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# Chest CT Findings in Patients with HIV Presenting to the Emergency Department: A Single Institute Experience



DIAGNOSTIC RADIOLOGY

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*Purpose:* The aim of this study was to analyze chest CT imaging findings and relevant clinical factors in patients with HIV presenting to the emergency department (ED). *Materials and methods:* A retrospective review was performed to identify patients with HIV who received chest CT imaging evaluation in the acute ED setting. Analyzed patients included adults with a known diagnosis of HIV who presented to the ED at a single tertiary care center between 2004 and 2020 and received chest CT imaging. Chest CT findings were assessed by 2 radiologist readers, and relevant clinical data were gathered. Statistical analysis was performed to determine if imaging and clinical factors demonstrate significant associations with CD4 count, viral load, and antiretroviral therapy status.

*Results:* A total of 113 patients with HIV were identified who presented to the ED and underwent chest CT imaging evaluation (mean age 47 ± 11 years). Frequently detected chest CT findings included infectious pneumonia (24%), malignancy (11%), pleural effusion (17%), pericardial effusion (13%), and pulmonary embolism (4%). CD4 count, viral load, and active retroviral therapy demonstrated statistically significant associations with a number of key imaging and clinical factors, including presence of pneumonia, malignancy, average length of hospital admission, and survival.

*Conclusion:* Patients with HIV present with a wide range of imaging findings when presenting in the acute ED setting. CD4 count, viral load, and active retroviral therapy status demonstrate statistically significant associations with multiple key imaging findings and clinical factors. Chest CT plays an integral role in the clinical management of this unique patient population.

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#### Introduction

According to the Centers for Disease Control and Prevention, the prevalence of HIV infection in the United States increased from 2014 to 2018 with over one million persons living with HIV (PLWH) in the United States at the end of 2018.<sup>1</sup> Among patients with PLWH, pulmonary disease is particularly common and is often the cause of acute symptoms that lead these patients to present to the emergency department (ED). Due to increased susceptibility to infection by common and opportunistic organisms as well as high rates of complications including malignancy and thromboembolism, PLWH presenting with respiratory symptoms often requires a broad differential diagnosis. Imaging plays an essential role in the clinical evaluation of these patients, requiring the radiologist interpreting ED studies to be familiar with the characteristic imaging findings of common cardiopulmonary complications of HIV infection. The limited sensitivity and specificity of radiographs for distinguishing these complications often makes chest CT studies the most appropriate study to ensure prompt and accurate diagnosis and targeted treatment.

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https://doi.org/10.1067/j.cpradiol.2022.09.002 0363-0188/© 2022 Published by Elsevier Inc. In this study, we sought to assess the cardiopulmonary complications of HIV that may present in the acute ED setting and their associated chest CT findings. Specifically, we aim to assess findings on chest CT studies obtained in the ED setting among patients with HIV presenting with acute respiratory symptoms. Furthermore, we evaluate whether specific imaging findings and clinical factors are associated with critical HIV-related clinical tests, including CD4 count and viral load. By presenting these findings in the context of clinical and laboratory data, we investigate associations of these imaging findings with HIV severity and survival.

## Methods

# Study design and setting

This retrospective study was conducted at a single tertiary care hospital with over 80,000 ED visits per year. Institutional review board approval was obtained with a waiver for informed consent. Patient medical records were reviewed, and data was analyzed in compliance with HIPAA.

#### Subjects and clinical data

Patients with established diagnoses of HIV/AIDS who sought care at the ED of this tertiary care center between 2004 and 2020 were identified through a search of the electronic medical record.

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Imaging records were then reviewed to identify those who received a chest CT study with or without intravenous contrast as part of their clinical workup in the ED. For these selected patients, clinical data regarding demographics, medical history, presentation, indications for imaging, hospital course, and survival were collected. Patients were excluded if provider documentation from the ED encounter was unavailable.

## Laboratory data

Laboratory studies obtained during the ED encounter as well as those obtained within 15 days prior to and following the encounter were reviewed to evaluate HIV disease severity. Specifically, within this time frame, the CD4+ T lymphocyte count and viral load in closest temporal proximity of the ED encounter were recorded for each patient. Individual CD4 counts for all patients were categorized into groups based upon specific values: CD4 count <200 vs >200 and CD4 count <200 vs >200-500 vs >500. Individual viral load counts for all patients were categorized into groups based upon specific values: viral load <20 vs >20 and viral load <20 vs >350. Additional pertinent labs including D-dimer level and infectious disease studies were reviewed on a case-by-case basis.

#### Imaging data and technique

All chest CT studies were obtained in the ED setting following clinical presentation. Chest CT examinations involved acquisition of axial CT images from the neck through the upper abdomen with 2 mm slice thickness using multidetector CT scanners. Intravenous administration of 80-120 mL of iodine-based contrast was selectively performed in accordance with CT angiography and pulmonary embolism protocols when indicated.

