Specificity and sensitivity of clinical diagnosis for chronic pneumonia

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نوعية وحساسية التشخيص السريري للالتهاب الرئوي المزمن

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الخلاصة: استهدفت هذه الدراسة المقارنة بين التشخيص السريري (غير الباضع) وبين التشخيص عن طريق تنظير القصبات (التشخيص الباضع)، في 50 مريضاً بالالتهاب الرئوي المزمن، ممّن كانت لطاخة البلغم لتحرِّي السل سلبية. وكانت أعمارهم تتراوح من 12 إلى 82 عاماً. وكانت حساسية التشخيص السريري 100٪ للسل، و81.8٪ لسرطان الرئة؛ في حين بلغت النَّوعية 67.5٪ للسل، 89.7٪ لسرطان الرئة. وقد كان التشخيص السريري صواباً في 43.4٪ من الحالات المشتبه بإصابتها بالسل، وفي 69.2٪ من الحالات المشتبه بإصابتها بسرطان الرئة. وبذلك يمكن أن يُعَوَّل على التشخيص في حالة المدخنات المسنَّات فقط. ونظراً للمبالغة في تشخيص السل في المناطق الموطونة، فيُوصَى بشدة باستخدام طريقة تنظير القصبات لتشخيص جميع الحالات المشتبه بإصابتها بالالتهاب الرئوي المزمن.

ABSTRACT To compare clinical (non-invasive) diagnosis with bronchoscopic (invasive) diagnosis, a total of 50 patients with chronic pneumonia (sputum smear-negative for tuberculosis) were examined. Age range was 12–82 years. Sensitivity of clinical diagnosis was 100% for tuberculosis and 81.8% for lung cancer; specificity was 67.5% for tuberculosis and 89.7% for lung cancer. Clinical diagnosis was correct in 43.4% of cases suspected of tuberculosis and 69.2% of cases suspected of lung cancer. It may be reliable only for elderly women smokers. Because tuberculosis is over-diagnosed in endemic areas, bronchoscopy is strongly recommended for all cases of chronic pneumonia.

Spécificité et sensibilité du diagnostic clinique pour la pneumonie chronique

RÉSUMÉ Afin de comparer le diagnostic clinique (non invasif) avec le diagnostic bronchoscopique (invasif), un effectif total de 50 patients souffrant de pneumonie chronique (frottis d'expectoration négatif pour la tuberculose) a été examiné. L'âge des patients était compris entre 12 et 82 ans. La sensibilité du diagnostic clinique était de 100 % pour la tuberculose et de 81,8 % pour le cancer du poumon ; la spécificité était de 67,5 % pour la tuberculose et de 89,7 % pour le cancer du poumon. Le diagnostic clinique était correct dans 43,4 % des cas suspects de tuberculose et dans 69,2 % des cas suspects de cancer du poumon. Il peut être fiable uniquement pour les femmes âgées qui fument. Étant donné que la tuberculose est surdiagnostiquée dans les zones d'endémie, la bronchoscopie est fortement recommandée pour tous les cas de pneumonie chronique.

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Introduction

Diagnosis of pneumonia is predominantly a clinical diagnosis. Signs and symptoms of lower respiratory tract infection are, however, not unique to pneumonia [*1*]. Pneumonia that fails to resolve at the expected rate, e.g. when the radiograph has failed to resolve by 50% in 2 weeks, or completely in 4 weeks [*2,3*], or does not show significant radiographic resolution after at least 10 days of antibiotic therapy [*4,5*], is considered to be chronic pneumonia [*3–5*], a diagnosis which to many clinicians conjures up an association with underlying neoplasm or less common pathogens [*6*].

The cause of non-resolving pneumonias may be non-infectious or infectious and usually invasive diagnostic techniques are required for confirmation [*7,8*]. It remains controversial to decide when to initiate an invasive diagnostic work-up for chronic infiltrates [*9*]. When clinical improvement has not occurred and chest radiographs remain unchanged or worsen, or in a situation with patients who are clinically stable or improving when the rate of radiographic resolution is delayed, then a more aggressive approach is warranted [*9*].

Fibreoptic bronchoscopy (FOB), which has minimal morbidity, is the preferred initial invasive method [*7*] and as the first step in the evaluation of non-resolving pneumonias after an appropriate period of observation [*4,10–12*].

