ORIGINAL ARTICLE

Multidrug-resistant pathogens in hospitalised patients coming from the community with pneumonia: a European perspective

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ABSTRACT

Background Probabilistic scores have been recently suggested to identify pneumonia caused by multidrug-resistant (MDR) bacteria. The aim of the study was to validate both Aliberti and Shorr scores in predicting MDR pneumonia, comparing them with healthcare associated pneumonia (HCAP) classification.
Methods Two independent European cohorts of consecutive patients hospitalised with pneumonia were prospectively evaluated in Barcelona, Spain (BC) and Edinburgh, UK (EC). Data on admission and during hospitalisation were collected. The predictive value of the three scores was explored for correctly indicating the presence of MDR pneumonia via a receiver-operating characteristic (ROC) curve.
Results A total of 1591 patients in the BC and 1883 patients in the EC were enrolled. The prevalence of patients with MDR pathogen among those with isolated bacteria was 7.6% in the BC and 3.3% in the EC. The most common MDR pathogen found in both cohorts was MRSA, followed by MDR *P aeruginosa*. A significantly higher prevalence of MDR bacteria was found among patients in the intensive care unit (ICU). The two probabilistic scores, and particularly the Aliberti one, showed an area under the ROC curve higher than the HCAP classification in predicting MDR pneumonia, especially in the ICU.
Conclusions Risk scores able to identify MDR pneumonia could help in developing strategies for antimicrobial stewardship.

Key messages

What is the key question?
Can we use probabilistic scores to predict the presence of multidrug-resistant (MDR) organisms in hospitalised patients coming from the community with pneumonia?

What is the bottom line?
Two probabilistic scores perform better than the healthcare-associated pneumonia classification in predicting the presence of pneumonia due to MDR bacteria in patients hospitalised both in the ward and in the intensive care unit.

Why read on?
The application of risk scores able to predict the presence of a MDR pneumonia in patients coming from the community could help to balance the need to treat infections appropriately while avoiding the overuse of broad-spectrum antibiotics.

INTRODUCTION

The presence of multidrug-resistant (MDR) organisms causing pneumonia in the community has emerged over the past decades as a critical problem.[1] Studies performed in the USA clearly documented the increasing prevalence of resistant organisms in patients with community-acquired pneumonia (CAP).[2] Data from European studies are limited and generally suggest a low frequency of MDR organisms in patients coming from the community with pneumonia.[3][4] Two probabilistic scores have been developed to assess the potential for MDR pathogens in CAP patients: the Aliberti score was prospectively derived from a European cohort of patients with CAP, while the Shorr score was derived from a retrospective analysis of patients with CAP in the USA.[3][5] However, neither

score has been prospectively validated in large and independent European cohorts of CAP patients.

The aims of the present study were (a) to externally validate the Aliberti and Shorr scores in predicting pneumonia caused by MDR bacteria and to compare them with the healthcare-associated pneumonia (HCAP) classification; (b) to evaluate the prevalence of *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA) and other MDR bacteria in two independent European cohorts of hospitalised patients coming from the community with pneumonia; and (c) to study characteristics and clinical outcomes of patients with pneumonia caused by MDR versus non-MDR bacteria.

MATERIALS AND METHODS

Two independent European cohorts of consecutive patients coming from the community and admitted with a diagnosis of pneumonia were prospectively evaluated in Barcelona, Spain, and Edinburgh, UK. The Barcelona cohort (BC) included patients admitted with a diagnosis of pneumonia to the Hospital Clínc in Barcelona, Spain, between January 2007 and March 2012. Patients who were

hospitalised in the previous 21 days, as well as those with a diagnosis of active tuberculosis or infection with fungi were excluded from the study. The Edinburgh cohort (EC) included patients admitted to National Health Service hospitals in Edinburgh with a diagnosis of pneumonia between January 2005 and December 2009. Exclusion criteria were (a) immunosuppression, defined as current, >28 days, use of oral prednisolone at any dose or other immunosuppressive drugs or (b) patients with solid organ transplantation; (c) known thoracic malignancy and (d) patients in whom active treatment was not considered appropriate; (e) hospitalisation in the preceding 14 days; and (f) patients who developed pneumonia >48 h after hospital admission.

Microbiological testings were conducted according to British Thoracic Society and European Respiratory Society recommendations. MRSA, *P aeruginosa* resistant to antipseudomonal penicillins, cephalosporins, carbapenems and quinolones, *Stenotrophomonas maltophilia*, vancomycin-resistant *Enterococcus*, *Acinetobacter baumanii*, Enterobacteriaceae producing extended-spectrum B-lactamases (ESBL) and other non-fermenting Gram-negative bacilli were considered to be MDR pathogens. Among patients with isolated bacteria, two study groups were identified: patients whose pneumonia was caused by at least one MDR bacteria and those whose pneumonia was caused only by non-MDR bacteria. Among patients with isolated bacteria, three risk scores were evaluated and tested against the isolation of MDR bacteria: the Aliberti and Shorr scores and HCAP classification, see online supplementary material.

The χ^2 test was used to compare categorical data between groups. The Mann–Whitney U test was used to compare two groups of non-parametric data. The area under the receiver-operating characteristic (ROC) curves, together with its 95% CIs, was calculated for the three scores.

RESULTS

A total of 1591 consecutive patients with pneumonia (63% men, median age: 70 years) in BC and 1883 patients (51% men, median age: 68 years) in EC were enrolled during the study periods. Demographics, severity of disease, clinical, laboratory and radiological findings on admission, initial antibiotic therapy and clinical outcomes of both study populations are summarised in the online supplementary material. A causative organism for pneumonia was identified in 691 patients (43%) in BC and in 557 patients (30%) in EC.