All chest CT studies obtained during each ED encounter were reviewed for relevant findings by a board-certified fellowshiptrained radiologist with approximately 23 years of experience and a 4th year radiology resident. Imaging findings were assessed as being either present or absent. Specific findings assessed included the presence of pleural effusion, pericardial effusion, pulmonary embolism, pneumonia, or malignancy. Any initial disagreements between these two reviewers were resolved via consensus agreement.

#### Statistical analysis

Statistical analysis was performed to assess for significant differences in various imaging and clinical factors based on groups defined by CD4 count, viral load, and ART status. Chi-square test was utilized to assess for significant associations between CD4 count (<200 vs >200 cells/mm<sup>3</sup>), viral load (<20 vs >20 copies/mL), or ART status and specific imaging findings (pleural effusion, pericardial effusion, pulmonary embolism, pneumonia, malignancy), and clinical findings (disposition from ED, and alive and/or deceased status). ANOVA was utilized to test for significant differences in the same imaging and clinical factors based on further subdivided groups defined by CD4 count (<200, 200-500, >500 cells/mm<sup>3</sup>) and viral load (<20, 20-350, >350 copies/mL). Unpaired t-test was utilized to assess for differences in length of admissions based upon groups defined by CD4 count (<200 vs >200 cells/mm<sup>3</sup>), viral load (<20 vs >20 copies/mL), or ART status.

For all statistical tests, a *P* value of <0.05 was considered to be statistically significant. All statistical analyses were performed using *Stata Statistical Software* (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.).

#### Results

## Clinical findings

Among the 591 PLWH who sought care at a single tertiary care center, we identified 119 patients who presented to the ED and received a CT scan of the chest. A total of 219 imaging studies, each representing a unique ED encounter, were obtained among these 119 patients. Sixteen encounters were excluded from analysis due to lack of available ED provider note, resulting in a final sample including 113 patients and 202 imaging studies (Fig 1). The distribution of number of ED visits were as follows: 1 ED visit (73 patients, 64.6%), 2 ED visits (18 patients, 15.9%), 3 ED visits (9 patients, 8.0%), 4 ED visits (5 patients, 4.4%), 5 ED visits (3 patients, 2.7%), 6 ED visits (4 patients, 3.5%), and 7 ED (1 patient 0.9%).

For these 113 patients (Table 1), the mean age at time of ED presentation was  $47 \pm 11$  years (range 24-79). The approximate date of HIV diagnosis was available for 96 patients, for whom the mean time from diagnosis to ED presentation was  $15 \pm 8$  years (range 0-34 years). A total of 71 patients, accounting for 142 imaging studies, were found to have a history of AIDS as determined by a previous documented CD4+ T-cell count <200 cells/mm<sup>3</sup> or a history of an AIDS-defining illness. A total of 38 patients, accounting for 61 imaging studies, had a history of malignancy, including lymphoma (n = 9), lung cancer (n = 7), rectal cancer (n = 4), anal cancer (n = 4), Kaposi sarcoma (n = 3), breast cancer (n = 2), colon cancer (n = 2), renal



FIG 1. Flow Diaphragm of Patient Selection.

## TABLE 1

Population characteristics and imaging indications

Characteristic	Value		
Total number of patients	113		
Mean age (years)	$47 \pm xx$ ; range: 24-79		
Mean time from HIV diagnosis (years)	$15 \pm xx$ ; range: 0-34		
History of AIDS	71 (63%)		
History of malignancy	38 (34%)		
Deceased	35 (31%)		
Total number of ED encounters/chest CT studies	202		
Studies obtained on ART	150 (74%)		
Imaging indication			
Shortness of breath	120 (59%)		
Chest pain	107 (53%)		
Cough	70 (35%)		
Elevated D-dimer	60 (30%)		
History of VTE	24 (12%)		
Known or suspected DVT	13 (6%)		
Hemoptysis	6 (3%)		
Syncope	4 (2%)		
Admitted from ED	144 (71%)		
Avg length of admission (days)	5; range: 1-48		
On ART	4; range 1-48		
Not on ART	7; range 1-44		

cancer (n = 2), head and neck cancer (n = 2), vulvar cancer (n = 1), gastric and prostate (n = 1), malignant pheochromocytoma (n = 1), and multiple myeloma (n = 1).

For 74% (150/202) of all imaging studies obtained, the patient was currently on active antiretroviral therapy (ART). The most common indication for obtaining a CT chest study upon presentation to the ED was shortness of breath (n = 120 studies). Other common indications included chest pain (n = 107), cough (n = 70), elevated d-dimer (n = 60), history of venous thromboembolism (VTE) (n = 24), known or suspected deep vein thrombosis (DVT) with extremity edema and/ or pain (n = 13), hemoptysis (n = 6), and syncope (n = 4). ED visits led to a hospital admission in 144 encounters (71%), and the average length of admission was 6 days (range: 1-48 days). Length of admission was found to differ significantly between patients who were on ART and those who were not, with patients on ART having shorter admissions (mean  $4.4 \pm 3.3$  vs  $7.1 \pm 8.9$  days; P = 0.029). Of the 113 patients, 35 patients (31%) were found to be deceased at the time of this study, with a median time between ED presentation and death of 376 days.

