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BRIEF REPORT

Limitations of Chest Radiography in Diagnosing Subclinical Pulmonary Tuberculosis in Canada

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Abstract

Subclinical pulmonary tuberculosis (PTB) is defined as "…a state of disease due to viable *Mycobacterium tuberculosis* that does not cause TB-related symptoms but does cause other abnormalities that can be detected using existing radiologic and mycobacteriologic assays." In high-income countries, subclinical PTB is usually diagnosed during active case finding, is acid-fast bacilli smear negative, and associated with minimal or no lung parenchymal abnormality on chest radiograph. In the absence of symptoms, the epidemiologic risk of TB and chest radiograph are critical to making the diagnosis. In a cohort of 327 patients with subclinical PTB, we address the question—how well field radiologists perform at identifying features important to the diagnosis of PTB, the presence or absence of which have been established by a panel of expert radiologists? Although not performing badly compared with this "gold standard," field readers were nevertheless susceptible to overread or underread films and miss key diagnostic features, such as the presence of a lung parenchymal abnormality, typical pattern, or cavitation. In the context of active case finding during which most patients with subclinical PTB are discovered, limitations of the chest radiograph need to be recognized, and sputum, ideally induced, should be submitted regardless of the radiographic findings.

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Subclinical pulmonary tuberculosis (PTB) is defined as "a state of disease due to viable *Mycobacterium tuberculosis* that does not cause TB-related symptoms but does cause other abnormalities that can be detected using existing radiologic or microbiologic assays."[1] Its diagnosis is often delayed, during which time tidal breathing alone may be sufficient to aerosolize the bacterium and lead to unrecognized transmission events.[2,3] In high-income countries, subclinical PTB is reported in approximately 20% of culture-positive patients with PTB.[4] In this setting, patients are usually diagnosed during active case finding, for example during the screening of immigrants and refugees, patients with a known diagnosis of extrapulmonary TB, or recently infected contacts.[4-6] At diagnosis, most subclinical patients are smear negative, and if they are HIV seronegative and have new active disease, they have minimal or no lung parenchymal abnormality on chest radiograph.[4] In the absence of symptoms, the epidemiologic risk of TB (ie, the reason for undertaking the active case finding) and the chest radiograph alone become central to considering a diagnosis of subclinical PTB and the submission of sputum for acid-fast bacillus smear and culture. With respect to the radiograph, reader experience and expertise may affect its utility. Herein, we address the following question: Herein, we address the following question as to how well do field radiologists perform at identifying features

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TABLE 1. Interreader Variability of Subclinical PTB Chest Radiograph Interpretations[a]

FEATURE	OBSERVER AGREEMENT	K STATISTIC	95% CI
EXPERT A VS EXPERT B			
Parenchymal abnormality	0.927	0.745	0.649-0.842
Typical Pattern[b]	0.896	0.754	0.677-0.832
Laterality (EOD)	0.835	0.724	0.656-0.791
Cavitation	0.921	0.494	0.327-0.661
Enlarged IT nodes	0.979	0.578	0.295-0.860
Pleural effusion	0.988	0.812	0.632-0.992
FIELD READERS VS EXPERT A			
Parenchymal abnormality	0.872	0.628	0.527-0.729
Typical Pattern[b]	0.880	0.672	0.588-0.755
Laterality (EOD)	0.765	0.619	0.545-0.693
Cavitation	0.902	0.234	0.062-0.406
Enlarged IT nodes	0.989	0.772	0.555-0.988
Pleural effusion	0.985	0.775	0.584-0.966
FIELD READERS VS EXPERT B			
Parenchymal abnormality	0.865	0.592	0.487-0.698
Typical Pattern[b]	0.850	0.664	0.579-0.748
Laterality (EOD)	0.737	0.568	0.490-0.646
Cavitation	0.939	0.384	0.172-0.596
Enlarged IT nodes	0.973	0.557	0.298-0.816
Pleural effusion	0.985	0.792	0.615-0.969

[a]EOD, extent of disease; IT, intrathoracic; PTB, pulmonary tuberculosis.
[b]Typical for "adult-type PTB," the latter defined as upper lung zone predominant PTB, with or without cavitation but with no discernable adenopathy. The upper lung zone was understood to include the superior segment of the lower lobe.

important to the diagnosis of PTB, the presence or absence of which have been established by a panel of expert radiologists.

