



## Original Article

## Adherence to antibiotic treatment guidelines and outcomes in the hospitalized elderly with different types of pneumonia



Raffaella Rossio <sup>a,1</sup>, Carlotta Franchi <sup>b,\*</sup>, Ilaria Ardoino <sup>c,1</sup>, Codjo D. Djade <sup>b</sup>, Mauro Tettamanti <sup>b</sup>, Luca Pasina <sup>b</sup>, Francesco Salerno <sup>d</sup>, Alessandra Marengoni <sup>e</sup>, Salvatore Corrao <sup>f</sup>, Maura Marcucci <sup>g</sup>, Flora Peyvandi <sup>a</sup>, Elia M. Biganzoli <sup>c</sup>, Alessandro Nobili <sup>b</sup>, Pier Mannuccio Mannucci <sup>h</sup>, REPOSI Investigators <sup>2</sup>

<sup>a</sup> Department of Pathophysiology and Transplantation, IRCCS Ca' Granda Maggiore Policlinico Hospital Foundation, Milan, Italy

<sup>b</sup> Department of Neuroscience, IRCCS – Istituto di Ricerche Farmacologiche “Mario Negri”, Milan, Italy

<sup>c</sup> Dipartimento di Scienze Cliniche e di Comunità, University of Milan, Italy

<sup>d</sup> Department of Medical and Surgery Sciences, IRCCS Policlinico San Donato, University of Milan, Italy

<sup>e</sup> Department of Clinical and Experimental Science, University of Brescia, Italy

<sup>f</sup> Dipartimento Biomedico di Medicina Interna e Specialistica, University of Palermo, Italy

<sup>g</sup> Geriatrics Unit, Foundation IRCCS Ca' Granda – Ospedale Maggiore Policlinico & Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

<sup>h</sup> Scientific Direction, IRCCS Ca' Granda Maggiore Hospital Policlinico Foundation, Milan, Italy

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## ABSTRACT

**Background:** Few studies evaluated the clinical outcomes of Community Acquired Pneumonia (CAP), Hospital-Acquired Pneumonia (HAP) and Health Care-Associated Pneumonia (HCAP) in relation to the adherence of antibiotic treatment to the guidelines of the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) in hospitalized elderly people (65 years or older).

**Methods:** Data were obtained from REPOSI, a prospective registry held in 87 Italian internal medicine and geriatric wards. Patients with a diagnosis of pneumonia (ICD-9 480–487) or prescribed with an antibiotic for pneumonia as indication were selected. The empirical antibiotic regimen was defined to be adherent to guidelines if concordant with the treatment regimens recommended by IDSA/ATS for CAP, HAP, and HCAP. Outcomes were assessed by logistic regression models.

**Results:** A diagnosis of pneumonia was made in 317 patients. Only 38.8% of them received an empirical antibiotic regimen that was adherent to guidelines. However, no significant association was found between adherence to guidelines and outcomes. Having HAP, older age, and higher CIRCS severity index were the main factors associated with in-hospital mortality.

**Conclusions:** The adherence to antibiotic treatment guidelines was poor, particularly for HAP and HCAP, suggesting the need for more adherence to the optimal management of antibiotics in the elderly with pneumonia.

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### 1. Introduction

Pneumonia is a common infectious disease and is among the leading causes of hospitalization and death [1]. In the frail elderly suffering from multiple chronic diseases pneumonia is more severe and leads to increased mortality [1]. Many scientific societies and working groups have prepared guidelines on the most suitable antibiotics for the empirical treatment of patients with different types of pneumonia. Among such guidelines the most used worldwide are those of the Infectious

Disease Society of America (IDSA) [2] and of the American Thoracic Society (ATS) [3], that include recommendations for the treatment of Community Acquired Pneumonia (CAP), Hospital Acquired Pneumonia (HAP), and for the new category Health Care-Associated Pneumonia (HCAP) [4,5].

