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Adherence to guidelines for hospitalized community-acquired pneumonia over time and its impact on health outcomes and mortality

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Abstract Compliance with validated guidelines is crucial to guide management of patients hospitalized with community-acquired pneumonia (CAP). Data describing real-life management and treatment of CAP are limited. We aimed to evaluate the compliance with guidelines over time, and to assess its impact on all-cause mortality and clinical outcomes. We retrospectively compared two cohorts of patients admitted to the hospital, throughout 2005, just after the implementation of a local clinical pathway based on CAP international guidelines, and 7 years later over 2012. We included all patients with a diagnosis of pneumonia and/or related complications. 564 patients were included. The Pneumonia Severity Index calculation was better documented in 2012 (25.23 %) compared to 2005 (17.70 %; $p = 0.032$), but compliance with guideline empirical antibiotic therapy was lower in 2012 (56.70 %) than in 2005 (68.75 %; $p = 0.004$). Performance of guideline recommended urinary antigen tests was higher in 2012, and associated with 57.3 % lower odds of in-hospital mortality (95 % CI 15.0–78.5 %) and with 65.9 % lower odds of 30-day mortality (95 % CI 31.5–83.0 %). Compliance with empirical antibiotic therapy was associated with 2.9 days lower mean length of hospital stay (95 % CI −4.2 to −1.6 days) and with 2.0 days lower mean duration of antibiotic therapy (95 % CI −3.3 to −0.7 days). Compliance with guidelines changed over time, with some effects on mortality and with an apparent reduction in the length of hospital stay and the duration of antibiotic therapy. Specific clinical training and hospital control policies could achieve greater compliance with guidelines, and thus reduce a burden on hospital services.

Keywords Community-acquired pneumonia · Guidelines · Adherence compliance

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Introduction

Community-acquired pneumonia (CAP) is the leading cause of death for infectious disease worldwide, representing a considerable cause of morbidity and mortality, especially among hospitalized patients [1, 2]. Both prevalence and hospitalization rates are particularly high in elderly and comorbid patients; [3, 4] for people over 65 years early readmission to hospital has also been increasing. [5] Today, if recurrences are excluded, the mean European length of hospital stay is 9.0 days and in-hospital mortality rates vary from 0 to 17.5 % across countries [6].

Given, the high burden of disease and the wide spectrum of clinical severity, use of validated guidelines are crucial in guiding diagnostic and therapeutic approaches. Compliance with guidelines has been found to improve clinical outcomes, independently of contextual and patient-specific

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variables (such as the decision to hospitalize and the rapidity of administration of the first antibiotic dose), [6] and to reduce unnecessary hospitalizations and readmissions, length of hospital stay, costs, and mortality [7–19].

Although compliance with guidelines varies among clinicians, and is conditioned by various factors, [20] site of care, i.e. management outside or inside hospital, and correct timing of antibiotic therapy are vital factors in reducing risk of complications and mortality from CAP [21]. These aspects, as well as choice of empirical antibiotic therapy, are most critical when applying guideline indications [6].

To comply with international guidelines, in 2005 we implemented a CAP clinical pathway (CP) based on American Thoracic Society and British Thoracic Society guidelines, which is still largely compatible with the most updated guidelines available in 2015 [22, 23].

Objectives

We aimed to evaluate to what extent compliance with the local CAP CP in our hospital changed over time from 2005 to 2012. We also aimed to evaluate the impact of hospital-wide compliance with the local CAP CP over time on (1) in-hospital all-cause mortality, (2) 30-day all-cause mortality, (3) length of hospital stay, and (4) length of antibiotic therapy.

Materials and methods

This report was written in compliance with the STROBE Statement for observational studies. [24]

Clinical pathway elaboration

In 2004 we outlined, and in 2005 implemented, a CAP CP based on then current American Thoracic Society and British Thoracic Society guidelines [22, 23]. Our intent was to provide hospital clinicians with a concise and useful tool to manage patients with CAP. Our CAP CP comprises tools (1) to stratify patient risk and select the most appropriate setting of care, (2) to indicate the fundamental diagnostic procedures, (3) to select the best timing and choice of empirical antibiotic therapy (see Fig. 1).

Study design

We conducted an observational retrospective study comparing two cohorts of patients admitted throughout 2005, the year the local CAP CP was implemented, and again in 2012, seven years after its original implementation. All patients in each cohort were followed up for 30 days from admission. The study was approved by the institutional ethics committee (study number: CE 157/14).

Setting

The study was conducted in a medium size teaching hospital in North-Western Italy. The hospital has 635 beds [25] and a catchment area of approximately half a million people [26]

Participants

We included all patients ≥18 years with a principal or secondary diagnosis of pneumonia and related complications (pleural effusion, empyema), i.e. ICD-9-CM codes 480-486, 510, 511, 518, consecutively admitted to our hospital from January 1st to December 31st in two separate years of 2005 and 2012. We also manually inspected medical records of patients with discharge diagnosis of other pulmonary diseases, to capture patients with respiratory failure that could represent CAP unreported in the Hospital Discharge Records (HDR), and included them in the study whenever appropriate.

