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Reliability of radiographic findings and the relation to etiologic agents in community-acquired pneumonia

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KEYWORDS Radiograph; CAP; Pneumonia; Infection **Summary** In a clinical setting the chest radiograph is the reference standard in establishing the diagnosis of community-acquired pneumonia (CAP). This study aimed to assess interobserver reliability (IR) of radiographic findings and the relationship to different causative pathogens in CAP.

Chest radiographs of 192 patients with pneumonia, obtained from a database, were reviewed by 2 radiologists and 1 respiratory physician without specific clinical information. Main pattern of infiltrate, extent of pneumonia, presence of pleural fluid, thickened bronchial walls, lymphadenopathy and air bronchogram were scored. Also, the involved lobes were identified. Sputum cultures, blood cultures and serological tests were performed to identify the causative pathogen.

IR was poor (kappa <0.4) for determining the main pattern of infiltrate and presence of air bronchogram, lymphadenopathy and thickening of bronchial walls. IR was fair to good (kappa 0.4–0.7) or even excellent (kappa > 0.7) for determining the presence of pleural effusion, the extent of pneumonia and for identifying the lobes involved. *Mycoplasma pneumoniae* was associated more often with patchy alveolar opacities than *Streptococcus pneumoniae* (P = 0.05). *Chlamydia* spp. were associated with unilobar involvement (86%), especially when compared to *M*. *Pneumoniae* (P = 0.03) and *S. pneumoniae* (P = 0.004).

In conclusion, simple features such as presence of pleural fluid, the extent of pneumonia and identifying the involved lobes show fair to excellent IR. Other features such as main pattern of infiltrate are difficult to assess and show poor IR. Hardly any relation between different pathogens and radiological features was found. Therefore, chest radiographs are of limited value in predicting the causative pathogen, but are of good use to determine the extent of pneumonia and to detect complications such as parapneumonic effusion. © 2005 Elsevier Ltd. All rights reserved.

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Introduction

Pneumonia is an inflammation of 1 or both lungs caused by a bacterial, viral or other pathogen. Community-acquired pneumonia (CAP) is contracted outside the hospital and is often preceded by a viral respiratory infection. Most episodes of (suspected) CAP are treated outside the hospital by general practitioners without further investigation. However, presenting symptoms and signs of CAP vary considerably which makes it difficult to establish the diagnosis by history taking and physical examination.¹⁻⁴ Once a patient is referred to the hospital chest radiography becomes the reference standard in establishing the diagnosis of CAP. Interpreting a chest radiograph requires the necessary skills and can be hindered by other diseases that mimic CAP. Interobserver variability for the presence or absence of pneumonia on chest radiograph varies between different studies from poor to good.^{5–7} Where Melbye and $Dale^5$ found that increasing experience contributes to better interobserver agreement, others did not.⁶

Once the diagnosis of pneumonia has been established the physician's main interest is to identify the causative pathogen in order to ensure optimal treatment. CAP may cause a number of patterns on chest radiograph such as alveolar, patchy alveolar, interstitial and mixed alveolo-interstitial patterns. Also features like air bronchogram, thickened bronchial walls and pleural fluid can be observed in some cases. It is not clear whether these specific findings on chest radiography are related to different causative pathogens. Albaum et al.⁷ investigated the interobserver reliability (IR) of chest radiograph for specific radiological patterns in patients with established CAP. Fair to good IR was found for pleural effusions and multilobar disease. However, poor IR was found for the pattern of the pulmonary infiltrate and the presence of air bronchograms.

Several authors have tried to relate radiographic patterns and their extent to different causative pathogens such as bacteria, viruses and atypical bacteria.^{8–19} Yet, no prospective investigation has been carried out to assess the correlation between patterns of pulmonary infiltrates and causative pathogens in CAP.

The aims of this study were to investigate the IR of radiographic findings in patients with CAP and to investigate the relationship of different radiological features with causative pathogens.

