

Patients Admitted to Hospital with Suspected Pneumonia and Normal Chest Radiographs: Epidemiology, Microbiology, and Outcomes

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PURPOSE: To describe the prevalence of patients admitted to hospital with a diagnosis of community-acquired pneumonia who have normal chest radiographs; the extent to which patients actually had pneumonia on radiographs; and to compare presentation and outcomes in patients with a lower respiratory tract infection and those whose clinical diagnosis of pneumonia was confirmed by radiography.

METHODS: We studied a population-based cohort of 2706 adults who were admitted with suspected pneumonia and managed using a clinical pathway. We stratified patients by presence or absence of radiograph-confirmed pneumonia, and compared their characteristics and in-hospital mortality. We also performed an independent review of a 10% sample of "normal" chest radiographs and classified them according to the presence or absence of pneumonia.

RESULTS: One third ($n = 911$) of patients admitted with pneumonia had their initial radiograph reported as "no pneumonia." Independent review found that only 7% (6/92) of radiographs developed an opacity that confirmed pneumonia. Characteristics were similar among admitted patients irrespec-

tive of radiographic findings, although patients without pneumonia on radiograph were older (mean [$\pm$ SD] age, 73 ± 15 years vs. 68 ± 19 years, $P < 0.001$) and had greater pneumonia-specific severity-of-illness scores (104 ± 32 vs. 99 ± 37 , $P = 0.004$). Patients without radiographic confirmation of pneumonia had similar rates of positive sputum cultures (32% [87/271] vs. 30% [208/706], $P = 0.42$) and blood cultures (6% [35/576] vs. 8% [100/1241], $P = 0.13$), but microbiology results differed, with a shift away from *Streptococcus pneumoniae* towards other streptococci species and gram-negative aerobic bacilli. In-hospital mortality was similar for both groups of patients (8% [64/911] in the unconfirmed pneumonia group vs. 10% [165/1795] in the confirmed group, adjusted $P = 0.09$).

CONCLUSION: One third of patients suspected of having pneumonia and admitted to hospital did not have pneumonia, but had serious lower respiratory tract infections with substantial rates of bacteremia and mortality. The absence of radiographic findings should not supercede clinical judgment and empiric treatments in these patients. *Am J Med.* 2004;117:305–311. ©2004 by Elsevier Inc.

Community-acquired pneumonia is the sixth leading cause of death in the United States and accounts for at least 600,000 hospital admissions each year (1,2). The majority of pneumonia-related morbidity, mortality, and health care expenditures occur among persons who are hospitalized at some point during their illness, making this group a key point of focus for studies of pneumonia (3–7). In an effort to improve quality of care and decrease unnecessary practice variations, a number of guidelines have been published to standardize

the diagnosis and treatment of this common disease (3–6).

Patients with pneumonia present with a spectrum of symptoms and signs. The clinical diagnosis includes combinations of fever, cough, sputum production, dyspnea, and physical findings suggestive of consolidation such as dullness on percussion and bronchial breathing (8–10). However, a systematic review of the utility of the clinical examination in diagnosing community-acquired pneumonia concluded that there were no combinations of the history and physical examination that could reliably confirm or refute the presence of pneumonia (10). Thus, at least for the purposes of research and disease epidemiology, chest radiography is required to confirm the presence of pneumonia (8,10–12).

Nevertheless, many patients who present with symptoms or findings suggestive of community-acquired pneumonia lack the necessary corroborating radiographic evidence at the time of presentation (9). These patients are often "clinically" diagnosed with pneumonia and are treated as such. Patients presenting with a serious lower respiratory tract infection (i.e., those suspected on clinical grounds of having community-acquired pneumonia but without chest radiography abnormalities sug-

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gestive of pneumonia) have not been well described. Indeed, these patients, by virtue of the absence of confirmatory radiographic findings, have been systematically excluded from randomized trials of treatment and from outcomes studies (8,10,12,13).

Therefore, we undertook the current study in a large population-based prospective cohort, with three main objectives in mind: to describe the prevalence of patients admitted to hospital with a diagnosis of community-acquired pneumonia and no evidence of pneumonia on initial chest radiography; to determine the extent to which the chest radiographs actually had abnormalities; and to compare the clinical presentation and outcomes of patients with and without a diagnosis of pneumonia confirmed by chest radiography.

