred to the Emergency Room (ER) of the IRCCS Fondazione Cà Granda, Ospedale Maggiore Policlinico, Milan, Italy, between January 2005 and December 2006 with a diagnosis of CAP. The Institutional Review Board of the hospital approved the study. Patients $\geq$ 18 years of age and satisfying the criteria for CAP were included in this study. Immunocompromised patients were excluded from the study, according to the design of the CURB-65 score derivation study.[4] Among the standard operating procedures adopted in the study center, neither the CURB-65 nor the Pneumonia Severity Index (PSI) are currently used by physicians in the ER for site-of-care decision that, thus, remains a clinical decision.

Records of all the enrolled patients were reviewed. Data were collected and included: demographic information, clinical data on admission to the ER, radiological findings and laboratory values, microbiological and in-hospital treatment data, length of stay in the hospital (LOS), in-hospital mortality. Severity of the pneumonia on admission was evaluated by the CURB-65 score.[4] Missing information was assumed to be negative or normal when determining the total score.

Study definitions

CAP was defined as the presence of a new pulmonary infiltrate seen on chest radiograph or computed tomography scan of the chest within 48 h after hospitalization with at least one of the following: 1) new or increased cough with/without sputum production; 2) fever (documented temperature -rectal or oral- $\geq$ 38.3 or $<$36° C); 3) evidence of systemic inflammation (such as abnormal white blood cell count -either leukocytosis, $>$10,000/cm^3, or leucopenia, $<$ 4000/cm^3- or C-reactive protein or procalcitonin values above the local upper limit). LOS was calculated as the number of days from the date of admission to the date of discharge. Immunodepression was considered in patients with neoplastic disease (defined as

any type of malignancy that was diagnosed in the previous 12 months or as active cancer), human immunodeficiency virus infection, autoimmune diseases, transplantation, and those undertaking immunosuppressive drugs and steroids. In-hospital mortality was defined as death by any cause during hospitalization. Patients were followed from day of admission to day 28; those who remained hospitalized for more than 28 days were considered alive. Any patient who was diagnosed and treated in the Emergency Room for less than 24 h before being discharged was regarded as discharged from the hospital.

Study groups

The CURB-65 score was calculated for every patient who referred to the ER during the study period. Among patients with a CURB-65 score of 0 or 1 on admission to the ER two groups of patients were identified: those who were hospitalized, Group 1, and those sent home, Group 2.

Analysis of the reasons for admission

Patients in Group 1 were identified as being potentially inappropriate for hospitalization. Each case record was submitted to the clinical judgment of a review committee of one infectious diseases, one internist and three pulmonary specialists. None of the reviewers was involved in the initial care of the patients and they were also blinded to patient outcomes. After discussion, the committee determined whether there was any clinical basis for hospital admission. If no clinical basis was determined, the hospital admission was deemed to be inappropriate. If there was a clinical basis for hospital admission of patients in Group 1, the reasons for hospitalization were classified as: (1) new or decompensated medical conditions other than CAP; (2) hypoxemia; (3) failure of outpatient therapy; (4) oral intolerance; (5) suspicion of sepsis; (6) bilateral pneumonia or pleural fluid drainage; (7) unmet social needs; (8) need of further work-up.

The category new or decompensated medical conditions other than CAP that required hospitalization included patients admitted to the hospital for treatment of a concomitant medical condition, new or decompensated. Among those, we identified cardiovascular events (i.e. acute myocardial infarction, acute decompensated heart failure, new arrhythmia or acute worsening of a long-term arrhythmia), neurological events (i.e. transient ischemic attack, cerebrovascular accidents seizure), exacerbations of chronic obstructive pulmonary disease (COPD) and exacerbations of asthma. Hypoxemia was defined as arterial oxygen saturation $<$90% or a PaO_2 value $<$60 mmHg or a PaO_2/FiO_2 ratio value $<$ 300) or clinical evidence of acute respiratory failure, such as respiratory distress. Failure of outpatient therapy was understood as meaning the patient was having persistent symptoms despite receiving appropriate oral antimicrobial treatment at home, consistent with the latest American Thoracic Society (ATS) guidelines.[3] Oral intolerance was defined as inability of the patient in gastrointestinal absorption of oral antibiotic therapy. Suspicion of severe sepsis was considered when the primary physician included sepsis in the differential diagnosis of the patient on hospital admission and a suspicion of severe sepsis was considered to be appropriate by the review committee. Unmet social needs included any non-medical reason that prevented adequate outpatient treatment of CAP (i.e, homelessness). Need of further work-up was described when urgent tests were performed in order to reach a diagnosis, such as the need to role out tuberculosis in the presence of haemoptysis. A consensus was reached with each case presented to the review committee. In cases where unanimous consensus was not reached, a majority decision was employed.

