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MAJOR ARTICLE

Incidence, Long-Term Outcomes, and Healthcare Utilization of Patients With Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome and Disseminated *Mycobacterium avium* Complex From 1992–2015

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Background. Despite the advent of combination antiretroviral therapy (cART), patients with human immunodeficiency virus (HIV) continue to develop late-stage complications including acquired immune deficiency syndrome (AIDS), disseminated *Mycobacterium avium* complex (DMAC), and death.

Methods. We performed an observational retrospective cohort study of HIV-infected adults who developed DMAC in the Duke University Health System from 1992 to 2015 to determine the incidence, long-term outcomes, and healthcare utilization of this population at high risk for poor outcomes. Findings were stratified by the "pre-cART" era (before January 1, 1996) and "post-cART" thereafter.

Results. We identified 330 adult HIV-infected patients newly diagnosed with DMAC, the majority (75.2%) of whom were male and non-Hispanic black (69.1%), with median age of 37 years. Incidence of DMAC declined significantly from 65.3/1000 in 1992 to 2.0/1000 in 2015, and the proportion of females and non-Hispanic blacks was significantly higher in the post-cART era. The standardized mortality ratios for DMAC patients who received cART were 69, 58, 27, 5.9, and 6.8 at years 1–5, respectively, after DMAC diagnosis. For patients diagnosed with DMAC in 2000 or later (n = 135), 20% were newly diagnosed with HIV in the 3 months preceding presentation with DMAC. Those with established HIV had a median time from HIV diagnosis to DMAC diagnosis of 7 years and were more likely to be black, rehospitalized in the 6 months after DMAC diagnosis, and die in the long term.

Conclusions. Disseminated *Mycobacterium avium* complex continues to be a lethal diagnosis in the cART era, disproportionately afflicts minority populations, and reflects both delayed entry into care and failure to consistently engage care.

Keywords. acquired immune deficiency syndrome; antiretroviral therapy; health disparities; human immunodeficiency virus; *Mycobacterium avium* complex.

The advent of combination antiretroviral therapy (cART) has dramatically changed the natural history of infection with human immunodeficiency virus (HIV). Patients with HIV who are treated with cART benefit from fewer opportunistic infections (OIs) and improved overall survival [1–6]. However, despite the efficacy, safety, and widespread availability of cART, late-stage complications of HIV continue to occur, including the development of acquired immune deficiency syndrome (AIDS), infection with disseminated *Mycobacterium avium* complex (DMAC), and death [7, 8].

The development of DMAC in patients with HIV typically occurs at a CD4 count of <50 cells/mm^3, and in the modern era of effective antiretroviral therapy, this generally reflects delayed entry into care. Before the availability of cART, the annual frequency of DMAC in patients with AIDS was approximately 10%–20% [9, 10]. Large cohort studies of patients with HIV in Atlanta and Baltimore described (1) a significant reduction in the rates of DMAC and other OIs after the introduction of cART as well as (2) a shift in epidemiology with females and blacks being at higher risk for DMAC in the post-cART era [11, 12]. Despite the large benefit of antiretroviral therapy, a recent single-center study highlights that the development of DMAC in patients with HIV is not uncommon and is associated with high mortality, even in the cART era [13]. Furthermore, even after adjustment for CD4 count, DMAC is an independent predictor of mortality in patients with AIDS [9].

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Our objectives were to describe the incidence of DMAC over time, long-term outcomes, and healthcare utilization of our cohort of HIV-infected patients at Duke University Health System presenting with DMAC from 1992 to 2015. A better understanding of the epidemiology, natural history, and pattern of hospitalizations of these high-need, high-cost patients [14] with HIV/AIDS is key for designing interventions to engage this population at high risk for poor outcomes.

METHODS

Study Population

We performed an observational retrospective cohort study of HIV-infected adult patients presenting with DMAC that included all patients initially diagnosed at our center. Subjects age 18 and older presenting to Duke University Health System between January 1, 1992 and June 30, 2015 with DMAC were ascertained using an existing research database (for patients presenting 1992–1999) and the Duke Enterprise Data Unified Content Explorer (DEDUCE) research tool (for patients presenting 2000–2015). The DEDUCE is an interface used to extract data from the electronic medical record [15].