Methods

Population

One hundred and ninety-six patients with CAP admitted at the department of pulmonary disaese of a large university hospital (1988–1992) were identified from a database. Chest radiography was performed in all patients on the day of admission. Age, sex and results of sputum, blood cultures and other microbial investigations such as serological testing, broncho-alveolar lavage and aspiration of pleural effusion were obtained from patient files.

Interpretation of chest radiographs

One hundred and ninety-six anterior/posterior or posterior/anterior views and 130 lateral views were obtained from the radiology archives. The chest radiographs were analyzed by 3 independent reviewers: 2 experienced radiologists (reviewers 1 and 2) and 1 experienced respiratory physician (reviewer 3). The reviewers were unaware of the patient's clinical data or the results of other diagnostic procedures. The radiographs were assessed according to protocol. First the type of infiltrate was identified as mainly lobar opacities, mainly patchy alveolar opacities, mainly interstitial opacities or mixed alveolar-interstitial opacities. Also, the radiographs were assessed for the presence of air bronchogram (yes, no, uncertain), presence of pleural effusion (yes, no, uncertain) and presence of lymphadenopathy (yes, no, uncertain). The extent of infiltrate was evaluated by identifying all involved lobes and the number of involved lobes (confined to 1 lobe, more than 1 lobe).

Different patterns of infiltrate were defined as described before.^{7,20-22} An alveolar infiltrate was defined as disease affecting the terminal air space characterized by a lobar or segmental distribution with a tendency to coalesce. Patchy alveolar infiltrate was defined as alveolar infiltrate with a non-continuous patchy distribution. An interstitial infiltrate was defined as disease in the connective tissue compartment with increased perivascular markings or peribronchial cuffing, with reticular or small irregular opacities present. Lymphadenopathy was defined as enlarged hilar lymph nodes. Air bronchogram, originally described by Fleischner,²³ was defined as a radiographic shadow of an air containing bronchus peripheral to the hilum and surrounded by airless lung.²¹

Microbiological analysis

Adequate sputum samples were collected if possible and sent to the microbiology laboratory for Gram's stain and culture. Sputa with >25 polymorphonuclear leucocytes and <10 squamous epithelial cells per low power field of a Gram's stain were defined as representative.²⁴ Representative sputa were cultured in a semiquantitative manner.^{25,26} If pleural effusion was present, thoraccentesis was performed and a sample was sent to the laboratory for Gram's stain and culture. In patients with fever of >38.5 °C, 3 blood samples were drawn. If indicated, serological tests were performed to screen for *Mycoplasma pneumoniae*, *Legionella pneumophila* and *Chlamydia* spp.

Statistical analysis

The percentage of interobserver agreement was measured for every feature. IR was tested by kappa statistics. A kappa of <0.4 indicates poor agreement, a kappa between 0.4 and 0.75 indicates fair tot good agreement and a kappa greater than 0.75 indicates excellent agreement between reviewers.²⁷ Correlation between radiographic patterns, identified by a majority of reviewers (2 out of 3), and etiologic agents was assessed with the Pearson chi-square test. If more than 20% of expected values was <5, Fisher's exact test was used. A *P*-value of <0.05 was considered statistically significant.

Results

Chest radiographs of the 196 consecutive patients were collected; 4 were excluded because their radiographs were not observed by all 3 radiologists. Characteristics of the remaining 192 patients are presented in Table 1. One hundred and fifteen (60%) were men and the mean age was 52 (19–89) years. Forty-five (23%) of CAP were caused by *Streptococcus pneumoniae*, 24 (13%) by *M. pneumoniae*, 21 (11%) by *Chlamydia* spp., 4 (2%) by *Haemophilus influenzae* and 5 (3%) by other pathogens. In 8 cases (4%) more than 1 pathogen was isolated and 68 (34%) pneumonias were of unknown etiology.

