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Prospective evaluation of radiographic manifestations of tuberculosis in relationship with CD4 count in patients with HIV/AIDS

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Abstract

A major risk factor to develop active tuberculosis (TB) is the infection with the human immunodeficiency virus (HIV). Chest radiography is the first-line imaging modality used to rule out TB. Coinfected individuals present often with atypical imaging patterns, due to the immunosuppression caused by the virus, making diagnosis difficult. In this prospective observational study 268 TB and HIV coinfected patients were included. During a follow-up period of 24 weeks, the predominant patterns on chest radiography were analyzed and compared to the cluster of differentiation 4 (CD4) count under antiretroviral and anti-TB therapy. Patients with low CD4 counts (<200 cells//μL) showed more often lymphadenopathy (62% vs 38%;*P* = .08) and a miliary pattern (64% vs 36%;*P* = .04) but less likely cavitation (32% vs 68%;*P* = .008) or consolidation (47% vs 63%;*P* = .002) compared to individuals with higher CD4 counts. Over the follow-up period, partial response to therapy was the most frequent radiological evolution (62%), mainly accompanied by an increase of CD4 cells (92%). Patients with a decrease in CD4 count mostly presented with a worsening in radiological findings (53%). Radiographic TB manifestation correlated with the immune status of patients coinfected with HIV. Low CD4 counts often showed atypical manifestation.

Abbreviations: ART = antiretroviral therapy, CD4 = cluster of differentiation 4, CXR = chest radiography, HIV = human immunodeficiency virus, PR = partial response, SD = stable disease, T1 = baseline, T3 = second follow-up (week 24), TB = tuberculosis, TR = total response.

Keywords: diagnosis, imaging, interstitial lung disease

1. Introduction

Recently, tuberculosis (TB) has surpassed the human immunodeficiency virus (HIV) as being the infectious disease causing the most deaths worldwide.[1] A major risk factor for the development of active TB is the infection with HIV.[2] Worldwide HIV infection is associated with poorer outcomes and higher relapse rates of pulmonary TB.[3] According to the world health organization HIV infected patients have a 21-fold higher risk to develop TB than patients without HIV infection.[4] Vice-versa TB is known to slow cluster of differentiation 4 (CD4) recovery and to increase progression to acquired immunodeficiency syndrome and death among HIV infected subjects.[1] The 2 infections are thus building a lethal synergy and it is fundamental to detect and exclude both diseases in everyone being infected with either 1.

Depending on the degree of immunosuppression, both typical and atypical radiographic patterns can be seen.[5,6] The CD4 count, being an indicator of the immune status, is known to influence radiographic features of TB on chest radiography (CXR) in HIV infected patients.[7] Typical manifestation of TB is defined as upper lung zone predominant consolidation with or without cavitation and absence of mediastinal lymphadenopathy.[8] Different studies suggest that CD4 counts < 200 cells//μL are highly associated with the presence of mediastinal lymphadenopathy, a lower prevalence of cavitation, and a higher incidence of extrapulmonary involvement, representing an atypical

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Informed consent was obtained from all subjects involved in the study.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study was approved by the "Joint Clinical and Research Centre Committee" ethics committee and the Uganda National Council for Science and Technology (reference number HS 1303).

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manifestation.[5,9,10] Further, it is known that immunosuppressed patients show higher rates of smear-negative TB.[11] Therefore, sputum culture for Mycobacterium tuberculosis is still the method of reference for diagnosing pulmonary TB, since the sensitivity is not influenced by HIV infection. Unfortunately, this is not always practicable due to the long time needed for growth and the extended need of resources. Therefore, HIV-associated TB is often diagnosed by combining clinical features, CXR and sputum microscopy.[11] It is thus desirable to identify atypical manifestations of TB in order to diagnose and treat the infection correctly to prevent further transmission.

Currently, CXR is the image modality of choice for screening, diagnosis and the evaluation of treatment-response as it is a cheap, widely accessible and cost-effective.[12,13] Furthermore, CXR has a lower radiation dose than computed tomography, where the sensitivity for the detection and characterization of infiltrates, cavities and lymphadenopathy would be higher.[9]

The purpose of this study was to evaluate the different CXR patterns of TB in patients with HIV-infection and to correlate them with CD4 count and the response to therapy.