## Imaging findings

A total of 202 CT scans of the chest were obtained in the ED among the 113 patients reviewed (Table 2). This included 18 routine noncontrast CT, 20 routine CT with IV contrast, 7 CT angiography, and 157 CT pulmonary angiography protocol studies. The most common finding was pneumonia (n = 55, 27%), manifesting as a single-lobe consolidation (n = 13, 24%), multilobar consolidations or opacities (n = 27, 49%), and ground glass opacities (n = 15, 27%) (Fig 2A-B). Cavitary lesions were observed in 5 studies (9%). Review of infectious workup for each case of pneumonia revealed the causative pathogen in 14 cases, including *Streptococcus pneumoniae* (n = 5), *Pneumocystis jirovecii* (n = 2), influenza (n = 2), *Pseudomonas aeruginosa* (n = 1), *Klebsiella pneumoniae* (n = 1), *Proteus mirabilis* (n = 1), *Cryptococcus neoformans* (n = 1), and *Mycobacterium peregrinum* (n = 1).

Evidence of malignancy was present in 22 chest CT studies (11%) (Fig 2C-E). Primary lung cancer in 7 patients accounted for 13 cases, metastatic disease in 3 patients accounted for 5 cases, and lymphoma in 4 patients accounted for 4 cases. In 59% of these studies, the malignancy was either a new finding or the extent of disease had worsened compared to prior imaging studies. Malignancy manifested as lung nodules or masses in 18 studies and as lymphadenopathy in 19

TABLE 2

ED Chest CT imaging findings

Imaging Findings	Value
Total number chest CT studies	202
Non-contrast CT	18 (9%)
Routine CT with IV contrast	20 (10%)
CT angiography	7 (3%)
CT pulmonary angiography	157 (78%)
Pneumonia	55 (27%)
Single-lobe	13 (24%)
Multi-lobe	27 (49%)
Ground glass opacities	15 (27%)
Cavitary lesions	5 (9%)
Pleural effusion	15 (27%)
Malignancy	22 (11%)
Туре	
Primary lung cancer	13 (59%)
Metastatic disease	5 (23%)
Lymphoma	4 (18%)
New or worsening	13 (59%)
Nodules/masses	18 (82%)
Lymphadenopathy	19 (86%)
Mediastinal	15 (68%)
Hilar	12 (55%)
Axillary	5 (23%)
Supraclavicular	4 (18%)
Pleural effusion	11 (50%)
Pericardial effusion	6 (27%)
Pleural effusion	34 (17%)
Unilateral	17 (50%)
Bilateral	17 (50%)
New or worsening	29 (85%)
Pericardial effusion	26 (13%)
New or worsening	19 (73%)
Pulmonary embolism	8 (4%)

studies. Lymphadenopathy was observed in the mediastinal (n = 15), hilar (n = 12), axillary (n = 5), and supraclavicular (n = 4) nodes. Evidence of pneumonia was concurrently present in 9 studies.

All cases of primary lung malignancy were non-small cell lung cancers (NSCLC), with 3 patients diagnosed with squamous cell carcinoma and 2 diagnosed with adenocarcinoma by pathology; the remaining 2 patients had poorly differentiated NSCLC. In all 7 patients, chest CT revealed a distinct nodule or mass which was centrally located in 2 patients and peripherally located with a lower lobe predominance in the other 5 patients. Among the 13 chest CTs obtained in these patients, lymphadenopathy was observed in 11 studies and pleural effusions in 8 studies.

Among the patients with pulmonary metastases, the primary malignancies included breast cancer, neck cancer, and malignant pheochromocytoma. Nodules and/or masses were present in all 5 chest CTs obtained in these patients, whereas lymphadenopathy was observed in 4 studies and pleural effusions in 2 studies.

The 4 patients with lymphoma included 1 case of classic Hodgkin lymphoma (HL) and 3 cases of non-Hodgkin lymphoma (NHL), more specifically 2 cases of diffuse large B cell lymphoma and 1 case of HHV8+, EBV+ lymphoproliferative disorder representing extra-cavitary primary effusion lymphoma. Lymphadenopathy was present in all 4 imaging studies, and nodules representing extra-nodal metastases were present in 1 study.

Pleural effusions were present in a total of 34 studies (17%), which were new or had increased in size compared to prior imaging in 29 studies. Fifty percent of these effusions were bilateral. Thoracentesis was performed in one case, and in 3 other cases a chest tube was already in place. Pleural effusion was associated with pneumonia in 15 studies and with malignancy in 11 studies.