Patients admitted from the community including nursing homes were included in the study in accordance with accepted definitions of CAP in the context of the pneumonia triad [27].

Patients diagnosed with nosocomial pneumonia, including patients hospitalized for ≥2 days during the prior 90 days, and immunocompromised patients were excluded. Patients with malignancies in active treatment were excluded (we included patients with malignancies in remission for at least 5 years). Patients whose medical records were not available were also excluded.

Variables

Variables are detailed in Fig. 2.

We investigated performance indicators suggested by Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) consensus guidelines. [28]

Data sources and measurements

Information about patients was gathered through the analysis of medical records, including attached documentation and hospital discharge data, by filling out an ad-hoc dataset. The lead author and last author manually inspected each record, and assessed whether or not the clinical practices were in line with those recommended by the local CAP CP. Any disagreement was resolved by consensus.

Data about 30-day mortality from admission were collected through telephone interview.

(i) Stratification risk and choice of the most appropriate setting of care

Pneumonia Severity Index calculation has to be performed in each patient presenting in A&D Department with signs or symptoms suggestive for CAP, in order to guide clinicians in the choice of the most appropriate site of care:
- I-II PSI* risk class: extra hospital management
- III PSI risk class: treatment in ambulatory setting or short hospitalization
- IV-V PSI risk class: in-hospital management

*PSI Pneumonia Severity Index

(ii) Fundamental diagnostic procedures

Performance of blood culture and urinary antigen tests for S. Pneumoniae and L. Pneumophila are recommended for each patient.

(iii) Empirical antibiotic therapy

First dose of empiric antibiotic therapy has to be performed within 4 hours from access to A&D Department.
The choice of the most appropriate antibiotic scheme might consider clinical aspects defining the following six category of patients:

Category 1: inpatient, non-invasive Care Unit treatment

- Macrolide
- Fluoroquinolone
- ß-lactam + fluoroquinolone or macrolide

Category 2: patient with suspected aspiration from home

- Amoxicilline-clavulanate
- Levofloxacin + clindamicyn/metronidazole

Category 3: patient with suspected aspiration from nursing home or Intensive Care Unit treatment

- ß-lactam (ampicillin/sulbactam or high dose ampicillin or other active ß-lactams) + clindamicyn/metronidazole

Category 4: patient with suspected P. Aeruginosa infection

- Anti-Pseudomonas ß-lactam (piperacillin/tazobactam, cefepime, imipenem or meropenem) + fluoroquinolone ± aminoglycoside
- Anti-Pseudomonas ß-lactam + aminoglycoside + macrolide

Category 5: inpatient, Intensive Care Unit treatment without risk for P. Aeruginosa infection

- ß-lactam + fluoroquinolone
- Fluoroquinolone ± clindamicin

Category 6: inpatient, Intensive Care Unit with risk for P. Aeruginosa infection

- Anti-Pseudomonas ß-lactam (piperacillin/tazobactam, cefepime, imipenem or meropenem) + fluoroquinolone
- Aminoglycoside + fluoroquinolone or macrolide
- Aztreonam + fluoroquinolone ± aminoglycoside

Fig. 1 Main recommendations contained in the local CAP clinical pathway

Statistical methods

We carried out descriptive analyses by testing the difference in proportions of binary mortality outcomes using χ^2 tests and the difference in means of continuous outcomes (length of hospital stay, duration of antibiotic therapy) using Student's *t* tests.

To estimate the independent effects of demographic and clinical characteristics on the outcomes of interests we utilized four multivariable generalized linear models assuming a Binomial distribution of mortality outcomes and a Normal distribution of continuous outcomes (length of hospital stay and duration of antibiotic therapy), including appropriate link functions. Regression models included four binary parameters indicating the compliance with diagnostic procedures such as execution of blood culture and urinary antigen tests, and the compliance with therapeutic interventions such as antibiotic therapy and treatment in intensive care unit (ICU). The models also included eight potential confounders of continuous age, gender, admission from nursing home or own home, presence of comorbidities, presence of criteria for severe CAP as identified by ATS, [28] year of admission to the hospital, stay in a respiratory or non-respiratory ward, performance of mechanical ventilation (MV). For the mortality binary outcomes, all predictor effects were exponentiated to allow interpretation as odds ratio.

(i) personal details and medical history
admission year, admission ward, sex, age, residence at home or nursing home, smoke, anti-Pneumococcal and anti-influenza vaccination
(ii) comorbidities
(iii) radiological characteristics of pneumonia
monolateral or bilateral infiltrates
(iv) presence of pleural effusion or empyema
(v) presence of criteria for severe CAP, as identified by American Thoracic Society [27]
(vi) risk stratification through Pneumonia Severity Index
(vii) diagnostic intervention
procedures aimed to obtain an etiological diagnosis (such as blood culture, urinary antigen tests for S. pneumoniae and L. pneumophila, sputum gram stain and culture, lung brushing or biopsy, bronchoalveolar lavage, bronchial lavage, quantitative endotracheal aspirate, other) and to manage pleural effusion and/or empyema (such as thoracentesis, chest drainage, video assisted thoracic surgery)
(viii) in-hospital therapeutic interventions
timing of administration of the first antibiotic dose, adherence of initial empiric antibiotic therapy to the recommendations of our local clinical pathway (see Figure 1), performance of switch therapy from intravenous to oral therapy, antibiotic therapy duration, oxygen and low molecular weight heparin administration
(ix) in-hospital clinical evolution
need for invasive or non-invasive mechanical ventilation (Mechanical Ventilation), transfer to Intensive Care Unit (ICU)
(x) clinical outcomes
length of hospital stay, in-hospital mortality, 30-day mortality

Fig. 2 Variables in detail

Results

Participants

564 patients were eligible for inclusion, 243 in 2005 and 321 in 2012 (Fig. 3).