METHODS

Subjects and Setting

Capital Health (Edmonton, Alberta) is considered one of the largest integrated health systems in Canada (14). It serves approximately 1 million people and has an annual health budget of almost 2 billion Canadian dollars (14). From November 15, 2000, to November 14, 2001, 2706 adults were admitted with a clinical diagnosis of pneumonia by 318 physicians to six regional hospitals (two tertiary care hospitals, two hospitals that provided secondary and some tertiary care, and two smaller community hospitals). This study was approved by the Institutional Health Research Ethics Board at the University of Alberta.

Starting on November 15, 2000, a "pneumonia critical pathway" was implemented at all hospitals in the Capital Health region. Patients 17 years of age or older were enrolled in the pathway if they presented to one of the study hospitals and were clinically diagnosed with community-acquired pneumonia of sufficient severity to require hospital admission. Patients were excluded if they had physician-diagnosed or suspected aspiration pneumonia, tuberculosis, or cystic fibrosis; were immunosuppressed (e.g., human immunodeficiency virus infection, current use of >10 mg/d of prednisone or other immunosuppressive agents, active treatment for cancer, history of organ transplantation, or pregnant or nursing); or required direct admission to the intensive care unit.

Regional Critical Pathway for Inpatients with Community-Acquired Pneumonia

Based on previously published work (13), a validated critical pathway for the management of pneumonia was developed with the goal of improving the quality and efficiency of care. A multidisciplinary team consisting of infectious disease specialists (including TJM), general internists (including SRM), respirologists, emergency medicine specialists, family physicians, pharmacists, nurses,

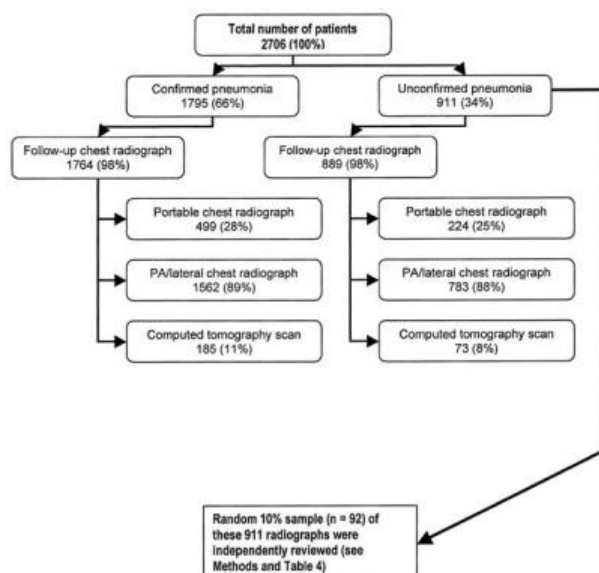


Figure. Flowchart of diagnostic imaging studies undertaken after admission to hospital in 2706 patients with suspected community-acquired pneumonia. PA = posteroanterior.

respiratory therapists, and dieticians developed and implemented the pathway at all regional hospitals. In summary, after initial triage and assessment in the emergency department, an inpatient physician was consulted for hospital admission. Patients were evaluated, and the pneumonia severity-of-illness score was calculated using the patient's age, sex, comorbid illnesses, physical findings, and laboratory results (11,12). Patients were given a pneumonia severity-of-illness risk class of I to V based on the method of Fine et al (12). Risk classes IV and V generally received inpatient care, although patients were admitted or discharged home from the emergency department based on the clinical judgment of the attending physicians. Once the admission decision was made, the pathway provided standardized management orders, algorithms for the prescription and discontinuation of antibiotics and oxygen therapy, and guidelines for discharge. Adherence to any aspect of the pathway itself was entirely voluntary and at the discretion of the responsible physician. Thus, for example, whether or not sputum cultures were collected, a follow-up radiograph was ordered, or an alternate diagnosis was pursued was left to the treating physicians. Six trained research nurses assisted with pathway implementation and prospectively collected standardized data on all inpatients.