2. Methods

2.1. Patient population

In this observational study between May 2013 and September 2015 patients with TB-HIV coinfection were prospectively included at the (*blinded for review*). This large outpatient clinic integrated an HIV-TB clinic in 2008 in order to improve outcomes of HIV infected patients with 350 to 400 new TB cases diagnosed annually.[14]

The patient cohort is part of the SOUTH study,[14] which was approved by the "Joint Clinical and Research Centre Committee" ethics committee and the Uganda national council for science and technology (reference number HS 1303). Inclusion and exclusion criteria are listed in Table 1.

2.2. Study characteristics and follow up investigations

After inclusion, the anti-TB therapy was initiated according to world health organization guidelines.[14,15] Patients who already received antiretroviral therapy (ART) continued their therapy. ART-naïve patients started ART 2 weeks later regardless of the CD4 count. The enrolled patients were followed up for 6 months and underwent several study visits: baseline, week 2, 8, and 24. At every visit, a short patient history including clinical features was conducted and blood samples were collected for the evaluation of CD4 and CD8 counts, viral load and medication concentrations to control the patients' compliance. CXR was performed at the radiology department of (*blinded for review*). CXRs were performed in postero-anterior projection at 3 different time points: before starting anti-TB therapy (baseline [T1]), at first follow-up (week 8) (T2), and second follow-up (week 24) (T3).[14]

2.3. Image evaluation

CXR with matching patient-IDs were photographed in Uganda using a digital still camera (Panasonic DMC-TZ56).[16] These photos were transferred to the (*blinded for review*) for further processing and evaluation. Two experienced radiologists (TF with 15 years and PV with 4 years of experience in radiology) analyzed CXR for the presence of 6 predefined factors representing the most common radiologic features in pulmonary TB, defined according to recently published studies,[15–18] were included: parenchymal consolidation; interstitial changes; diffuse micronodular (miliary) pattern; pleural effusion; presence of lung cavities; and the occurrence of mediastinal lymphadenopathy. Readers evaluated CXR for presence/absence of these features on baseline and follow-up CXR at first follow-up (week 8) and T3 for response/changes. The following response criteria were defined: total response (TR) to therapy (TR: X-ray turned normal), partial response (PR) to therapy (PR: ≥1 feature disappeared), (stable disease [SD]: no change) and (progressive disease: ≥1 feature new/progression). In the event of a reading mismatch, the readers reevaluated the images until consensus was sought. Readers were blinded to clinical information.

2.4. Measurement of CD4 and CD8

CD4 cell count and viral load measurements were performed at (*blinded for review*). CD4 cell count was performed at T1 and at T3.

2.5. Statistics

Kappa test was performed to access interreader reliability. *T* test was used to compare between different CD4 count groups. As the cutoff between high and low increase of CD4 counts from T1 to T3 we used a median increase of 100% of all CD4 increase-ratios. Microsoft Excel was used for table presentation and GraphPad PRISM for statistic calculations. Statistical significance was defined for $P < .05$.

3. Results

3.1. Patient population

Overall, a total 166 patients were included (69 female; median age 33 years, range 17–59 years). Inclusion details can be found Figure 1.

3.2. Sputum and CD4 count

At T1 in 86% of patients (n = 142) sputum cultures were positive. At T3 only in 2% of patients (n = 4) sputum culture remained positive. At T1 mean CD4 count was 230 cells/μL (range 2–1171cells/μL). The average CD4 cell count at T1 in patients with positive culture results was slightly higher compared to the culture negative group (231cells/μL vs 222cells/μL; $P = .001$.) At T3 the CD4 cell count increased by 68% in the

Table 1

Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Age: ≥ 18 yr	-Extrapulmonary TB
HIV infection proven (receiving antiretroviral therapy (ART) or not)	-Active/ planned pregnancy
Pulmonary Tuberculosis (TB) newly diagnosed based on:	-Participation in another study
-Clinical symptoms (cough, fever, weight loss, night sweats)	-Life expectancy < a yr due to comorbidities (e.g., Kaposi sarcoma)
-Chest X-ray	-Decompensated liver disease
-Sputum fluorescent microscopy	-Aminotransferases > 5 times upper limit of normal
-xPert MTB/RIF (nucleic acid amplification test for rapid TB diagnosis and antibiotic sensitivity test)	-Glomerular filtration rate (GFR) < 50 mL/min
-Sputum culture	
Exclusion criteria during study	
-Extraordinary medical conditions	
-New pregnancy	
-Resistance to first-line anti-TB drug	
-Immune Reconstitution Inflammatory Syndrome in organs other than the lungs (e.g., tuberculous meningitis)	
-Baseline culture showing Mycobacteria other than Mycobacteria tuberculosis	

ART = antiretroviral therapy, HIV = human immunodeficiency virus, TB = tuberculosis.