Pericardial effusions were observed in 26 studies (13%). Twenty-two of these effusions were small, 2 were moderate, and 2 were large in size. These effusions were new or worsening in 19 studies, with one



**FIG 2.** For example chest CT findings in patients with HIV presenting to the emergency department (ED). (A-B) 59-year-old male with history of HIV and prior right pneumonectomy who presented to the ED with new shortness of breath, pleuritic chest pain, and elevated D-dimer. Coronal (A) and axial (B) CT contrast-enhanced CT images of the chest in lung window show patchy ground glass and consolidative airspace opacities in the left upper and lower lobes (arrows), as well as a small left-sided pleural effusion. The patient was admitted and treated with antibiotics for management of multifocal pneumonia. (C-E) 56-year-old man with history of HIV who presented for evaluation in the ED with worsening pain associated with inspiration. Axial CT images of the chest reveal an area of dense masslike consolidation in the right lower lobe (arrow in C), right hilar adenopathy (arrow in D), and complete occlusion of the right lower lobe bronchi. An FDG-PET/CT study was obtained for further evaluation. Axial FDG-PET CT image demonstrates markedly increase meta-bolic activity associated with a masslike area in the right lower lobe (arrow in E). The patient underwent transbronchial biopsy, which confirmed the diagnosis of poorly differenti-ated adenocarcinoma. (F-G) 61-year-old man with history of HIV who presented with acutely worsening shortness of breath and elevated D-dimer. Axial contrast-enhanced CT image of the chest demonstrates a pulmonary embolism in the right nump artery and bilateral lobar and segmental pulmonary artery branches (arrows in F). Note is also made of flattening of the intraventricular septum (arrow in G) and enlargement of the right ventricle, consistent with right heart strain. The patient was started on treatment with therapeutic warfarin and ultimately discharged from the hospital following clinical improvement during a 7-day hospital admission.

causing cardiac tamponade requiring a pericardial window. A total of 6 of the observed pericardial effusions were in patients with concurrent chest malignancy and 10 were in patients with concurrent pneumonia.

Eight studies were positive for new pulmonary embolism (Fig 2F-G), with two additional studies demonstrating known, residual emboli. Of the 60 studies in which elevated D-dimer level was an indication, pulmonary embolism was found in 4 cases. D-dimer level was not measured in the other 4 cases of pulmonary embolism. Pulmonary embolism was in the setting of pneumonia in 2 cases and malignancy in 1 case.

#### Associations with CD4 T-cell Count

CD4+ T-cell count was available within 15 days of the ED encounter for 167 encounters (83%). Of these encounters, 76 (46%) were associated with a CD4 count <200 cells/mm<sup>3</sup>, 47 (28%) with a CD4 count between 200 and 500 cells/mm<sup>3</sup>, and 44 (26%) with a CD4 count >500 cells/mm<sup>3</sup> (Table 3). When CD4 count was <200 cells/mm<sup>3</sup>, the patient was more likely to be deceased at the time of this study when compared to patients with CD4 count >200 cells/mm<sup>3</sup> (47% vs 29%; *P* = 0.012). On imaging, patients with CD4 count <200

cells/mm<sup>3</sup> were more likely to have pleural effusions (24% vs 12%; P = 0.049) and pneumonia (38% vs 19%; P = 0.005) when compared to patients with CD4 count >200 cells/mm<sup>3</sup>. Further, when CD4 count was stratified into 3 groups (<200, 200-500, >500 cells/mm<sup>3</sup>), analysis also yielded significant differences in the presence of pneumonia (P = 0.001), length of admission (P = 0.003), and whether the patient was deceased (P = 0.002).

## Associations with Viral Load

Measures of viral load were available within 15 days of the ED encounter for 157 encounters (78%). Viral load was found to be <20 copies/mL for 56 encounters (36%), between 20 and 350 copies/mL for 37 encounters (24%), and >350 copies/mL for 64 encounters (41%) (Table 4). For these 64 encounters in which viral load was elevated above 350 copies/mL, the patient was documented to be on ART for 31 of the encounters (48%). In contrast, 33 patients were not currently on ART (52%). Patients with viral load >20 copies/mL were more likely to be deceased compared to patients with viral loads <20 (45% vs 25% P = 0.015). Additionally, there were also significant differences were detected in groups defined by viral