Data Procurement

The existing research database (for patients presenting 1992–1999) was constructed in the early 2000s by searching for "*Mycobacterium avium* complex" (MAC) in the Duke University microbiology culture records and then building a clinical database by manual chart review of all patients with positive culture results. The clinical database included demographic information, HIV status (defined below), laboratory and radiographic data, and treatment regimens for both DMAC and HIV/AIDS if applicable. For patients presenting 2000–2015, subjects were ascertained by searching for the *International Classification of Diseases, Ninth Revision* code 031.2 via the DEDUCE research tool and then confirming culture positivity for DMAC and virologic or serologic evidence of HIV by manual chart review (see definition below). Persons with a diagnosis of HIV/AIDS-DMAC had data extracted from DEDUCE including demographic, clinical, and microbiological variables. Additional review of the electronic medical record was performed to extract diagnostic, treatment, and outcome data for patients presenting 2000–2015.

Disseminated *Mycobacterium avium* Complex Incidence, Epidemiology, and Long-Term Outcomes

To determine the incidence of DMAC in patients with HIV presenting for care at Duke from 1992 to 2015, HIV clinic census data were obtained from institutional administrative reports and DEDUCE searches. To evaluate the epidemiology and long-term outcomes of patients with HIV/AIDS who developed DMAC before and after the availability of cART, the following data elements were extracted from both research tools (the existing clinical database and DEDUCE) and supplemented by manual chart review: patient age, gender, race/ethnicity, timing of cART initiation in relation to DMAC diagnosis (if applicable), presence of other OIs, and development of immune reconstitution inflammatory syndrome (IRIS). For patients presenting 2000–2015, mortality data were obtained from DEDUCE as well as by review of the electronic medical record, and for those presenting 1992–1999, mortality data were obtained by manual chart review. For patients not known to be deceased, survival was censored either at the most recent visit to the Duke University Health System or June 30, 2015, whichever was earlier.

Timing of Human Immunodeficiency Virus Diagnosis and Hospitalization Patterns

For patients with HIV presenting to the Duke University Health System from 2000 to 2015, DEDUCE allowed for capture of additional data elements to study the timing of HIV diagnosis in relation to the diagnosis of DMAC and the hospitalization pattern of patients with HIV/AIDS who developed DMAC. The number of hospitalizations and associated admission diagnoses were recorded for all patients with HIV/AIDS-DMAC in the year before and 2 years after first positive sterile culture for DMAC.

Definitions

A diagnosis of DMAC was defined as (1) confirmed diagnosis of HIV infection plus (2) a positive culture for *Mycobacterium avium* complex from blood, bone marrow, or biopsy of a sterile site. Patients with positive cultures only from nonsterile sites such as sputum, stool, or bronchoalveolar lavage were excluded from the cohort. Human immunodeficiency virus diagnosis was confirmed by positive HIV-1 antibody testing or viral load. The date of DMAC diagnosis was defined by the date on which the first diagnostic specimen that grew MAC was obtained. A "new" diagnosis of HIV was defined as documentation of HIV initially diagnosed within the 3 months before DMAC presentation.

The "pre-cART era" was defined as before January 1, 1996, and the "cART era" was defined as January 1, 1996 or later. Combination antiretroviral therapy was defined by an antiretroviral regimen that included (1) a protease inhibitor plus 2 nucleoside reverse-transcriptase inhibitors, (2) a nonnucleoside reverse-transcriptase inhibitor plus 2 nucleoside reverse-transcriptase inhibitors, (3) an integrase inhibitor plus 2 nucleoside reverse-transcriptase inhibitors, or (4) an integrase inhibitor plus a boosted protease inhibitor. Human immunodeficiency virus-associated OIs were defined using the Centers for Disease Control and Prevention criteria [16]. Immune reconstitution inflammatory syndrome was defined by clinical manifestations of inflammation after initiation of cART, with pretreatment CD4 count <200 cells/mm and positive virologic and/or immunologic response to cART.

Statistical Analysis

The annual incidence of DMAC was calculated using the number of newly diagnosed DMAC patients as the numerator and the population of patients with HIV seen at least once in the Duke Adult Infectious Diseases Clinic during the same year as the denominator. Survival was measured using the Kaplan-Meier method. Differences in survival among groups were assessed using Cox proportional hazard modeling. A standardized mortality curve was constructed using US life expectancy tables (available at http://www.cdc.gov/nchs/fastats/life-expectancy.htm) for a cohort of the same age, gender, and race/ethnicity composition as the DMAC patient cohort. Differences in continuous variables were assessed using the Wilcoxon rank-sum test, and differences in categorical variables were assessed using the χ^2 or Fisher's exact test, as appropriate. Statistical analysis was performed with R version 3.2.3 (R Core Team [2016]).