Chest Radiograph Review

Of the 2706 patients who had an initial chest radiograph, 2653 (98%) had at least one follow-up radiograph within 72 hours of hospital admission (Figure). There was no difference in ascertainment of follow-up radiographs in patients with confirmed (98% [1764/1795]) or unconfirmed (98% [889/911]) pneumonia. We undertook an

independent review of a 10% random sample of all patients hospitalized with suspected community-acquired pneumonia whose chest radiographs were reported as not having abnormalities consistent with pneumonia. A standardized data abstraction form was used to record the presence of any radiographic abnormalities. A new opacity within 72 hours of admission was considered evidence that the illness triggering the admission was pneumonia (8,10,13).

Measurements

The main variable of interest was the presence or absence of radiograph-confirmed pneumonia in patients admitted to hospital with a clinical diagnosis of community-acquired pneumonia. Hereafter, we refer to those patients with radiograph-confirmed pneumonia as the “confirmed” group and those without radiographic confirmation of pneumonia as the “unconfirmed” group.

Extensive prospective data were collected on all patients, including sociodemographic data, clinical information (e.g., symptoms, signs, pneumonia severity-of-illness scores, and laboratory values), microbiology results, official radiography reports, and outcomes such as length of stay and in-hospital mortality.

Statistical Analysis

We present descriptive statistics, stratified by the presence or absence of radiographic confirmation of pneumonia. Chi-squared tests were used for nonparametric data, and *t* tests were used for parametric data. To assess differences in in-hospital mortality according to the presence or absence of radiographic abnormalities, multivariate logistic regression models were used, adjusted for age, sex, site of treatment, pneumonia severity-of-illness score, and any sociodemographic and clinical variables that differed at a *P* value ≤ 0.10 . We present adjusted odds ratios and their 95% confidence intervals, and considered a two-tailed *P* value < 0.05 to be statistically significant. Analyses were performed using SPSS 11.5 (SPSS, Chicago, Illinois).

RESULTS

Over 1 year, a total of 2706 patients with clinically suspected community-acquired pneumonia were admitted to our hospitals and enrolled in the pneumonia pathway. Of these patients, 1795 (66%) had radiograph-confirmed pneumonia and 911 (34%) did not have radiographic confirmation of the disease. Only 53 patients (2%) in the cohort did not have at least one follow-up chest radiograph after admission (Figure).

Patients with unconfirmed pneumonia were older than those with radiograph-confirmed pneumonia (mean $\pm$ SD age, 73 ± 15 years vs. 68 ± 19 years, *P* < 0.001) (Table 1). They also had more severe illness (pneumonia severity-of-illness score, 104 ± 32 vs. $99 \pm$

37 , *P* = 0.004). In the unconfirmed pneumonia group, 14% of patients (*n* = 128) were considered to be at low risk (risk class I-II) of mortality or complications compared with 22% of those with confirmed pneumonia (*n* = 395). Most patients (89% [2408/2706]) had at least one pulmonary symptom of cough, shortness of breath, sputum production, or wheezing. There was no difference in the presence of pulmonary symptoms according to radiographic findings (90% [*n* = 816] in the unconfirmed group vs. 89% [*n* = 1592] in the confirmed group, *P* = 0.49). There were few clinically important features that distinguished patients with radiographic confirmation of pneumonia from those without radiographic confirmation.

Laboratory Tests

There were few laboratory tests that appreciably distinguished these patients (Table 1). In particular, based on the serum levels of blood urea nitrogen and creatinine at presentation, patients without radiographic confirmation of pneumonia were not more likely to be intravascular volume depleted than those with radiographic confirmation.

Microbiology of Blood and Sputum Cultures

The microbiologic results of sputum samples and blood cultures demonstrated some significant differences between unconfirmed and confirmed patients (Tables 2 and 3). Blood cultures were obtained from about two thirds (1817/2706) of patients (Table 2), and positivity rates were similar in unconfirmed and confirmed patients (6% [35/576] vs. 8% [100/1241], *P* = 0.13). However, the relative frequency of pathogens isolated from the two groups differed. For example, *Streptococcus pneumoniae* bacteremia accounted for 14% (5/35) of all positive blood cultures in unconfirmed pneumonia patients compared with 64% (64/100) of positive cultures in confirmed patients (*P* < 0.001). Conversely, gram-negative bacteremias were much more common in the unconfirmed pneumonia group.

An organism was isolated from the sputum samples in about a third of cases (295/977) (Table 3). Most organisms would be considered typical for respiratory tract infections. In contrast to the findings for blood cultures, we observed no significant differences in the percentages of organisms cultured from the sputum of unconfirmed and confirmed pneumonia patients. *S. pneumoniae*, *Staphylococcus aureus*, *Hemophilus* species, and *Moraxella catarrhalis* accounted for the vast majority of all positive sputum cultures in either group of patients.