Statistical analysis

All data were statistically analyzed with SPSS (version 14.0, Chicago, Il). Descriptive statistics were reported at baseline with continuous data expressed as a mean $\pm$ SD and categorical data expressed as counts. Summary statistics for all continuous explanatory variables were presented as means with differences between groups compared by means of independent *t*-tests. Categorical explanatory variables were summarized as percentages with differences between groups analyzed using the chi-square test or the Fisher exact test were appropriate. The positive predictive value of the CURB-65 as an indicator of inappropriate hospitalization was determined by calculating the proportion of patients with CURB-65 score 0 and 1 in whom we were unable to find any justification for hospitalization, out of the total number of inpatients with a score 0 and 1, that is, by dividing the number of outpatients or unjustified patients who had been admitted to the hospital by the total number of patients with score 0 and 1.

Results

A total of 714 patients were enrolled during the study period, and among them 134 were excluded from the analysis due to the presence of immunosuppression. The final study population was composed of 580 patients. Demographics, comorbidities, severity of disease on admission, radiological, physical and laboratory findings on admission of the study population are summarized in Table 1. The flow chart of the study population is depicted in Fig. 1, according to the CURB-65 score, as well as the final site of care.

A total of 218 patients were classified with a CURB-65 score of 0 or 1 on admission to the ER, and among them 127 (58%) were hospitalized (Group 1), while 91 were sent home (Group 2). Demographics, comorbidities, severity of disease on admission, radiological, physical and laboratory findings on admission, microbiology data and outcomes of patients with CURB-65 score of 0 and 1 are summarized in Table 2, according to final the site of care decision. Patients in Group 1 were older, with a higher prevalence of chronic cardiovascular and pulmonary diseases, and more severe presentation on admission. More than one-third needed oxygen therapy in the ER, while almost 8% needed either continuous positive airway pressure or non-invasive mechanical ventilation on admission.

A consensus among the reviewers was achieved in 100% of cases for assigning reasons for hospitalization, with an

Table 1 Demographics, comorbidities, severity, radiological, physical and laboratory findings on admission of the study population.