Human Subjects

This retrospective record review was deemed minimum risk and approved by the Duke University Medical Center Institutional Review Board.

RESULTS

We identified 330 adult HIV-infected patients newly diagnosed with DMAC in the Duke University Health System from 1992 to 2015. The majority of patients were male (75.2%) and non-Hispanic black (69.1%), with a median age of 37 years (interquartile range [IQR] = 31–43 years, range 19–71) as shown in Table 1. The median age of patients was approximately the same in the pre-cART compared with cART era, although the proportion of females (18.4% versus 29.6%, $P = .03$) and non-Hispanic blacks (55.3% versus 79.4%, $P < .001$) was significantly higher in the cART era (Table 1).

Table 1. Clinical and Demographic Characteristics of Patients With HIV/AIDS and Disseminated *Mycobacterium avium* Complex Infection From 1992 to 2015

Characteristic	Pre-cART Era (n = 141)	cART Era (n = 189)	P Value
Age (median, range)	36 (19–55)	38 (22–71)	.06
%Female	18.4%	29.6%	.03
Race/ethnicity			<.001
Black, non-Hispanic	78 (55.3%)	150 (79.4%)	
White, non-Hispanic	61 (43.3%)	27 (14.3%)	
Hispanic	0 (0%)	5 (2.6%)	
Native American	1 (0.7%)	2 (1.1%)	
Asian	1 (0.7%)	1 (0.5%)	
Unknown	0 (0%)	4 (2.1%)	
Antiretroviral therapy (at the time of DMAC diagnosis)			(not relevant)
Never received	135 (95.7%)	46 (24.3%)	
Already prescribed	0 (0%)	83 (43.9%)	
Started within 30 days	0 (0%)	31 (16.4%)	
Started within 31–180 days	0 (0%)	17 (9.0%)	
Started >180 days	6 (4.3%)	9 (4.8%)	
Unknown	0 (0%)	3 (1.6%)	

Abbreviations: AIDS, acquired immunodeficiency syndrome; cART, combination antiretroviral therapy; DMAC, disseminated *Mycobacterium avium* complex; HIV, human immunodeficiency virus.

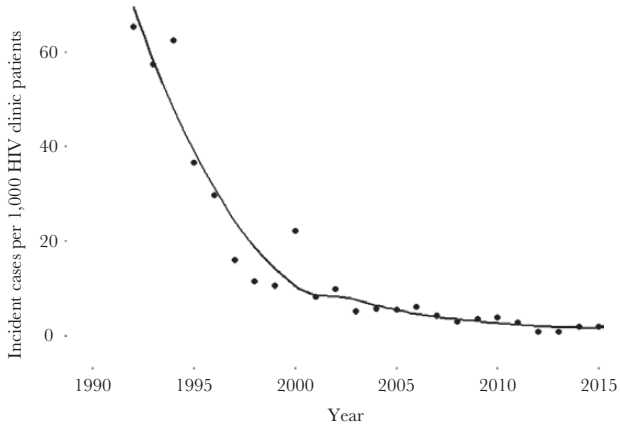

Figure 1. The incidence of disseminated *Mycobacterium avium* complex human immunodeficiency virus (HIV)-infected patients declined from a peak of 65.3/1000 in 1992 to 2.0/1000 in 2015.

The incidence of DMAC in HIV-infected patients declined from a peak of 65.3/1000 in 1992 to 2.0/1000 in 2015 (Figure 1). More than half of the total cohort of patients (54.8%) was never started on cART, including 46 of the 189 patients (24.3%) diagnosed in the post-cART era (Table 1). A minority of individuals diagnosed with DMAC before the availability of cART (4.3%) survived long enough to start this therapy. Of the 57 of 189 patients in the cART era who were initiated on cART after presentation with DMAC, more than half (53.4%) were prescribed antiretroviral therapy within 30 days after DMAC diagnosis. Of all patients prescribed cART, IRIS occurred in 26 of 150 (17.3%) of patients newly diagnosed with DMAC.