METHODS

In a previously well-defined population-based cohort of HIV-seronegative, sputum culture-positive adult (aged >14 years) patients with subclinical PTB notified in Canada between 2005 and 2020, diagnostic chest radiographs had been reread for the presence or absence of specific features by 2 expert chest radiologists (A and B, with 25 and 15 years of experience, respectively) and discrepant interpretation arbitrated by a third expert chest radiologist (C, with 15 years of experience) (Supplemental Materials 1, 2 and 3, available online at http://www.mcpiqojournal.org/).[4,7] The number of radiographs requiring arbitration varied according to feature from 1.2% (pleural effusion) to 9.5% (laterality). Expert radiologists were aware that the patient had been given a diagnosis of PTB; field radiologists were aware of the indications for the radiograph.[4-6] In the present study, field radiology reports were retrieved and information was systematically abstracted from them as follows: whether i) a lung parenchymal abnormality was reported, and if so, whether it was ii) unilateral or bilateral, iii) typical for adult-type PTB—ie, involved predominantly the "lung apices," "upper lobes" or "upper lung zones," iv) cavitary, and v) were enlarged intrathoracic nodes, or vi) a pleural effusion reported. It is conservatively estimated on the basis of past epidemiologic studies in the province that over the 16 years during which the cohort of subclinical patients was diagnosed, approximately 15,000 to 20,000 chest radiographs would have been read in connection with active case finding by field readers.[5,6,8-10]

Analysis

For each of the above features we quantified the level of agreement between expert readers A and B, between field readers and expert reader A, and between field readers and expert reader B, using generalized kappa statistics. For each feature, we also determined the proportion of radiographs that were underread (U, with 1-U = sensitivity) or overread (O, with 1-O = specificity), by field readers, relative to expert readers A and B and the consensus of expert readers A, B, and C.[11] Underreading and overreading of expert readers A and B, relative to the consensus of expert readers A, B, and C is also provided in a supplement. Finally, for each feature we also compared the proportion of patients with the feature, as reported by the field readers, vs the proportion of patients with the feature, as reported by the consensus of expert readers (A, B, and C), using chi-square and Fisher exact tests (Stata version SE14.2). These comparisons included all patients and those stratified according to sputum smear status and the reason for assessment (active case finding vs miscellaneous). Institutional approval was obtained from the Health Research Ethics Board of the University of Alberta, Canada (Identifier: PR00108560).

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TABLE 2. Overreading and Underreading of Chest Radiographs by Field Readers in Patients With Subclinical PTB[a]

Feature	Reading	Field vs Expert A	Field vs Expert B	Field vs Consensus	Range
		Proportion (%)	Proportion (%)	Proportion (%)	
Parenchymal abnormality	Over	10/61 (16.4)	7/51 (13.7)	9/61 (14.8)	13.7-16.4
	Under	31/266 (11.7)	37/276 (13.4)	30/266 (11.3)	11.3-13.4
Typical pattern[b]	Over	17/106 (16.0)	11/92 (12.0)	13/98 (13.3)	12.0-16.0
	Under	31/221 (14.0)	39/235 (16.6)	40/229 (17.5)	14.0-17.5
Laterality (EOD)[c]	Over	27/231 (11.7)	27/236 (11.4)	27/238 (11.3)	11.4-11.7
	Under	51/266 (19.2)	58/276 (20.7)	49/266 (18.4)	18.4-21.0
Cavitation	Over	4/294 (1.4)	4/304 (1.3)	4/302 (1.3)	1.3-1.4
	Under	27/33 (81.8)	16/23 (69.6)	17/25 (68.0)	68.0-81.8
Enlarged IT nodes	Over	4/320 (1.3)	5/317 (1.6)	5/318 (1.6)	1.3-1.6
	Under	0/7 (0.0)	4/10 (40.0)	3/9 (33.3)	0.0-40.0
Pleural effusion	Over	4/317 (1.2)	2/315 (0.6)	4/318 (1.3)	0.6-1.3
	Under	1/10 (10.0)	1/12 (8.3)	0/9 (0.0)	0.0-10.0

[a]EOD, extent of disease; IT, intrathoracic; PTB, pulmonary tuberculosis.
[b]Typical for "adult-type PTB," the latter defined as upper lung zone predominant PTB, with or without cavitation but with no discernable adenopathy. The upper lung zone was understood to include the superior segment of the lower lobe. If the expert reader read as typical and the field reader read as normal or atypical = underreading. If the expert reader read as normal or atypical and the field reader read as typical = overreading.
[c]If the expert reader read as unilateral and field reader read as normal, or the expert reader read as bilateral and the field reader read as unilateral or normal = underreading and vice-versa for overreading.