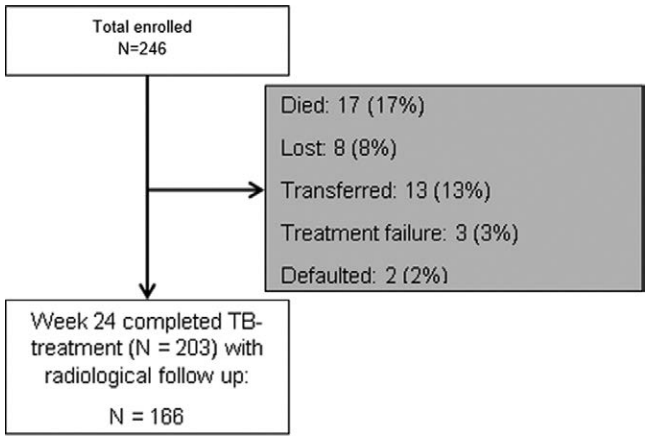

Figure 1. Study cohort: enrolled, withdrawn and followed up.

culture negative group but decreased by 39% in the remaining positive patients (Table 2).

3.3. Image evaluation

Overall, mean interreader-agreement was substantial (kappa = 0.74; range 0.57–0.95). At T1, the most frequently detected patterns were consolidations, followed by mediastinal lymphadenopathy, while the military pattern was found rarely. While 8% of patients (n = 13) showed normal CXR at T1, 48% (n = 80) presented with 1 pattern and 44% (n = 73) showed 2 to 4 patterns (Fig. 2 and Table 3).

3.4. Correlation of CD4 and CXR features at T1

CD4 cell counts were divided into 4 groups (0–100, 101–200, 201–300, and > 300cells/μL) and listed against radiological features (Table 4 and Fig. 3). While consolidation and pleural effusion did not differ significantly among all 4 CD4 cell count groups, the miliary pattern and mediastinal lymphadenopathy occurred more often in patients with low CD4 cell counts (64% and 62%; respectively). Patients with higher initial CD4 cell counts presented more often with cavities (68%) (Fig. 4). The 13 patients presenting with a normal CXR had a median CD4 count of 131 cells/μL (8 cells/μL–689 cells/μL).

3.5. Changes in CD4 and CXR-features over time

Regardless of the dominant image feature at T1, overall, most patients showed an increase in the CD4 cell count (89%). This was most pronounced for the miliary pattern or in cases with pleural effusion. Patients with consolidations showed a lower increase in CD4 counts over time. The highest number of cases with a decrease in CD4 counts was found in patients showing interstitial changes or lymphadenopathy at T1. When comparing these values to the image-based response, we saw a high increase of CD4 count in patients with PR, whereas patients with TR and low CD4 count at baseline showed a decrease in CD4 count (Table 5). Regarding PR and SD, patients with low initial CD4 cell counts (<200) were more likely to have an increase in CD4 counts (71% and 89%; respectively). Contrary to this, patients with initial high CD4 cell count (>200) showed slightly higher percentages of decrease or stable CD4 cell counts (57% and 64%; respectively).

3.6. Image based therapy response

62% of patients (n = 103) showed PR to therapy at T3 regardless of the radiological pattern at T1. progressive disease was only found in patients with CD4 counts above 100 cells/μL and mostly in patients with CD4 counts above 300 cells/μL at T1 (Table 6 and Fig. 5).

4. Discussion

In this retrospective study, we found a correlation between the radiographic TB manifestation and the immune status of patients coinfected with TB and HIV. Unlike other HIV-associated opportunistic infections, TB can present at any CD4-level but is more likely to present with progressive immunosuppression. The typical radiographic alterations (infiltrates and cavitation) in TB are consequence of a normal functioning immune response.[18] Therefore, patients with a low CD4 count have a higher likelihood to present with atypical manifestations such as mediastinal lymphadenopathy and lung changes with a miliary pattern. The lower the CD4 count, the less the ability of the immune system to fight and destroy any intruder resulting in a less TB-typical radiological pattern. Cavitation for example appeared twice as often with a CD4 count above 200 cells/μL compared to cases where the CD4 count was below this level. Unspecific patterns, such as diffuse consolidation, are frequent in any of the 4 defined CD4 stages. The correlation of the radiographic abnormalities with the CD4 count have the potential to be useful in diagnosis and clinical staging of TB.[19] In our dataset however, we were not able to find a specific pattern for any single CD4 stage in order to predict the grade of immunosuppression based on the CXR findings.

