

# Preliminary Observations of Veterans Without HIV Who Have *Mycobacterium avium* Complex Pulmonary Disease

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**Background:** Nontuberculous *Mycobacterium*-related pulmonary disease (NTM-PD) is commonly caused by *Mycobacterium avium* complex (MAC) and is increasingly recognized in veterans. NTM-PD carries an increased risk of mortality, and lack of treatment is an predictor of increased mortality.

**Methods:** We describe the clinical characteristics of veterans diagnosed with MAC-pulmonary disease (MAC-PD) followed in a health care setting with varying treatment practices. We reviewed the electronic health records of veterans without HIV who had sputum culture-positive MAC-PD followed at the Jesse Brown Veteran Affairs Medical Center in Chicago, Illinois.

**Results:** We identified 19 veterans diagnosed with MAC-PD between 2008 and 2019. They were predominantly male (89.5%),

Black (73.6%), and had a median age of 74 years. Sixteen veterans (84.2%) had underlying lung disease, and 16 (84.2%) were current or former smokers. Respiratory symptoms were reported in 17 veterans (89.5%). Guideline-directed combination antimycobacterial therapy was initiated in 10 veterans (52.6%); however, only 5 (50.0%) completed treatment. Comorbidities, symptoms, and findings on chest imaging at diagnosis were similar among treated and untreated veterans.

**Conclusions:** Clinical, imaging, and treatment attributes of MAC-PD in veterans without HIV who reside in metropolitan Chicago are heterogeneous and are associated with a relatively high mortality rate. Further studies are warranted to characterize MAC-PD and its treatment in veterans without HIV who reside in underresourced urban communities in the US.

Nontuberculous *Mycobacterium* (NTM) is a ubiquitous organism known to cause a variety of infections in susceptible hosts; however, pulmonary infection is the most common. *Mycobacterium avium* complex (MAC) is the most prevalent cause of NTM-related pulmonary disease (NTM-PD) and is associated with underlying structural lung disease, such as chronic obstructive pulmonary disease (COPD) and noncystic fibrosis bronchiectasis.<sup>1-3</sup>

Diagnosis of NTM-PD requires (1) symptoms or radiographic abnormality; and (2) at least 2 sputum cultures positive with the same organism or at least 1 positive culture result on bronchoscopy (wash, lavage, or biopsy).<sup>1</sup> Notably, the natural history of untreated NTM-PD varies, though even mild disease may progress substantially.<sup>4-6</sup> Progressive disease is more likely to occur in those with a positive smear or more extensive radiographic findings at the initial diagnosis.<sup>7</sup> A nationwide Medicare-based study showed that patients with NTM-PD had a higher rate of all-cause mortality than did patients without NTM-PD.<sup>8</sup> In a study of 123 patients from Taiwan with MAC-PD, lack of treatment was an independent predictor of mortality.<sup>9</sup> Given the risk of progressive morbidity and mortality, recent guidelines recommend initiation of a susceptibility

driven, macrolide-based, 3-drug treatment regimen over watchful waiting.<sup>10</sup>

MAC-PD is increasingly recognized among US veterans.<sup>11,12</sup> The Jesse Brown Veterans Affairs Medical Center (JBVAMC) in south/west Chicago serves a large, predominantly Black male population of veterans many of whom are socioeconomically underresourced, and half are aged  $\geq 65$  years. We observed that initiation of guideline-directed therapy in veterans with MAC-PD at JBVAMC varied among health care professionals (HCPs) in the pulmonary clinic. Therefore, the purpose of this retrospective study was to describe and compare the characteristics of veterans without HIV were diagnosed with MAC-PD and managed at JBVAMC.