113

TABLE 3

#### Associations with CD4+ T lymphocyte count

Imaging or Clinical Variable	$\begin{array}{l} CD4 < 200 \\ cells/mm^3 \end{array}$	CD4 > 200 cells/mm <sup>3</sup>	CD4 200-500 cells/mm <sup>3</sup>	CD4 > 500 cells/mm <sup>3</sup>	<i>P</i> value (CD4 <200 vs >200 cells/mm <sup>3</sup> )	<i>P</i> value (CD4 <200 vs 200- 500 vs >500 cells/mm <sup>3</sup> )
Number of encounters	76	91	47	44	-	-
Admitted from ED	59 (77%)	66 (72%)	38 (81%)	28 (64%)	P = 0.449	P = 0.126
Avg length of admission	6 days	4 days	5 days	3 days	P = 0.109	P = 0.002
Deceased	36 (47%)	26 (29%)	20 (43%)	6(14%)	P = 0.012	P = 0.003
Pneumonia	29 (38%)	17 (19%)	14 (30%)	3 (7%)	P = 0.005	P = 0.001
Malignancy	13 (17%)	8 (9%)	5 (11%)	3 (7%)	P = 0.107	<i>P</i> = 0.234
Pleural effusion	18 (24%)	11 (12%)	8 (17%)	3 (7%)	P = 0.049	P = 0.063
Pericardial effusion	11 (14%)	11 (12%)	6(13%)	5 (11%)	P = 0.650	P = 0.885
Pulmonary embolism	4 (5%)	4 (4%)	2 (4%)	2 (5%)	P = 0.794	<i>P</i> = 0.073

load of <210, 20-350, and >500 based on the prevalence of pneumonia (P = 0.008), length of hospital admission (P = 0.000), and whether the patient was deceased (P = 0.030).

# Discussion

In this study we present a comprehensive retrospective analysis of chest CT findings amongst PLWH presenting acutely in the ED setting. Given the wide variety of potential complications of HIV infection, the radiologist must be familiar with the imaging manifestations of the many infectious, malignant, and thromboembolic processes to which these patients are susceptible in order to ensure appropriate management is achieved. The results of this single-institution study highlight the imaging correlates of several processes that may cause acute cardiopulmonary symptoms in PLWH, including pneumonia, lung cancer, lymphoma, pleural and pericardial effusions, and pulmonary embolism. Statistically significant associations were found between CD4 count and several key imaging and clinical factors, including pneumonia, pleural effusions, average length of hospital admission, and survival. Significant associations were also identified between viral load and factors including pneumonia, survival, and average length of hospital admission.

Pneumonia is a major cause of morbidity among PLWH given their increased susceptibility to severe disease from both typical community-acquired and opportunistic pathogens. Bacterial community-acquired pneumonia (BCAP) caused by *Streptococcus pneumoniae* remains the most common pulmonary infection in PLWH on ART, typically manifesting on chest CT as areas of patchy consolidation and bronchiectasis.<sup>2-5</sup> In this study, 27% of chest CT scans obtained in the ED demonstrated findings consistent with pneumonia. Among those with a causative organism identified, *S. pneumoniae* was the most common etiology, with chest CT showing lobar consolidations as expected. We found a significant association between the rate of pneumonia and the severity of HIV, with a higher frequency of infection among patients with low CD4 counts and high viral loads, which is consistent with previous studies that have found higher frequencies of both BCAP and opportunistic pneumonia in patients with low CD4 counts.<sup>6,7</sup>

We also reported multiple cases of opportunistic infections, including pneumonia caused by Pneumocystis jirovecii, Cryptococcus neoformans, and non-tuberculous mycobacterium. Among the 2 cases of PCP proven by broncho-alveolar lavage and tissue biopsy, both presented with bilateral ground glass opacities on chest CT, which is the main imaging finding in 92% of cases of PCP according to a previous study by Hartman et al.<sup>8</sup> Cryptococcal infection in PLWH more commonly presents as disseminated disease and meningitis rather than pneumonia; however, when there is pulmonary involvement, the most common finding is bilateral interstitial infiltrates.<sup>9</sup> Other possible findings include nodules with or without cavitation, consolidations, lymphadenopathy, and pleural effusions.<sup>9-12</sup> In this study, we found 1 case of cryptococcal pneumonia with positive blood antigen that presented as diffuse, bilateral ground glass opacities, similar in appearance to PCP. Lastly, we found 1 case of Mycobacterium peregrinum pneumonia, diagnosed by sputum culture, which presented with multiple areas of linear atelectasis. Cases of pneumonia caused by this mycobacterium species are sparsely reported in the existing literature, with one previous case reported in a patient with HIV.<sup>13-16</sup>

Of note, we also reported 1 case of pneumonia due to *Proteus mir-abilis*, a rare cause of mostly hospital-acquired pneumonia, although few reports of community-acquired pneumonia from *Proteus* exist.<sup>17</sup> The patient in our study had a history of recurrent pneumonia, with 2 previous episodes of pneumococcal pneumonia and 2 episodes of unknown etiology. In this case chest CT revealed numerous scattered tree-in-bud opacities, consolidative opacities, and cavitary lesions which had been present on previous studies but since increased in size. These findings are similar to the radiographic findings previously described by Unger et al., which consisted of predominantly lower lobe opacities with areas of cavitation present in 63% of cases and effusions present in 38% of cases.<sup>18</sup>

Malignancy is one of the most common long-term complications of HIV infection. In this study, we demonstrate that new or worsening malignancy is a common reason for patients with HIV presenting to the ED. Since the advent of ART, the incidences of AIDS-defining malignancies, such as NHL, have decreased significantly, while the incidences of non-AIDS-defining malignancies, including lung cancer,