Nevertheless, our findings are consistent with recent studies, showing "atypical" presentation in patients with severe immunosuppression.[18,20] A study from Ethiopia[19] comparing CXR of smear-positive TB patients coinfected with HIV versus HIV-negative individuals showed, that the atypical presentation in the CXR, like lymphadenopathy and pleural effusion, were associated with HIV coinfection. Similarly, Kisembo et al[21] described typical patterns associated with HIV-positivity and severely immunosuppressed patients. A retrospective study performed in Iran evaluating 15 HIV-TB-coinfected patients failed to reveal any statistically significant correlation between CD4 cell count and radiographic manifestation or severity of infection.[22] Nevertheless, they found that the dominant radiographic pattern of TB in patients with CD4 cell count < 500cells/μL was atypical. Pleural effusion reflects a strong immune reaction in the pleura occurring mainly in patients with CD4 count above 200 cells/μL.[23] In our study, we could not demonstrate any difference regarding pleural effusion among the 4 CD4 groups.

Table 2

Mean and standard deviation of CD4 cell count at baseline (T1) and at end of follow-up 24 weeks later (T3) sorted according to sputum culture results.

T1, Culture	CD4 (cells/ μL)	T3, Culture	CD4 (cells/ μL)
Positive (142, 86%)	231 ± 220	Positive (4, 3%)	142 ± 166
Negative (24, 14%)	222 ± 220	Negative (138, 97%)	374 ± 259