Even though several studies have evaluated the degree of adherence to guidelines for empirical antibiotic therapy, especially in CAP [6], very few of them did evaluate adherence for the different categories of pneumonia and its impact on clinical outcomes [7]. Furthermore, a paucity of studies has specifically considered the hospitalized elderly population [8]. With this background, the aims of this study were to evaluate adherence to IDSA/ATS guidelines and its relationship with the main clinical outcomes (length of hospital stay, re-hospitalization rate, in-hospital and 3-month mortality) in elderly people consecutively admitted to Italian internal medicine and geriatric wards participating in the prospective REPOSI registry.

\* Corresponding author at: Laboratory for Quality Assessment of Geriatric Therapies and Services, IRCCS – Istituto di Ricerche Farmacologiche “Mario Negri”, Via Giuseppe La Masa, 19 20156 Milan, Italy. Tel.: +39 02 39014580; fax: +39 02 39001916.

E-mail address: [carlotta.franchi@marionegri.it](mailto:carlotta.franchi@marionegri.it) (C. Franchi).

<sup>1</sup> Equally contributing authors.

<sup>2</sup> REPOSI denotes the Registro Politerapie SIMI, Società Italiana di Medicina Interna.

## 2. Methods

### 2.1. Data collection

This study was conducted in internal medicine and geriatric wards participating to REPOSI (Registro Politerapie SIMI), a collaborative and independent registry of the Italian Society of Internal Medicine (SIMI), IRCCS Fondazione Cà Granda Policlinico Hospital, and the IRCCS Istituto di Ricerche Farmacologiche Mario Negri. The registry design was described in details elsewhere [9]. In brief, patients aged 65 years or more consecutively admitted to hospital during four index periods which lasted one week each separated from each other by 3 months were enrolled in the biannual study runs in 2008, 2010, and 2012.

The principal data collected included socio-demographic factors, clinical parameters, patterns of comorbidities according to the Cumulative Illness Rating Scale (CIRS), and medications prescribed. In particular, CIRS was developed in 1968 and successively reviewed for elderly patients in 1991. It allows to calculate the number and functional severity (score) of chronic illnesses in the frame of the comorbid state of a given patient, according to 13 items, one for each biological system, plus one for psychiatric conditions. Thus, a comorbidity index was computed by counting the number of items for which moderate to severe illness was reported (scores  $\geq 3$ ), while overall illness severity was represented by the mean of the (score for) first 13 CIRS items [10].

Participation was voluntary and all patients provided signed informed consent. In this study on pneumonia, patients from REPOSI 2008 were excluded because no information about their living environments and previous hospitalizations and hospital visits were available, preventing the accurate classification of the type of pneumonia and making particularly difficult the distinction between CAP and HCAP.

### 2.2. Criteria for pneumonia classification

All patients with a diagnosis of pneumonia [International Classification of Diseases – Ninth Revision (ICD9) codes 480–487] or prescribed antibiotic therapy with pneumonia as an indication were included. We classified patients as having CAP when the onset of symptoms did occur outside the hospital setting or alternatively within 48 h since hospital admission. Patients were classified as having HAP if diagnosed with pneumonia after being hospitalized for more than 48 h. They were classified as HCAP if hospitalized in an acute care ward for two or more days within 90 days before the infection; or resided in a nursing home or long-term care facility; or had received intravenous antibiotic therapy, chemotherapy or wound care within the past 30 days before the current infection; or had attended a hospital or hemodialysis clinic [2,3,5].