Diagnostic Imaging

The majority of radiographs (92% [1643/1795]) in the confirmed pneumonia group revealed a lower lobe infiltrate, and about one quarter (*n* = 425) had an associated pleural effusion. In the independent review of a 10% ran-

Table 1. Sociodemographic, Clinical, and Laboratory Characteristics of the 2706 Patients Admitted to Hospital with Suspected Community-Acquired Pneumonia

Characteristic	Confirmed Pneumonia (n = 1795)	Unconfirmed Pneumonia (n = 911)	P Value
	Mean $\pm$ SD or Number (%)		
Age (years)	68 $\pm$ 19	73 $\pm$ 15	<0.001
Male sex	946 (53)	465 (51)	0.43
Admitted from home	1361 (76)	708 (78)	0.50
Aboriginal Canadian	74 (4)	24 (3)	0.05
Current smoker	464 (29)	195 (24)	0.02
Current substance abuse	96 (5)	18 (2)	<0.001
Pneumonia severity index score	99 $\pm$ 37	104 $\pm$ 32	0.004
Fever	789 (44)	393 (43)	0.69
Shaking chills	414 (23)	180 (20)	0.05
Cough	1274 (71)	672 (74)	0.13
Shortness of breath	1199 (67)	661 (73)	0.002
Sputum production	817 (46)	452 (50)	0.04
Hemoptysis	114 (6)	25 (3)	<0.001
Pleurisy	206 (12)	69 (8)	0.001
Wheezing	345 (19)	246 (27)	<0.001
Crackles on auscultation	683 (38)	331 (36)	0.38
Nausea	263 (15)	106 (12)	0.03
Vomiting	260 (15)	93 (10)	0.06
Abdominal pain	63 (4)	28 (3)	0.55
Diarrhea	114 (6)	41 (5)	0.05
Chronic obstructive pulmonary disease	322 (18)	198 (22)	0.02
Liver disease	67 (4)	13 (1)	0.001
Heart failure	280 (16)	185 (20)	0.002
Hemoglobin (g/dL)	12.4 $\pm$ 2.0	12.8 $\pm$ 2.0	<0.001
White blood cells ($\times 10^3/\mu\text{L}$)	14 $\pm$ 15	13 $\pm$ 22	0.02
Neutrophils ($\times 10^3/\mu\text{L}$)	11 $\pm$ 7	9 $\pm$ 5	<0.001
Blood urea nitrogen (mg/dL)	25 $\pm$ 20	22 $\pm$ 17	0.45
Creatinine (mg/dL)	1.3 $\pm$ 1.0	1.2 $\pm$ 0.9	0.67
Po ₂ (mm Hg)	65 $\pm$ 24	66 $\pm$ 27	0.25
Pco ₂ (mm Hg)	38 $\pm$ 11	40 $\pm$ 11	0.006

Pco₂ = partial pressure of carbon dioxide; Po₂ = partial pressure of oxygen.

dom sample (92/911) of “normal” chest radiographs for patients with unconfirmed pneumonia (Figure), 7% of radiographs (n = 6) were completely normal, while 87% (n = 80) showed some nonpneumonia-related radiographic abnormality (Table 4), such as chronic obstructive pulmonary disease, heart failure, and atelectasis. Only six radiographs (7%) had any opacities consistent with pneumonia demonstrated within 72 hours of presentation.

Outcomes

Patients with radiographic confirmation of pneumonia had an appreciable risk of in-hospital mortality (10% [165/1795]), although patients without radiographic confirmation of pneumonia had a similar mortality risk (8% [64/911]). In multivariate logistic regression models that adjusted for potentially confounding variables, including pneumonia-specific disease severity, these differ-

ences in mortality were not significant (odds ratio = 1.4; 95% confidence interval: 0.95 to 2.1; $P = 0.09$).