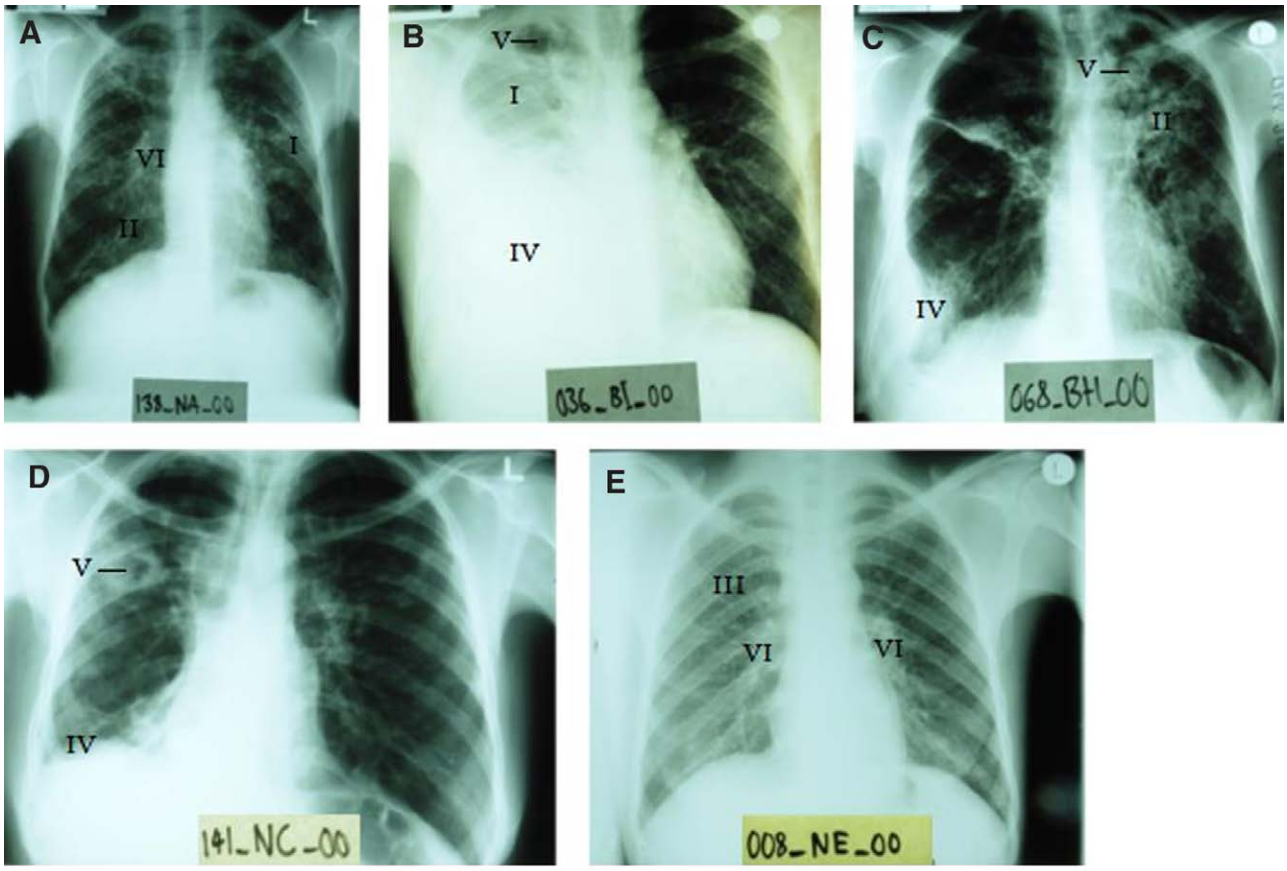

Figure 2. Photographed chest X-ray with typical tuberculosis patterns: parenchymal consolidation (I), interstitial changes (II), miliary pattern (III), pleural effusion (IV), cavitation (V), mediastinal lymphadenopathy (VI).

Table 3

Chest X-ray findings in 166 patients listed by frequency. Multiple patterns per patient possible.

Chest X-ray findings	Number of patients
1.Consolidation	91 (55%)
2.Mediastinal lymphadenopathy	47 (28%)
3.Interstitial changes	43 (25%)
4.Cavitation	28 (17%)
5.Pleural effusion	22 (13%)
6.Miliary pattern	14 (8%)

Under therapy, overall an increase of CD4 counts could be seen regardless of the dominant image feature at baseline, though it showed a broad variance of range. The most significant rise of CD4 count was achieved in patients who showed a miliary pattern or pleural effusion at T1, indicating a good response to therapy. The highest number of cases with a decrease in CD4, was found in patients with lymphadenopathy or interstitial changes at T1. When comparing these values to the image-based response, we saw a high increase of CD4 count in patients with PR, whereas patients who showed a decrease in CD4 count were more likely to have TR.

Patients with low initial CD4 counts and with a high increase were more likely to show PR or SD. After 24 weeks of therapy, only 4 patients still showed positive culture results – all having a remarkably low CD4 count. While most people can achieve viral suppression and a rise of the CD4 count under therapy, some might obtain viral suppression without any significant increase in CD4 counts, due to advanced age, and a low nadir CD4 count or other not yet known factors.[24] It would further be interesting to compare drug resistant cases with radiographic pattern and CD4 count in order to detect drug-resistance earlier and initiate culture-based drug

Table 4

Occurrence of radiological patterns depending on CD4 cell counts.

CD4 (T1) cells/µL	Overall	Consolidation	Interstitial changes	Miliary pattern	Pleural effusion	Cavitation	Mediastinal lymphadenopathy
	166 (100%)	91 (55%)	43 (25%)	14 (8%)	22 (13%)	28 (17%)	47 (28%)
0–100	55 (33%)	24 (26%)	13 (30%)	8 (58%)	7 (32%)	3 (11%)	20 (43%)
101–200	33 (20%)	19 (21%)	10 (23%)	1 (7%)	6 (27%)	6 (21%)	9 (19%)
201–300	31 (19%)	20 (22%)	5 (12%)	3 (21%)	6 (27%)	7 (25%)	8 (17%)
> 300	47 (28%)	28 (31%)	15 (35%)	2 (14%)	3 (14%)	12 (43%)	10 (21%)
0–200	88 (53%)	43 (47%)	23 (53%)	9 (64%)	13 (59%)	9 (32%)	29 (62%)
> 200	78 (47%)	48 (53%)	20 (47%)	5 (36%)	9 (41%)	19 (68%)	18 (38%)