Median follow-up time after DMAC diagnosis was 259 days (IQR = 82–581 days, range 0–7544), resulting in 679 total patient-years of follow-up. Median survival was 189 days in patients who never started cART (95% confidence interval [CI], 152–255 days), but the median survival was not reached (60% still alive at median follow-up time of 454 days) among patients who received cART (Figure 2A). Of patients who ever received cART, 37 of 150 (25%) were known to be alive at 5 years post-DMAC and 10 (7%) were alive at 10 years post-DMAC diagnosis. To put this in context, the expected mortality of a cohort of the same age, gender, and racial/ethnic makeup in the general US population would be approximately 1.5% over 5 years; the standardized mortality ratios for all DMAC patients who received cART (n = 144; 6 patients of Asian, Native American, or unknown race, for whom life tables were not available, were excluded for this analysis) were 69 (95% CI, 42–94), 58 (95% CI, 44–70), 27 (95% CI, 21–33), 5.9 (95% CI, 4.5–7.3), and 6.8 (95% CI, 4.8–8.7) at years 1–5, respectively, after DMAC diagnosis. In contrast, standardized mortality ratios for patients who never

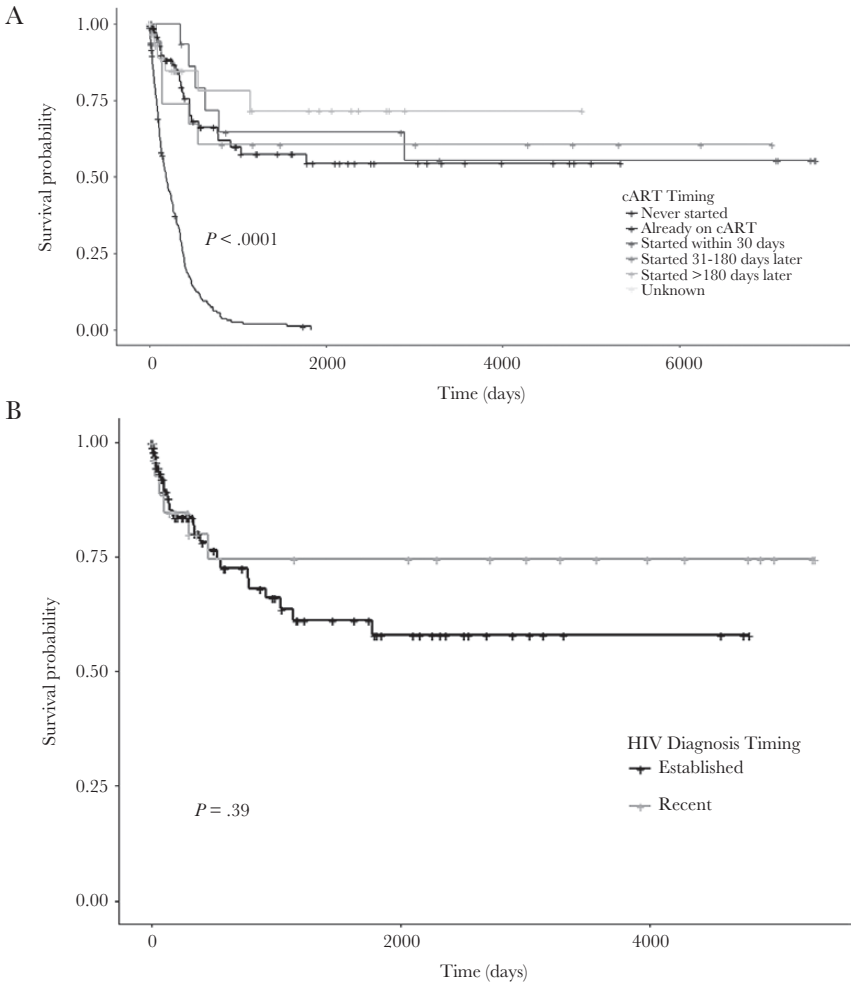

Figure 2. Median survival was 189 days in patients who never started combination antiretroviral therapy (cART), but the median survival was not reached among patients who received cART (A). Survival was not significantly different between newly diagnosed and established patients overall, but the survival curves diverge at approximately the first year after disseminated *Mycobacterium avium* complex diagnosis, with continued mortality in the established patient group but no further deaths in the newly diagnosed group (B). HIV, human immunodeficiency virus.

received cART were 275 (95% CI, 245–298), 280 (95% CI, 246–303), 236 (95% CI, 167–278), 0 (95% CI, 0–283), and 99 (95% CI, 41–143) at years 1–5 (the standardized mortality ratio for year 4 is 0 because none of the 4 patients living at the start of year 4 died that year).