TABLE 4
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Associations with viral load

Imaging or Clinical Variable	$VL < 20 \ copies/mL$	$VL > 20 \ copies/mL$	VL 20-350 copies/mL	VL > 350 copies/mL	<i>P</i> value (CD4 <20 vs >20 copies/mL)	<i>P</i> value (CD4 <20 vs 20- 359 vs > 350 copies/mL)
Number of encounters	56	101	37	64		
Admitted from ED	41 (73%)	79 (78%)	27 (73%)	52 (81%)	P = 0.479	P = 0.498
Avg length of admission	4 days	6 days	4 days	7 days	P = 0.082	P = 0.000
Deceased	14 (25%)	45 (45%)	14 (38%)	31 (48%)	P = 0.015	<i>P</i> = 0.030
Pneumonia	15 (27%)	32 (32%)	5 (14%)	27 (42%)	P = 0.521	P = 0.008
Malignancy	4 (7%)	13 (13%)	7 (19%)	6 (9%)	P = 0.269	P = 0.179
Pleural effusion	11 (20%)	13 (13%)	4(11%)	9(14%)	P = 0.259	P = 0.480
Pericardial effusion	10(18%)	10 (10%)	2 (5%)	8 (13%)	P = 0.152	P = 0.211
Pulmonary embolism	1 (2%)	7 (7%)	3 (8%)	4 (6%)	P = 0.157	<i>P</i> = 0.498

VL = Viral load

have remained stable or potentially even increased in PLWH.<sup>19-22</sup> Similar to the general population, lung cancer is the most common cause of cancer-associated mortality in PLWH; however, multiple studies have shown that PLWH have an increased risk of developing the disease (relative risk of 2.2 to 4.7 per Sigel et al.), a tendency to develop the disease at a younger age, and poorer survival rates.<sup>21-27</sup> The association between HIV infection and lung cancer is likely multifactorial, with higher rates of smoking among PLWH as well as direct immunosuppressive mechanisms of HIV infection contributing.<sup>21,22,25,28</sup>

Previous studies of the imaging characteristics of lung cancer in PLWH have reported parenchymal masses or nodules, predominantly peripherally located in the upper lobes, to be the most common imaging feature.<sup>26,29</sup> Additionally, lymphadenopathy and pleural effusions are frequently observed, with Fishman et al. reporting lymphadenopathy in 10 cases and pleural effusions in 10 cases in their study of 30 PLWH with bronchogenic carcinoma.<sup>26</sup> In our study, 13 chest CT studies obtained in 7 patients demonstrated findings of primary lung cancer, with 8 studies demonstrating evidence of new or progressive disease compared to prior imaging. Imaging findings were consistent with previous reports, with peripheral pulmonary mass or nodule being the most common disease manifestation; however, these were more frequently located in the lower lobes. Lymphadenopathy and pleural effusions were present in the majority of studies, suggesting these may be more common adjunct findings than previously reported.

The association between HIV and the development of lymphoma is even more profound. HIV is associated with up to a 30-fold increase in the risk of developing HL and up to a 165-fold increase in the risk of developing NHL.<sup>30,31</sup> In our study, we found 1 case of HL and 3 cases of NHL with disease manifestations evident on chest CT. Progression of disease, represented as worsening lymphadenopathy and new pulmonary nodules, was noted in 3 of these cases, and, in each case, the patient presented with complaint of shortness of breath and cough. These findings are consistent with those previously reported by Eisner et al. who found cough and dyspnea to be the most common symptoms of HIV+ patients with NHL with pulmonary involvement. They also found lymphadenopathy and pulmonary nodules to be among the most common imaging findings, although they reported a greater prevalence of pleural effusions (68%) than observed here (33%).<sup>32</sup> It is important to note that for the 2 cases of progressive NHL included in our study, the patients were concurrently diagnosed with pneumonia based on CT findings of ground glass opacities. While it is unclear whether a separate infectious process or the patient's advancing malignancy was the cause of the patient's symptoms, our findings underscore the need to have a high suspicion for potential malignancy in PLWH presenting with new nodules or lymphadenopathy on chest CT even when an infectious etiology seems likely given the patient's immunosuppressed state.