Patients were admitted to 11 hospital departments: A&E, cardiology, infectious diseases, ICU, 3 internal medicine divisions, nephrology and dialysis, geriatrics, respiratory, and thoracic surgery.

Information about patients and disease characteristics is illustrated in Tables 1 and 2.

Mean age and proportion of patients with 5 or more comorbidities were both greater in 2012 than 2005 (respectively 75.4 vs. 69.0 years; $p < 0.001$; and 19.3 vs. 9.1 % of patients; $p = 0.001$), despite a significant reduction, in 2012, of proportion of severe CAP as defined by ATS criteria [28] (5.6 % of patients in 2012 vs. 10.7 % in 2005; $p = 0.026$).

Compliance with diagnostic procedures

PSI was reported in 25.2 % of patients in 2012 vs. 17.7 % in 2005 ($p = 0.032$) (Table 3).

Influenza and pneumococcal vaccination was only recorded for one patient.

Urinary antigen tests for *S. pneumoniae* and *L. pneumophila* were performed in a greater percentage of patients in 2012 compared to 2005 (56.4 and 57.6 %, respectively in 2012 vs. 22.6 and 48.6 % in 2005), although there was a significant reduction of other diagnostic tests such as sputum Gram stain and culture, brushings and bronchial lavage in the later year.

Compliance with therapeutic interventions

Compliance with clinical pathway in choice of initial empiric antibiotic therapy was 56.7 % in 2012 vs. 68.8 % in 2005 ($p = 0.004$) (Table 4). The most common