RESULTS

There were 327 patients with subclinical PTB among whom 286 (87.5%) had new active disease and 289 (88.4%) were smear negative.[4] The mean ± SD age of the patients was 47.4±19.6 years; 152 (46.5%) were woman; and 297 (90.8%) were non-Canadian-born. The indications for the radiograph were as follows: i) active case finding: 170 (52.0%) immigration referrals, 43 (13.1%) extrapulmonary TB, and 38 (11.6%) TB contact and ii) workup of other miscellaneous conditions, such as cancer or trauma, 76 (23.2%). Posterior-anterior and lateral views were obtained in 305 (93.3%) patients. Kappa statistics were highest for expert readers A vs B and, for most features, lower for field readers vs expert reader A or B—agreement was minimal for cavitation (kappa 0.234-0.384) (Table 1). Underreading and overreading of major features by field readers (vs expert reader A or B or vs the consensus of expert readers A, B, and C) was not uncommon; underreading of lung parenchymal disease ranged from 11.3% to 13.4%, a typical pattern from 14.0% to 17.5%, extent of disease from 18.4% to 21.0%, and cavitation from 68.0% to 81.8% (Table 2). Underreading by expert reader A or B compared with the consensus of readers A, B, and C was uncommon, but the groups were not independent of one another (Supplement Table 1, available online at http://www.mcpiqojournal.org/). Overall, field readers were less likely to report parenchymal disease, a typical pattern, and cavitation than the consensus of expert readers (74.9% vs 81.3%, 62.4% vs 70.0% and 3.4% vs 7.6%, respectively) (Table 3). Field readers appeared to perform better in smear-positive than smear-negative cases, although the numbers were small. Lack of foreknowledge that PTB was high on the differential diagnosis, as was the case in those patients whose radiograph had been ordered for other miscellaneous conditions, had no discernible effect on the performance of field readers relative to the consensus of expert readers Table 4.

DISCUSSION

The chest radiographic features of subclinical PTB, as reported in high-income countries, are known to be subtle.[4-6] In the present

TABLE 3. Radiographic Features in Patients With Subclinical PTB According to Sputum Smear Status—Field vs Consensus of Expert Readers[a]

	Smear (+), (n=38)			Smear (-), (n=289)			Smear (+) and (-), (n=327)		
Radiographic feature	Field No (%)	Expert No (%)	*P* value[c]	Field No (%)	Expert No (%)	*P* value[c]	Field No (%)	Expert No (%)	*P* value[c]
Parenchymal Abnormality									
Yes	35 (92.1)	36 (94.7)		210 (72.7)	230 (79.6)		245 (74.9)	266 (81.3)	.047
No	3 (7.9)	2 (5.3)	.65	79 (27.3)	59 (20.4)	.051	82 (25.1)	61 (18.7)	
Pattern[b]									
Typical	28 (73.7)	30 (78.9)		176 (60.9)	199 (68.9)		204 (62.4)	229 (70.0)	.039
Atypical of Normal	10 (26.3)	8 (21.1)	.59	113 (39.1)	90 (31.1)	.045	123 (37.6)	98 (30.0)	
Laterality (EOD)									
Unilateral	20 (52.6)	23 (60.5)		137 (47.4)	155 (53.6)		157 (48.0)	178 (54.4)	.11
Bilateral	15 (39.5)	13 (34.2)	.76	73 (25.3)	75 (26.0)	.13	88 (26.9)	88 (26.9)	
Normal	3 (7.9)	2 (5.3)		79 (27.3)	59 (20.4)		82 (25.1)	61 (18.7)	
Cavitation									
Yes	1 (2.6)	3 (7.9)		10 (3.5)	22 (7.6)		11 (3.4)	25 (7.6)	.016
No	37 (97.4)	35 (92.1)	.62	279 (96.5)	267 (92.4)	.029	316 (96.6)	302 (92.4)	
Enlarged IT Nodes									
Yes	0 (0.0)	1 (2.6)		11 (3.8)	8 (2.8)		11 (3.4)	9 (2.8)	.65
No	38 (100.0)	37 (97.4)	Not statistically significant	278 (96.2)	281 (97.2)	.48	316 (96.6)	318 (97.2)	
Pleural Effusion									
Yes	3 (7.9)	3 (7.9)		10 (3.5)	6 (2.1)		13 (4.0)	9 (2.8)	.39
No	35 (92.1)	35 (92.1)	Not statistically significant	279 (96.5)	283 (97.9)	.31	314 (96.0)	318 (97.2)	

[a]EOD, extent of disease; IT, intrathoracic; PTB, pulmonary tuberculosis.
[b]Typical for "adult-type PTB," the latter defined as upper lung zone predominant PTB, with or without cavitation but with no discernable adenopathy. The upper lung zone was understood to include the superior segment of the lower lobe.
[c]Chi-square and Fisher exact tests.

comparative study of using chest radiography to report subclinical PTB, we found that the level of agreement between field and expert readers was lower than among expert readers themselves for most radiographic features. Compared with a "gold standard" set by a panel of expert readers, underreading and overreading of subclinical PTB radiographs by field readers was not uncommon. Field readers were less likely to report a lung parenchymal abnormality, typical pattern, or cavitation. Field interpretations tended to be better in smear-positive than smear-negative cases, although the numbers were small. The absence of forewarning of PTB as a leading diagnostic consideration in the group whose reason for assessment was "miscellaneous conditions" did not result in poorer performance by field readers.