Table 2 shows the frequencies of positive results identified by each reviewer. The majority of pulmonary infiltrates (72–90%) were lobar alveolar opacities. Mixed alveolar–interstitial and interstitial patterns were hardly observed. Air bronchogram was identified in 26–50% of patients. The presence of thickened bronchial walls was very Table 1Patient characteristics.

Characteristics	No. (%)
Age, years*	51.8 (19–89)
Sex Male Female	115 (60) 77 (41)
Chest radiograph AP or PA view Lateral view	192 (100) 126 (65)
Etiologic agent Streptococcus pneumoniae Mycoplasma pneumoniae Chlamydia spp. Legionella pneumophila Haemophilus influenzae Other, one pathogen Mixed pathogens Unknown	45 (23) 24 (13) 21 (11) 17 (9) 4 (2) 5 (3) 8 (4) 68 (34)

AP, anterior/posterior; PA, posterior/anterior. *Mean (range).

variable among the reviewers (2-23%). Most pneumonias were confined to 1 lobe (53-61%) and the lower lobes were predominantly affected. Pleural fluid was present in 10-24% of patients and lymphadenopathy in 2-27%.

IR is presented in Table 3. IR for determining the pattern of the infiltrate, presence of air bronchogram and thickening of bronchial walls was poor throughout (kappa <0.4). Extent of pneumonia showed better agreement and fair to good IR (kappa 0.50–0.67). Good agreement and good to excellent IR was found for identifying the involved lobes (kappa 0.53–0.77). Agreement between reviewers on presence of pleural fluid was fair to good and presence of lymphadenopathy was poor. No significant differences were observed when comparing agreement and IR among radiologists with agreement and IR between radiologists and respiratory physician.

Several differences in radiological features (agreement by 2 out of 3 reviewers) between pneumonias with different causative pathogens were observed (Table 4). Air bronchograms were observed more often in pneumonias caused by *Chlamydia* spp., *S. pneumoniae* and *L. pneumophila* than in pneumonias caused by *M. pneumoniae*. *M. pneumoniae* was associated more often with patchy alveolar opacities than *S. pneumoniae* (P = 0.05). *Chlamydia* spp. was associated with unilobar involvement (86%), especially when compared to *M. pneumoniae* (P = 0.03) and *S. pneumoniae* (P = 0.004). Pleural effusion was presented

	Characteristics	Reviewer 1 n (%)	Reviewer 2 n (%)	Reviewer 3 n (%)
Main radiological pattern	Lobar alveolar opacities	173 (90)	139 (72)	172 (90)
5 1	Patchy alveolar opacities	9 (5)	38 (20)	16 (8)
	Mixed alveolar-interstitial opacities	3 (2)	7 (4)	2 (1)
	Interstitial opacities	5 (3)	6 (3)	0 (0)
	Missing	2 (1)	2 (1)	2 (1)
Air bronchogram	Yes	79 (41)	116 (60)	50 (26)
-	No	70 (36)	66 (34)	125 (65)
	Uncertain	43 (22)	10 (5)	17 (9)
Thickened bronchial walls	Yes	45 (23)	13 (7)	4 (2)
	No	127 (66)	177 (92)	186 (97)
	Uncertain	20 (10)	2 (1)	2 (1)
Extent of pneumonia	Confined to 1 lobe	109 (57)	118 (61)	102 (53)
	>1 lobe	83 (43)	74 (39)	90 (47)
Lobes involved	RUL	45 (23)	41 (21)	41 (21)
	RML	50 (26)	52 (27)	49 (26)
	RLL	93 (48)	82 (43)	89 (46)
	LUL	46 (24)	57 (30)	50 (26)
	LLL	86 (45)	78 (41)	82 (43)
Pleural effusion	Yes No Uncertain	46 (24)	44 (23)	20 (10)
		111 (58)	124 (65)	124 (64)
		35 (18)	24 (13)	48 (25)
Lymphadenopathy	Yes No Uncertain	52 (27)	5 (3)	3 (2)
		140 (73)	137 (71)	173 (90)
		0 (0)	50 (26)	16 (8)