## METHODS

The hospital microbiology department identified veterans diagnosed with NTM at JBVAMC between October 2008 and July 2019. Veterans included in the study were considered to have MAC-PD per American Thoracic Society (ATS)/Infectious Diseases Society of America (ISDA) guidelines and those diagnosed with HIV were excluded from analysis. The electronic health record (EHR) was queried for pertinent demographics, smoking history, comorbidities,

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**TABLE Patient Demographics (N = 19)**

Characteristics	Results
Race, No. (%)	
Black	14 (73.7)
White	5 (26.3)
Sex, No. (%)	
Male	17 (89.5)
Female	2 (10.5)
Age at diagnosis, median (range), y	74 (45-92)
Body mass index, mean (range)	26.2 (14.3-35.4)
Smoking status, No. (%)	
Never	3 (15.8)
Current	2 (10.5)
Former	14 (73.7)
Comorbidities, No. (%)	
Chronic obstructive pulmonary disease	12 (63.2)
Lung cancer	3 (15.8)
Obstructive sleep apnea	9 (47.4)
Other lung disease <sup>a</sup>	4 (21.1)
Gastroesophageal reflux disease	7 (36.8)
Symptoms, No. (%) <sup>b</sup>	
Any respiratory symptoms	17 (89.5)
Dyspnea	10 (52.6)
Chronic cough	15 (78.9)
Sputum production	12 (63.2)
Acid-fast bacillus sample source, No. (%)	
Sputum	16 (84.2)
Bronchoalveolar lavage	3 (15.8)
Chest computed tomography findings, No. (%)	15
Mediastinal/hilar lymph node	7 (46.7)
Nodular/tree-in-bud opacities	13 (86.7)
Bronchiectasis	6 (40.0)
Emphysema	7 (46.7)
Cavity	4 (26.7)
Fibrosis	8 (53.3)
Treatment initiated, No. (%)	10 (52.6)
Deceased at follow-up, No. (%)	6 (31.6)

<sup>a</sup>Other lung disease includes sarcoidosis, bronchiectasis, and chronic thromboembolic pulmonary hypertension.

<sup>b</sup>Reported in isolation but may occur in combination.

and symptoms at the time of a positive mycobacterial culture. Computed tomography (CT) and pulmonary function tests (PFTs) performed within 1 year of diagnosis were included. PFTs were assessed in accordance with Global Initiative for Obstructive Lung Disease (GOLD) criteria, with normal forced expiratory volume in 1 second (FEV<sub>1</sub>) and forced vital capacity (FVC) values defined as  $\geq 80\%$  and a normal FEV<sub>1</sub>/FVC ratio defined as  $\geq 70$ . The diffusion capacity of lung for carbon monoxide (DLCO)

was assessed per 2017 European Respiratory Society (ERS) technical standards and was considered reduced if below the lower limit of normal.<sup>13</sup> Information regarding treatment decisions, initiation, and cessation were collected. All-cause mortality was recorded if available in the EHR at the time of data collection.

Statistical analysis was performed using Mann-Whitney U and Fisher exact tests where appropriate.  $P < .05$  was considered statistically significant. The study was approved by the JBVAMC Institutional Review Board.

## RESULTS

We identified 43 veterans who had a positive culture for MAC; however, only 19 veterans met the diagnostic criteria for MAC-PD and were included in the study (Table). The cohort included predominantly Black and male veterans with a median age of 74 years at time of diagnosis (range, 45-92). Sixteen veterans had underlying lung disease (84.2%), and 16 (84.2%) were current or former smokers. Common comorbidities included COPD, obstructive sleep apnea, gastroesophageal reflux disease, and lung cancer. Respiratory symptoms were reported in 17 veterans (89.5%), 15 (78.9%) had a chronic cough, and 10 (52.6%) had dyspnea. Fifteen veterans had a chest CT scan within 1 year of diagnosis: A nodular and tree-in-bud pattern was most commonly found in 13 (86.7%) of veterans. Thirteen veterans had PFTs within 1 year of MAC-PD diagnosis, of whom 6 had a restrictive pattern with percent predicted FVC  $< 80\%$ , and 9 had evidence of obstruction with FEV<sub>1</sub>/FVC  $< 70$ . DLCO was below the lower limit of normal in 18 veterans. Finally, 6 veterans were deceased at the time of the study.

Of the 19 veterans, guideline-directed, combination antimycobacterial therapy for MAC-PD was initiated in only 10 (52.6%) patients due to presence of symptoms and/or imaging abnormalities. Treatment was deferred due to improved symptoms, concern for adverse events (AEs), or lost to follow-up. Five veterans stopped treatment prematurely due to AEs, lost to follow-up, or all-cause mortality. Assessment of differences between

treated and untreated groups revealed no significant difference in race, sex, age, body mass index (BMI), symptom presence, or chest CT abnormalities. There was no statistically significant difference in all-cause mortality (40% and 22.2% in treated and untreated group, respectively).