Additional data were available from the DEDUCE system for HIV-infected patients diagnosed with DMAC in 2000 or later (n = 135). At the time of presentation of DMAC, 10 of 135 (7%) patients were unaware of their HIV diagnosis, and an additional 18 (13%) had been newly diagnosed with HIV in the prior 3 months. Table 2 compares patients newly diagnosed with HIV (n = 28) to patients with an established HIV diagnosis (n = 107). Patients with an established HIV diagnosis had a median time from HIV diagnosis to DMAC diagnosis of 7 years (IQR = 4–10 years, range 4 months–22 years). Those with longstanding HIV at the time of DMAC presentation, compared with their newly diagnosed counterparts, were more likely to be black (84% vs 64%, P = .008) and more likely to have never started cART (18% vs 4%, P < .001) as shown in Table 2. Survival was not significantly different (log-rank P = .39) between newly diagnosed and established patients overall, but the survival curves diverge at approximately the first year after DMAC diagnosis, with continued mortality in the established patient group but no further deaths in the newly diagnosed group (Figure 2B).

Figure 3 illustrates the pattern of hospitalization for a period spanning the year before DMAC diagnosis to 2 years after DMAC diagnosis, stratified by timing of HIV diagnosis. Hospitalization both before and after DMAC diagnosis was common; however, persons newly diagnosed with HIV had fewer hospitalizations overall compared with those known to have HIV for at least 3 months before DMAC diagnosis. Of note, 1 patient was admitted twice to the hospital within the year before DMAC diagnosis but was not diagnosed with HIV until 10 days before DMAC diagnosis and died less than 1 month after DMAC diagnosis.

Table 2. Comparison of Patients With Disseminated *Mycobacterium avium* Complex Infection Newly Diagnosed With HIV and Patients With an Established HIV Diagnosis From 2000 to 2015

Characteristic	Newly Diagnosed (n = 28)	Established Diagnosis (n = 107)	P Value
Year DMAC diagnosed (median, IQR)	2004 (2001–2008)	2004 (2001–2007)	.81
Age (median, IQR)	41 (36–45)	38 (32–44)	.28
Female (%)	32%	31%	1.0
Race/ethnicity			.008
Black, non-Hispanic	18 (64%)	90 (84%)	
White, non-Hispanic	6 (21%)	10 (9%)	
Hispanic	3 (11%)	1 (1%)	
Native American	0 (0%)	2 (2%)	
Asian	1 (4%)	0 (0%)	
Unknown	0 (0%)	4 (4%)	
Antiretroviral therapy			<.001
Never received	1 (4%)	19 (18%)	
Already prescribed	8 (29%)	62 (58%)	
Started within 30 days	11 (39%)	17 (16%)	
Started within 31–180 days	5 (18%)	5 (5%)	
Started >180 days	2 (7%)	2 (2%)	
Unknown	1 (4%)	2 (2%)	

Abbreviations: DMAC, disseminated *Mycobacterium avium* complex; HIV, human immunodeficiency virus; IQR, interquartile range.

The majority of patients with DMAC (59%) were rehospitalized in the 6 months after DMAC diagnosis (median 1 hospitalization, IQR = 0–2, range 0–8); another 42% of those still alive at 7 months after DMAC diagnosis were also hospitalized between 7 and 12 months after DMAC diagnosis (median number of hospitalizations 0, IQR = 0–1.8, range 0–7). Patients with newly diagnosed HIV were less likely to be rehospitalized in the 6 months after DMAC diagnosis (10 of 28, 36%) than patients with HIV status known for at least 3 months before DMAC diagnosis (69 of 107, 64%, P = .011 for comparison).