Added to the already recognized subtlety of the radiographic findings in subclinical PTB and the potential for underreading, is the possibility that a radiographic abnormality, when present, is dismissed on account of not being new. In an earlier study, we found that most immigration referrals, when assessed in-country and determined to have active PTB, are asymptomatic. When their diagnostic chest radiographs are compared to earlier radiographs performed during the immigration process, most are found to be stable for 6 months or more, a period of stability that is normally associated with inactivity.[4] Among the subgroup of patients in the present cohort that were discovered during active case finding, 52% were immigration referrals. Unsurprisingly, even when "expert-read" the chest radiograph in subclinical PTB significantly under-detects abnormalities present on computed tomographic scan.[12]

In the context of our active case-finding exercises, sputum or another airway secretion specimen was submitted independent of the

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TABLE 4. Radiographic Features in Patients With Subclinical PTB According to Reason For Assessment (Active Case-Finding vs Miscellaneous)—Field vs Consensus of Expert Readers[a]

	Active Case Finding (n=251)			Miscellaneous (n=76)			All groups		
Radiographic feature	Field No (%)	Expert No (%)	*P* value[c]	Field No (%)	Expert No (%)	*P* value[c]	Field No (%)	Expert No (%)	*P* value[c]
Parenchymal Abnormality									
Yes	180 (71.7)	196 (78.1)		65 (85.5)	70 (92.1)	.198	245 (74.9)	266 (81.3)	.047
No	71 (28.3)	55 (21.9)	.10	11 (14.5)	6 (7.9)		82 (25.1)	61 (18.7)	
Pattern[b]									
Typical	153 (61.0)	173 (68.9)		51 (67.1)	56 (73.7)		204 (62.4)	229 (70.0)	.039
Atypical of Normal	98 (39.0)	78 (31.1)	.061	25 (32.9)	20 (26.3)	.374	123 (37.6)	98 (30.0)	
Laterality (EOD)									
Unilateral	113 (45.0)	129 (51.4)		44 (57.9)	49 (64.5)		157 (48.0)	178 (54.4)	.11
Bilateral	67 (26.7)	67 (26.7)		21 (27.6)	21 (27.6)	.419	88 (26.9)	88 (26.9)	
Normal	71 (28.3)	55 (21.9)	.21	11 (14.5)	6 (7.9)		82 (25.1)	61 (18.7)	
Cavitation									
Yes	3 (1.2)	15 (6.0)		8 (10.5)	10 (13.2)		11 (3.4)	25 (7.6)	.016
No	248 (98.8)	236 (94.0)	.007	68 (89.5)	66 (86.8)	.616	316 (96.6)	302 (92.4)	
Enlarged IT Nodes									
Yes	9 (3.6)	5 (2.0)		2 (2.6)	4 (5.3)		11 (3.4)	9 (2.8)	.65
No	242 (96.4)	246 (98.0)	.42	74 (97.4)	72 (94.7)	.681	316 (96.6)	318 (97.2)	
Pleural Effusion									
Yes	11 (4.4)	7 (2.8)		2 (2.6)	2 (2.6)		13 (4.0)	9 (2.8)	.39
No	240 (95.6)	244 (97.2)	.34	74 (97.4)	74 (97.4)	NS	314 (96.0)	318 (97.2)	

[a]EOD, extent of disease; IT, intrathoracic; NS, not significant; PTB, pulmonary tuberculosis.
[b]Typical for "adult-type PTB," the latter defined as upper lung zone predominant PTB, with or without cavitation but with no discernable adenopathy. The upper lung zone was understood to include the superior segment of the lower lobe.
[c]Chi-square and Fisher exact test

incident chest radiograph interpretation (as per the protocol in our immigration referrals and most extrapulmonary cases, and discretionary in our tuberculin skin test/interferon gamma release assay-positive cases). Had sputum not been submitted in patients with normal or atypical radiographic findings, over one-third of our patients with subclinical PTB would have been missed. Whether sputum, preferably induced given the absence of cough, should be submitted as a routine practice in such patients is not clearly recommended in the literature[13]; however, our findings suggest that it should be. In patients whose reason for assessment was "miscellaneous," radiograph requisitions did not usually forewarn of PTB, and sputum was submitted on the basis of pathologic or computed tomographic findings or absence of alternative diagnoses.

In conclusion, there are limitations to chest radiography in diagnosing subclinical PTB in high-income countries. If the radiograph alone, without sputum, is used during active case finding to rule out subclinical PTB, many patients with subclinical PTB would be missed. The impact of treating such patients with preventive therapy alone on outcomes and drug resistance is still uncertain. It is possibly not that large.[14,15]

POTENTIAL COMPETING INTERESTS

The authors report no competing interests.

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SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **PTB,** pulmonary tuberculosis; **TB,** tuberculosis

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