### 2.3. Antibiotic treatment adherence

In the REPOSI database microbiological investigations were not recorded. We are cognizant that in the presence of microbiological methods identifying etiology of CAP, antimicrobial therapy should be specifically directed to that pathogen [2]. However, in the present analysis, because this specific information was missing, adequacy of antibiotic therapy according to microbiological tests could not be evaluated. Hence we defined empirical antibiotic regimens those administered on the first day of therapy for pneumonia and considered the antibiotic regimen adherent to IDSA/ATS guidelines if concordant with the current recommendations for CAP, HAP, and HCAP [2,3]. For treatment of CAP, the use of beta-lactam antibiotics (ceftriaxone, cefotaxime, amoxicillin, amoxicillin/clavulanate, and ampicillin/sulbactam) in combination with a macrolide (azithromycin or clarithromycin) and that of a respiratory fluoroquinolone alone (moxifloxacin or levofloxacin) was considered treatments consistent with guidelines. In the presence of risk factors for *Pseudomonas* species, the use of an antipseudomonas antibiotic (piperacillin/tazobactam, ceftazidime, cefepime, imipenem or

meropenem) in combination with ciprofloxacin or with an aminoglycoside was considered consistent.

For treatment of HAP, provided that the infection began within the first 4 days of hospitalization, ceftriaxone, levofloxacin, moxifloxacin, ciprofloxacin, ampicillin/sulbactam or ertapenem were considered consistent with the guidelines. For late onset HAP or in the presence of risk factors for multi-drug resistant (MDR) pathogens, antipseudomonas cephalosporins or carbapenems or beta-lactam/beta-lactamase inhibitors plus antipseudomonas fluoroquinolone or an aminoglycoside plus linezolid or vancomycin were prescribed. Most patients with HCAP are at risk of infection with MDR pathogens: accordingly, the recommended therapy is that of late-onset HAP.

### 2.4. Statistical analysis

Data were summarized as frequencies (%), means and standard deviations or medians and interquartile ranges, as appropriate. The association between pneumonia types and socio-demographic factors and other co-morbidities was assessed by univariable multinomial logistic regression model (CAP was the reference category). Multivariable selection was performed according to the results of univariable analysis and then assessed by a lasso regularized multinomial regression [11]. Adherence to clinical guidelines was assessed by means of a mixed effect logistic regression model, in order to account for possible withinward correlation [12]. Three regression models were fitted to account for pneumonia classification (model 1), age and gender (model 2), and clinical features affecting classification (model 3). The year of REPOSI enrolment was also considered in adjusted models.

The main clinical patient outcomes (re-hospitalization, in-hospital and 3-month mortality) were analyzed by means of a logistic regression model, accounting for pneumonia classification, adherence to clinical guidelines, demographic characteristics and possible clinical features. Length of hospital stay was evaluated as a continuous variable.

The analysis was performed using the SAS/STAT software Version 9.1 (SAS Institute Inc., Cary, NC, USA). The Proc GLIMMIX was used to fit mixed effect models.

## 3. Results

### 3.1. Demographic characteristics

Among 4035 patients included in the REPOSI registry, a sample of 529 had a diagnosis of pneumonia at the time of admission or during hospitalization. From the REPOSI 2010 and 2012 runs 142 patients were excluded because of missing data, 58 because enrolled in 2008 and 12 because they have viral or fungal pneumonia, so that a total of 317 patients enrolled in 72 wards were available for analysis (Fig. 1): 167 (53.6%) were males and mean age was 80.7 years. Overall, 191 patients had CAP, 55 HAP, and 71 HCAP.

Table 1 reports the socio-demographic and main clinical characteristics at the time of hospital admission according to the type of pneumonia. Compared to those with CAP, HAP patients were significantly older and presented with a slight lower degree of physical ability (Barthel index). Patients with HCAP were also less likely to live alone or with relatives, used a higher number of medications, had more co-morbidities at admission and also a higher illness severity score (CIRS severity index). The multivariate multinomial regression model confirmed the results of univariable analysis: almost the same factors were independently associated to the pneumonia type with almost the same effect, but no association was seen for the number of co-morbidities and a lower BMI seemed to be associated to HCAP. Pertaining to the comorbidity profiles, no relevance between-group differences were found, but HCAP patients were more often affected by malignancies and vascular diseases ( $p$ -value  $< 0.1$ ), HAP patients by genitourinary diseases ( $p$ -value  $< 0.1$ ).

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