Pericardial effusion is one of the most common cardiac complications of HIV, frequently developing in the setting of malignancy such as Kaposi sarcoma or lymphoma. This complication may also develop in the setting of various infections, such as mycobacterial or *Staphylococcus aureus* infection.<sup>33,34</sup> However, more recent studies in the post-ART era have reported lower rates of pericardial effusion compared to pre-ART times, which may be in part related to lower rates of opportunistic infections given better control of HIV progression.<sup>35</sup> In this study, 26 chest CTs were remarkable for pericardial effusion, and a majority of these studies did not demonstrate concurrent infectious or malignant disease. We did not find a significant association between the presence of pericardial effusion and HIV severity as measured by lower CD4 count or higher viral load, in contrast to the findings of Heidenreich et al. who reported lower average CD4 count among patients with AIDS with pericardial effusion than those without effusion. However, our other findings show strong concordance, with majority of effusions being small, asymptomatic, and not requiring intervention.<sup>33</sup>

Previous studies have shown that PLWH are at an increased risk of thromboembolic disease compared to patients without HIV.<sup>36,37</sup> Specifically, Malek et al. reported a 43% increase in odds of developing a PE among PLWH relative to those without the disease.<sup>36</sup> HIV infection produces a hypercoagulable state through several mechanisms, with protein S deficiency as one of the most accepted etiologies. This prothrombotic state is heightened in the setting of opportunistic infection or HIV- associated malignancy. Further, VTE risk has been shown to correlate with the severity of HIV infection, with studies showing greater frequency of VTE among patients with low CD4 counts.<sup>38</sup> In this study, PE was present in 4% of chest CT studies performed in the ED. This is much higher than the prevalence of PE of less than 0.5% found in previous studies of PLWH, suggesting PE may be a more common cause of acute ED presentation in PLWH than previously recognized.<sup>36,39</sup> Additionally, there was no significant difference in the risk of PE among patients with CD4 count < 200 compared to patients with CD4 count >200, and there was no clear association between the findings of pulmonary embolism and pneumonia or malignancy; however, these comparisons were significantly limited given the small sample size.

There are several limitations to note in this retrospective study. The included sample size of 113 patients and 202 chest CT studies represents a reasonably sized study compared to existing studies in the literature. Nevertheless, a larger sample size would likely have been beneficial and may have yielded additional significant results. Expanding the study beyond a single tertiary care center could also have improved the generalizability of our results. Additionally, it is unclear why patients documented to be on ART were found to have elevated viral load >350 copies/mL; medication noncompliance and ineffective medication are possible contributing factors, but further investigation is required to determine the nature of such poorly controlled disease.

In conclusion, patients with HIV can present with a wide range of chest CT imaging findings upon during acute presentations to the emergency department. Commonly detected findings in this patient population included pneumonia, new or worsening malignancy, pleural or pericardial effusions, and pulmonary embolism. Significant associations were found between CD4 count, viral load, with various imaging and clinical factors including pneumonia, pleural effusion, average hospital admission length, and survival. These findings highlight the critical importance of chest CT imaging in the clinical management of patients with HIV presenting in the acute ED setting.

## References

- 1. Centers for Disease Control and Prevention. HIV Surveillance Report. 2018, 31.
- Bordon J, Kapoor R, Martinez C, et al. CD4+ cell counts and HIV-RNA levels do not predict outcomes of community-acquired pneumonia in hospitalized HIV-infected patients. Int J Infect Dis IJID Off Publ Int Soc Infect Dis 2011;15:e822–7.
- Cribbs SK, Crothers K, Morris A. Pathogenesis of HIV-Related Lung Disease: Immunity, Infection, and Inflammation. Physiol Rev 2020;100:603–32.
- Madeddu G, Porqueddu EM, Cambosu F, et al. Bacterial community acquired pneumonia in HIV-infected inpatients in the highly active antiretroviral therapy era. Infection 2008;36:231–6.
- Shah RM, Salazar AM. CT manifestations of human immunodeficiency virus (HIV)related pulmonary infections. Semin Ultrasound CT MR 1998;19:167–74.
- Hirschtick RE, Glassroth J, Jordan MC, et al. Bacterial pneumonia in persons infected with the human immunodeficiency virus. Pulmonary Complications of HIV Infection Study Group. N Engl J Med 1995;333:845–51.
- Jung AC, Paauw DS. Diagnosing HIV-related disease: using the CD4 count as a guide. J Gen Intern Med 1998;13:131–6.
- Hartman TE, Primack SL, Müller NL, Staples CA. Diagnosis of thoracic complications in AIDS: accuracy of CT. AJR Am J Roentgenol 1994;162:547–53.
- Pupaibool J, Limper AH. Other HIV-associated pneumonias. Clin Chest Med 2013;34:243–54.
- Huang L, Crothers K. HIV-associated opportunistic pneumonias. Respirology 2009;14:474–85.
- Logan PM, Finnegan MM. Pulmonary complications in AIDS: CT appearances. Clin Radiol 1998;53:567–73.
- Marchiori E, Müller NL, Soares Souza AJ, Escuissato DL, Gasparetto EL, Franquet T. Pulmonary disease in patients with AIDS: high-resolution CT and pathologic findings. AJR Am J Roentgenol 2005;184:757–64.