In some conditions there is a long time between the initial and final diagnosis of chronic pneumonia, which usually occurs after failure of treatment for tuberculosis or lung cancer. Because many chronic pneumonia patients are treated by general practitioners in the absence of a diagnosis, it is important that they have knowledge of the sensitivity and specificity of clinical diagnosis for chronic pneumonia as they are the ones who gene-rally make the primary diagnosis.

In reality, very little is known regarding the sensitivity and specificity of clinical diagnosis. In other words, how sensitive and specific is this method of diagnosis? Is it reliable? When should an invasive method of diagnosis be requested? These questions need to be answered. It is important that the reliability of the non-invasive method is assessed, particularly for tuberculosis. Additionally, it has been recommended that FOB be performed early in heavy smokers and patients > 50 years of age with slow or non-resolving pneumonia [*5*]. The aim of this study was, therefore, to compare the primary or clinical diagnosis with final diagnosis done by FOB and to find out how well matched they were.

Methods

This study was conducted in the infectious and tropical diseases clinic and ward of Al-Zahra Hospital, which is affiliated to Isfahan University of Medical Sciences, with the cooperation of the pulmonology, radiology and pathology departments. Al-Zahra Hospital is a specialty and sub-specialty hospital which is equipped with the latest modern facilities. An evaluation study was carried out from January 2004 to June 2004 on 50 patients who were examined using FOB because of non-resolving pneumonia.

Many patients treated in private clinics of our infectious diseases clinic with acute presentation of pneumonia failed to respond to treatment. They were then referred by their physicians to the pulmonology unit for bronchoscopy.

Inclusion criteria for this study were: non-resolved signs and symptoms (cough or sputum) despite at least 10 days antibiotic therapy against community acquired

pneumonia [*3–5*]; lung infiltration in chest X-ray for at least 2 weeks (indicated in 2 chest X-rays); and negative sputum smear for tuberculosis.

There were many patients with acute presentation of pneumonia such as fever, cough, sputum and lobar or segmental infiltration of the chest X-ray who had been diagnosed and treated as acute community acquired pneumonia. The usual treatment regimen was ceftriaxon 1 g every 12 hours for 10 days plus erythromycin 400 mg every 6 hours for 10 days. Patients who showed no clinical response (continuous fever, sputum and cough) were re-evaluated. At this stage any patients having the first criteria were sent for a second chest X-ray (second criteria) and they were also referred to the reference laboratory for tuberculosis in Isfahan to exclude tuberculosis by sputum smear (× 3) (third criteria).

The exclusion criteria were: patients with definitive diagnosis; testing positive for human immunodeficiency virus (HIV); patients without previous chest X-rays (at least 2 X-rays are needed to confirm chronic pneumonia); patients with previous bronchoscopy; and patients who did not have a complete history taken and had not had a physical examination.

We selected 50 patients consecutively during the period January 2004–June 2004 who had been diagnosed with chronic pneumonia and who met the inclusion and exclusion criteria. There were about 70 patients who did not meet the criteria, mainly not showing lung infiltration in 2 chest X-rays. All of the patients who were selected for the study were informed and completed a consent form. There were no refusals to participate.

The data collected included information obtained from the patient, demographic characteristics, chief complaints, course and duration of symptoms, history of smoking (packs per year), previous underlying disease, previous therapy and management recorded on the base of declarations of patients. Data regarding clinical diagnosis (non-invasive method) was based on the first diagnosis of the infectious diseases specialist (history taking, physical examination). The findings of chest X-ray (postero-anterior and lateral) were recorded from the radiologist's report.

All patients had 3 negative sputum smears for acid-fast bacilli. The clinical diagnosis (non-invasive method) was based on the first diagnosis of an infectious diseases specialist (history taking, physical examination), report and suggestion of a radiologist for 2 chest X-rays. In this step, according to this diagnosis, all patients were classified as: tuberculosis, lung cancer or others (bronchectasia, chronic bronchitis, aspiration pneumonia and non-specific diagnosis).