Table 2	Observed	radiological	features	by th	e three	reviewers.
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RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; reviewers 1 and 2, radiologists; reviewer 3, respiratory physician.

more often in pneumococcal pneumonia (27%) than in pneumonias caused by other pathogens (6–17%), although this difference was not significant. Figure 1 shows the location of pneumonias of the 4 most represented pathogens. The distribution of the pathogens in the lungs is largely identical with overall predominance in the lower lobes. *S. pneumoniae* was more frequently present in the right middle lobe (RML) and the right lower lobe (RLL) than *Chlamydia* spp. (P = 0.03 and 0.05).

Discussion

In the present study we aimed to assess the IR for radiographic findings in patients with CAP. We found that IR among 2 radiologists and 1 respiratory physician was poor for determining the main pattern of a pulmonary infiltrate and the presence of air bronchogram, thickened bronchial walls and lymphadenopathy. Simple radiological features such as the extent of pneumonia, the presence of pleural fluid and identifying the involved lobes were associated with fair to good and even excellent IR. These findings are largely in accordance with the results of Albaum et al.⁷ In this study IR between 2 radiologists was investigated in 288 patients with possible pneumonia. IR for determining the main pattern of infiltrate, presence of air bronchogram and lymphadenopathy was poor, while IR for the presence of pleural fluid and the extent of pneumonia was fair to good.

Young and Marrie⁶ found a considerable degree of interobserver variability in 4 groups of reviewers with increasing experience. This effect was most predominant in patients with patchy opacities. In our study no statistically significant differences in agreement and IR were observed between 2 radiologists and 1 respiratory physician. To our knowledge this has not been investigated previously. We find this result not surprising since both radiologists and respiratory physicians read chest radiographs daily.

Characteristics	Reviewers 1–2 % Agreement/Kappa	Reviewers 1–3 % Agreement/Kappa	Reviewers 2–3 % Agreement/Kappa
Main radiological pattern	77/0.26	86/0.20	77/0.30
Air bronchogram	57/0.31	51/0.22	53/0.21
Thickened bronchial walls	68/0.14	68/0.06	92/0.26
Extent of pneumonia	81/0.67	73/0.54	61/0.50
Involved lobes RUL	91/0.73	88/0.64	90/0.69
RML	85/0.70	84/0.58	82/0.53
RLL	87/0.65	83/0.67	78/0.55
LUL	87/0.67	89/0.70	87/0.68
LLL	89/0.77	78/0.56	78/0.55
Pleural effusion	70/0.46	65/0.37	71/0.45
Lymphadenopathy	74/0.38	77/0.27	73/0.19

Table 3 Interobserver agreement (%) and variability (kappa statistics) between the three reviewers.

RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe

Radiological pattern	S. pneumoniae n = 45 (%)	M. pneumoniae n = 24 (%)	Chlamydia spp. n = 21 (%)	L. pneumophila n = 17 (%)
Main radiological pattern				
Lobar alveolar opacities	40 (89)	17 (71)	18 (86)	16 (94)
Patchy alveolar opacities	1 (2)	4 (17) [#]	2 (10)	0 (0)
Mixed alveolar-interstitial	2 (4)	2 (8)	0 (0)	0 (0)
opacities				
Interstitial opacities	0 (0)	0 (0)	0 (0)	0 (0)
No agreement between 2 reviewers	2 (4)	1 (4)	1 (5)	1 (6)
Air bronchogram	21 (47)	7 (29)	12 (57)	9 (53)
Thickened bronchial walls	2 (44)	3 (13)	1 (48)	1 (6)
Extent of pneumonia				
Confined to 1 lobe	22 (49)	14 (58)	18 (86)*	11 (65)
More than 1 lobe involved	23 (51)	10 (42)	3 (14)	6 (35)
Pleural effusion	12 (27)	4 (17)	3 (14)	1 (6)
Lymphadenopathy	1 (2)	0 (0)	0 (0)	0 (0)

 Table 4
 Frequencies of radiological patterns observed by 2 out of 3 reviewers for different causative agents.