Characteristic	Study population $n = 580$
Demographics	
Male, n (%)	322 (56)
Age, mean ± SD years	68 ± 20
Current tobacco smoker, n (%)	68 (12)
Comorbidities	
Cardiovascular disease, n (%)	295 (51)
Chronic obstructive pulmonary disease, n (%)	148 (26)
Diabetes mellitus, n (%)	82 (14)
Chronic renal insufficiency, n (%)	42 (7.2)
Neurological diseases, n (%)	149 (26)
Asthma, n (%)	13 (2.2)
Severity on admission	
Oxygen therapy, n (%)	256 (44)
NIV and/or CPAP use, n (%)	73 (13)
Radiological findings	
Bilateral pneumonia, n (%)	62 (11)
Pleural effusion, n (%)	119 (21)
Physical findings	
Temperature, mean ± SD°C	37.4 ± 1.2
Systolic Blood Pressure, mean ± SD mmHg	133 ± 25
Diastolic Blood Pressure, mean ± SD mmHg	75 ± 15
Heart rate, mean ± SD beats/minute	97 ± 21
Respiratory Rate, mean ± SD breath/minute	25 ± 10
Arterial Oxygen Saturation, mean ± SD (%)	92 ± 7
Laboratory values	
Arterial pH, mean ± SD	7.43 ± 0.08
$PaCO_2$, mean ± SD mmHg	38 ± 12
PaO2/FiO2 ratio, mean ± SD	275 ± 81
White Blood Cell, mean ± SD cell/L^{-1}	12.5 ± 6.8
Creatinine, mean ± SD mg/dL	1.5 ± 1
Urea, mean ± SD mg/dL	61 ± 47
Empiric antibiotic therapy	
Azithromycin, n. (%)	290 (50)
Ceftriaxone, n. (%)	208 (36)
Levofloxacin, n. (%)	119 (21)
Piperacillin/tazobactam, n. (%)	55 (9.5)
Imipenem, n. (%)	25 (4.3)
Monotheray, n. (%)	51 (8.8)
Microbiology	
S. pneumoniae, n. (%)	36 (6.2)
S. aureus, n. (%)[a]	17 (2.9)
L. pneumoniae, n. (%)	15 (2.6)
M. pneumoniae, n. (%)	9 (1.6)
P. aeruginosa, n. (%)	8 (1.4)
Enterococcus, n. (%)	8 (1.4)
C. pneumoniae, n. (%)	6 (1.3)
Other	11 (1.9)

PaO_2: partial pressure of oxygen in arterial blood; $PaCO_2$: partial pressure of carbon dioxide in arterial blood; FiO2 fraction of inspired oxygen; SD Standard deviation; *n*: number; SAPS: simplified acute physiology score; NIV: non-invasive ventilation; CPAP: non-invasive continuous positive airway pressure.

[a] 7 methicillin-resistant *S. aureus*.

unanimous decision in 95% of the cases. Among the 127 patients belonging to Group 1, reasons that justified hospitalization were found in 104 (83%) patients, see Table 3. No clinical justification for hospitalization was identified in 23 patients (17%). The calculated positive predictive value of the CURB-65 score as a sole indicator for inappropriate hospitalization was 52%. Among those in Group 1, one patient died.

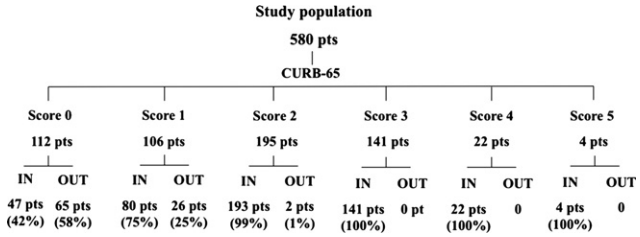

Figure 1 Flow chart of the study population according to the CURB-65 score risk classes and the final site of care (IN: hospitalized; OUT: sent home).

A total of 362 patients were classified with a CURB-65 score of 2-to-5 on admission to the ER, and among them 360 (99%) were hospitalized, while 2 were sent home. Among patients with CURB-65 score of 2-to-5 who were hospitalized, 54 (15%) patients died.

Discussion

The main findings of the present study are: 1) among patients presenting in the Emergency Room with a CURB-65 score of 0 or 1, almost 50% are appropriately hospitalized based on clinical judgment; 2) main reasons for hospitalization of patients with CURB-65 of 0 and 1 include the presence of hypoxemia on admission, failure of outpatient therapy and the presence of cardiovascular events on admission; 3) used as the sole indicator for inappropriate hospitalization, the CURB-65 score had a poor positive predictive value of 52%.

A major concern exists in literature whether the prediction of death performed by the CURB-65 score could also be an appropriate criterion for hospitalization, in view of the fact that the CURB-65 score was not initially developed to choose the site of care for CAP patients. Based on the CURB-65 ability in predicting mortality, guidelines have suggested its use to decide the site-of-care. However, some data showed discrepancy between the CURB-65 score and clinical judgment, as well as a misleading performance of this score in young adults.[9]

We found that the site-of-care decision based on the CURB-65 score was inconsistent with clinical judgment in one out of five CAP patients presenting at the ER. In almost the total of the cases, the discrepancy involved hospitalization of CAP patients with a score of 0 and 1 due to the presence of hypoxemia on admission, failure of outpatients therapy and decompensated medical conditions. Our data are consistent with those recently published by Choudhury and coworkers who identified reasons justifying hospitalization in 83% of patients with CURB-65 score of 0 and 1 who were admitted to the hospital.[10] Similarly to our results, these authors found hypoxemia and decompensated comorbidities playing a major role in this decision.