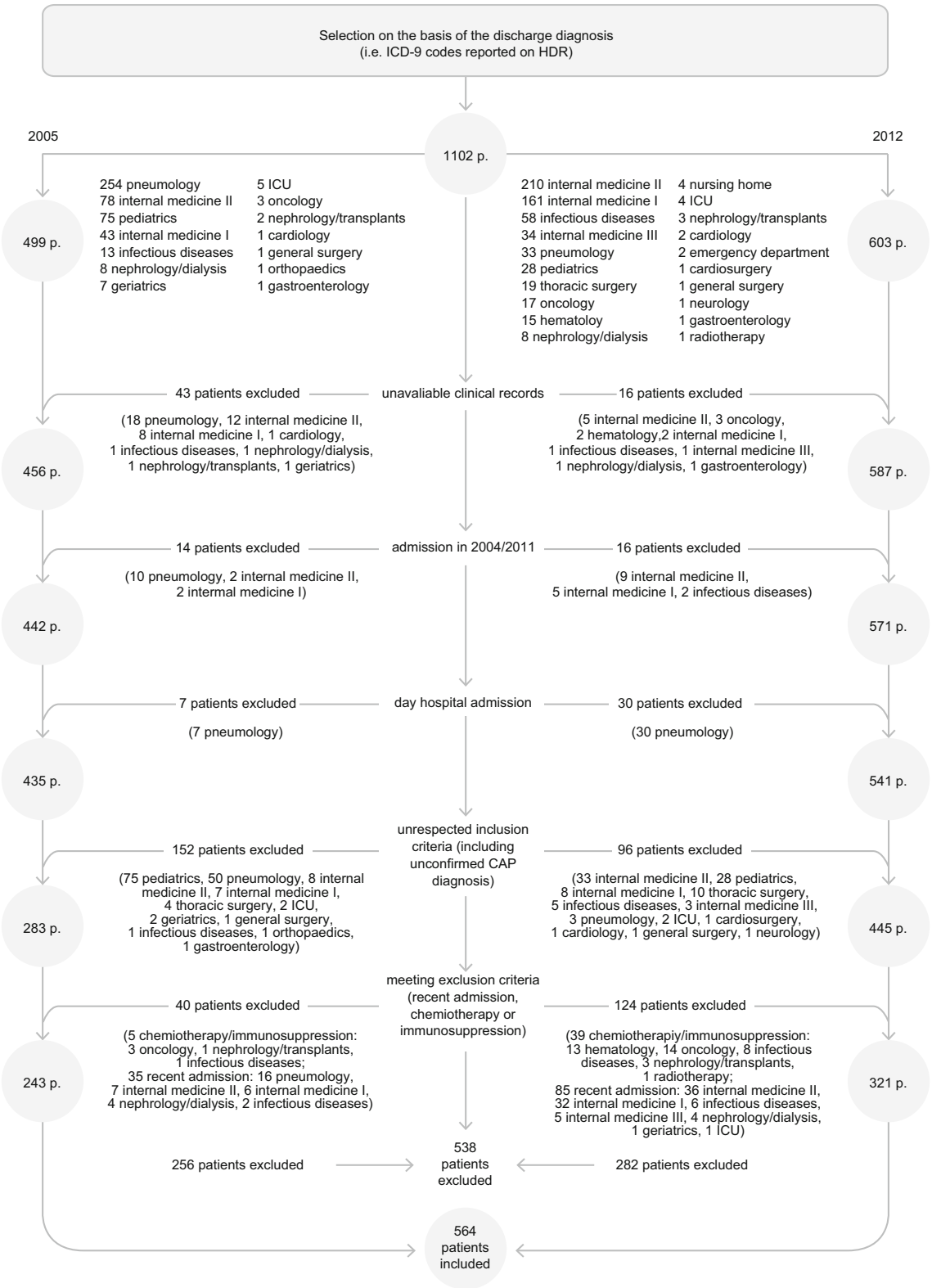

Fig. 3 Flow diagram of patients included and excluded from study. *CAP* community-acquired pneumonia, *HDR* hospital discharge register, *ICU* intensive care unit

Table 1 Socio-demographic and clinical characteristics of the sample

	2005	2012	Total	*p* value
Age in years, mean (SD)	**69.03 (20.69)**	**75.36 (15.58)**	**72.64 (18.22)**	**<0.0001**
Sex, % (*n*)				
Male	57.61 (140)	56.39 (181)	56.91 (321)	0.771
Female	42.39 (103)	43.61 (140)	43.09 (243)	
Admission from, % (*n*)				
Home	90.95 (221)	85.98 (276)	88.12 (497)	0.071
Nursing home	9.05 (22)	14.02 (45)	11.88 (67)	
Smoking, % (*n*)				
Smokers	20.58 (50)	16.20 (52)	18.09 (102)	0.087
Never smokers	38.68 (94)	35.83 (115)	37.06 (209)	
Ex smokers	20.16 (49)	29.28 (94)	25.35 (143)	
Not assessed	20.58 (50)	18.69 (60)	19.50 (110)	
Comorbidity, % (*n*)				
Systemic hypertension	**36.21 (88)**	**51.40 (165)**	**44.86 (253)**	**<0.001**
Ischemic cardiopathy	17.28 (42)	19.00 (61)	18.26 (103)	0.601
Heart failure	19.34 (47)	25.55 (82)	22.87 (129)	0.082
Cerebrovascular disease	**18.11 (44)**	**35.20 (113)**	**27.84 (157)**	**<0.001**
Diabetes mellitus	16.05 (39)	21.18 (68)	18.97 (107)	0.124
Malignancy	**11.52 (28)**	**24.92 (80)**	**19.15 (108)**	**<0.001**
Chronic liver disease	9.05 (22)	11.53 (37)	10.46 (59)	0.342
Chronic kidney disease	13.99 (34)	12.15 (39)	12.94 (73)	0.519
Chronic lung disease	24.69 (60)	28.66 (92)	26.95 (152)	0.293
Non-neoplastic haematological disease[a]	**2.06 (5)**	**6.54 (21)**	**4.61 (26)**	**0.012**
Diseases non otherwise classified	**65.02 (158)**	**76.01 (244)**	**71.28 (402)**	**0.004**
≥5 Comorbidities	**9.05 (22)**	**19.31 (62)**	**14.89 (84)**	**0.001**

In *bold* are the variables for which there is evidence at the 5 % level of a difference between 2005 and 2012

[a] Non-immunosuppressive non-neoplastic haematological disease such as anemia and myelodysplastic diseases

antibiotic treatment schemes in both years were levofloxacin (16.5 % in 2012 vs. 11.5 % in 2005), co-amoxiclav plus macrolide (14.9 vs. 11.5 %) and levofloxacin plus ceftriaxone (10.0 vs. 12.8 %) (data not shown in tables).

There was no evidence of a difference ($p = 0.183$) in the overall duration of antibiotic therapy between the 2 years.

75.7 % of patients admitted in 2012 and 58.9 % of those admitted in 2005 appropriately received oxygen therapy ($p < 0.001$). 9.35 % of patients in 2012 vs. 2.06 % in 2005 ($p < 0.001$) were treated with Mechanical Ventilation (MV): in detail, 9.0 % of patients in 2012 vs. 1.2 % in 2005 ($p < 0.001$) were treated with non-invasive ventilation (NIV), while 1.3 % of patients in 2012 vs. 1.7 % in 2005 ($p = 0.691$) were treated with invasive ventilation.

2.2 % of patients in 2012 vs. 1.7 % in 2005 were treated in ICU ($p = 0.649$).

In-hospital and 30-day mortality

Mortality rates did not change significantly over time. In-hospital mortality was 13.1 % in 2012 and 15.2 % in 2005 ($p = 0.468$). Thirty-day mortality was 15.9 % in 2012 and 19.6 % in 2005 ($p = 0.283$).