DISCUSSION

In a large prospective cohort of patients admitted to hospital with a clinical diagnosis of pneumonia, we found that one third of patients did not have radiographic confirmation of this diagnosis. In fact, of the chest radiographs read as “no pneumonia” by the radiologist, only 7% (6 of 92 sampled) had opacities consistent with pneumonia. Thus, by the currently accepted definition, 93% of these patients did not have pneumonia; rather, they most likely had a serious lower respiratory tract infection. There were few sociodemographic or clinical characteristics that distinguished patients with a serious lower respiratory tract infection from patients with confirmed pneu-

Table 2. Results of the 1817 Blood Cultures Obtained from the 2706 Patients Admitted to Hospital with Suspected Community-Acquired Pneumonia

Results	Confirmed Pneumonia (n = 1795)	Unconfirmed Pneumonia (n = 911)	P Value
	Number (%)		
Blood cultures performed	1241 (69)	576 (63)	0.002
Blood cultures positive	100 (8)	35 (6)	0.13
Organisms cultured			
<i>Streptococcus pneumoniae</i>	64 (64)	5 (14)	<0.001
Other <i>Streptococcus</i> species	2 (2)	8 (23)	<0.001
<i>Staphylococcus aureus</i>	14 (14)	5 (14)	0.97
<i>Enterococcus</i> species	0	3 (9)	0.02
<i>Hemophilus influenzae</i>	1 (1)	0	1.0
Gram-negative aerobic bacilli	14 (14)	14 (40)	0.001
Anaerobes	5 (5)	0	0.32

monia. In fact, these patients had a greater severity of illness than, and similar mortality to, patients with radiographically confirmed disease.

The major difference that we observed between patients with and without pneumonia as defined by chest radiograph was in the microbial spectrum. *S. pneumoniae*, which accounted for 64% of infections associated with bacteremia in the confirmed group, was present in only 14% of the unconfirmed group with bacteremia, although the overall rates of bacteremia were similar. There was also a shift away from the more commonly reported organisms (3–7) towards nonpneumococcal streptococci and gram-negative aerobic bacilli such as *Escherichia coli*. According to the results of sputum cultures, the microbial spectrum of both groups of

patients was similar to that usually cited (3–7). It may be that empirical treatment strategies need to be reconsidered for patients who present with a serious lower respiratory tract infection but without radiographic abnormalities of pneumonia.

The chest radiograph has been used as the reference standard for the diagnosis of pneumonia in most (15) but not all (9) previous studies. Nevertheless, technical limitations as well as interobserver and intraobserver variability in the interpretation of chest radiographs of patients with possible pneumonia are well known (8,15). For example, in a study involving 15 patients with pneumonia, a panel of 3 radiologists agreed with the original radiologist on the diagnosis 87% of the time, whereas 21

Table 3. Results of the 977 Sputum Cultures Obtained from the 2706 Patients Admitted to Hospital with Suspected Community-Acquired Pneumonia

Results	Confirmed Pneumonia (n = 1795)	Unconfirmed Pneumonia (n = 911)	P Value
	Number (%)		
Sputum cultures performed	706 (40)	271 (30)	<0.001
Sputum cultures positive	208 (30)	87 (32)	0.42
Organisms cultured*			
<i>Streptococcus pneumoniae</i>	73 (35)	22 (25)	0.10
Other <i>Streptococcus</i> species	16 (8)	3 (3)	0.18
<i>Staphylococcus aureus</i>	32 (15)	16 (18)	0.52
<i>Enterococcus</i> species	4 (2)	2 (2)	0.83
<i>Hemophilus</i> species	47 (23)	24 (28)	0.36
<i>Moraxella catarrhalis</i>	16 (8)	10 (11)	0.29
Gram-negative aerobic bacilli	39 (19)	16 (18)	0.94
Anaerobes	8 (4)	6 (7)	0.26
Miscellaneous [†]	3 (1)	4 (5)	0.10

* Because some samples grew more than one organism, there are more organisms than the total number of sputum cultures.

† Includes *Aspergillus* species, *Nocardia* species, and *Pneumocystis carinii*.