The CURB-65 score suffers of a lack a formal assessment of hypoxemia, a major drawback in light of the importance of assessing oxygenation immediately on arrival at the ER. We found that hypoxemia was a reason for hospitalization in almost one-third of CAP patients with CURB-65 score of 0 and 1. Our data are consistent with a recent prospective, multicenter study by Sanz and coworkers who identified hypoxemia at the time of admission in almost 50% of patients with CURB-65 score of 0-1.[11] The authors found that these patients had a prolonged length of hospital stay, higher rate of admissions in the intensive care unit and development of severe sepsis as well as mortality in comparison to non-hypoxemic patients. Our data are also consistent with findings reported by Ronan et al. who identified bilateral/multilobar appearance of the chest

Table 2 Findings on admission of patients with CURB-65 score of 0 and 1.

Characteristic	Group 1 $n = 127$	Group 2 $n = 91$	p
Demographics			
Male, n. (%)	69 (54)	48 (53)	0.885
Age, mean ± SD years	58 ± 19	41 ± 16	<0.001
Current tobacco smoker, n. (%)	17 (13)	0 (0)	<0.001
Comorbidities			
Cardiovascular disease, n. (%)	41 (32)	10 (11)	0.001
Chronic obstructive pulmonary disease, n. (%)	30 (24)	2 (2.2)	<0.001
Diabetes mellitus, n. (%)	12 (10)	2 (2.2)	0.036
Neurological diseases, n. (%)	14 (11)	5 (5.6)	0.155
Severity on admission			
Oxygen therapy, n. (%)	46 (36)	0	<0.001
NIV/CPAP use, n. (%)	10 (7.9)	0	0.006
Physical findings			
Systolic Blood Pressure, mean ± SD mmHg	135 ± 20	127 ± 16	0.005
Diastolic Blood Pressure, mean ± SD mmHg	78 ± 12	74 ± 11	0.020
Heart rate, mean ± SD beats/minute	97 ± 21	97 ± 19	0.977
Respiratory Rate, mean ± SD breath/minute	21 ± 7	15 ± 4	<0.001
Arterial Oxygen Saturation, mean ± SD (%)	95 ± 4	97 ± 2	<0.001

Group 1: patients who were hospitalized; Group 2: patients who were sent home; SD Standard deviation; *n*: number; NIV: non-invasive ventilation; CPAP: non-invasive continuous positive airway pressure.

Table 3 Reasons that justified hospitalization among patients with a CURB-65 score of 0 or 1.

Reasons	N. (%)
1. Hypoxemia	36 (35)
2. Failure of outpatient therapy	15 (14)
3. Cardiovascular events	10 (9.7)
4. Further Work-up	8 (7.8)
5. Neurological events	7 (6.7)
6. Exacerbation of COPD	6 (5.8)
7. Exacerbation of asthma	4 (3.8)
8. Bilateral pneumonia	3 (2.9)
9. Unmet social needs	3 (2.9)
11. Severe hemoptysis	1 (0.9)
12. Suspicion of severe sepsis	1 (0.9)
13. Oral intolerance	1 (0.9)
14. Others	9 (8.7)

N: number; COPD: chronic obstructive pulmonary disease.

radiograph to be associated with mortality in CAP patients with CURB-65 score of 0-2.[12] The lack of evaluation by the CURB-65 score of hypoxemia on admission is important in view of the fact that current guidelines clearly consider hypoxemia as an absolute contraindication to outpatient treatment of CAP.[13]

We found that failure of outpatient therapy was one of the main reasons for hospitalization in patients with CURB-65 score of 0 and 1. The majority of the panel agreed to hospitalize these patients in order to increase spectrum of pathogen coverage with endovenous antibiotics. This decision is in accordance with the latest guidelines published by the ATS in 2007 indicating failure of outpatient therapy as clinical indication for more extensive diagnostic testing.