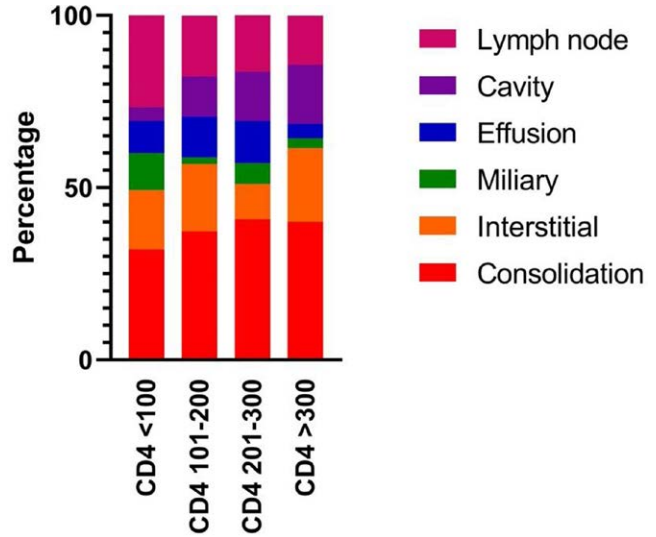

Figure 3. Frequency of the radiological features depending on CD4 count at baseline. CD4 = cluster of differentiation 4.

susceptibility testing. Limitations of this study are as follows: First, the quality of the CXR which were only scanned by a photograph of a digital camera. The quality, however, was high enough for the purpose of this study. Second, images were only read for presence/absence of a certain pattern, but not for its location or magnitude. Third, from the initial study population of 268 patients, we could only include 166 in this retrospective analysis, due to missing follow-ups and dropouts. This could lead to an asymmetric distribution with an attrition bias. Fourth, in this study we have only focused on pulmonary TB. It is known that 70% of patients with CD4 counts under 100 cells/μL show extrapulmonary manifestations, mostly peripheral lymphadenitis.[11] It would be desirable to include these cases in a further study to evaluate all elements of the disease.

5. Conclusions

In this retrospective study with 166 HIV and TB coinfected patients, we have demonstrated that there is an association of the CD4 count with the radiographic pattern on CXR. Imaging correlates with the change of CD4 count and reflects the response to therapy. Furthermore, an increase of CD4 counts under therapy was indicative for partial radiographic response, whilst a decrease of CD4 counts indicated stable disease.

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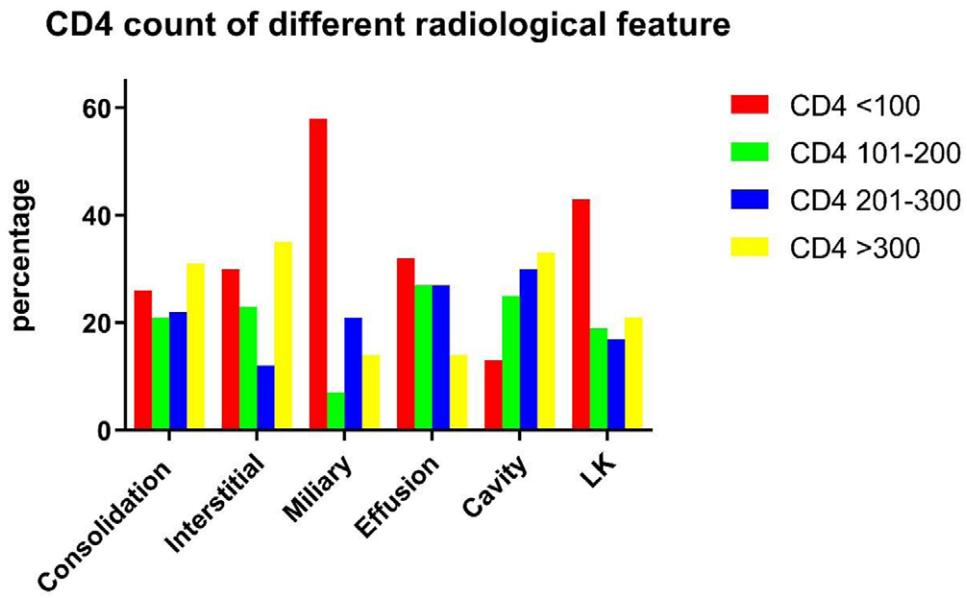

Figure 4. Percentage distribution of CD4-counts per radiological pattern. CD4 = cluster of differentiation 4.

Table 5

Occurrence of CD4 count-changes under therapy based on radiological therapy response and initial CD4 cell count.