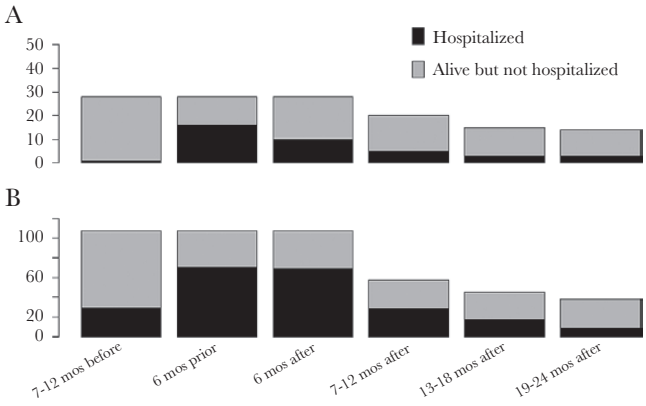

Figure 3. Pattern of hospitalization for a period spanning the year before disseminated *Mycobacterium avium* complex (DMAC) diagnosis to 2 years after DMAC diagnosis, stratified by timing of human immunodeficiency virus diagnosis.

DISCUSSION

We describe the incidence, epidemiology, long-term outcomes, and healthcare utilization of patients with HIV/AIDS who develop DMAC in the cART era. Our study is novel in that (1) few studies in the cART era have focused specifically on DMAC [11–13], (2) we report on a prolonged observation period (>20 years), and (3) hospitalization patterns in a population of HIV/AIDS-DMAC patients have not previously been described. We found that although incidence has significantly decreased since the advent of cART, DMAC continues to be a lethal diagnosis for patients with HIV, disproportionately afflicts minority populations, and reflects both delayed entry into care and failure to consistently engage in care. Furthermore, frequent hospital utilization by this medico-psychosocially complex patient group highlights the need for individual- and systems-based interventions to improve care delivery and engagement for this high-need, high-cost population [14] at substantial risk of poor outcomes.

We found the incidence of DMAC has dramatically declined since the advent of cART in 1996 and has approximately stabilized since 2005. This finding is consistent with multicohort analyses of AIDS-defining OIs in North America [6, 17], which highlight DMAC as one of the most common OIs before and after the availability of cART. Corroborating prior studies [11, 12], we demonstrated that the proportion of females (18.4% versus 29.5%) and non-Hispanic blacks (55.3% versus 79.5%) was significantly higher in the cART era. This underscores the persistence over time of racial/ethnic and gender disparities in HIV care, with black persons being particularly vulnerable to such inequality [18, 19]. Factors associated with disparities in antiretroviral therapy prescription and viral suppression differ for men and women of the same race/ethnicity [19], suggesting that gender—in addition to race—contributes to inequity in access and outcomes along the HIV care continuum.

Success across the multistep "HIV treatment cascade" from timing of diagnosis to virologic suppression [20–22] is severely challenged for patients with HIV who develop DMAC. We identify 2 distinct populations of patients who experience breakdown in this cascade at varying points: (1) those with significantly delayed entry into care who are newly diagnosed with HIV near the time of presentation with DMAC, and (2) those with longstanding known HIV who fail to consistently engage in care and ultimately develop late-stage complications of AIDS, such as DMAC. Our data suggest that these groups are slightly different; in our cohort, patients with an established HIV diagnosis who presented with DMAC were more likely to be black, more likely to never initiate antiretroviral therapy, more likely to be rehospitalized in the 6 months after DMAC diagnosis, and more likely to die in the long term than patients newly diagnosed with HIV. This dramatically divergent "natural history" of patients with known HIV that is longstanding—often on the order of several years—who nevertheless fail to engage in

care reliably enough to begin cART, unmasks the severity of racial disparity in contributing to breakdown in the HIV care cascade, with resultant devastating outcomes including death. Furthermore, the stuttering engagement over time by patients in minority groups likely reflects the complex interplay of personal and societal stigma related to HIV as well as logistical barriers to accessing care such as unstable or lack of housing, transportation, and/or health insurance.