Adjusted regression analyses (Table 5) showed that mortality was positively associated with age and severity of pneumonia and negatively associated with performance of urinary antigen tests for *S. pneumoniae* and *L. pneumophila*. Mortality was not associated with to compliance with empirical antibiotic treatment in the CAP clinical pathway.

With each 1 year increase in age there was an 8.1 % increase in odds of in-hospital mortality (95 % CI 4.9–11.4 %) and a 10.5 % increase in odds of 30-days mortality (95 % CI 6.8–14.3 %), while keeping all other predictors constant. Subjects meeting the criteria for severe CAP had 74.3 % greater odds of in-hospital mortality (95 % CI 38.3–119.6 %) and 86.8 % greater odds of 30-day mortality (95 % CI 46.2–138.5 %) compared to subjects not meeting such criteria, while holding all other predictors constant. Performance of urinary antigen test was associated with 42.7 % lower odds of in-hospital mortality (95 % CI 21.5–85.0 %) and 34.1 % lower odds

Table 2 Radiological aspects of pneumonia and criteria for severe CAP

	2005	2012	Total	*p* value
Radiological aspect, % (*n*)				
XR monolateral infiltrates	79.83 (190)	80.70 (255)	80.32 (445)	0.800
XR bilateral infiltrates	20.17 (48)	19.30 (61)	19.68 (109)	
Pleuric effusion	31.69 (77)	30.22 (97)	30.85 (174)	0.708
Pleuric empyema	3.29 (8)	3.12 (10)	3.19 (18)	0.906
Criteria for severe CAP, % (*n*)				
Invasive mechanical ventilation	1.65 (4)	1.25 (4)	1.42 (8)	0.691
Septic shock	2.47 (6)	2.18 (7)	2.30 (13)	0.821
Respiratory rate >30 breaths/min	**7.82 (19)**	**0.93 (3)**	**3.90 (22)**	**<0.001**
paO_2/FiO_2 <250	0.41 (1)	0.62 (2)	0.53 (3)	0.732
Multilobar infiltrates	25.51 (62)	24.30 (78)	24.82 (140)	0.741
Confusion/disorientation	20.16 (49)	19.00 (61)	19.50 (110)	0.730
Uremia (Blood Urea Nitrogen >20 mg/dl)	**26.75 (65)**	**3.12 (10)**	**13.30 (75)**	**<0.001**
Leukopenia (WBC <4000/mm^3)	6.17 (15)	4.36 (14)	5.14 (29)	0.335
Thrombocytopenia (platelets <100,000/mm^3)	8.64 (21)	6.54 (21)	7.45 (42)	0.347
Hypothermia (body temperature <36 °C)	0	0	0	–
Systolic blood pressure <90 mmHg	2.47 (6)	4.05 (13)	3.37 (19)	0.303
Severe CAP as defined by ATS, % (*n*)[a]	**10.70 (26)**	**5.61 (18)**	**7.80 (44)**	**0.026**
At least 1 major criteria	3.29 (8)	3.12 (10)	3.19 (18)	0.906
At least 2 of the first 3 minor criteria	1.23 (3)	2.18 (7)	1.77 (10)	0.399
At least 3 minor criteria	**9.05 (22)**	**2.18 (7)**	**5.14 (29)**	**<0.001**

In *bold* are the variables for which there is evidence at the 5 % level of a difference between 2005 and 2012

[a] American Thoracic Society

of 30-day mortality (95 % CI 17.0–68.5 %) compared to subjects who were not tested for urinary antigens, while holding all other predictors constant.

Association between treatment in the ICU and mortality did not reach statistical significance at the 5 % level. However, treatment in the ICU appears to result in lower odds of both in-hospital mortality (OR 0.5; 95 % CI% CI 0.1–2.8) and 30-day mortality (OR 0.3; 95 % CI 0.1–2.0).

Length of hospital stay and duration of antibiotic therapy

Mean length of hospital stay was 11.5 days in 2012 and 11.7 days in 2005 ($p = 0.831$). Mean duration of antibiotic therapy was 12.8 days in 2012 and 13.7 days in 2015 ($p = 0.183$).

Regression analyses (Table 5) showed compliance with CP antibiotic treatment was associated with shorter mean length of hospital stay (−2.9 days; 95 % CI% CI −4.2 to −1.6 days) and with shorter mean duration of antibiotic therapy (−2.0 days; 95 % CI −3.3 to −0.7 days). Admission from nursing home was associated with 3.2 days shorter mean length of hospital stay (95 % CI −5.2 to −1.2 days) compared with admission from home. Mean duration of antibiotic therapy was 1.1 days shorter for subjects meeting the criteria for severe CAP (95 % CI −1.7 to −0.5 days). With each one year increase in age there was a 0.1 day increase in mean duration of hospital stay (95 % CI 0.02–0.1 days). Factors associated with increased length of hospital stay and the duration of antibiotic therapy were: performance of MV (4.6 days; 95 % CI 1.7–7.6 days; and 5.0 days; 95 % CI 2.1–7.9 days, respectively), admission to ICU (8.4 days; 95 % CI 3.6–13.3 days; and 6.2 days; 95 % CI 1.2–11.3 days, respectively), admission to respiratory ward (4.2 days; 95 % CI 2.2–6.3 days; and 4.4 days; 95 % CI 2.4–6.4 days, respectively) and performance of blood cultures (2.6 days; 95 % CI 1.3–4.0 days; and 2.7 days; 95 % CI 1.4–4.0 days, respectively).