To further understand the differences of this cohort, the 13 veterans alive at time of the study were compared with the 6 who had since died of all-cause mortality. No statistically significant differences were found.

## DISCUSSION

Consistent with previous reports in the literature, veterans in our cohort were predominantly current or former smoking males with underlying COPD and bronchiectasis.<sup>1-3,11,12</sup> Chest CT findings varied: Most veterans presented not only with nodules and tree-in-bud opacities, but also a high frequency of fibrosis and emphysema. PFTs revealed a variety of obstruction and restrictive patterns, and most veterans had a reduced DLCO, though it is unclear whether this is reflective of underlying emphysema, fibrosis, or an alternative cardiopulmonary disease.<sup>13,14</sup>

While underlying structural lung disease may have been a risk factor for MAC-PD in this cohort, the contribution of environmental and domiciliary factors in metropolitan Chicago neighborhoods is unknown. JBVAMC serves an under-resourced population who live in the west and south Chicago neighborhoods. Household factors, ambient and indoor air pollution, and potential contamination of the water supply and surface soil may contribute to the prevalence of MAC-PD in this group.<sup>15-19</sup> Further studies are warranted to characterize MAC-PD and its treatment in veterans without HIV who reside in under-resourced urban communities in the US.

Recent ATS, European Society of Clinical Microbiology and Infectious Diseases, and IDSA guidelines recommend combination antimycobacterial therapy for patients who meet clinical, radiographic, and microbiologic criteria for the diagnosis of MAC-PD.<sup>10</sup> Patients who meet these diagnostic criteria, particularly patients with smear positivity or fibrocavitary disease, should be treated because of risk of un-

favorable outcomes.<sup>15,20-22</sup> However, we found that the initiation of guideline-recommended antimycobacterial therapy in veterans without HIV with MAC-PD were inconsistent among HCPs. The reasons underlying this phenomenon were not apparent beyond cited reasons for treatment initiation or deference. Despite this inconsistency, there was no clear difference in age, BMI, symptom burden, radiographic abnormality, or all-cause mortality between treatment groups. Existing studies support slow but substantial progression of untreated MAC-PD, and while treatment prevents deterioration of the disease, it does not prevent progression of bronchiectasis.<sup>6</sup> The natural history of MAC-PD in this veteran cohort has yet to be fully elucidated. Furthermore, the 50% treatment dropout rate was higher than previously reported rates (11-33%).<sup>5</sup> However, the small number of veterans in this study precludes meaningful comparison with similar reports in the literature.

We did note a relatively high all-cause mortality in this cohort (n = 6, 32%); however, this rate is comparable to the all-cause mortality rate of 27% observed in a 2018 meta-analysis of 9035 patients with MAC-PD.<sup>23</sup> Although there was no major difference in those deceased and those alive at the time of data collection in our study, previously described predictors of mortality included male sex, advanced age, presence of fibrocavitary disease, decreased FVC, and presence of comorbidities.<sup>8,23</sup> Larger prospective studies evaluating veterans with MAC-PD are needed to further evaluate contributors to mortality in veterans with MAC-PD.

## Limitations

The limitations of this small, single-center, retrospective study prevent a robust, generalizable comparison between groups. Further studies are warranted to characterize MAC-PD and its treatment in veterans without HIV who reside in under-resourced urban communities in the US.<sup>24-26</sup>

## CONCLUSIONS

These data suggest that clinical, imaging, and treatment attributes of MAC-PD in veterans without HIV who reside in

metropolitan Chicago are heterogeneous and are associated with a relatively high mortality rate. Although there was no difference in the attributes or outcomes of veterans who did and did not initiate treatment despite current recommendations, further studies are needed to better explore these relationships.

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### Disclaimer

The opinions expressed herein are those of the authors and do not necessarily reflect those of *Federal Practitioner*, Frontline Medical Communications Inc., the US Government, or any of its agencies.

### Ethics and consent

This study was approved by the Jesse Brown Veterans Affairs Medical Center Institutional Review Board (VA Chicago [WS], IL-537).

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