Response		CD4 change	
	Initial CD4	Decrease/Stable (11%)	Increase (89%)
Total response (7%)	< 200	100%	0%
	> 200	46%	54%
Partial response (62%)	< 200	29%	71%
	> 200	57%	43%
Stable disease (27%)	< 200	11%	89%
	> 200	64%	36%
Progressive disease (4%)	< 200	0%	100%
	> 200	33%	67%

Table 6

Radiological response under therapy from T1 (baseline) to T3 (week 24) depending on baseline CD4 count.

CD4 count cells/µL	Overall n (%)	TR n (%)	PR n (%)	SD n (%)	PD n (%)
<100	55 (33)	5 (1)	32 (58)	18 (33)	0 (0)
101–200	33 (20)	1 (3)	23 (70)	7 (21)	2 (6)
201–300	31 (19)	2 (6)	23 (74)	4 (13)	2 (6)
>300	47 (28)	4 (9)	25 (53)	15 (32)	3 (6)
Total	166 (100)	12 (7)	103 (62)	44 (27)	7 (4)

CD4 = cluster of differentiation 4, PD = progressive disease, PR = partial response, SD = stable disease, T1 = baseline, T3 = second follow-up (week 24), TR = total response.

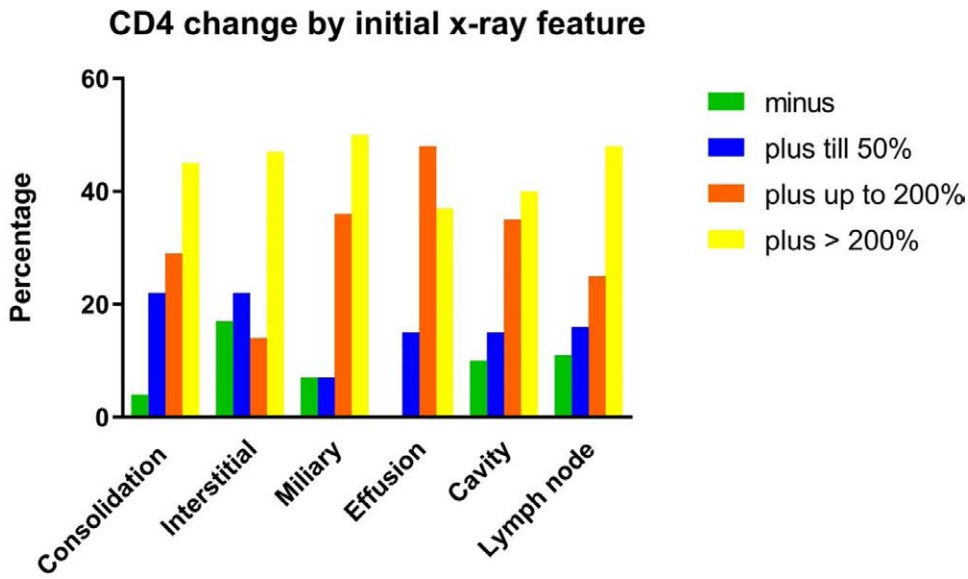

Figure 5. Percentage changes in CD4 over time in relation to the initial pattern. CD4 = cluster of differentiation 4.