All patients were then examined by FOB for a definitive diagnosis. In this study, FOB diagnosis (invasive method), which was conducted by a pulmonologist in the pulmonology unit of the hospital, was the gold standard. It included all procedures done by FOB: bronchial washing, bronchial biopsy, bronchial brushing, bronchoalveolar lavage and transbronchial biopsy. The samples obtained by FOB were sent to the hospital laboratory for cytological analysis and to the reference laboratory for tuberculosis in Isfahan for direct smear and culture for acid-fast bacilli.

All acid-fast bacilli sputum smears or cultures positive in the bronchoalveolar lavage procedure were classified as having tuberculosis. Patients with positive findings indicating cancer (cytology) in bronchoalveolar lavage were classified as having lung cancer.

Patients were divided into 2 groups by history of smoking: non-smokers or light

smokers (≤ 40 packs per year) and heavy smokers (> 40 packs per year) [*5*].

Statistical analysis was performed using the binominal test to compare data for each method of diagnosis. The chi-squared test was used to compare the results of sex difference and type of smoking and also Fisher's exact test to compare the results for age group (≤ 50 years and > 50 years) using *SPSS*, version 11. The level of significance was $P < 0.05$.

Results

The study sample included 23 males and 27 females (male to female ratio 0.85:1) (Table 1). In terms of age, 78% were > 50 years and 8% were ≤ 30 years. Mean (standard deviation) age was 57 (20.1) years for men and 66 (15.4) years for women.

The main clinical diagnoses for these patients with chronic pneumonia were tuberculosis (23 patients) and lung cancer (13 patients) (Table 2).

Of the 23 patients who had a clinical diagnosis of tuberculosis, only 10 were confirmed by FOB (Table 3). Clinical diagnosis of not having tuberculosis was the same. Only 9 of the 13 patients clinically diagnosed with lung cancer were confirmed by FOB (Table 4). Two of those diagnosed as not having lung cancer were eventually diagnosed with the disease and were added to lung cancer category but they are not in the group diagnosed by clinical diagnosis.

So in 23 out of 50 patients, positive diagnosis of using the non-invasive method was as the same as for the invasive method of diagnosis. The binominal test indicated a highly significant difference between the invasive and the non-invasive methods of diagnosis, indicating that the non-invasive method was not a reliable method for cases of chronic pneumonia ($P < 0.001$) (Table 2).

The sensitivity of clinical diagnosis for tuberculosis was 100% but specificity was 67.5% (Table 3). The sensitivity of clinical diagnosis for lung cancer was 81.8% but specificity was 89.7% (Table 4).

Overall, the correct diagnosis was found in 34.7% (8 out of 23) of males by the no-ninvasive method of diagnosis, (confirmed by FOB) and 55.5% (15 out of 27) of females (Table 5). The difference was not significant using the chi-squared test ($P = 0.142$).

Ten of the males (43.4%) and 1 of the females (3.7%) (/27) were classed as heavy smokers (≥ 40 packs/year). The non-invasive method produced a correct diagnosis in 63.6% of heavy smokers and 41.0% of non-smokers or light smokers (Table 6). However, the chi-squared test showed the difference was not significant ($P = 0.184$).

The non-invasive method gave the correct diagnosis in 27.2% of patients ≤ 50 years and 48.5% of patients > 50 years. Fisher's exact test showed there was no significant difference ($P = 0.189$).

Table 1 **Distribution of patients by age and sex**

Sex	Age (years)								
	11–20 No.	21–30 No.	31–40 No.	41–50 No.	51–60 No.	61–70 No.	71–80 No.	> 80 No.	Total No.
Male	2	1	1	3	4	5	6	1	23
Female	0	1	1	2	3	6	11	3	27

Table 2 **Comparison of non-invasive (clinical) diagnosis and invasive diagnosis (fibreoptic bronchoscopy)**

Disease	Non-invasive diagnosis[a] No.	Invasive diagnosis Confirmed No.	Invasive diagnosis Ruled out No.
TB	23	10	13[a]
Lung cancer	13	9	4[b]
Other			
Chronic bronchitis or bronchectasia	8	4	4
Aspiration pneumonia	4	0	4[c]
Non-specific diagnosis	2	0	2[d]
Total	50	23	27

TB = tuberculosis.
P < 0.001.
[a]2 cancer, 11 healthy.
[b]3 healthy.
[c]3 healthy.
[d]Both healthy.