Discussion

Our study aimed to provide an analysis of the clinical experience of a medium sized Italian teaching hospital, which is likely to be similar in other Western-European settings.

Summary of findings

Compliance with clinical pathway. In our hospital, compliance changed over time. PSI calculation was better

Table 3 Adherence to diagnostic procedures and its main findings

	2005	2012	Total	*p* value
PSI (Pneumonia Severity Index) calculation, % (*n*)	**17.70 (43)**	**25.23 (81)**	**21.99 (124)**	**0.032**
I class	4.65 (2)	12.35 (10)	9.68 (12)	
II class	4.65 (2)	8.64 (7)	7.26 (9)	
III class	13.95 (6)	20.99 (17)	18.55 (23)	0.146
IV class	60.47 (26)	37.04 (30)	45.16 (56)	
V class	16.28 (7)	20.99 (17)	19.35 (24)	
History investigation about vaccinations, % (*n*)	0.41 (1)	0	0.01 (1)	0.250
Procedures for etiological diagnosis, % (*n*)				
Blood culture	60.91 (148)	64.17 (206)	62.77 (354)	0.426
Positive	**24.32 (36)**	**9.71 (20)**	**15.82 (56)**	**<0.001**
S. pneumoniae	**2.78 (1)**	**35.00 (7)**	**14.29 (8)**	**0.020**
S. aureus	**2.78 (1)**	**10.00 (2)**	**5.36 (3)**	
Coagulase-negative *Staphylococci*	**66.67 (24)**	**40.00 (8)**	**57.14 (32)**	
Pseudomonas vesicularis	**2.78 (1)**	**0**	**1.79 (1)**	
Enterobacteriaceae	**8.33 (3)**	**5.00 (1)**	**7.14 (4)**	
Saprophytic	**16.67 (6)**	**10.00 (2)**	**14.29 (8)**	
Urinary antigen test for *S. pneumoniae*	**22.63 (55)**	**56.39 (181)**	**41.84 (236)**	**<0.001**
Positive	3.64 (2)	6.08 (11)	5.51 (13)	0.487
Urinary antigen test for *L. pneumophila*	**48.56 (118)**	**57.63 (185)**	**53.72 (303)**	**0.032**
Positive	1.69 (2)	4.32 (8)	3.30 (10)	0.212
Sputum Gram stain	**19.75 (48)**	**0.93 (3)**	**9.04 (51)**	**<0.001**
Sputum culture	**29.63 (72)**	**19.31 (62)**	**23.76 (134)**	**0.004**
Lung brushing or biopsy	**4.94 (12)**	**1.25 (4)**	**2.84 (16)**	**0.009**
Bronchoalveolar lavage (BAL)	4.94 (12)	8.72 (28)	7.09 (40)	0.083
Bronchial lavage (BL)	**10.70 (26)**	**0.31 (1)**	**4.79 (27)**	**<0.001**
Quantitative endotracheal aspirate	1.23 (3)	2.49 (8)	1.95 (11)	0.285
Other	**61.73 (150)**	**45.17 (145)**	**52.30 (295)**	**<0.001**
Procedures for pleural effusion/empyema, % (*n*)				
Thoracentesis	22.35 (19)	14.95 (16)	18.23 (35)	0.187
Chest drainage	9.41 (8)	9.35 (10)	9.38 (18)	0.988
Video-assisted thoracic surgery	37.50 (3)	10.00 (1)	22.22 (4)	0.163

In *bold* are the variables for which there is evidence at the 5 % level of a difference between 2005 and 2012

documented in 2012 compared to 2005, although the proportion of patients that received antibiotic therapy adherent to clinical pathway (CP) was lower in 2012.

Concerning the performance of procedures aimed at obtaining an aetiological diagnosis, urinary antigen tests for *S. pneumoniae* and *L. pneumophila* were significantly increased in 2012 compared to 2005, despite a significant reduction in most other diagnostic tests, and performed in a significantly greater proportion of patients in the respiratory ward than in other wards.

Mortality In-hospital and 30-day mortality did not significantly change over time after adjustment for adherence to CP, although their point estimates were lower in 2012 compared to 2005. In the adjusted regression analyses, age and severity of pneumonia emerged as the only predictors associated with an increased risk of in-hospital and 30-day mortality. Patients who were tested for urinary antigens had lower odds of in-hospital and 30-day mortality. Administration of empirical antibiotic therapy compliance with CP did not have a significant impact on mortality from CAP.

Clinical outcomes Mean length of hospital stay and mean length of antibiotic therapy remained almost unchanged in 2012 and 2005, although they were significantly higher among patients hospitalized in the respiratory ward compared to those treated in other departments. The administration of an empirical antibiotic therapy compliance with CP was associated with a reduction in length of stay and duration of antibiotic therapy. Regression analysis confirmed these observations, and also provided some evidence of an increased mean length of hospital stay and duration of antibiotic therapy associated with execution of blood culture, mechanical ventilation (MV) and treatment in ICU.