Author contributions

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References

[1] Tornheim JA, Dooley KE. Tuberculosis associated with HIV infection. Microbiol Spectr. 2017;5:S50–5.
[2] Mayer KH, Dukes Hamilton C. Synergistic pandemics: confronting the global HIV and tuberculosis epidemics. Clin Infect Dis. 2010;50 Suppl 3:S67–70.
[3] Perriëns JH, Colebunders RL, Karahunga C, et al. Increased mortality and tuberculosis treatment failure rate among human immunodeficiency virus (HIV) seropositive compared with HIV seronegative patients with pulmonary tuberculosis treated with "standard" chemotherapy in Kinshasa, Zaire. Am Rev Respir Dis. 1991;144:750–5.
[4] The World Health Organization. HIV-associated Tuberculosis: 2017. Available at: https://apps.who.int/iris/bitstream/handle/10665/254824/SEA-TB-370.pdf;jsessionid=A10206B690AD1B941DBBB21081BCE69C?sequence=1 [access date February 3, 2023].
[5] Affusim C, Abah V, Kesieme EB, et al. The effect of low CD4+ lymphocyte count on the radiographic patterns of HIV patients with pulmonary tuberculosis among Nigerians. Tuberc Res Treat. 2013;2013:535769.
[6] Keiper MD, Beumont M, Elshami A, et al. CD4 T lymphocyte count and the radiographic presentation of pulmonary tuberculosis. A study of the relationship between these factors in patients with human immunodeficiency virus infection. Chest. 1995;107:74–80.
[7] Lawn SD, Evans AJ, Sedgwick PM, et al. Pulmonary tuberculosis: radiological features in west Africans coinfected with HIV. Br J Radiol. 1999;72:339–44.
[8] Lau A, Barrie J, Winter C, et al. Chest radiographic patterns and the transmission of tuberculosis: implications for automated systems. PLoS One. 2016;11:e0154032.
[9] Jeong YJ, Lee KS. Pulmonary tuberculosis: up-to-date imaging and management. AJR Am J Roentgenol. 2008;191:834–44.
[10] Garcia GF, Moura AS, Ferreira CS, et al. Clinical and radiographic features of HIV-related pulmonary tuberculosis according to the level of immunosuppression. Rev Soc Bras Med Trop. 2007;40:622–6.
[11] Gray JM, Cohn DL. Tuberculosis and HIV coinfection. Semin Respir Crit Care Med. 2013;34:32–43.
[12] van Cleeff MR, Kivihya-Ndugga LE, Meme H, et al. The role and performance of chest X-ray for the diagnosis of tuberculosis: a cost-effectiveness analysis in Nairobi, Kenya. BMC Infect Dis. 2005;5:111.
[13] de Albuquerque YM, Lima AL, Brandão e Silva AC, et al. Chest radiographic findings in patients with HIV/AIDS and pulmonary tuberculosis. Int J STD AIDS. 2013;24:951–6.

[14] Sekaggya-Wiltshire C, Castelnuovo B, von Braun A, et al. Cohort profile of a study on outcomes related to tuberculosis and antiretroviral drug concentrations in Uganda: design, methods and patient characteristics of the south study. BMJ Open. 2017;7:e014679.
[15] World Health Organization. Treatment of Tuberculosis: Guidelines. 4th ed. World Health Organization; 2010. Available at: https://apps.who.int/iris/handle/10665/44165 [access date February 3, 2023].
[16] Becker AS, Blüthgen C, Phi van VD, et al. Detection of tuberculosis patterns in digital photographs of chest X-ray images using deep learning: feasibility study. Int J Tuberc Lung Dis. 2018;22:328–35.
[17] da Silva RM, da Rosa L, Lemos RN. Radiographic alterations in patients presenting human immunodeficiency virus/tuberculosis coinfection: correlation with CD4+ T cell counts. J Bras Pneumol. 2006;32:228–33.
[18] Padyana M, Bhat RV, Dinesha M, et al. HIV-tuberculosis: a study of chest X-ray patterns in relation to CD4 count. N Am J Med Sci. 2012;4:221–5.
[19] Post FA, Wood R, Pillay GP. Pulmonary tuberculosis in HIV infection: radiographic appearance is related to CD4+ T-lymphocyte count. Tuber Lung Dis. 1995;76:518–21.
[20] Getachew A, Idh J, G/Sillasie S, et al. Chest radiographic patterns of smear positive tuberculosis in relation to HIV: a cross-sectional study in a population with a high burden of HIV and tuberculosis. Br J Med Med Res. 2014;4:5474–83.
[21] Kisembo HN, Boon SD, Davis JL, et al. Chest radiographic findings of pulmonary tuberculosis in severely immunocompromised patients with the human immunodeficiency virus. Br J Radiol. 2012;85:e130–9.
[22] Bakhshayesh-Karam M, Tabarsi P, Mirsaiedi SM, et al. Radiographic manifestations of tuberculosis in HIV positive patients: correlation with CD4+ T-cell count. Int J Mycobacteriol. 2016;5:S244–S5.
[23] Jones BE, Young SM, Antoniskis D, et al. Relationship of the manifestations of tuberculosis to CD4 cell counts in patients with human immunodeficiency virus infection. Am Rev Respir Dis. 1993;148:1292–7.
[24] World Health Organization. Chest Radiography in Tuberculosis Detection: Summary of Current WHO Recommendations and Guidance on Programmatic Approaches. World Health Organization; 2016. Available at: https://apps.who.int/iris/handle/10665/252424 [access date February 3, 2023].