Discussion

The presentation of chronic pneumonia syndrome is varied and may mimic neoplasm, interstitial lung disease, or chronic fungal or mycobacterial infection [*6*].

In this study, sensitivity of clinical diagnosis for tuberculosis and lung cancer, the 2 main diagnoses for patients with chronic pneumonia, was high, 100% and 81.8% respectively. Specificity of clinical diagnosis was lower, especially for tuberculosis (67.5%); it was higher for lung cancer (89.7%). It must be remembered that many of the patients in this study had first been managed by general practitioners, who use clinical diagnosis as the baseline of management. This indicates that in endemic

Table 3 **Specificity and sensitivity of clinical diagnosis for tuberculosis among chronic pneumonia patients, measured by bronchoscopy**

Disease	Non-invasive diagnosis No.	Invasive diagnosis (bronchoscopy) TB confirmed No.	Invasive diagnosis (bronchoscopy) TB ruled out No.
TB	23	10	13[a]
Non-TB	27	0	27
Total	50	10	40

TB = tuberculosis.
[a]2 of these 13 patients were eventually diagnosed as having lung cancer.
Sensitivity of clinical diagnosis = 10/(10 + 0) = 100%.
Specificity of clinical diagnosis = 27/(27 + 13) = 67.5%.

Table 4 **Specificity and sensitivity of clinical diagnosis of lung cancer among chronic pneumonia patients measured by bronchoscopy**

Disease	Non-invasive diagnosis	Invasive diagnosis (bronchoscopy)	
		Lung cancer confirmed	Lung cancer ruled out
	No.	No.	No.
Lung cancer	13	9	4
Non-lung cancer	37	2[a]	35
Total	50	11	39

[a]*These 2 patients were originally diagnosed as having tuberculosis.*
Sensitivity of clinical diagnosis = 9/(9 + 2) = 81.8%.
Specificity of clinical diagnosis = 35/(35 + 4) = 89.7%.

areas, clinical diagnosis may give an over-diagnosis of tuberculosis of up to 32.5%, an alarming rate given that in some endemic areas FOB is not available and these patients are at risk of being wrongly treated.

It is important to differentiate slowly resolving from non-resolving pneumonias because the cause of each is different. In general, slowly resolving pneumonias are caused by antimicrobial or host defence factors [*7*] but the cause of non-resolving or progressive pneumonia may be infectious or non-infectious [*8*]. Several risk factors have been established for delayed radiographic resolution of pneumonia and should be considered in patient evaluation. They include coexisting medical conditions, history of smoking, advanced age, diabetes mellitus, chronic obstructive pulmonary disease and conditions that mimic pneumonia (e.g. neoplasms) [*13*]. Some of the patients in this study of chronic pneumonia syndrome also

Table 5 **Comparison of clinical diagnosis (non-invasive) and final diagnosis (invasive) by sex**

Disease	Non-invasive diagnosis	Invasive diagnosis (bronchoscopy)	
		Confirmed	Ruled out
	No.	No.	No.
Tuberculosis	23	10	13[a]
Male	7	2	5
Female	16	8	8
Lung cancer	13	9	4
Male	6	4	2
Female	7	5	2
Bronchitis	8	4	4
Male	5	2	3
Female	3	2	1
Other	6	0	6
Male	5	0	5
Female	1	0	1
Total	50	23	27

[a]*2 of these 13 patients were eventually diagnosed as having lung cancer.*

Table 6 **Comparison of clinical diagnosis (non-invasive) and final diagnosis (invasive) by smoking habit**

Category	Non-invasive diagnosis No.	Invasive diagnosis (bronchoscopy) Confirmed No.	Ruled out No.
Heavy smoker[a]	11	7	4
TB	4	2	2
Lung cancer	5	4	1
Other	2	1	1
Non-smoker/light smoker[a]	39	16	23
TB	19	8	11
Lung cancer	8	5	3
Bronchitis	12	3	9
Total	50	23	27

TB = tuberculosis.
[a]*Heavy smoker: ≥ 40 packs/year; light smoker: < 40 packs per year.*

had underlying predisposing conditions, advanced age (78% > 50 years) and history of heavy smoking: more than 20% of patients were heavy smokers.