Table 4. Results of an Independent Review of 92 Chest Radiographs from 911 Patients Admitted to Hospital with Suspected Community-Acquired Pneumonia Whose Initial Chest Radiographs Were Reported as “No Pneumonia”

Findings	Number (%)
Normal radiograph	6 (7)
Pneumonia present	6 (7)
Other abnormalities present*	80 (87)
Chronic obstructive pulmonary disease	31 (34)
Heart failure	17 (18)
Atelectasis	17 (18)
Pleural effusion	14 (15)
Granulomatous disease	7 (8)
Interstitial lung disease	4 (4)
Coronary bypass surgery	4 (4)

* Patients could have more than one abnormality present on the radiograph.

internists agreed with the original radiologist only 72% of the time (8). In one study that did not require a positive chest radiograph for the diagnosis of pneumonia (rather, the investigator’s definition was an acute lower respiratory tract infection with new focal findings on chest examination that required treatment with antibiotics), 60% (93/236) of patients never developed radiographic findings consistent with pneumonia (9). However, only 22% of this cohort required admission to hospital, whereas we studied only inpatients. Thus, these findings are not directly comparable with ours.

The vast majority (87%) of patients in the unconfirmed pneumonia group did have radiographic findings on diagnostic imaging. These abnormal findings, however, were not necessarily suggestive of pneumonia and included chronic obstructive pulmonary disease, heart failure, or atelectasis. These findings may indicate the existence of underlying lung pathologies or predisposing illnesses in the unconfirmed group, very early atypical changes related to pneumonia, or even misdiagnosis. It is particularly noteworthy that only 7% of the patients with suspected pneumonia and “normal” chest radiographs developed an opacity that was consistent with the diagnosis of pneumonia. In a study in which simultaneously obtained high-resolution computed tomographic scans of the chest and chest radiographs were compared in 47 patients presenting with presumed community-acquired pneumonia, scanning identified all 18 cases that were apparent on chest radiograph as well as an additional 8 cases, indicating that 31% of their radiograph-confirmed pneumonias were not initially identified by chest radiography (16).

Should all patients with a serious lower respiratory tract infection and normal chest radiographs undergo further imaging, for example, with high-resolution computed tomography (15–17)? For clinical purposes, radio-

logic confirmation of pneumonia would unlikely have changed management or improved outcomes in our sample because patients were clinically diagnosed and risk stratified, and managed according to a standardized pneumonia pathway. Still, there is little evidence to support this statement, and further study is needed to examine whether additional imaging improves processes of care or outcomes, and whether routine additional diagnostic imaging is feasible or cost-effective (15).

We found that the clinical presentation and outcomes were similar for patients, irrespective of the presence of radiographic confirmation of pneumonia. Although it appeared that patients with confirmed disease might have had higher in-hospital mortality, this was not the case after adjustment for potentially confounding variables. This would suggest that the absence of typical radiographic findings in a patient with clinical findings suggestive of severe pneumonia should not necessarily play an important part in management issues regarding empiric treatment or the decision to admit to hospital. It is possible that the difficulty in diagnosing “pneumonia” in the absence of a confirmatory chest radiograph led to a delay in treatment and hospitalization, and contributed to the somewhat higher than expected mortality, among patients with lower respiratory tract infection. Unfortunately, our data do not allow us to further explore this hypothesis.

There are several limitations that need to be considered when interpreting our results. First, the diagnostic label of “serious lower respiratory tract infection” that we applied to our sample of patients without radiographic confirmation of pneumonia may be questioned. However, the following findings attest to the diagnosis: all patients presented with acute illness, 89% had respiratory symptoms and signs that were sufficient to require hospital admission and placement on a pneumonia critical pathway, treatment involved antibiotics directed at pulmonary pathogens, and there was no (at least at presentation) convincing alternate or competing diagnosis. Second, we did not collect sputum and blood cultures from every patient. These, as well as other tests and management decisions, were only suggested by the pathway and left to the discretion of the attending physicians. Third, we reviewed only a 10% random sample of the “normal” radiographs, which could reflect a biased or nonrepresentative sample. Fourth, there were no data on the clinical course or mortality of patients after they were discharged. Finally, although these population-based data were drawn from six hospitals in one region in Canada, our results may not be generalizable to other settings or other countries.

With these limitations in mind, we conclude that one third of all patients with clinically suspected pneumonia do not actually have pneumonia. Rather, they have a serious lower respiratory tract infection with associated

high rates of bacteremia and substantial mortality. Further study of this population is clearly warranted, and our results may have implications for both researchers (in terms of future definitions of pneumonia) and for guideline framers (in terms of empiric management recommendations for this group of patients). Hopefully, our findings will help clinicians to better appreciate the severity of illness and mortality associated with a clinical suspicion of pneumonia irrespective of the presence of radiographic findings.

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