Table 4 Adherence to therapeutic interventions

	2005	2012	Total	*p* value
Distribution of patients within clinical categories identified by guidelines % (*n*)				
Inpatient, non-ICU treatment[a]	96.71 (235)	96.26 (309)	96.45 (544)	0.151
Patient with suspected aspiration from home	1.23 (3)	0.62 (2)	0.89 (5)	
Patient with suspected aspiration from nursing home or in ICU treatment	0.41 (1)	1.56 (5)	1.06 (6)	
Patient with suspected *P. aeruginosa* infection	0.41 (1)	1.25 (4)	0.89 (5)	
Inpatient, ICU treatment without risk for *P. aeruginosa* infection	1.23 (3)	–	0.53 (3)	
Inpatient, ICU treatment with risk for *P. aeruginosa* infection	–	0.31 (1)	0.18 (1)	
Antibiotic therapy adherent to guidelines, % (*n*)				
In patients of category 1	**70.26 (163)**	**58.58 (181)**	**63.59 (344)**	**0.005**
In patients of category 2	33.33 (1)	0	20.00 (1)	0.361
In patients of category 3	0	0	0	–
In patients of category 4	0	25.00 (1)	20.00 (1)	0.576
In patients of category 5	33.33 (1)	–	33.33 (1)	–
In patients of category 6	–	0	0	–
Administration of the first antibiotic dose, % (*n*)				
Within 4 h from A&E presentation	**96.00 (24)**	**99.59 (243)**	**99.26 (267)**	**0.047**
Within 4 h from admission to ward	**54.92 (106)**	**69.66 (202)**	**63.77 (308)**	**<0.001**
Switch therapy, % (*n*)	**23.31 (55)**	**30.94 (99)**	**27.70 (154)**	**0.047**
Intra-hospital antibiotic therapy duration in days, mean (SD)	10.71 (7.17)	10.56 (6.39)	10.63 (6.73)	0.7925
Post-discharge prescription duration in days, mean (SD)	**6.20 (2.52)**	**4.79 (2.33)**	**5.39 (2.33)**	**<0.0001**
Antibiotic therapy total duration in days, mean (SD)	13.66 (8.18)	12.78 (6.65)	13.14 (7.33)	0.1825
Oxygen administration, % (*n*)	**58.85 (143)**	**75.70 (243)**	**68.44 (386)**	**<0.001**
MV (mechanical ventilation), % (*n*)	**2.06 (5)**	**9.35 (30)**	**6.21 (35)**	**<0.001**
Administration of low molecular weight heparin, % (*n*)	53.09 (129)	58.88 (189)	56.38 (318)	0.170

In *bold* are the variables for which there is evidence at the 5 % level of a difference between 2005 and 2012

[a] Intensive care unit

Comparison with the literature

Compliance with clinical pathway. The few studies carried out so far suggest that severity scores for pneumonia are rarely used in clinical practice [21, 29, 30]. The results of our study are in accord with those reported in the study by Blasi et al., [6] which shows that in Europe the application of PSI and CURB-65 appears well below the threshold recommended by the guidelines. The most encouraging results emerge from university hospitals, where PSI calculation was done in approximately 30 % of cases, compared with 6 % of cases in non-university hospitals, and CURB-65 calculations in around 40 vs. 14 %.

In line with Dambrava et al. [31] we demonstrate an association between compliance with CP in choice of initial antibiotic therapy and reduced length of hospital stay and the duration of antibiotic therapy.

The use of NIV in patients with CAP, both in the literature and in our study, remains controversial. [32, 33]

Mortality. In-hospital mortality in our sample is in line with European hospital mortality rates (0–17.5 %) [6].

In our study, performance of urinary antigen tests is associated with lower mortality, although performance of blood cultures did not yield similar results. This is difficult to compare with existing literature; as such variables are often estimated in combination. For example, Uematsu et al. [11] in 2014 report that combined performance of blood culture, sputum investigations and urinary antigen tests is associated with a 36 % reduction of 30-day mortality ($p < 0.001$).

Some studies have found lower mortality when antibiotic treatment is compliant with guidelines [15, 17–19]. Menéndez et al. demonstrated that noncompliance is an independent risk factor for treatment failure and mortality [18]. Nevertheless, Dambrava et al. [31] find compliance not to be associated with mortality, also consistent with our findings.