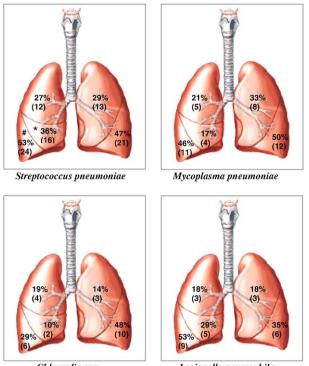
^{*}Significantly more patchy alveolar densities compared to S. *pneumoniae* (P = 0.046),

*Significant difference with S. pneumoniae and M. pneumoniae (P = 0.034 and 0.004).

While reading the presented IR data one should realize however that kappa values are dependent on the prevalence of the measured feature. Especially features with a high prevalence (e.g. the presence of an infiltrate) have a higher interobserver agreement by chance than features with a lower prevalence. This may produce low kappa values since the kappa value is a measure for the rate of agreement on top of the agreement by chance.

The second aim of our study was to compare radiological features between pneumonias caused by different pathogens. We found that *Chlamydia*

spp. was more frequently associated with unilobar involvement, compared to *S. pneumoniae* and *M. pneumoniae*. Only few studies have been performed comparing radiological findings in pneumonias caused by different pathogens. Kauppinen et al.¹⁵ compared radiographic features caused by *S. pneumoniae* with those caused by *C. pneumoniae* and found no differences. Different authors found that the majority of Chlamydia pneumonias (60–100%) were confined to 1 lobe.^{15–18} We found that only 49% of pneumococcal pneumonias were limited to 1 lobe. Although the classical manifestation of pneumococcal pneumonia is a lobar



Chlamydia spp

Legionella neumophila

Figure 1 Distribution of pneumonias caused by the 4 most represented pathogens. *S. pneumonia* was more frequently observed in the middle lobe^{*} (P = 0.027) and lower right lobe[#] (P = 0.045) than *Chlamydia* spp.

consolidation with presence of air bronchogram, a variety of patterns has been documented in pneumococcal pneumonia.^{28–31} Most often a bronchopneumonia pattern is observed with patchy and sometimes confluent air-space disease, often multifocal or bilateral.^{28,29} Another finding was that S. pneumoniae was associated less often with patchy alveolar opacities than M. pneumoniae. Finnegan et al.³² studied a group of 60 patients with mycoplasma pneumonia in which patchy airspace diasease was most common. Ettinger¹⁹ found that M. pneumoniae was associated with diffuse bilateral interstitial or mixed alveolo-interstitial opacities. In a series by Putman et al.³³ with acute mycoplasma pneumonia most patients had airspace disease with lobar or segmental distribution.

The distribution of different pathogens between the lobes was mostly identical with predominance in the lower lobes. However, *S. pneumoniae* was localized more frequently in the RML and the RLL than *L. pneumophila*. In a study by Albaum et al.⁷ the distribution of different pathogens in both lungs was not documented.

In conclusion, we can confirm that IR for determining the main pattern of an infiltrate and presence of air bronchogram, lymphadenopathy and thickened bronchial walls is poor. IR for simple characteristics such as presence of pleural effusion and extent of pneumonia is fair to good or even excellent. Few correlations were found between radiological features and different causative pathogens. Combined with previously published data, this implies that interpretation of a chest radiograph in a patient with CAP does not give a physician useful clues about the causative pathogen. On the other hand, accurately studying chest radiographs does provide the physician with useful information about the location of the pneumonia, its extent and the presence of pleural effusion.

This may guide the physician in estimating the severity of pneumonia and the recognition of complications of CAP such as parapneumonic effusion or empyema. As a consequence we believe that chest radiograph is essential for diagnosing CAP and its extent. Determining the antibiotic(s) of choice however should not be based on radiographic findings but on the whole clinical picture including microbiological tests.

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