Concerning reliability of clinical diagnosis, FOB confirmed the diagnosis made by non-invasive methods in no more than 23 (46.0%) patients. In other words, in 54.0% of patients in this study the clinician had failed to reach a correct diagnosis. Could it be a reliable method? There was a statistically significant difference between the non-invasive and the invasive method of diagnosis ($P < 0.001$). So the non-invasive method of diagnosis was not a reliable method for chronic pneumonia syndrome. This may result in over-diagnosis of tuberculosis and lung cancer.

Non-invasive methods of diagnosis may, however, be correct in some circumstances. For example, it was correct in 34.7% of men and 55.5% of women. It was correct in 63.6% of heavy smokers and 41.0% of light smokers/non-smokers. It was also diagnostic in 48.5% of patients ≥ 50 years old. But after statistical analysis, there was no significant difference.

Non-resolving or slowly resolving pulmonary infiltrates constitute a clinical diagnostic challenge for physicians [*7*]. Invasive techniques such as FOB with bronchoalveolar lavage and appropriate culture for bacteria, *Legionella* spp., fungi, and mycobacterium can also be deferred when unequivocal, albeit incomplete, radiographic resolution can be demonstrated [*9*]. The technique is extremely useful in finding a specific diagnosis for a non-resolving pneumonia (in those cases where a specific diagnosis can be made) [*4*]. In other words, FOB, in the absence of any indications, is rarely diagnostic and should not be routinely employed [*14*]; it may be required in selected cases for the diagnosis of tuberculosis [*15*]. It should, however, be accompanied by bronchoalveolar lavage, bronchial washings and post-bronchoscopy sputum smears.

Fibreoptic bronchoscopy procedures have provided overall diagnostic yields in 5.8% [*16*], 32.5% [*17*], 87.1% [*18*] and 90% [*19*] of patients suspected of having tuberculosis. In the present study, overall

diagnostic yield was 43.5%. Moreover, lung cancer was diagnosed in 2 of the patients who were ruled out for tuberculosis. As in a previous study, these results suggest that in an area with high prevalence of tuberculosis, FOB procedures should be performed in patients with chronic pneumonia syndrome where other conditions (such as tuberculosis or malignancy) must be ruled out [*17*].

Fibreoptic bronchoscopy may be the best means of evaluating the bronchial tree and adjacent lung parenchyma [*20*] and bronchoalveolar lavage can provide diagnostic information in cases of primary and metastatic disease of the lung [*21*]. Bronchoscopic material can be obtained in about 50% of primary lung cancers, with more accuracy in bronchoalveolar cell carcinoma and adenocarcinoma than in squamous cell carcinoma [*21*]. It is most useful (73%) in the diagnosis of bronchogenic carcinoma [*12*]. Of the 11 lung cancer patients in our study, 91% were diagnosed as bronchogenic carcinoma and 1 patient as adenocarcinoma, a finding which is similar those of some previous studies [*12,21*].

Bronchoscopic procedures in the suspected cancer cases in this study provided overall diagnostic yields in 69.2% (9/13) of patients. In 2 patients with suspected tuberculosis, this was ruled out and they were finally confirmed as having lung cancer. Overall diagnostic yield was 66.7% (10/15). These results show the importance of FOB in the diagnosis of tuberculosis and lung cancer in patients with chronic pneumonia.

To sum up, the sensitivity of the non-invasive method of diagnosis was 100% for pulmonary tuberculosis and 81.8% for lung cancer. Specificity was 67.5% for pulmonary tuberculosis and 89.7% for lung cancer. Therefore, this method may not be reliable, at least for tuberculosis. Also, it suggests that FOB is a necessary option in every chronic pneumonia patient. In fact, as indicated in a previous study, FOB must be performed early in heavy smokers and patients > 50 years of age with slow or non-resolving pneumonia [*5*]. In contrast, in light smokers/non-smokers or younger patients, it should only be performed after 4–8 weeks unless clinical symptoms justify an earlier intervention [*6*].

Acknowledgements

My sincere thanks to Dr Soleiman Kheiri of the Biostatistics Department for his critical statistical review of the manuscript. Special thanks to Dr Farid Karimi who helped in this work and Maria Gillies who helped in the final edit. Thanks also to the Research Deputy of Isfahan University of Medical Sciences and the pulmonology, radiology and pathology departments of Al-Zahra Hospital for their help in conducting this study.

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