The prevalence of patients with at least one MDR pathogen was 2.4% in BC and 0.9% in EC and among those with isolated bacteria, 7.6% in BC and 3.3% in EC. The most common MDR pathogen found in both cohorts was MRSA, followed by MDR

P aeruginosa and ESBL+ pathogens. Characteristics and outcomes of patients whose pneumonia was due to *P aeruginosa* and MRSA are reported in the online supplementary material. A significantly higher prevalence of MDR bacteria was found among patients admitted to the intensive care unit (ICU) in comparison with those admitted to the ward in both cohorts. In comparison with patients with pneumonia caused by non-resistant bacteria, those with a least one MDR bacteria came more frequently from a nursing home, had been more frequently hospitalised in the prior 90 days, were more immunosuppressed (in BC) and had more severe pneumonia on admission in terms of use of mechanical ventilation, acidemia and alteration of gas exchange. Patients with MDR bacteria also showed a significant longer hospital stay, a significant higher frequency of treatment failure and higher mortality, up to 40%, in comparison with subjects with a pneumonia caused by a non-resistant bacteria.

At least one risk factor for MDR organisms was identified in 41% and 31% of the patients in BC and EC, respectively. The ROC curves evaluating the performance of the three scores with respect to the presence of MDR bacteria are reported in table 1 for both study cohorts. In the entire BC, the area under the ROC curve for the Aliberti score was 0.89, the Shorr score was 0.89 and HCAP classification was 0.77. In the entire EC, the area under the ROC curve for the Aliberti score was 0.77, the Shorr score was 0.75 and HCAP classification was 0.66. The performance of the three scores was evaluated among patients admitted to ICU and among those admitted to the ward. The Aliberti score showed a higher area under the curve in both populations of patients in BC admitted to ICU and ward patients and in ICU patients in EC in comparison with the Shorr score and HCAP classification.

DISCUSSION

This study shows a low prevalence of MDR bacteria in CAP patients in three hospitals in a single Scottish region in Northern Europe and in one hospital in Barcelona in Southern Europe. Patients suffering from pneumonia caused by MDR bacteria show more severe disease on presentation and worse clinical outcomes in comparison with those with non-MDR bacteria. Finally, two probabilistic scores (Aliberti and Shorr) perform better than HCAP classification in predicting the presence of pneumonia due to MDR bacteria. The Aliberti score shows a slightly better performance in both the entire population of patients with pneumonia and among ICU patients in comparison with the Shorr score.

Our data confirm a low percentage of pneumonia caused by MDR bacteria in Europe: 7.6% in Spain and 3.3% in the UK. A difference seems to be emerging in the prevalence of CAP

Table 1 Area under the receiver-operating characteristic curve in the entire population, patients admitted to the intensive care unit (ICU) and those admitted to the ward in the Barcelona cohort (BC) and Edinburgh cohort (EC) according to the Aliberti and Shorr scores and healthcare-associated pneumonia (HCAP) classification

| Study cohorts | Score | Area under the curve | | |
		Entire population	ICU patients	Ward patients
BC	Aliberti score	0.89 (0.83–0.95)	0.85 (0.75–0.96)	0.91 (0.84–0.98)
	Shorr score	0.89 (0.82–0.96)	0.77 (0.58–0.96)	0.89 (0.80–0.97)
	HCAP classification	0.77 (0.69–0.83)	0.83 (0.71–0.95)	0.75 (0.68–0.83)
EC	Aliberti score	0.77 (0.71–0.84)	0.79 (0.68–0.89)	0.77 (0.70–0.84)
	Shorr score	0.75 (0.68–0.81)	0.74 (0.63–0.86)	0.80 (0.73–0.87)
	HCAP classification	0.66 (0.59–0.73)	0.60 (0.49–0.71)	0.73 (0.64–0.82)

caused by MDR bacteria between the USA and Europe. Reasons for this finding could be related to the enrolment of more severe and immunocompromised patients in the US studies as well as the presence of some differences in the organisation of healthcare systems in terms of decentralisation of care on the territory and different policies and guidelines related to the use of antibiotics (11, 18). These final considerations could be also responsible for the slight difference in MDR prevalence between Southern (Spain and Italy) Europe and Northern (UK) Europe (6).

We showed a superiority of both Aliberti and Shorr scores in comparison with HCAP classification. Differences in ROC values of both Aliberti and Shorr scores between the two study cohorts could be mainly due to the difference in prevalence of MDR bacteria. The knowledge of population characteristics, the presence and degree of immunosuppression and background resistance rates is therefore critical to optimise the use of these scores.

We found a high prevalence of MDR bacteria among patients with pneumonia who were admitted to ICU and, particularly, those who received mechanical ventilation. These findings raise the question whether all severe patients with pneumonia admitted to ICU should receive a broad-spectrum antibiotic treatment against MDR bacteria regardless of the presence of risk factors. Although in daily clinical practice patient disease severity often leads physicians to prescribe a broad-spectrum antibiotic coverage in order to prevent excess mortality due to treatment failure, a probabilistic approach based on score system could be suggested. The Aliberti score has been proved to have a role in evaluating the presence of MDR infection also in CAP patients admitted to ICU.

In conclusion, a low prevalence of MDR organisms could be found among patients coming from the community and who are hospitalised because of an episode of pneumonia, with MRSA identified as the most frequent pathogen. The application in clinical practice of risk scores able to predict the presence of MDR pneumonia in patients coming from the community could help in developing strategies for healthcare workers to balance the need to treat infections appropriately while avoiding the overuse of broad-spectrum antibiotics.

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