Combination antiretroviral therapy has substantially improved the overall survival of persons with HIV [1–3, 5, 23]; however, HIV mortality due to AIDS-OIs persists in the cART era [24–26], and we found the risk of death associated with DMAC to be particularly high. Median survival in our cohort was significantly affected by initiation of cART: 189 days in patients never started on therapy, compared with 60% of patients still alive at 454 days after diagnosis of DMAC in those who were prescribed cART. Even with cART, patients with HIV who develop DMAC were far more likely to die (27- to 69-fold) in the first 3 years after diagnosis than age, gender, and race-matched persons in the general population, and this increased risk of death persisted, albeit at a lower level (5.9- to 6.8-fold) in years 4 and 5. Although the overall prognosis for patients with HIV/AIDS-DMAC is better in the cART era, it lags behind the improved median survival associated with other common OIs, such as *Pneumocystis jirovecii* pneumonia and Kaposi's sarcoma, which increased from <5 years pre-cART to >15 years post-cART [27]. The high mortality associated with DMAC in HIV-infected patients is often attributed to the more profound immunosuppression at which MAC typically occurs; however, even after adjusting for CD4 count, DMAC remains an independent predictor of death [9, 13, 27]. Well described risk factors for AIDS-related death exactly mirror those for developing DMAC: lower CD4 counts, late presentation to care, and failure to engage in care [7, 20]. Furthermore, racial disparities in HIV mortality persist in the cART era [28, 29]. Taken together, biological factors as well as structural barriers to engagement in care are both critical contributors to the high death rates observed in patients with HIV/AIDS and DMAC, even in the era of cART.

There is conflicting evidence surrounding the impact of cART on healthcare utilization of patients with HIV/AIDS [30–36]. In evaluating the hospitalization pattern of patients with HIV who develop DMAC in the cART era, we found that hospitalization before and after presentation with DMAC was common. In addition, rehospitalization is common in this population, particularly in the first couple of years after diagnosis with DMAC (Figure 3). Patients with newly diagnosed HIV—approximately the time of DMAC—had a lower proportion of hospitalizations surrounding DMAC diagnosis, which is not surprising given their late presentation to care. More importantly, delayed presentation to care serves as a negative prognosticator of success along the HIV care continuum, given the associated subsequent risk of limited engagement in care and death [6, 7, 20, 21]. As exampled in our study, one patient was admitted twice to the hospital for recurrent methicillin-resistant *Staphylococcus aureus* skin and soft tissue infections within the year before DMAC but was not diagnosed with HIV until 10 days prior and died less than 1 month after DMAC diagnosis—this represents a missed opportunity for earlier HIV diagnosis and linkage to care.

In the modern era of antiretroviral therapy, which is increasingly effective, safe, and available [37], the persistence of DMAC as a complication in patients with HIV/AIDS represents a profound breakdown in the HIV treatment cascade. We believe that 2 key interventions will be necessary to improve outcomes in this high-risk population: (1) more available and destigmatized outreach and testing in high-risk groups to diagnose HIV earlier and (2) intensive interventions for patients with known HIV who develop DMAC, using this potentially lethal diagnosis as a stimulus to more consistently engage in care. Given that the median time from HIV diagnosis to viral suppression ranges from 19 months to 6 years in developed countries [38, 39], and that only 25% of patients with HIV in the United States are virologically suppressed [20], we must urgently prioritize bridging these chasms in the HIV care continuum to successfully care for HIV/AIDS-DMAC patients who are particularly vulnerable to poor outcomes.

Our study has several limitations. The single-center, retrospective design limits generalizability, although this criticism is mitigated by the consistency of our findings with other published studies. We did not capture healthcare data and utilization outside our health system, limiting the ability to fully assess hospitalizations before and after DMAC. Therefore, the high rates of hospitalization observed here should be considered the lower bounds of what actually occurred. To assess incidence over time, we used a denominator of HIV-seropositive patients seen in our clinic during the year, recognizing that some of the DMAC patients seen in our health system may not have been seen in the clinic before the DMAC diagnosis and may have received HIV-related healthcare elsewhere. We did not assess HIV viral suppression, which is a key correlate of healthcare engagement and mortality. Finally, the electronic health record data that formed the basis for our analysis may underestimate retention-in-care estimates when compared with integration with HIV surveillance data [40].

CONCLUSIONS

In conclusion, although the incidence of DMAC in persons with HIV infection has diminished over time, patients who receive a diagnosis in the post-cART era remain at high risk for complications and recurrent hospitalizations. Disseminated *Mycobacterium avium* complex is a late-stage OI that increasingly and disproportionately afflicts racial minorities, reflecting both trends in HIV epidemiology in the United States as well as

delays in access to care among minority groups. Patients with HIV who develop DMAC are at very high risk for death and hospitalization for several years after diagnosis. Encouragingly, we demonstrate that long-term survival may be achieved with cART, even for patients with delayed presentation to care and/or those who fail to engage in care. Continued prioritization of strategy development and implementation to link and engage this medico-behaviorally complex population of patients in HIV care is critically needed.

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