- Marie I, Heliot P, Roussel F, Hervé F, Muir JF, Levesque H. Fatal Mycobacterium peregrinum pneumonia in refractory polymyositis treated with infliximab. Vol. 44, Rheumatology (Oxford, England). England; 2005. p. 1201–2.
- Omar S V, Allam M, Joseph L, Mtshali S, Ismail NA, Ismail A. Draft Genome Sequence of Mycobacterium peregrinum Isolated from an HIV-Positive Patient in South Africa. Genome Announc 2017;5(31):e00759-17.
- Sawahata M, Hagiwara E, Ogura T, et al. [Pulmonary mycobacteriosis caused by Mycobacterium peregrinum in a young, healthy man]. Nihon Kokyuki Gakkai Zasshi 2010;48:866–70.
- 16. Sharma M, Malhotra B, Tiwari J, Bhargava S. Profile of nontuberculous mycobacteria in patients suspected of tuberculosis and drug-resistant tuberculosis. J Lab Physicians 2020;12:203–11.
- Okimoto N, Hayashi T, Ishiga M, et al. Clinical features of Proteus mirabilis pneumonia. J Infect Chemother Off J Japan Soc Chemother 2010;16:364–6.
- Unger JD, Rose HD, Unger GF. Gram-negative pneumonia. Radiology 1973; 107:283–91.
- Diamond C, Taylor TH, Aboumrad T, Anton-Culver H. Changes in acquired immunodeficiency syndrome-related non-Hodgkin lymphoma in the era of highly active antiretroviral therapy: incidence, presentation, treatment, and survival. Cancer 2006;106:128–35.
- **20.** Simard EP, Pfeiffer RM, Engels EA. Cumulative incidence of cancer among individuals with acquired immunodeficiency syndrome in the United States. Cancer 2011;117:1089–96.
- Mani D, Haigentz MJ, Aboulafia DM. Lung cancer in HIV Infection. Clin Lung Cancer 2012;13:6–13.
- Sigel K, Pitts R, Crothers K. Lung Malignancies in HIV Infection. Semin Respir Crit Care Med. 2016;37:267–76.
- Cadranel J, Garfield D, Lavolé A, Wislez M, Milleron B, Mayaud C. Lung cancer in HIV infected patients: facts, questions and challenges. Thorax 2006;61:1000–8.
- 24. Hou W, Fu J, Ge Y, Du J, Hua S. Incidence and risk of lung cancer in HIV-infected patients. J Cancer Res Clin Oncol 2013;139:1781–94.
- Sigel K, Makinson A, Thaler J. Lung cancer in persons with HIV. Curr Opin HIV AIDS 2017;12:31–8.

- 26. Fishman JE, Schwartz DS, Sais GJ, Flores MR, Sridhar KS. Bronchogenic carcinoma in HIV-positive patients: findings on chest radiographs and CT scans. AJR Am J Roentgenol 1995;164:57–61.
- Karp J, Profeta G, Marantz PR, Karpel JP. Lung cancer in patients with immunodeficiency syndrome. Chest 1993;103:410–3.
- Shcherba M, Shuter J, Haigentz MJ. Current questions in HIV-associated lung cancer. Curr Opin Oncol 2013;25:511–7.
- 29. Bazot M, Cadranel J, Khalil A, et al. Computed tomographic diagnosis of bronchogenic carcinoma in HIV-infected patients. Lung Cancer 2000;28:203–9.
- Kaplan L. HIV-related lymphomas: Epidemiology, risk factors, and pathobiology. In: Post T, editor. UpToDate. Waltham, MA: UpToDate; 2020.
- Vishnu P, Aboulafia DM. AIDS-Related Non-Hodgkin's Lymphoma in the Era of Highly Active Antiretroviral Therapy. Adv Hematol 2012;2012: 485943.
- Eisner MD, Kaplan LD, Herndier B, Stulbarg MS. The pulmonary manifestations of AIDS-related non-Hodgkin's lymphoma. Chest 1996;110:729–36.
- Heidenreich PA, Eisenberg MJ, Kee LL, et al. Pericardial effusion in AIDS. Incidence and survival. Circulation 1995;92:3229–34.
- 34. Chen Y, Brennessel D, Walters J, Johnson M, Rosner F, Raza M. Human immunodeficiency virus-associated pericardial effusion: report of 40 cases and review of the literature. Am Heart J 1999;137:516–21.
- **35.** Lind A, Reinsch N, Neuhaus K, et al. Pericardial effusion of HIV-infected patients ? Results of a prospective multicenter cohort study in the era of antiretroviral therapy. Eur J Med Res 2011;16:480–3.
- Malek J, Rogers R, Kufera J, Hirshon JM. Venous thromboembolic disease in the HIV-infected patient. Am J Emerg Med 2011;29:278–82.
- Rasmussen LD, Dybdal M, Gerstoft J, et al. HIV and risk of venous thromboenbolism: a Danish nationwide population-based cohort study. HIV Med 2011;12:202– 10.
- Bibas M, Biava G, Antinori A. HIV-Associated Venous Thromboembolism. Mediterr J Hematol Infect Dis 2011;3:e2011030.
- Howling SJ, Shaw PJ, Miller RF. Acute pulmonary embolism in patients with HIV disease. Sex Transm Infect 1999;75:25–9.