Table 5 Multivariable regression analyses for in-hospital and 30-day mortality, length of hospital stay and duration of antibiotic therapy

	In-hospital mortality		30-day mortality		Length of hospital stay		Duration of antibiotic therapy	
	$N = 561$		$N = 495$		$N = 561$		$N = 505$	
	OR	95 % CI	OR	95 % CI	MD	95 % CI	MD	95 % CI
Socio-demographic characteristics and other potential confounders								
Age in years (continuous)	**1.081**	**1.049, 1.114**	**1.105**	**1.068, 1.143**	**0.052**	**0.016, 0.089**	−0.003	−0.038, 0.033
Male gender (vs. female gender)	0.803	0.454, 1.419	0.628	0.348, 1.133	0.850	−0.424, 2.124	0.411	−0.792, 1.615
Admission from nursing home (vs. from own home)	1.118	0.544,2.300	1.409	0.648, 3.063	**−3.222**	**−5.232, −1.213**	−1.770	−3.619, 0.079
Five or more comorbidities (vs. less than five)	1.601	0.827, 3.102	1.243	0.627, 2.464	1.150	−0.621, 2.921	1.421	−0.233, 3.075
ATS criteria for CAP severity (continuous)	**1.743**	**1.383, 2.196**	**1.868**	**1.462, 2.385**	-0.287	−0.903, 0.329	**−1.111**	**−1.694, −0.527**
Admission in 2012 (vs. admission in 2015)	1.081	0.491, 2.377	0.863	0.387, 1.923	1.297	−0.723, 3.318	0.659	−1.224, 2.541
Stay in a respiratory ward (vs. stay in a non-respiratory ward)	0.847	0.351, 2.042	0.750	0.304, 1.851	**4.225**	**2.152, 6.299**	**4.363**	**2.377, 6.349**
Mechanical ventilation	0.968	0.289, 3.243	1.102	0.340, 3.575	**4.638**	**1.688, 7.587**	**5.017**	**2.115, 7.919**
Adherence to diagnostic procedures								
Blood culture	0.677	0.377, 1.213	0.600	0.328, 1.097	**2.631**	**1.259, 4.003**	**2.728**	**1.417, 4.039**
Urinary Antigen tests	**0.427**	**0.215, 0.850**	**0.341**	**0.170, 0.685**	0.033	−1.407, 1.473	−0.164	−1.535, 1.207
Adherence to therapeutic interventions								
Antibiotic therapy adherent to clinical pathway	0.830	0.468, 1.471	0.957	0.526, 1.738	**−2.868**	**−4.186, −1.550**	**−2.004**	**−3.265, −0.743**
Treatment in ICU	0.452	0.073, 2.817	0.305	0.047, 1.983	**8.409**	**3.547, 13.272**	**6.237**	**1.170, 11.303**

In *bold* are the variables for which there is evidence at the 5 % level of a difference between 2005 and 2012

Clinical outcomes In our study, the average length of hospital stay is in line with the European mean duration documented by Blasi et al. (9.0 days) [6].

Data interpretation

Overall, results from this study showed that clinical practice in our hospital changed over time. Compliance with CP in the choice of empirical antibiotic therapy appeared to be reduced over time, while main diagnostic and therapeutic interventions (i.e. PSI calculation, execution of urinary antigen tests, administration of oxygen therapy) improved.

These mixed results may explain why in-hospital and 30-day mortality did not significantly change in 2012 compared to 2005. Mortality does not appear to be associated with compliance with CP, except for performance of urinary antigen test, but does show association with patient age and CAP severity. It is possible that impact on mortality due to poor compliance with guideline recommended antibiotic therapy could have been cancelled out by improvements in compliance with other diagnostic and therapeutic interventions.

Reduced compliance with CP empiric antibiotic therapy in 2012 compared to 2005 may be due to lack of dedicated resources available for implementation of the clinical guidelines. Although recently in Italy there have been some efforts to promote implementation of clinical guidelines, [34] the frequency and quality of dissemination is still subject to local initiative. A recent Italian study [35] finds that implementation of therapeutic recommendations, including empirical antibiotic therapy, leads to significantly better outcomes of CAP and return to prior health status, especially in more severe cases of CAP.

Limitations of our study

Our study limitations primarily stem from the observational study design, although we have accounted for the most common potential confounders of the association between compliance with CAP CP and clinical outcomes. As in any retrospective study, missing data can influence the effect size of associations as well as their precision. Particularly, the data relating to administration of antibiotics within 4 h from access to A&E, and data about pneumococcal and influenza vaccinations were only partially complete, and such variables could not be accounted for the analyses. However, most variables were carefully recorded and could be included in the analyses.

In 2005 the majority (62.96 %) of CAP patients were treated in the hospital's respiratory ward, while in 2012, due to a hospital-wide reorganisation, all CAP patients were treated in non-respiratory wards. This could have potentially influenced both compliance with CAP CP and the clinical outcomes assessed in our study. However, we have accounted for this potential confounding effect by including ward type in the regression model.

Conclusion

Compliance with CAP guidelines can progressively change over time, suggesting the need for continual efforts to promote compliance with clinical guidelines.

In our study, mortality is not associated with compliance with the clinical pathway, but it is positively associated with patient age and CAP severity, and negatively associated with performance of urinary antigen tests. Compliance with CP empirical antibiotic treatment is associated with a lower length of hospital stay and shorter duration of antibiotic therapy, suggesting overall improvement in clinical care with compliance with the CP. Ongoing and comprehensive approaches to favour guidelines implementation may result in improvement of the overall management of CAP and help to reduce a burden on hospital services.

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Compliance with ethical standards

Conflict of interest The authors declares that they have no conflict of interest.

Statement of human and animal rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study formal consent is not required.

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