There are some concerns in clinical practice that the CURB-65 score may not be easily applied in older patients who may still have substantial mortality risk, even if a mild form of CAP destabilizes a chronic, but compensated, disease process. Our findings confirmed this hypothesis with the identification of the concomitant presence of CAP and other decompensated comorbidities that influenced the admission decision in 32% of the patients. Among the decompensated comorbidities, we mainly identified cardiovascular and neurological events, as well as exacerbations of chronic obstructive pulmonary disease. The impact of cardiovascular events in CAP patients has been recently analyzed by different groups of investigators. Perry et al. used data from administrative databases of the Department of Veterans Affairs in the USA and found that hospitalization for pneumonia is associated with a clinically significant number of cardiovascular events and that the majority of these events occur during the initial hospitalization.[14] The incidence of acute myocardial infarction (AMI) at the time of hospital admission in patients with CAP has been shown to be up to 7% in different settings.[15,16] Moreover, we recently identified AMI to be also one of the main causes for clinical failure during hospitalization for patients with CAP.[17]

When we analyzed clinical judgment *versus* the CURB-65 score 2-to-5, we found an almost complete concordance in the decision of the site of care for CAP patients. We can speculate that the presence of at least two out of five criteria of the CURB-65 is able to recognize those patients who could need hospitalization.

Our study has different limitations. In view of the retrospective design of the study, we did not have enough data to perform a full analysis of patients who were discharged from the ER. Furthermore, missing information regarding the use of vasopressors as well as respiratory rate values on admission was present and we assumed the patient had normal respiratory rate if otherwise reported in the ER charts. Furthermore, we were not able to identify patients with healthcare associated pneumonia, in order to evaluate the CURB-65 score in the site-of-care decision for these group of patients.

Our study is strengthened by the evaluation of a consecutive population of patients with CAP in a teaching hospital. Likewise, another strength is the incorporation of a multidisciplinary review committee that judged the appropriateness of hospitalization for every case by consensus. Similar clinical consensus methods have been previously used in studying the etiology of mortality in cancer, cardiovascular disease and pneumonia.[17]

Our findings have different implications. From a clinical point of view, as suggested by the BTS guidelines, the CURB-65 should be strongly supported by clinical judgment in order to decide the site of care for CAP patients, especially if a score of 0 or 1 is present. In this case, an accurate evaluation of the presence of acute respiratory failure as well as other decompensated comorbidities is needed. From a research point of view, since the CURB-65 is not a good tool in deciding the site-of-care in CAP patients with score 0 and 1, further research is needed to improve the predictability of CURB-65 in low score patients. Furthermore, a comparison between the CURB-65 score and the PSI is also needed in order to evaluate the concordance of the two scoring systems in deciding the site of care for patients with CAP. Findings from the present study could be useful in modifying the CURB-65 score in order to maintain its simplicity and improve site-of-care ability.

Although the CURB-65 has been proposed as a tool to guide the site of care decision by international guidelines, this score is not ideal by itself, and should not be regarded

as providing decision support information if a score of 0 and 1 is present. In CAP patients with CURB-65 scores of 0 or 1, further evaluation of the presence of hypoxemia, as well as decompensated comorbidities should be performed and completed by clinical judgment.

Authors' contributions

All authors have revised the manuscript for important intellectual content and approved the final version. SA, JR, FB conceived the study, and participated in its design and coordination. SA, RC, AMB, PT, and FB participated in the analysis of the data. VR participated in acquisition of the data and analysis of data. AMZ performed the statistical analysis. SA, RC, AMB, JR, PP, PT, FP and FB have been involved in drafting the manuscript or revising it critically for important intellectual content.

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Conflict of interests

No financial and non-financial competing interests (political, personal, religious, ideological, academic, intellectual, commercial or any other) are present in relation to this manuscript for all the authors.

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